

LATIN AMERICAN

4TH INTERNATIONAL CONGRESS ON NATURAL AND APPLIED SCIENCES

EDITORS
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4TH INTERNATIONAL LATIN AMERICAN CONGRESS ON NATURAL AND APPLIED SCIENCES

March 13-15, 2023 / Rio de Janeiro, Brazil

EDITORS

Mijael Altamirano Santiago Isi Verónica Lara Andrade María Cruz Cuevas Álvarez Marcos Pérez Mendoza

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CONGRESS TITLE

4th International Latin American Congress on Natural and Applied Sciences

DATE AND PLACE

March 13-15, 2023 / Rio de Janeiro, Brazil

ORGANIZATION

IKSAD INSTITUTE

Universidad Abierta y a Distancia UNAD, Colombia Universidad Juárez Autónoma de Tabasco, México Institute Of Economic Development And Social Research Violence and Abuse Studies Platform

EDITORS

Mijael Altamirano Santiago Isi Verónica Lara Andrade María Cruz Cuevas Álvarez Marcos Pérez Mendoza

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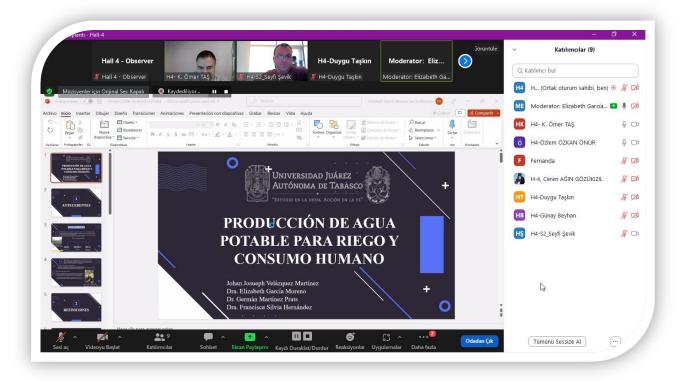
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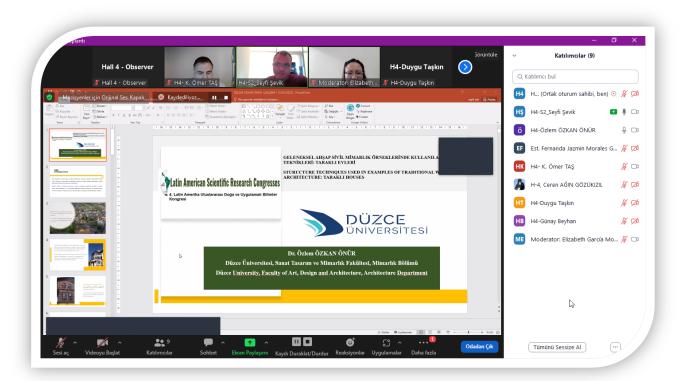
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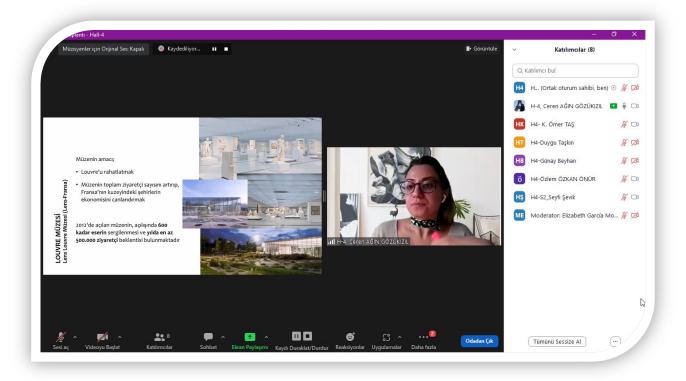
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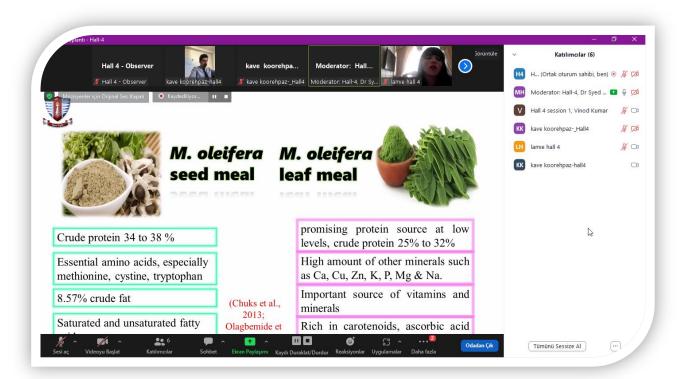
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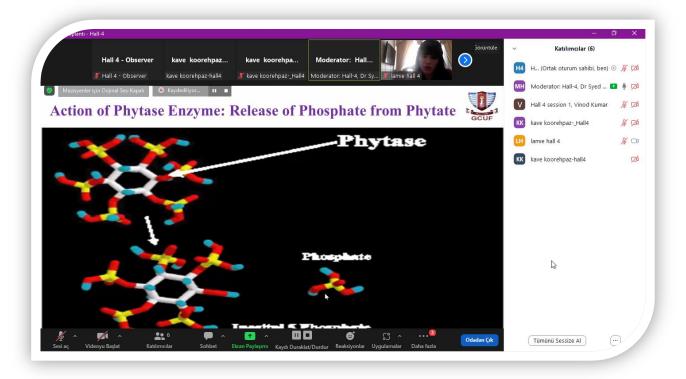
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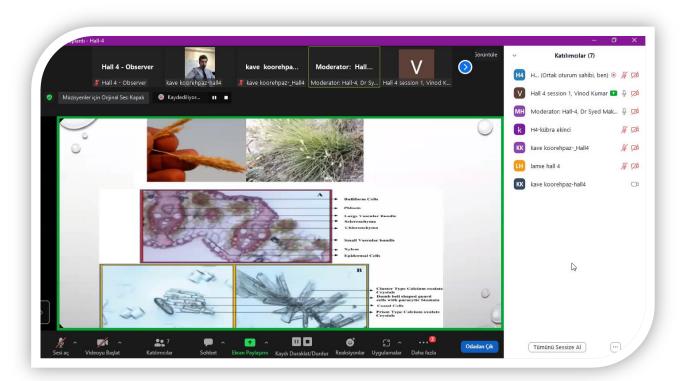


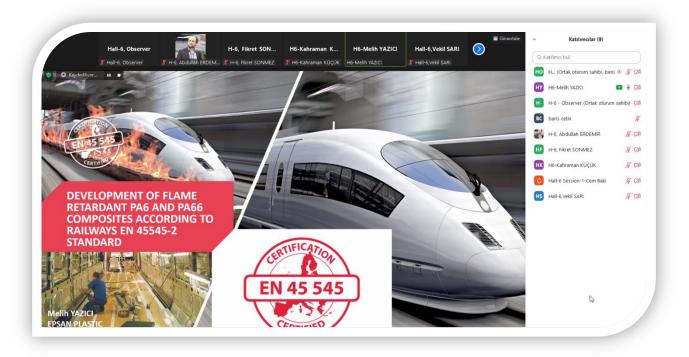


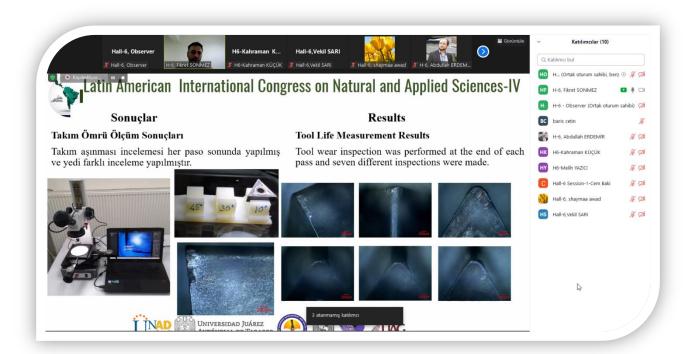




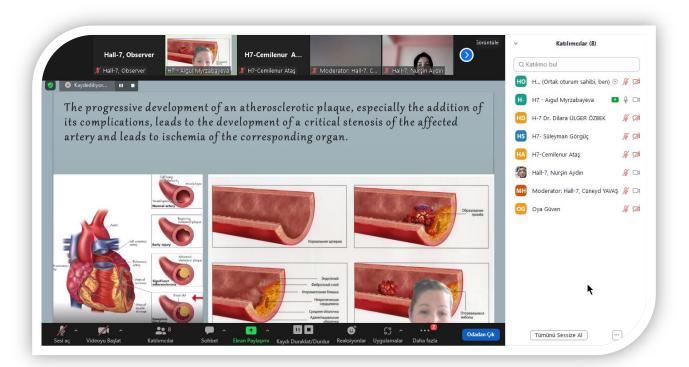


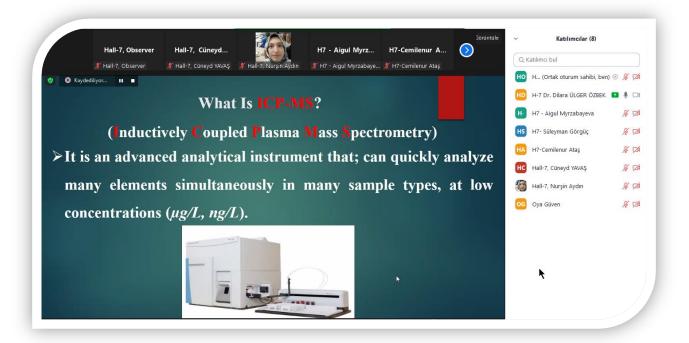


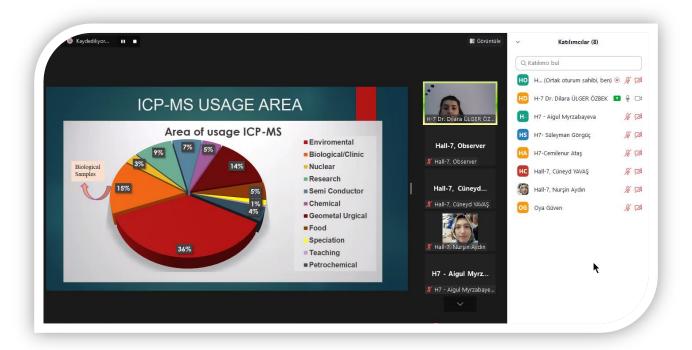




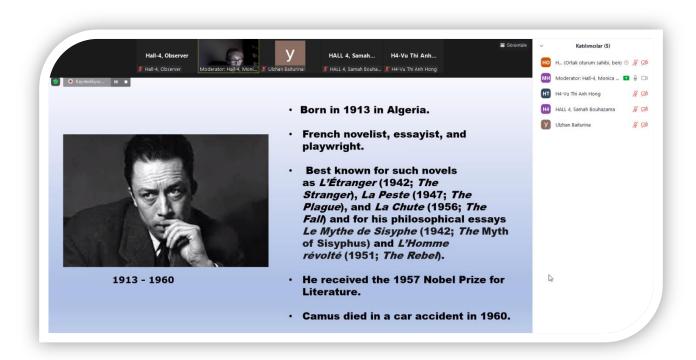




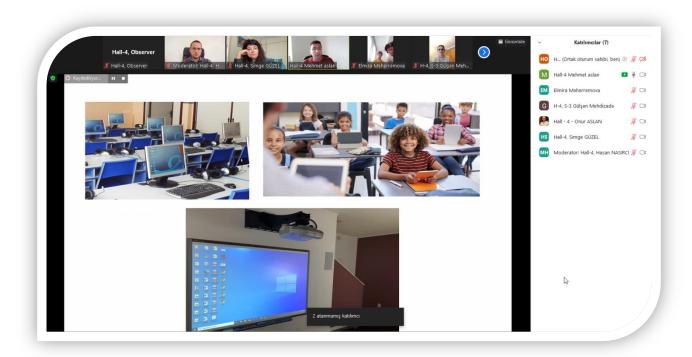


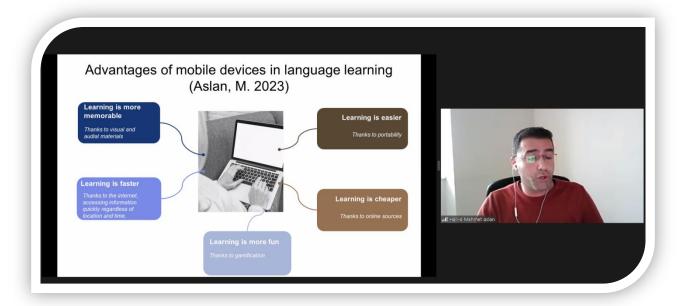




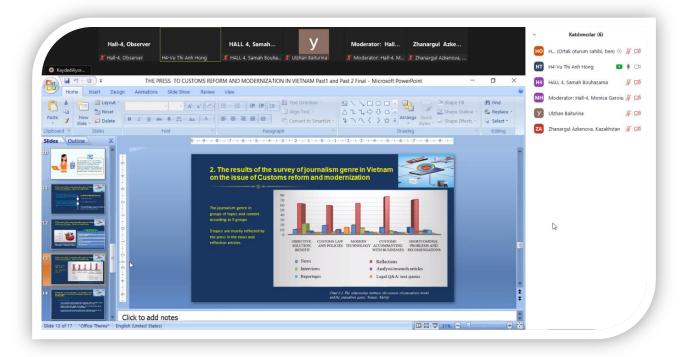
















Latin American

International Congress on Natural and Applied Sciences -IV

March 13-15, 2023 / Rio de Janeiro, Brazil

CONFERENCE PROGRAM

Online (with Video Conference) Presentation



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-Opening Ceremony-

13.03.2023

RIO DE JANEIRO LOCAL TIME - 10 00: 10 30

MEXICO LOCAL TIME - 07 00: 07 30

ANKARA LOCAL TIME - 16 00: 16 30

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ONLINE PRESENTATIONS

13.03.2023 / Hall-6, Session-1



RIO DE JANEIRO LOCAL TIME

08 00 : 10 00



ANKARA LOCAL TIME



HEAD OF SESSION: Prof. Dr. Salah BELAIDI		
G.P. Ashwinkumar C. Sulochana N.Sandeep	Vijayanagara Sri Krishnadevaraya University Gulbarga University Central University of Karnataka India	NUMERICAL INVESTIGATION OF CHEMICALLY REACTING MHD FLOW DUE TO A ROTATING CONE WITH THERMOPHORESIS AND BROWNIAN MOTION
Hamza Assila Younes Zaoui Issam Ameziane El hassani Abderrazzak El Moutaouakil Ala Allah Youssef Ramli M'Hammed Ansar	Mohammed V University in Rabat Morocco	SYNTHESIS OF ETHYL 2-(4-BENZYL-3- METHYL-6-OXO-1,6- DOIHYDROPYRIDAZIN-1-YL)ACETATE: CRYSTAL STRUCTURE AND HIRSHFELD SURFACE ANALYSIS
Chennai Yassmine Belaidi Salah	University of Biskra	QSAR MODELING USING GAUSSIAN PROCESS APPLIED FOR A SERIES OF FLAVONOIDS AS POTENTIAL ANTIOXIDANTS
Chennai Yassmine Ouassaf Mebarka	University of Biskra	QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP (QSAR) INVESTIGATIONS AND MOLECULAR DOCKING ANALYSIS OF PLASMODIUM PROTEIN FARNESYLTRANSFERASE INHIBITORS AS POTENT ANTIMALARIAL AGENTS
Dr.Yassmine CHENNAI Dr.Assma FETTEH	Mohamed Khaidhar University	ANTIBACTERIAL AND ANTI- OXIDANT ACTIVITIES OF EXTRACTS FROM MEDICINAL PLANTS
Prof. Dr. Salah BELAIDI Dr.Yassmine CHENNAI	Mohamed Khaidhar University	IN SILICO INVESTIGATION OF SEVERAL SERIES OF HETEROCYCLIC MOLECULES FOR DRUG DISCOVERY
Chennai Yassmine Ouassaf Mebarka	University of Biskra	CONTRIBUTION TO DRUG DISCOVERY THROUGH COMPUTATIONAL ANALYSIS OF SEVERAL SERIES OF HETEROCYCLIC MOLECULES



ONLINE PRESENTATIONS

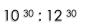
13.03.2023 / Hall-6, Session-2



RIO DE JANEIRO LOCAL TIME



ANKARA LOCAL TIME





16 30: 18 30

HEAD OF SESSION: Prof. Dr. Huma Ali		
Rima SAADBOUZID Radhia BOUZIDI Imane SARHANI Donia HELLAL Leilia OUMDDOUR Massouda IBRIR Hachani KHADRAOUI Ghania BELAALOUI	Batna 2 University Batna	BREAST CANCER; PRELIMINARY RESULTS OF A RETROSPECTIVE STUDY IN EASTERN ALGERIA
Eman Bunyan Ibrahim Rana Adil Hanoon	Universty of Duhok Iraq	DETECTION OF THE MUTATIONS ASSOCIATED WITH HEMOPHILIA A AND B IN DUHOK PROVINCE
Sidra Mohiuddin Soofi Dr. Afshan Siddiq	University of Karachi Pakistan	MORUS ALBA; A RAY OF HOPE FOR MENTAL ILLNESSES
Yusuf Rabe Yusuf Muhammad Sanyinna Abdulhamid Ahmed	Nigerian Defence Academy Nigerian Army University Biu Umaru Musa Yar'adua University	MOSQUITO VECTOR ABUNDANCE AND DISTRIBUTION ASSOCIATED WITH THE PREVALENCE OF MALARIA IN ZANGO LOCAL GOVERNMENT AREA, KATSINA STATE, NIGERIA
Prof. Dr. Huma Ali Dr. Saba Zubair	Jinnah Sindh Medical University	TRENDS AND ROLE OF PHARMACIST IN COMMUNITY PHARMACY SERVICES AND FACILITATION PROTOCOL: CHALLENGES IN REAL TIME PRACTICES
Özgür Ülkü ÖZDEMİR Şeyda BERK	Sivas Cumhuriyet University Türkiye	GLUCOSE TRANSPORTERS IN CANCER METABOLISM
Rabia KALELİ Şeyda BERK	Sivas Cumhuriyet University Türkiye	THE MOLECULAR MECHANISM OF CANCER METASTASIS
Istemi SERIN	University of Health Sciences Türkiye	LYMPHOCYTE LEVEL AT DIAGNOSIS IN HODGKIN LYMPHOMA: COULD IT BE AN INDICATOR OF THE STAGE AT INITIAL DIAGNOSIS?
P.H. Najafgulieva R.Sh.Qasimov	Azerbaijan Medical University	COMPARATIVE ANALYSIS OF NEW OPPORTUNITES FOR PHARMACOTHERAPY OF NON-SPECIFIC ULCERATIVE COLITS AND WAYS TO IMPROVE ITS PERFORMANCE EVALUATION



ONLINE PRESENTATIONS

14.03.2023 / Hall-4, Session-1



RIO DE JANEIRO LOCAL TIME

08 00 : 10 00



ANKARA LOCAL TIME



HEAD OF SESSION: Dr. Syed Makhdoom Hussain		
Lyudmila Kabaivanova Lilyana Nacheva Venelin Hubenov Juliana Ivanova	Bulgarian Academy of Sciences Bulgaria	BIOACTIVE PRODUCTS FROM RED MICROALGAE GROWN IN DIGESTATE
Dr. Syed Makhdoom Hussain	Government College University pakıstan	USE OF OILSEEDS BY-PRODUCTS IN AQUA-FEEDS
Aminu Ado Kaugama Mahrazu A. Yusuf Phd Ushie Onumashi Afi Phd Yusha'u Safiyanu Muhammad Ansar Bilyamin Adam Jabir Abdullahi Muhammad	Federal University Wukari Bayaro University Kano Chemistry Kano University	IMPACT OF HEAVY METALS CONTENT FOUND IN IRRIGATED RED PEPPER IN CHALLAWA INDUSTRIAL AREA
M. Mileva N. Vilhelmova-Ilieva G. Jovchev S. Gateva Tz. Gerasimova A. Dobreva	Bulgarian Academy of Sciences Bulgaria	BENEFICIAL BIOLOGICAL AND MEDICINAL EFFECTS OF THE BULGARIAN OIL-BEARING ROSE
Jyoti Sinha Vinod Kumar	Sushant University	PREPARATION AND EVALUATION OF TOPICAL PREPARATION OF EULALIOPSIS BINATA EXTRACT
Kave Koorehpaz	Urmia University	NOVEL CRYOPROTECTANTS AND THEIR EFFECTS ON DECREASING GLYCEROL CONCENTRATION DURING CRYOPRESEVVATION
Novotorzhina Nelya Rzayeva Irada Kazimzadeh Shafa Safarova Mehpara Gahramanova Gariba Mustafayeva Yegana	Institute of Additive Chemistry	HYDROXYMETHYL-P- TOLUENESULFONAMIDE AS AN ANTIOXIDANT ADDITIVE TO DIESEL FUELS



ONLINE PRESENTATIONS

14.03.2023 / Hall-5, Session-1



RIO DE JANEIRO LOCAL TIME

08 00 : 10 00



ANKARA LOCAL TIME



HEAD OF SESSION: Nebi BİLİR		
Allahverdiyev Elxan Rəcəf oğlu Abbasova Nahidə Şavaat qizi	Azərbaycan Dövlət Aqrar Universiteti Azərbaycan	DETERMINATION OF THE INFLUENCE OF STRUCTURE, SIZE OF WORKING NESTS AND THEIR FORAGING ON THE DEVELOPMENT OF FIELD MOUSE IN SOWN AREAS
Nilüfer YAZICI Nebi BİLİR	Isparta University Türkiye	GROWTH VARIATION IN FOREST TREE SPECIES IN AFFORESTATION OF GRADONI TERRACING
Nilüfer YAZICI Nebi BİLİR	Isparta University Türkiye	EFFECT OF TERRACING ON GROWTH OF TAURUS CEDAR (CEDRUS LIBANI): A CASE STUDY FROM ISPARTA DISTRICT
Oktay TOMAR Alptekin Mert YILMAZ	Kocaeli University Türkiye	FOOD WASTE AND FOOD LOSS: CAUSES, EFFECTS AND SOLUTIONS
Alptekin Mert YILMAZ Abdullah ÇAĞLAR Oktay TOMAR	Kocaeli University Türkiye	UPCYCLING IN THE AGRICULTURE AND FOOD SECTOR
Serim Tuna KOÇ	Trakya University Türkiye	ARONIA AND ANTHOCYANINS



ONLINE PRESENTATIONS

14.03.2023 / Hall-6, Session-1



RIO DE JANEIRO LOCAL TIME

08 00 : 10 00



ANKARA LOCAL TIME



HEAD OF SESSION: Prof. Zviad Kovziridze			
Prof. Zviad Kovziridze Prof. Natela Nizharadze Assoc. Gulnazi Tabatadze Dr. Vera Kinkladze Dr. Nino Darakhvelidze Dr. Maia Balakhashvili	Georgian Technical University Georgia	OBTAINING AND STUDYING OG A HIGHLY REFRACTORY COMPOSITE BASED ON SIC BY HOT PRESSING	
Prof.Dr. Qassim Shamkhi al khafaji Prof.Dr. Shaymaa Awad Kadhim Noor Ali jaafar Hasanain Alawadi PhD.lhab Alfadhel	University of Kufa	EVALUTION OF ATOMIC PROPERTIES FOR LI-LIKE IONS SYSTEMS USING HARTREE- FOCK AND CONFIGURATION INTERACTION METHODS	
Vekil SARI	Sivas Cumhuriyet University Türkiye	DESIGN AND MODEL OF AN INDUCTIVE WIRELESS POWER TRANSFER SYSTEM FOR ELECTRIC VEHICLES	
Fatma MEYDANERİ TEZEL	Karabük University Türkiye	ELECTRICAL AND STRUCTURAL CHARACTERIZATION OF PBS THIN FILMS PRODUCED BY SPRAY METHOD	
Fatma MEYDANERİ TEZEL NECMİ SERKAN TEZEL	Karabük University Türkiye	Pbs supercapacitor electrode structures	
Kahraman KÜÇÜK Fatih Mehmet BOTSALI	Türk Traktör ve Ziraat Makineleri A.Ş. Konya Technical University	EXPERIMENTAL INVESTIGATION OF THE EFFECT OF DIFFERENT DIAMETER CYLINDER USED IN HYDRO-PNEUMATIC SUSPENSION SYSTEM ON THE STRUCTURE	
Fikret SÖNMEZ	Manisa Celal Bayar University Türkiye	ANALYSIS OF TOOL WEAR AND SURFACE ROUGHNESS VALUES IN THE MACHINING OF STAINLESS STEEL MATERIALS	
Abdullah ERDEMİR Mete KALYONCU	MPG Machinery Production Group Inc. Co., Konya Technical University	MODELING IMPEDANCE CONTROL WITH LIMITED INTERACTION POWER FOR A 2R PLANAR ROBOT ARM	
Melih Yazıcı	Bursa Technical University Türkiye	DEVELOPMENT OF FLAME RETARDANT PA6 AND PA66 COMPOSITES ACCORDING TO RAILWAYS EN 45545-2 STANDARD	
C. BAKİ B. ÇETİN B. SAFRAN C. TANCI C. BAKRAÇ	Vector BTC Ltd. Şti Türkiye FNSS Defense Systems Inc. Türkiye Tura Design and Engineering Ltd. Sti Türkiye	FINITE ELEMENT ANALYSIS BASED DEFORMATION ANALYSIS OF A SPESIFIC UNI-AXIAL COMPRESSION TEST SET-TO FOR DETERMINATION OF CIRCLIP LIMIT FORCE	



ONLINE PRESENTATIONS

14.03.2023 / Hall-7, Session-1



RIO DE JANEIRO LOCAL TIME

08 00 : 10 00



ANKARA LOCAL TIME



HEAD OF SESSION: Cüneyd YAVAŞ		
Sadriddinova Dilobar Husniddin qizi	Bukhara State University Uzbekistan	THE IMPORTANCE OF PHYSICAL ACTIVITY IN IMPROVING PUBLIC HEALTH
Aigul Myrzabayeva	Al-Farabi Kazakh National University	ROLE OF APOPTOSIS AND PROLIFERATION OF VASCULAR WALL CELLS IN ATHEROGENESIS
Oya GÜVEN Dilek VURAL KELEŞ	Kırklareli University Türkiye	THE RELATIONSHIP OF NEUTROPHIL- LYMPHOCYTE RATIO AND PROGNOSIS IN COVID-19 PATIENTS
Nurşin AYDIN	Dicle University Türkiye	MATERNAL IMMUNITY TOLERANCE
Cüneyd YAVAŞ Savaş BARIŞ	Başakşehir Çam and Sakura City Hospital Türkiye Aydın Gynecology and Pediatrics Hospital Türkiye	A RARE CASE OF NOVEL MUTATION IN THE KIFBP GENE
Dilara ÜLGER ÖZBEK	Sivas Cumhuriyet University Türkiye	USAGE OF ICP-MS IN BIOLOGICAL SAMPLES
Süleyman Görgüç Cemilenur Ataş Kübra Yıldırım Ece Şimsek Ahmet Yılmaz Çoban	Akdeniz University	INVESTIGATION OF THE BLOOD MICROBIOME PROFILE
Cemilenur Ataş Majda Ličina Kübra Yıldırım Ece Şimsek Ahmet Yılmaz Çoban	Akdeniz University	IN VITRO CULTURE MODELS IN LATENT TUBERCULOSIS INFECTION



ONLINE PRESENTATIONS

14.03.2023 / Hall-4, Session-2



RIO DE JANEIRO LOCAL TIME

10 30 : 12 30



ANKARA LOCAL TIME



16 30: 18 30

HEAD OF SESSION: Dr. German Martinez Prats, Dr. Francisca Silvia Hernández, Dr. Elizabeth García Moreno

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Oliva Atiaga Fernanda Guerrero Fernando Páez Rafael Castro Edison Collahuazo Luís Miguel Nunes Marcelo Grijalva ván Grijalva Xosé Luis Otero	Universidad de las Fuerzas Armadas ESPE Universidade Compostela Universidade do Algarve Universidade de Lisboa University of Compostela	VARIATION OF AIR QUALITY DUE TO CONFINEMENT BY COVID-19 IN CITIES OF ECUADOR WITH THE USE OF SATELLITE DATA
Seyfi ŞEVİK	Hitit University	INVESTIGATION OF THE USABILITY OF THE HIGHWAY SURFACE DRAINAGE SYSTEM AS A PRECIPITATION WATER HARVESTING SYSTEM
K. Ömer TAŞ Günay BEYHAN H. Haluk SELİM	Sakarya University Türkiye National Defence University Türkiye	GEOMORPHOLOGIC ANALYSIS OF THE YENIŞEHIR (BURSA) BASIN
Duygu TAŞKIN Günay BEYHAN	Sakarya University Türkiye	PALEOSEISMIC STUDIES ON THE NORTH ANATOLIAN FAULT AND THE EAST ANATOLIAN FAULT AND EVALUATION OF ACTIVE FAULTS
Özlem ÖZKAN ÖNÜR	Düzce University Türkiye	STURUCTURE TECHNIQUES USED IN EXAMPLES OF TRADITIONAL WOOD CIVIL ARCHITECTURE: TARAKLI HOUSES
Özlem ÖZKAN ÖNÜR	Düzce University Türkiye	IN HISTORICAL BUILDINGS DAMAGE CAUSITIVE STRUCTURE PHYSICS FACTORS
Res. Assist. Dr. Ceren AĞIN GÖZÜKIZIL Dr. Senem TEZCAN	Muş Alparslan University Türkiye The Istanbul Metropolitan Municipality	SATELLITE MUSEUMS AND ITS IMPACT ON URBAN SPACE
Johan Josueph Velazquez Martinez Dr. German Martinez Prats Dr. Francisca Silvia Hernández Dr. Elizabeth García Moreno	Universidad Juárez Autónoma de Tabasco	LA CONDENSACIÓN DE LA HUMEDAD ATMOSFÉRICA
Johan Josueph Velazquez Martinez Dr. German Martinez Prats Dr. Francisca Silvia Hernández Dr. Elizabeth García Moreno	Universidad Juárez Autónoma de Tabasco	PRODUCCIÓN DE AGUA POTABLE PARA RIEGO Y CONSUMO HUMANO



ONLINE PRESENTATIONS

14.03.2023 / Hall-5, Session-2



RIO DE JANEIRO LOCAL TIME

10 30 : 12 30



ANKARA LOCAL TIME



16 ³⁰ : 18 ³⁰

HEAD OF SESSION: Asst. Prof. Dr. İsa AVCI		
Asst. Prof. Dr. Murat KOCA Asst. Prof. Dr. İsa AVCI	Van Yuzuncu Yil University Karabük University	SECURITY VULNERABILITIES IN CLOUD TECHNOLOGY
PUSHKAR PANDEY	Indian Institute of Technology	APPLYING UX PRINCIPLES TO FIND PRE- PATTERNS IN HANDHELD AUGMENTED REALITY GAMES
Marilda de los Angeles Carvalho Marquez Yazmin Isolda Álvarez García	Universidad Juárez Autónoma de Tabasco	COMERCIO ELECTRONICO
Aniekan Essienubong Ikpe Michael Okon Bassey Etuk Ekom Mike	Akwa Ibom State Polytechnic University of Benin	MULTIAXIAL NON-PROPORTIONAL RANDOM ANALYSIS OF A TYPICAL HUB STEERING KNUCKLE WITH RESPECT TO IN-SERVICE LOADING EFFECTS ON ITS GEOMETRIC MODEL
Abir Bounaama	-	EXISTENCE OF SOLUTIONS FOR QUASI- LINEAR HYPERBOLIC WEIGHTED EQUATION WITH SOURCE TERMS
Feyza ALTUNBEY ÖZBAY Erdal ÖZBAY	Firat University Türkiye	PERFORMANCE ANALYSIS OF SWARM- BASED METAHEURISTIC ALGORITHMS ON CONTINUOUS OPTIMIZATION PROBLEMS
Assist. Prof. Ayfer TEKİN ATACAN Emre Can BAYKURT	Yildiz Technical University Türkiye	NONLINEAR BEHAVIOR OF CIRCULAR SHALLOW ARCHES



ONLINE PRESENTATIONS

14.03.2023 / Hall-6, Session-2



RIO DE JANEIRO LOCAL TIME

10 30 : 12 30



ANKARA LOCAL TIME



16 ³⁰ : 18 ³⁰

HEAD OF SESSION: Dr. Ivan PAVLOVIC		
Muhammad Adnan Arshad Asif Iqbal Umair Gull Muhammad Abdullah Saleem Saira Jamil Abid Shehzad	University of Agriculture Faisalabad	YIELD RESPONSES OF WHEAT (TRITICUM AESTIVUM L.) TO EXOGENOUS APPLIED MORINGA LEAF EXTRACT (MLE)
Bisma Yaseen Asif Iqbal Umair Gull Muhammad Abdullah Saleem Saira Jamil Abid Shehzad	University of Agriculture Faisalabad	EFFECT OF DIFFERENT SEEDING RATE AND HARVESTING INTERVAL ON THE FORAGE YIELD AND QUALITY OF MAIZE
Dr. Milena Milojević PhD student Suzana Knežević Dr. Biljana Delić Vujanović Dr.Goran Stanišić	Unit of Agricultural and Business	MILK PRODUCTION IN ACCORDANCE WITH THE PRINCIPLES OF SUSTAINABLE DEVELOPMENT: THE CASE OF FARM "KOJIĆ"
Dr. R. Saravanan	Bharath Institute of Higher Education and Research	PRODUCTION OF TRANSGENIC EDIBLE BANANA PLANT CONTAIN CT B GENE
Dr. Ivan PAVLOVIC	Scientific Institute of Veterinary Medicine of Serbia	BIODIVERSITY AND SEASONAL DISTRIBUTION OF CULICOIDES SPP.IN NORTH PART OF SERBIA (VOJVODINA)
Shoaib Alam Pharm.D	University Of Karachi	SCREENING OF PHASEOLOUS VULGARIS LINN. FOR PHARMACOLOGICAL AND TOXICOLOGICAL EFFECTS
Salma ELAMIRI Soumia ABOUL-HROUZ Achraf CHAKIR Mohamed ZAHOUILY	Hassan II University - Casablanca, Morocco	APPLICATION OF NOVEL SLOW- CONTROLLED RELEASE FERTILIZER (SCRF): MONITORING THE RELEASE PROFILE OF NITROGEN, PHOSPHORUS AND POTASSIUM IN WATER AND SOIL



ONLINE PRESENTATIONS

14.03.2023 / Hall-7, Session-2



RIO DE JANEIRO LOCAL TIME



ANKARA LOCAL TIME



16 ³⁰ : 18 ³⁰

$10^{30}:12^{30}$		
	10 30 •	12 30

HEAD OF 3	ESSION: Major Gne	orgne GlukGlu
Major Gheorghe GIURGIU Prof. dr. Manole COJOCARU	Titu Maiorescu University	MICROBIOTA MODULATION AS THERAPEUTIC APPROACH IN THE NEUROPATHIC PAIN IN DOG WITH SPINAL CORD INJURY: IMPACT OF POLENOPLASMIN
Milivoje Urošević Milosava Matejević Milena Milojević Tsegmid Namsraijav	University of Novi Sad Mongolian University of life sciences	BASIC MORPHOMETRIC PARAMETERS OF THE ANTLERS OF THE GOLDEN TROPHY RED DEERS (Cervus elaphus L.)
Muhammad Waris MAJEED Hafiz Qadeer AHMED	University of Agriculture Pakistan	PREPARATION AND EVALUATION OF NANOPARTICLES OF ZINC OXIDE COATED INTRAMAMMARY INFUSION FOR THE TREATMENT OF SUBCLINICAL BOVINE MASTITIS
Memiş Özdemir Zekrullah Motmain Kübra Ekinci Esranur Saygılı	Atatürk University Türkiye	A META-ANALYSIS OF THE ASSOCIATION BETWEEN PROLACTIN (PRL) GENE POLYMORPHISM WITH LACTATION MILK AND PROTEIN PRODUCTION TRAITS IN CATTLE
Memiş Özdemir Zekrullah Motmain Kübra Ekinci Esranur Saygılı	Atatürk University Türkiye	INVESTIGATION OF THE RELATIONSHIP BETWEEN KAPPA-CASEIN GENE POLYMORPHISM AND MILK PRODUCTION HARACTERISTICS IN HOLSTEIN BREED CATTLE: META- ANALYSIS
Dr. Wafa Majeed Dr. Muhammad Saad Tariq	University of Agriculture	ROLE OF RUTIN IN ATTENUATION OF METABOLIC GLUCOSE AND INSULIN IMPAIRMENT
Rodolfo Reda Renzo Guarnieri Alessio Zanza Marco Seracchiani Dario Di Nardo Luca Testarelli	Sapienza University of Rome	PERI-IMPLANT MARGINAL BONE LOSS PROGRESSION AND A-MMP-8

CONTENT

Author	Title	No
Johan Josueph Velazquez Martinez Dr. German Martinez Prats Dr. Francisca Silvia Hernández Dr. Elizabeth García Moreno	LA CONDENSACIÓN DE LA HUMEDAD ATMOSFÉRICA	1
Johan Josueph Velazquez Martinez Dr. German Martinez Prats Dr. Francisca Silvia Hernández Dr. Elizabeth García Moreno	PRODUCCIÓN DE AGUA POTABLE PARA RIEGO Y CONSUMO HUMANO	3
G.P. Ashwinkumar C. Sulochana N.Sandeep	NUMERICAL INVESTIGATION OF CHEMICALLY REACTING MHD FLOW DUE TO A ROTATING CONE WITH THERMOPHORESIS AND BROWNIAN MOTION	5
Chennai Yassmine Belaidi Salah	QSAR MODELING USING GAUSSIAN PROCESS APPLIED FOR A SERIES OF FLAVONOIDS AS POTENTIAL ANTIOXIDANTS	6
Chennai Yassmine Ouassaf Mebarka	QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP (QSAR) INVESTIGATIONS AND MOLECULAR DOCKING ANALYSIS OF PLASMODIUM PROTEIN FARNESYLTRANSFERASE INHIBITORS AS POTENT ANTIMALARIAL AGENTS	7
Dr. Yassmine CHENNAI Dr. Assma FETTEH	ANTIBACTERIAL AND ANTI- OXIDANT ACTIVITIES OF EXTRACTS FROM	8
Prof.Dr. Salah BELAIDI Dr. Yassmine CHENNAI	IN SILICO INVESTIGATION OF SEVERAL SERIES OF HETEROCYCLIC MOLECULES FOR DRUG DISCOVERY	9
Chennai Yassmine Ouassaf Mebarka	CONTRIBUTION TO DRUG DISCOVERY THROUGH COMPUTATIONALANALYSIS OF SEVERAL SERIES OF HETEROCYCLIC MOLECULES	10
Rima SAADBOUZID Radhia BOUZIDI Imane SARHANI Donia HELLAL Leilia OUMDDOUR Massouda IBRIR Hachani KHADRAOUI Ghania BELAALOUI	BREAST CANCER; PRELIMINARY RESULTS OF A RETROSPECTIVE STUDY IN EASTERN ALGERIA	11
Sidra Mohiuddin Soofi Dr. Afshan Siddiq	MORUS ALBA; A RAY OF HOPE FOR MENTAL ILLNESSES	13
Yusuf Rabe Yusuf Muhammad Sanyinna Abdulhamid Ahmed	MOSQUITO VECTOR ABUNDANCE AND DISTRIBUTION ASSOCIATED WITH THE PREVALENCE OF MALARIA IN ZANGO LOCAL GOVERNMENT AREA, KATSINA STATE, NIGERIA	14
Prof. Dr. Huma Ali Dr. Saba Zubair	TRENDS AND ROLE OF PHARMACIST IN COMMUNITY PHARMACY SERVICES AND FACILITATION PROTOCOL: CHALLENGES IN REAL TIME PRACTICES	15
Özgür Ülkü ÖZDEMİR Şeyda BERK	GLUCOSE TRANSPORTERS IN CANCER METABOLISM	16
Rabia KALELİ Şeyda BERK	THE MOLECULAR MECHANISM OF CANCER METASTASIS	28

Istemi SERIN	LYMPHOCYTE LEVEL AT DIAGNOSIS IN HODGKIN LYMPHOMA: COULD IT BE AN INDICATOR OF THE STAGE AT INITIAL DIAGNOSIS?	41
P.H. Najafgulieva R.Sh.Qasimov	COMPARATIVE ANALYSIS OF NEW OPPORTUNITES FOR PHARMACOTHERAPY OF NON-SPECIFIC	44
Dr. Syed Makhdoom Hussain	USE OF OILSEEDS BY-PRODUCTS IN AQUA-FEEDS	46
Aminu Ado Kaugama Mahrazu A. Yusuf Phd Ushie Onumashi Afi Phd Yusha'u Safiyanu Muhammad Ansar Bilyamin Adam Jabir Abdullahi Muhammad	IMPACT OF HEAVY METALS CONTENT FOUND IN IRRIGATED RED PEPPER IN CHALLAWA INDUSTRIAL AREA	47
Jyoti Sinha Vinod Kumar	PREPARATION AND EVALUATION OF TOPICAL PREPARATION OF EULALIOPSIS BINATA EXTRACT	48
Kave Koorehpaz	NOVEL CRYOPROTECTANTS AND THEIR EFFECTS ON DECREASING GLYCEROL CONCENTRATION DURING CRYOPRESEVVATION	49
Novotorzhina Nelya Rzayeva Irada Kazimzadeh Shafa Safarova Mehpara Gahramanova Gariba Mustafayeva Yegana	HYDROXYMETHYL-P-TOLUENESULFONAMIDE AS AN ANTIOXIDANT ADDITIVE TO DIESEL FUELS	50
Associate Professor Allakhverdiyev Elkhan Rajaf D. student, Abbasova Nahida Shavaat	DETERMINATION OF THE INFLUENCE OF STRUCTURE, SIZE OF WORKING NESTS AND THEIR FORAGING ON THE DEVELOPMENT OF FIELD MOUSE IN SOWN AREAS	53
Nilüfer YAZICI Nebi BİLİR	GROWTH VARIATION IN FOREST TREE SPECIES IN AFFORESTATION OF GRADONI TERRACING	56
Nilüfer YAZICI Nebi BİLİR	EFFECT OF TERRACING ON GROWTH OF TAURUS CEDAR (CEDRUS LIBANI): A CASE STUDY FROM ISPARTA DISTRICT	58
Nilüfer YAZICI Nebi BİLİR	GROWTH VARIATION IN FOREST TREE SPECIES IN AFFORESTATION OF GRADONI TERRACING	65
Serim Tuna KOÇ	ARONIA AND ANTHOCYANINS	72
Prof.Dr.Qassim Shamkhi al khafaji Prof.Dr.shaymaa Awad Kadhim Noor Ali jaafar Hasanain Alawadi PhD.Ihab Alfadhel	EVALUTION OF ATOMIC PROPERTIES FOR LI-LIKE IONS SYSTEMS USING HARTREE-FOCK AND CONFIGURATION INTERACTION METHODS	74
Vekil SARI	DESIGN AND MODEL OF AN INDUCTIVE WIRELESS POWER TRANSFER SYSTEM FOR ELECTRIC VEHICLES	76
Fatma MEYDANERİ TEZEL	ELECTRICAL AND STRUCTURAL CHARACTERIZATION OF PBS THIN FILMS PRODUCED BY SPRAY METHOD	77
Prof. Dr., Fatma MEYDANERİ TEZEL Prof. Dr.NECMİ SERKAN TEZEL	PbS SUPERCAPACITOR ELECTRODE STRUCTURES	85
Kahraman KÜÇÜK Prof. Dr. Fatih Mehmet BOTSALI	EXPERIMENTAL INVESTIGATION OF THE EFFECT OF DIFFERENT DIAMETER CYLINDER USED IN HYDRO- PNEUMATIC SUSPENSION SYSTEM ON THE STRUCTURE	94
Fikret SÖNMEZ	ANALYSIS OF TOOL WEAR AND SURFACE ROUGHNESS VALUES IN THE MACHINING OF STAINLESS STEEL MATERIALS	96
Abdullah ERDEMİR Prof. Dr. Mete KALYONCU	MODELING IMPEDANCE CONTROL WITH LIMITED INTERACTION POWER FOR A 2R PLANAR ROBOT ARM	107

Melih Yazıcı	DEVELOPMENT OF FLAME RETARDANT PA6 AND PA66 COMPOSITES ACCORDING TO RAILWAYS EN 45545-2 STANDARD	120
C. BAKİ B. ÇETİN B. SAFRAN C. TANCI C. BAKRAÇ	FINITE ELEMENT ANALYSIS BASED DEFORMATION ANALYSIS OF A SPESIFIC UNI-AXIAL COMPRESSION TEST SET-TO FOR DETERMINATION OF CIRCLIP LIMIT FORCE	122
Sadriddinova Dilobar Husniddin qizi	THE IMPORTANCE OF PHYSICAL ACTIVITY IN IMPROVING PUBLIC HEALTH	123
Aigul Myrzabayeva	ROLE OF APOPTOSIS AND PROLIFERATION OF VASCULAR WALL CELLS IN ATHEROGENESIS	127
Oya GÜVEN Dilek VURAL KELEŞ	THE RELATIONSHIP OF NEUTROPHIL-LYMPHOCYTE RATIO AND PROGNOSIS IN COVID-19 PATIENTS	128
Doktorant Nurşin AYDIN	MATERNAL IMMUNITY TOLERANCE	130
Cüneyd YAVAŞ Savaş BARIŞ	A RARE CASE OF NOVEL MUTATION IN THE KIFBP GENE	132
Dilara ÜLGER ÖZBEK	USAGE OF ICP-MS IN BIOLOGICAL SAMPLES	134
Süleyman Görgüç Cemilenur Ataş Kübra Yıldırım Ece Şimsek Ahmet Yılmaz Çoban	INVESTIGATION OF THE BLOOD MICROBIOME PROFILE	142
Cemilenur Ataş Majda Ličina Kübra Yıldırım Ece Şimsek Ahmet Yılmaz Çoban	IN VITRO CULTURE MODELS IN LATENT TUBERCULOSIS INFECTION	144
Seyfi ŞEVİK	INVESTIGATION OF THE USABILITY OF THE HIGHWAY SURFACE DRAINAGE SYSTEM AS A PRECIPITATION WATER HARVESTING SYSTEM	146
Özlem ÖZKAN ÖNÜR	IN HISTORICAL BUILDINGS DAMAGE CAUSITIVE STRUCTURE PHYSICS FACTORS	160
Ceren AĞIN GÖZÜKIZIL Senem TEZCAN	SATELLITE MUSEUMS AND ITS IMPACT ON URBAN SPACE	174
Asst. Prof. Dr. Murat KOCA Asst. Prof. Dr. İsa AVCI	SECURITY VULNERABILITIES IN CLOUD TECHNOLOGY	176
PUSHKAR PANDEY	APPLYING UX PRINCIPLES TO FIND PRE-PATTERNS IN HANDHELD AUGMENTED REALITY GAMES	183
Aniekan Essienubong Ikpe Michael Okon Bassey Etuk Ekom Mike	MULTIAXIAL NON-PROPORTIONAL RANDOM ANALYSIS OF A TYPICAL HUB STEERING KNUCKLE WITH RESPECT TO INSERVICE LOADING EFFECTS ON ITS GEOMETRIC MODEL	184
Dr. Feyza ALTUNBEY ÖZBAY Dr. Erdal ÖZBAY	PERFORMANCE ANALYSIS OF SWARM-BASED METAHEURISTIC ALGORITHMS ON CONTINUOUS OPTIMIZATION PROBLEMS	198
Ayfer TEKİN ATACAN Emre Can BAYKURT	NONLINEAR BEHAVIOR OF CIRCULAR SHALLOW ARCHES	199
Muhammad Adnan Arshad Asif Iqbal Umair Gull Muhammad Abdullah Saleem Saira Jamil Abid Shehzad	YIELD RESPONSES OF WHEAT (TRITICUM AESTIVUM L.) TO EXOGENOUS APPLIED MORINGA LEAF EXTRACT (MLE)	201

Bisma Yaseen Asif Iqbal Umair Gull Muhammad Abdullah Saleem Saira Jamil Abid Shehzad	EFFECT OF DIFFERENT SEEDING RATE AND HARVESTING INTERVAL ON THE FORAGE YIELD AND QUALITY OF MAIZE (Zea mays L.)	203
Dr. R. Saravanan	PRODUCTION OF TRANSGENIC EDIBLE BANANA PLANT CONTAIN CT B GENE	205
Academician., PrincipalRes.Fell., Dr. Ivan PAVLOVIC	BIODIVERSITY AND SEASONAL DISTRIBUTION OF CULICOIDES SPP.IN NORTH PART OF SERBIA (VOJVODINA)	206
Major Gheorghe GIURGIU Prof. dr. Manole COJOCARU	MICROBIOTA MODULATION AS THERAPEUTIC APPROACH IN THE NEUROPATHIC PAIN IN DOG WITH SPINAL CORD INJURY: IMPACT OF POLENOPLASMIN	207
Milivoje Urošević Milosava Matejević Milena Milojević Tsegmid Namsraijav	BASIC MORPHOMETRIC PARAMETERS OF THE ANTLERS OF THE GOLDEN TROPHY RED DEERS (Cervus elaphus L.)	208
Muhammad Waris MAJEED Hafiz Qadeer AHMED	PREPARATION AND EVALUATION OF NANOPARTICLES OF ZINC OXIDE COATED INTRAMAMMARY INFUSION FOR THE TREATMENT OF SUBCLINICAL BOVINE MASTITIS	209
Memiş Özdemir Zekrullah Motmain Kübra Ekinci Esranur Saygılı	A META-ANALYSIS OF THE ASSOCIATION BETWEEN PROLACTIN (PRL) GENE POLYMORPHISM WITH LACTATION MILK YIELD AND PROTEIN PRODUCTION TRAITS IN CATTLE	211
Dr. Wafa Majeed Dr. Muhammad Saad Tariq	ROLE OF RUTIN IN ATTENUATION OF METABOLIC GLUCOSE AND INSULIN IMPAIRMENT	218
Rodolfo Reda Renzo Guarnieri Alessio Zanza Marco Seracchiani Dario Di Nardo Luca Testarelli	PERI-IMPLANT MARGINAL BONE LOSS PROGRESSION AND A- MMP-8 CAN BE CONSIDERED AS INDICATORS OF THE SUBSEQUENT ONSET OF PERI-IMPLANTITIS. A 5-YEAR STUDY	219

4TH INTERNATIONAL LATIN AMERICAN CONGRESS ON NATURAL AND APPLIED SCIENCES

LA CONDENSACIÓN DE LA HUMEDAD ATMOSFÉRICA

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RESUMEN

La falta de infraestructura hídrica genera una escasez económica de agua y no garantiza el acceso al agua. El tener más desarrollo de infraestructura hídrica alivia por mucho la escasez pero de igual manera se debe considerar los impactos del cambio climático, siendo importante tomar en cuenta que el agua sostiene los ecosistemas terrestres (pastizales, ríos, lagos, etc.) que al contar con la infraestructura y la aplicación correcta proporcionan servicios importantes como la purificación para consumo humano, suministro de agua, producción de alimentos y actividades económicas

Siempre es importante buscar soluciones eficientes que estos abastezcan el agua potable para todos los ciudadanos que carecen. Es por ello por lo que se crean innovadoras tecnologías para extraer el agua de la humedad del aire; Se considera es posible utilizar energías renovables como es la energía eólica, cubriendo y solucionando a un problema generalizado. Se considera que estas innovaciones permiten que el acceso al agua potable a muchas personas usando simplemente la energía eólica.

Estas innovaciones tienen la tendencia de mejorar por mucho la calidad de vida de las personas, permitiendo que haya producción de agua extrayéndola de la humedad del aire aplicando el proceso de condensación; considerándose que depende de una fuente de energía sencilla que se conoce desde hace miles de años.

Todos los proyectos cuentan con una gran relevancia, sistemas complejos y diferentes pero al mismo tiempo buscan resolver la problemática presentada desde mucho tiempo atrás y gracias a los avances tecnológicos y métodos es posible la generación de agua a partir de la condensación del aire, aun habiendo muchas alternativas en prototipos siempre está abierta la índole de afrontar las problemáticas de todo tipo y mejorarlas, principalmente en base a un

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desarrollo sostenible siempre y cuando contando con el diseño e implementaciones de nuevas tecnologías.

ABSTRACT

The lack of water infrastructure generates an economic shortage of water and does not guarantee access to water. Having more development of water infrastructure greatly alleviates scarcity but in the same way the impacts of climate change must be considered, being important to take into account that water sustains terrestrial ecosystems (grasslands, rivers, lakes, etc.) that by having the infrastructure and the correct application provide important services such as purification for human consumption, Water supply, food production and economic activities

It is always important to look for efficient solutions that supply drinking water for all citizens who lack. That is why innovative technologies are created to extract water from moisture in the air; It is considered possible to use renewable energies such as wind energy, covering and solving a widespread problem. These innovations are considered to allow access to drinking water to many people simply using wind energy.

These innovations have the tendency to greatly improve the quality of life of people, allowing water production by extracting it from the humidity of the air by applying the condensation process; considering that it depends on a simple energy source that has been known for thousands of years.

All projects have great relevance, complex and different systems but at the same time seek to solve the problem presented for a long time and thanks to technological advances and methods it is possible to generate water from air condensation, even if there are many alternatives in prototypes is always open the nature of facing problems of all kinds and improving them, mainly based on sustainable development as long as it has the design and implementation of new technologies.

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PRODUCCIÓN DE AGUA POTABLE PARA RIEGO Y CONSUMO HUMANO

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RESUMEN

El agua es esencial para la vida en la Tierra, es necesaria para la vida, la salud y el medio ambiente. Sin agua, la vida tal como la conocemos no existiría. El problema de la escasez de agua potable es una preocupación importante en muchas áreas del mundo. Varios países han producido agua potable a partir de recursos renovables durante siglos. Los países también recolectan agua de lluvia para complementar sus fuentes naturales de agua potable. Sin embargo, hay formas de recolectar agua potable de manera segura si es necesario.

Muchas personas en áreas rurales recolectan agua potable de fuentes contaminadas. El agua contaminada es cuando las sustancias nocivas contaminan la fuente recolectada. Algunas fuentes comunes de agua contaminada son los abrevaderos de animales y los pantanos. Esto se debe a la eliminación inadecuada de los desechos animales. El agua contaminada puede ser letal si no se trata. Sin embargo, hay formas de tratar el agua potable contaminada con cloro y

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otros productos químicos. Estas soluciones ayudan a prevenir enfermedades fatales causadas por bacterias en el agua contaminada. Incluso entonces, las fuentes de agua potable tratada y no contaminada cuestan dinero y requieren un mantenimiento continuo.

ABSTRACT

Water is essential for life on Earth, it is necessary for life, health and the environment. Without water, life as we know it would not exist. The problem of drinking water scarcity is a major concern in many areas of the world. Several countries have produced drinking water from renewable resources for centuries. Countries also collect rainwater to supplement their natural sources of drinking water. However, there are ways to collect drinking water safely if needed.

Many people in rural areas collect drinking water from contaminated sources. Contaminated water is when harmful substances contaminate the collected source. Some common sources of contaminated water are animal troughs and swamps. This is due to improper disposal of animal waste. Contaminated water can be lethal if left untreated. However, there are ways to treat drinking water contaminated with chlorine and other chemicals. These solutions help prevent fatal diseases caused by bacteria in contaminated water. Even then, sources of treated and uncontaminated drinking water cost money and require ongoing maintenance.

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NUMERICAL INVESTIGATION OF CHEMICALLY REACTING MHD FLOW DUE TO A ROTATING CONE WITH THERMOPHORESIS AND BROWNIAN MOTION

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ABSTRACT

In this study we analysed the momentum, heat and mass transfer behaviour of magnetohydrodynamic flow towards a vertical rotating cone in porous medium with thermophoresis and Brownian motion effects. Further, the numerical solutions are elucidated by using Runge-Kutta based shooting technique. Obtained results are validated with open literature and found an excellent agreement. The influence of non-dimensional governing parameters on velocity, temperature and concentration profiles along with the friction factor, local Nusselt and Sherwood numbers are determined and discussed with the help of graphs and tables. Results proved that the thermophoresis and Brownian motion parameters have tendency to control the heat and mass transfer rates. It is also found that a raise in the porosity parameter develops the heat and mass transfer rate.

Keywords: MHD, Rotating cone, Thermophoresis, Brownian motion, Chemical reaction.

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QSAR MODELING USING GAUSSIAN PROCESS APPLIED FOR A SERIES OF FLAVONOIDS AS POTENTIAL ANTIOXIDANTS

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ABSTRACT

For decades, flavonoids have been the core of diverse research, especially for their significant antioxidant activity. They have several biological activities, and they are used as anticancer, antileishmanial, anti-inflammatory, and antiaging compounds. However, current researchers are very much interested in the antioxidant activity of flavonoids since oxidative stress is strongly related to several diseases. In this study, we have chosen to elaborate on a quantitative structure-antioxidant activity relationship (QSAR) using a statistical method called Gaussian process (GP). The main advantage of this method compared to other techniques currently used in QSAR studies is that it does not increase the complexity of learning tests. Typical QSAR studies use common techniques such as the artificial neural method, multiple linear regression, and partial least squares regression. The aim of this work was to use a statistical technique little known in pharmaceutical chemistry, the Gaussian process regression which is rarely used to build a QSAR model. Finally, we have also demonstrated that GP is reliable and capable of predicting the antioxidant activity with a respectable record (R 2 pred) which is equal to 0.86, so it is much higher than the reference value of 0.6. Therefore, we estimate that this reliable model can be used to predict the antioxidant activity of a series of new molecules. Also, based on the HC results, our set was divided into four separate clusters according to the presence of glycosides and the molar weight of the flavonoids.

Keywords: Flavonoids, Antioxidant, QSAR, Gaussian process, PCA, HCA.

QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP (QSAR)
INVESTIGATIONS AND MOLECULAR DOCKING ANALYSIS OF PLASMODIUM
PROTEIN FARNESYLTRANSFERASE INHIBITORS AS POTENT
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ABSTRACT

The development of farnesyltransferase inhibitors based on the benzophenone scaffold directed against Plasmodium falciparum is considered a strategy in malaria treatment. In this work, quantitative structure-activity relationship (QSAR) was performed to predict the protein farnesyltransferase (PFT) inhibitory activities for a series of 36 benzophenone derivatives. The data set was divided into two subsets of training and test sets, and the best model using multiple linear regression (MLR), with the values of internal and external validity (R2 = 0.884, R2adj = 0.865, R2pred = 0.821, Q2cv = 0.822 and R2p=0.811) was found in agreement with the Tropsha and Golbraikh criteria. The applicability domain (AD) was determined using the Williams plot to describe the chemical space for the model used in this study. The model shows that antimalarial activities of benzophenone depend on logP, bpol, MAXDn, and FMF descriptors. These indications prompted us to design new benzophenones PFT inhibitors and predict the value of their anti-malarial activities based on the MLR equation. Docking results reveal that the newly designed benzophenones bind to the hydrophobic pocket and polar contact with high affinity. The predicted results from this study can help to design novel benzophenone as inhibitors of human PFT with high antimalarial activities.

KeyWord: QSAR, docking, benzophenone, PFT inhibitory, antimalarial.

ANTIBACTERIAL AND ANTI- OXIDANT ACTIVITIES OF EXTRACTS FROM

medicinal plants

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ABSTRACT

The algerian flora provides a diverse range of aromatic plants with a high therapeutic interest due to their secondary biologically active metabolites, which have sparked scientific interest. In this study, we are interested in the plants Ocimum basilicum L. of the Lamiaceae family and Artemisia campestris A. of the Asteriaceae family, which are well known locally and have a variety of curative properties in traditional medicine. The first part of this study is devoted to the quality control of the plant powder and the investigation of the metabolites. The phytochemical screening revealed the presence of flavonoids, tannins, coumarine, essential oil, and other metabolic compounds. The HE were obtained using hydrodistillation with a yield of 2.4% for O.basilicum L. and 1.8% for A.campestris A.The phenolic compounds were obtained by a series of extractions with four solvants of increasing polarity. The concentration of these extracts in total polyphénols, flavonoids, and tanins was determined by using the reactif Folin Ciocalteu, aluminum trichlorure, and vanilline with the addition of chlorhydric acid. In the second section, we investigated the antioxidative capacity of extracts (HE and phenolic compounds) in vitro using the DPPH method. The results show that our extraits have interesting antioxidant properties, with ethyl acetate being the most effective. Furthermore, the essential oil has a very low antioxidative activity when compared to the benchmark for the two plants. Finally, we assessed the antibacterial activity of our extracts against ten pathogenic bacteria using the MH diffusion method. The results show that phenolic extracts of O.basilicum L. have higher activity for HE.Unlike A.campestris A., the acétate of éthyle extract is the most active on the majority of Gram+ souches.

Keywords: O.basilicum L., Artemisia campestris A, Antibacterial, oxidant activities

IN SILICO INVESTIGATION OF SEVERAL SERIES OF HETEROCYCLIC MOLECULES FOR DRUG DISCOVERY

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ABSTRACT

Drug discovery and design are inextricably linked to various branches of chemistry, particularly organic chemistry. Many aspects of chemistry must be involved in order to translate knowledge of the molecular, genetic, and cellular bases of cancer into effective therapies. Thus, the goal of this research is to identify promising active compounds for coumarin as CK2 protein kinase inhibitors using a QSAR model and drug similarity analysis.CK2 is a ubiquitous Ser/Thr-specific protein kinase that is required for cell cycle viability and progression. CK2 levels are particularly high in proliferating, normal, or transformed tissues, and transgenic mice expressing its catalytic subunit are responsible for lymphomas. The work began with the optimization of the equilibrium structures of the basic coumarin in order to select the most reliable forecasting approach compared to experimentation and at the lowest computational cost. Following our research, we conduct a multiple linear regression (MLR) analysis to generate QSAR models. An external validation research was done because the results show that the QSAR model of CK2 inhibitory activity is robust and has extremely strong prediction capacity, as indicated by R2 values of 0.951 and 0.927, respectively, following linear regression analysis. The investigation using QSAR models is successful in screening 34 candidate chemicals. Following that, the compounds under consideration were evaluated for drug-likeness and reactivity (ADME, golden triangle, lipophylicity indices). The results reveal that when supplied orally, the majority of the substances have no bioavailability issues.

The data also aid in determining which chemicals do not have clearance issues, as well as which are the most stable and reactive among those examined. The anticipated findings of this study may aid in the development of novel coumarins with significant CK2 inhibitor activity.

Keywords: coumarine, CK2, QSAR, MLR.

CONTRIBUTION TO DRUG DISCOVERY THROUGH COMPUTATIONALANALYSIS OF SEVERAL SERIES OF HETEROCYCLIC MOLECULES

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ABSTRACT

Breast cancer is the most common type of female cancer. One class of hormonal therapy for breastcancer drugs -non steroidal aromatase inhibitors- are triazole analogues. In this work a fundamentaland original research was made on the molecule of triazole heterocyclic, whose the aim is topredict the reactivity and biological activity studied of the compound. It is based on different computational and approaches used in computer aided -drug-design. (SPR, QSAR, moleculardocking, ADMET). A study of structure – property relationships (SPR) for 1,2,3 triazole derivatives has been carried. A linear quantitative structure activity relationship model is obtained using Multiple LinearRegression (MLR) analysis as applied to a series of triazole derivatives with inhibitory activity of the aromatase. The accuracy of the proposed MLR model is illustrated using the following evaluation techniques: cross validation, and external test.Docking process, the interaction and binding of ligands - protein were done and visualized using software Molegro Virtual Docking. Molinspiration and ADMETSAR web servers used to calculate ADMET and physicochemical properties of the target compounds respectively. The results are reported and discussed in the present investigation. A close agreement with experimental results was found which improves the affinity of the present work.

KeyWord:1,2,3-triazole, aromatase inhibitory, density functional theory, QSAR, MLR, ADMET, docking molecular

BREAST CANCER; PRELIMINARY RESULTS OF A RETROSPECTIVE STUDY IN EASTERN ALGERIA

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ABSTRACT

Breast cancer is the most frequently diagnosed cancer and the second cause of death worldwide and in Algeria. We can distinguish different histological and molecular entities in breast cancer. The objective of this work is to report the preliminary results of a molecular and histological characterization of breast cancer in CLCC Batna center during the period from 2018 to 2022.

Clinical and pathological characteristics of 570 breast cancer cases were collected from the archives of the pathology department of CLCC and CHU hospital Batna. To analyze their characteristics, age, histological type, SBR grade, hormone receptor status, HER2 status were taken in account, and molecular phenotypes were compared.

The results revealed that the mean age of the selected population is 51 years with a predominance of the age group 50 to 59 years. The proportions of luminal A, luminal B, TNBC and HER2 breast cancer subtypes were 23.5%, 49.51%, 16.8% and 10.5%, respectively. The invasive ductal carcinoma (IDC) was the most common histological type (85.4%) followed by the invasive lobular carcinoma (9.5%), The SBR grade II was the most common in the population. We noticed a higher frequency of IDC in the young [40 - 49 y] and middle aged groups [50 - 59 y], while all the IDC were of Luminal B molecular type.

Although our results are preliminary, some of them are concordant with other Algerian studies. A more extended molecular and immunohistological characterization is ongoing.

Key words: Breast Cancer, Histological type, sub-molecular type, Aures region, immunohistochemistry

MORUS ALBA; A RAY OF HOPE FOR MENTAL ILLNESSES

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ABSTRACT:

Over the years, plants have been used in treatment of various health ailments. *Morus alba* also

known as White Mulberry is a deciduous tree which belongs to family *Moraceae*. Mulberry is

rich in antioxidants such as hydrophobic flavonoids, polyphenols, carotenoids, vitamin A, C

and E. This study analyses the central nervous system activities including memory

enhancement, learning abilities, changes in behavior, cognition, anxiety and depression. These

effects will be studied on experimental mice, which will be distributed in control and test

groups. Aqueous fruit extract prepared by Maceration extraction will be given to test group in

three different doses per oral over a time period of 30 days, whereas control will be given

water for injection for same duration. Afterwards, changes in aforementioned effects will be

observed to determine the pharmacological effects of plant.

Key Words *Morus alba* White Mulberry Anxiolytic Cognition Antidepressant Antioxidant

Maceration

13

MOSQUITO VECTOR ABUNDANCE AND DISTRIBUTION ASSOCIATED WITH THE PREVALENCE OF MALARIA IN ZANGO LOCAL GOVERNMENT AREA, KATSINA STATE, NIGERIA

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ABSTRACT

Mosquitoes are group of small insects distributed among 41 genera and about 3500 species responsible for transmitting malaria and other infectious diseases worldwide. This study examined mosquito vector abundance and distribution associated with the prevalence of malaria in Zango Local Government Area, Katsina State, Nigeria. This is a descriptive cross sectional research that employed survey and laboratory practical to generate data. A total of 305 individuals involving pregnant women, children and other patients attending the selected Health Centres randomly selected from 4 communities were examined. Eight houses were randomly selected from each community for entomological studies of indoor-biting and resting mosquitoes. Ladles/pipetting were used for collection of larvae in small ground pools, earthen pots and discarded tyres whereas dipping method was used to collect larvae in large breeding sites such as ponds and dams. MS-Excel and Graph Pad Instat software were used for data analysis. Five hundred and thirty one (531) mosquito larvae and 785 adult mosquitoes were collected from 35 breeding sites and 32 households respectively. Majority of the larvae collected belong to the genus Anopheles with A. gambiae species accounting for 56.3%. The adult mosquito species collected were identified as: Anopheles gambiae (69.2%), Anopheles arabiensis (5.7%) and Anopheles funestus (4.5%), while non- malaria vectors are: Culex quinquefasciatus (14.4%) and Aedes aegypti (6.2%) respectively. The prevalence of Plasmodium falciparum infection among the subject was 59.0%. This study provides a baseline data on the mosquito vector species (especially Anopheles) in the area, giving an insight into the high prevalence of malaria recorded in the locality. Proper environmental sanitation, proper sewage system, clearing bushes around house and any possible mosquito breeding sites are therefore, recommended.

Keywords: Mosquito; Abundance; Distribution; Prevalence; Malaria; Zango Local Government Area.

TRENDS AND ROLE OF PHARMACIST IN COMMUNITY PHARMACY SERVICES AND FACILITATION PROTOCOL: CHALLENGES IN REAL TIME PRACTICES

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ABSTRACT

Background: Community Pharmacy is most debatable part of practice in Pakistan with respect to its application and existence. There are many reasons behind the implications of long-term growth plans of this valuable Practice. In Pakistan major challenges associated may be enlisted as lack of significant information, least priority from higher stack holders, less incentive in terms of job and retention, limited opportunities, no mass level communication for pharmacy setups offering community services, ranges of services offered and trained staff availability, absence of counselling and education activities, limited media coverage and social responsibility, prioritizes and resources allocation and maintenance. **Study Design** and Methodology: A cross sectional descriptive study design was used to evaluate the information and perception of public towards community pharmacy setup in Pakistan and role of Pharmacist in drugs management system. Moreover multiple groups of Pharmacy related professionals including community pharmacist's, technician and other healthcare professionals were also included to determine the related practices and scope of work. Data Collection was carried out using a well constructed questionnaire and validation was performed prior to this study. Results: Values of Cronbach's alpha and spearman correlation were found satisfactory. It was revealed during the study that pharmacist's recognition at mass level is comparatively very low in this region. Moreover costly community related services are one other discouraging factor from public perspective. Basic health indicators are relatively low and people's levels of knowledge was much less towards any available pharmacy services. Conclusion: Incentive should be attractive to maintain long-term relationships and growth of community pharmacy service. Service providers and public relations must be encouraged to build with proper media support towards better quality of medication provisions in presence of trained and qualified pharmacist. Campaigns for education and awareness should be placed on regular basis in various territories across the country. All stakeholders should develop a reflective practice model with clear provision of policies and feedback to improve and expand community services in order to improve better system.

Keywords: Community Pharmacy Pharmacist role , real time Challenges and practice, policy, service

GLUCOSE TRANSPORTERS IN CANCER METABOLISM

KANSER METABOLİZMASINDAKİ GLUKOZ TAŞIYICILARI

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ÖZET

Kontrolsüz, sonsuz çoğalma, tümörlerin temel bir özelliğidir. Bu nedenle, son araştırmalar, kanser hücreleri ve normal hücreler arasındaki metabolik süreçlerdeki farklılıkları vurgulamaktadır. Kanser tedavisinde hastanın sağ kalımını ve yasam kalitesini artırmak çok önemlidir ve bu alanda önemli gelişmeler olmuştur. Buna rağmen kansere bağlı ölümlerde sürekli artışlar gözlenmektedir. Kanser hücresi gelişiminin ayırt edici özelliklerinden biri, yeni biyokütle üretimi ve besin sinyalleşmesini kolaylaştırmak için gerekli hücresel metabolitlerin artan üretimi için aerobik glikolize yakıt sağlamak için glukoza artan bağımlılıktır. Kanser hücrelerinin, oksijen varlığında bile ATP üretme aracı olarak glikolizin tercihli kullanımına başvurmaları Warburg etkisi olarak tanımlanmıştır. Glukozun hücresel homeostaz ve metabolizmada merkezi bir rol oynaması nedeniyle, memeli hücrelerinin plazma zarı boyunca glukozun taşınması, en önemli hücresel besin taşıma olaylarından birini temsil etmektedir. Neredeyse tüm memeli hücrelerinin plazma zarlarının, kolaylaştırıcı difüzyon tipinde glukoz için bir taşıma sistemine sahip olduğu uzun zamandır tespit edilmiştir; bu taşıyıcılar, glukozun hücre içine veya dışına kimyasal gradyanı boyunca plazma zarı boyunca hareketine izin vermektedir. Aerobik glikolizin mitokondriyal solunumdan çok daha az verimli olduğu ve son yıllarda araştırmacıların kanser hücrelerinin bu yolu kullanmasının nedenlerden biri, kanser hücresi büyümesinde önemli olan hücre sinyal yollarının metabolik yolların düzenlenmesidir. Metabolik yolların bu düzenlemesinin önemi, bunun hücre çoğalması için gerekli olan besinlerin biyokütleye dahil edilmesini kolaylaştırmasıdır. Ayrıca, örneğin c-myc, ras ve src gibi bazı onkogenlerin aktivasyonunun ve hipoksi ile indüklenebilir faktör-la gibi transkripsiyon faktörlerinin aşırı ekspresyonu ve glikolitik enzimlerin ve glukoz tasıyıcıların (GLUT) aktivitesini indükleyebildiği birçok çalışmada ispatlanmıştır. Glukozun hücresel homeostaz ve metabolizmada merkezi bir rol oynaması nedeniyle, memeli hücrelerinin plazma zarı boyunca glukozun taşınması, en önemli hücresel besin taşıma olaylarından birini temsil etmektedir. Neredeyse tüm memeli hücrelerinin plazma zarlarının, kolaylaştırıcı difüzyon tipinde glukoz için bir taşıma sistemine sahip olduğu uzun zamandır tespit edilmiştir; bu taşıyıcılar, glukozun hücre içine veya dışına kimyasal gradyanı boyunca plazma zarı boyunca hareketine izin vermektedir. Bu taşıyıcılar, glukozun D-enantiyomerine özgüdür ve ATP (Adenozin trifosfat) hidrolizi veya bir H+ gradyanı gibi enerji gerektiren herhangi bir bileşene bağlanmamaktadır. Kolaylaştırıcı glukoz taşıyıcıları, aktif olarak glukoz biriktiren Na+ bağımlı taşıyıcılardan farklıdır. Glukoz taşıyıcılar (GLUT) arasında, GLUT1'in glukoz için yüksek bir afinitesi vardır ve bu nedenle, enerji için glukoza yüksek oranda bağımlı olan dokularda önemli bir rol oynamaktadır. GLUT1 dahi olmak üzere diğer glukoz taşıyıcıların hem katı hem de hematolojik

malignitelerin çeşitli türlerinde eksprese edildiği çeşitli çalışmalarla elde edilmiştir ve bu kanserlerde, glukoz taşıyıcıların aşırı ekspresyonunun derecesinin tümörün derecesi, kanserin evresi ve klinik sonuçla ilişkili olduğu dair veriler mevcuttur. Glukozun bir hücreye kolaylaştırıcı girişini sağlayan GLUT'ların, kanserde artan bir şekilde serbest bırakıldığı bulunmuştur. GLUT'lar için kansere özgü ekspresyon paternleri tanımlanıyor olsa da bireysel GLUT'lar için bir rolü kanıtlayan kapsamlı analizler hala gereklidir.

Anahtar Kelimeler: Kanser metabolizması, Glukoz taşıyıcıları, Warburg etkisi

ABSTRACT

One of the main characteristics of tumors is unchecked, unending expansion. The variations in metabolic processes between cancer cells and normal cells are thus highlighted by recent studies. Enhancing patient survival and quality of life during cancer therapy is crucial, and there have been considerable advancements in this field. Despite this, the number of deaths from cancer is continuing to rise. The increasing reliance on glucose to power aerobic glycolysis for the synthesis of new biomass and the increased generation of cellular metabolites required to promote nutritional signaling are characteristics of cancer cell development. The Warburg effect is characterized by cancer cells' preference for glycolysis over other ATP-producing processes, even when oxygen is present. One of the most significant cellular nutrient transport processes involves the movement of glucose across the plasma membrane of mammalian cells since glucose is essential for cellular homeostasis and metabolism. It has long been known that almost all mammalian cells feature facilitative diffusion-type glucose transport systems in their plasma membranes, which allow glucose to move into or out of the cell along a chemical gradient across the plasma membrane. Aerobic glycolysis is significantly less effective than mitochondrial respiration, however researchers have recently exploited this method for cancer cells due to the regulation of metabolic pathways and cell signaling pathways that are crucial for the proliferation of cancer cells. This metabolic pathway control is significant because it makes it easier to incorporate nutrients needed for cell proliferation into the biomass. Also, it has been demonstrated in numerous studies that various oncogenes, including c-myc, ras, and src, as well as excessive production of transcription factors such hypoxia-inducible factor-a, can activate glycolytic enzymes and glucose transporters (GLUT). The movement of glucose through the plasma membrane of mammalian cells is one of the most significant cellular nutrient transport processes because glucose is essential for cellular homeostasis and metabolism. It has long been known that practically all mammalian cells' plasma membranes have a glucose transport system of the facilitator diffusion type. These transporters allow glucose to go in or out of the cell via the chemical gradient across the plasma membrane. These transporters are specialized for the Denantiomer of glucose and don't bind to any substances that need energy to function, including an H+ gradient or ATP (adenosine triphosphate) hydrolysis. Different from Na+ dependent transporters, which actively collect glucose, are facilitating glucose transporters. As GLUT1 is one of the glucose transporters with a high affinity for glucose, it is crucial in tissues that depend heavily on glucose for energy. There is evidence that additional glucose transporters, including GLUT1, are overexpressed in a variety of solid and haematological tumors, and that this overexpression is correlated with the tumor grade, cancer stage, and clinical outcome in these cancers. It has been discovered that GLUTs are released more frequently in cancer. GLUTs help glucose enter a cell. Comprehensive analyses showing a role for specific GLUTs are still needed despite the discovery of cancer-specific expression patterns for GLUTs.

Keywords: Cancer metabolism, Glucose Transporters, Warburg effect

GİRİS

Kanser metabolizmasının kökleri, mitokondriyal solunum zinciri kompleksi IV 1'i keşfiyle 1931 Nobel Tıp veya Fizyoloji Ödülü sahibi Otto Warburg tarafından yapılan gözlemlere dayanmaktadır. Warburg, normal dokularla karşılaştırıldığında, in vitro kanser dokusu dilimlerinin, oksijen varlığında bile laktat üretmek için bol miktarda glukoz kullandığını gözlemledi. Bu, aerobik glukoliz veya Warburg etkisi olarak adlandırılan bir olgudur (Warburg, 1956). Kanser hücrelerinin çoğu, tümör büyümesi için trikarboksilik asit (TCA) döngüsü boyunca akışı teşvik etmek için solunum yapar (Bonekamp et al., 2020; DeBerardinis & Chandel, 2020; Hollinshead et al., 2020; Krall et al., 2021; Martínez-Reyes et al., 2020; Vasan et al., 2020). Solunum yapmayan ancak yine de büyüme için gerekli metabolitleri sağlamak üzere TCA döngüsünü kullanan tümörler vardır (Cardaci et al., 2015). Bununla birlikte. Warburg etkisi hem kanserli fare modellerinde hem de kanserli insan hastalarda in vitro ve in vivo olarak gözlemlenebilen gerçek bir olgudur (Engelman et al., 2008; Gatenby & Gillies, 2004). Son 25 yılda kanser metabolizmasının yeniden canlanması, kanser hücrelerinin neden Warburg etkisini sergilediğini açıklamaya yardımcı olan keşiflerle aynı zamana denk geliyor (Vander Heiden et al., 2009). 1990'larda, glukolitik enzim laktat dehidrojenaz A'nın (LDHA) miyelositomatozis viral onkogen homologu (MYC)'nin transkripsiyonel bir hedefi olduğu ve kanser hücrelerinin artan glukoliz ve tümörijenik potansiyeli için gerekli olduğu kabul edildi. Böylece Warburg etkisi için moleküler bir temel sağlamaktadır (Shim et al., 1997). Ayrıca, kanserde sıklıkla serbest bırakılan ve tümörün hayatta kalması ve büyümesi için gerekli olan AKT serin-treonin kinaz (AKT), Rapamisin protein kompleksinin memeli hedefi (mTOR) ve hipoksi ile indüklenebilir faktörler (HIF'ler) de 1990'larda keşfedilmiştir (Hoxhaj & Manning, 2020; Hurst, 2016; Sabatini, 2017). Bu yollar, glukoz taşıyıcılarının ve glukolitik enzimlerin transkripsiyonel yukarı regülasyonu ve fosforilasyonu yoluyla bireysel olarak glukolizi arttırır (Hoxhaj & Manning, 2020; Hurst, 2016; Sabatini, 2017).

Glukoz Taşıyıcı Ailesi:

GLUT'ların ana işlevi, metabolizma için glukozun sürekli kullanılabilirliğini sağlamaktır ve bunu glukozun hücre içi ve hücre dışı bölmeler arasındaki hareketini kontrol ederek yaparlar (Augustin, 2010; Medina & Owen, 2002). GLUT ailesinin genleri, 2A çözünen taşıyıcı ailesine aittir ve *SLC2A* gen sembolüne sahiptirler. Şu anda açıklanan *GLUT* genlerinin 14 izoformu vardır ve bu izoformlar, birincil sekanslarına göre üç sınıfa ayrılabilir (Augustin, 2010; Krzeslak et al., 2012; Macheda et al., 2005). Birinci sınıf genler (sınıf I) klasik taşıyıcılar olarak bilinir ve *GLUT 1-4* ve *GLUT* tan oluşur. 14, *GLUT 3*'ün gen kopyası olarak kabul edilir. Sınıf II, GLUT 5, 7, 9 ve 11'den oluşurken, sınıf III, *GLUT 6, 8, 10, 12* ve *13*'ten oluşur. H+ miyoinositol taşıyıcı (HMIT) olarak bilinir (Macheda et al., 2005).

GLUT'ların pek çok izoformu mevcut olmasına rağmen, büyük, oldukça korunmuş bir transmembran alanı ve asimetrik, daha az korunmuş bir sitoplazmik ve ekzoplazmik alan ile benzer transmembran anatomisine sahiptirler (Medina & Owen, 2002). Bununla birlikte, hücre altı lokalizasyon, substrat tanıma ve taşıma kinetiği açısından işlevlerinde farklılık gösterirler (Macheda et al., 2005; Medina & Owen, 2002). 14 izoform, kendi aralarında %14-63 oranında özdeş protein dizilerine sahiptir ve bunların %30-79'u korunur (Augustin, 2010). Tüm izoformlar aynı zamanda GLUT 1 için orijinal hidropati grafiğine dayanan 12 transmembran sarmalına sahiptir. Farklı GLUT'lar dokuda çeşitli dağılımlara sahiptir ve genellikle hücreye özgüdür. Ayrıca glukoz, fruktoz ve galaktoz gibi diğer heksozlara karşı farklı afiniteleri vardır (Augustin, 2010; Macheda et al., 2005; Medina & Owen, 2002).

Glukoz Taşıyıcı Sınıf I:

Bu GLUT ailesi, tanımlanan ilk gruptur ve en karakterize edilen gruptur. GLUT 1 ve GLUT 4 en çok çalışılanlardır (Frolova & Moley, 2011). 1985 yılında, GLUT 1 klonlanan ilk izoform olmuştur. GLUT1 eritrositler, plasenta, endotelyal hücrelerde eksprese edilir ve bu nedenle kan-beyin bariyerinden girişi düzenler; büyüme faktörleri, insülin ve stres varlığında, hücresel farklılaşma ve transformasyon koşullarında değiştiği bulunmuştur (Jun et al., 2011). Diğer GLUT'larla karşılaştırıldığında, GLUT1'in glukoz için yüksek afinitesi vardır ve bu nedenle enerji için glukoza yüksek oranda bağımlı olan dokularda önemli bir rol oynar (Luo et al., 2010). GLUT1'in çeşitli katı ve hematolojik malignitelerde aşırı eksprese edildiği bulunmuştur (Grabellus et al., 2012; Jun et al., 2011). GLUT 1'in aşırı eksprese edildiği kanser çeşitleri arasında, bunlarla sınırlı olmamak üzere, diffüz büyük B hücreli lenfoma, kolorektal karsinomlar, hepatoselüler karsinom, baş ve boyun kanseri, gastrointestinal stromal tümör (GIST), prostat karsinomu, tiroid karsinomu, böbrek hücreli kanser, akciğer kanseri, pankreas kanseri, sarkomlar ve gırtlak karsinomlarıdır. Bu kanserlerde, GLUT1 aşırı ekspresyon derecesinin tümörün derecesi, kanserin evresi ve klinik sonuç ile ilişkili olduğu konseptine karşı olan ve olmayan veriler vardır (Carvalho et al., 2011; Luo et al., 2010; Reinicke et al., 2012).

GLUT4 kalp, iskelet ve kas dokusu gibi genellikle insüline duyarlı dokularda bulunur. Tip II şeker hastalığı ve obezitede geniş çapta çalışılmıştır ve tümöri-genezdeki rolü daha az ölçüde incelenmiştir (Augustin, 2010). GLUT4'ün uyarılması ve ardından dokuda glukoz alımı, fosfatidilinositol 3-kinaz-AKT yolunun aktivasyonu ile ilişkilendirilmiştir. GLUT4'ün çoklu miyelom hücre canlılığını ve proliferasyonunu sürdürmede kilit bir rol oynadığını görülmüştür (McBrayer et al., 2012). İmatinib ile tedaviden sonra GIST hücrelerinde plazma zarında bulunan GLUT4'te bir azalma olduğu da görülmüştür (Tarn et al., 2006). Bunun, plazma zarından GLUT4'ün endositozunun veya hücre içi mikrozomların tecrit edilmesinin bir sonucu olduğu ve AKT'nin ekspresyonundan bağımsız olduğunu bu da GLUT4'ün bu kanserlerin idamesindeki rolünün altını çizmektedir (Tarn et al., 2006).

Hiperbolik eğrinin denklemi olan Michaelis-Menten denklemininden türetilen Lineweaver-Burk denklemi olan (Km)'si yaklaşık 17 mmol/l olan *GLUT*2, glukoz için en düşük afiniteye sahiptir. İnce bağırsak, böbrek, meme, insülinoma, kolon ve pankreasın kanser hücre hatlarında ifade edilmiştir. *GLUT*2 ve *GLUT*5, insanlarda fruktoz taşınmasında birincil olarak belirtilen taşıyıcılardır, ancak *GLUT*2, *GLUT*5'ten daha az ölçüdedir (Augustin, 2010; Medina & Owen, 2002; Reinicke et al., 2012). *GLUT*3, nispeten iyi çalışılmış ve ağırlıklı olarak beyinde eksprese edildiği bulunan, bu sınıftaki başka bir taşıyıcıdır. Bununla birlikte plasenta ve testisler gibi yüksek glukoz ihtiyacı olan dokularda da bulunur (Augustin, 2010). *GLUT*3'ün araştırıldığı kanser hücre dizileri arasında meme, koriokarsinom, yumurtalık, kolorektal, retinoblastom ve rabdomiyosarkom yer alır (Medina & Owen, 2002). *GLUT* 3'ün düzenlenmesinde tümör *proteini* 53'ün (*P*53) rolüne ilişkin çelişkili raporlar vardır; *GLUT* 3 ekspresyonunun p53'ten bağımsız bir yolakla düzenlendiğine dair raporlar varken başka bir grup, *p*53 vahşi tipin aşırı ekspresyonunun *GLUT* 3 supresyonuna yol açtığını öne sürmektedir (Kawauchi et al., 2008; Watanabe et al., 2010).

Glukoz Taşıyıcı Sınıf II:

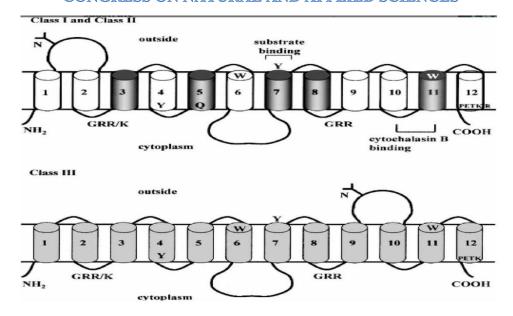
Bu GLUT grubu bazen 'farklı' GLUT'lar olarak anılır ve bu sınıfın başlıca özelliği fruktozu taşıma yetenekleridir (Medina & Owen, 2002). GLUT 2 ve GLUT 5, tarihsel olarak insan fruktoz naklinde belirtilen taşıyıcılardı, ancak daha yakın zamanlarda bu sınıftaki diğer GLUT'ların fruktoz taşınmasındaki rolü tarif edilmiştir (Augustin, 2010; Reinicke et al., 2012).

GLUT 5 böbreklerde, testislerde, ince bağırsakta, kas ve yağ dokusunda bol miktarda bulunur. Fruktozu taşıma eyleminde oldukça spesifiktir ve diğer heksoz şekerlerini taşıma yeteneğinden yoksundur (Medina Villaamil et al., 2011). GLUT 5'in tümörijenezde önemli olduğu öne sürülmüştür ve örneğin renal hücreli karsinom (RCC), meme ve prostat kanseri gibi bazı kanser türlerinde normal hücrelere kıyasla aşırı eksprese edildiği bulunmuştur (Medina Villaamil et al., 2011; Reinicke et al., 2012; Wuest et al., 2011). Bu ailenin klonlanan son üyesi olan GLUT 7, ince bağırsakta, kolonda ve daha az oranda prostat ve testislerde eksprese edilir. İnsanlarda hem glukoz hem de fruktoz için yüksek bir afiniteye sahiptir ve kanser metabolizmasındaki rolü henüz aydınlatılmamıştır (Augustin, 2010; Cheeseman, 2008).

GLUT 9 öncelikle karaciğer ve böbrekte bulunur, fakat aynı zamanda akciğer, lökositler ve ince bağırsakta da bulunmuştur. Bir glukoz/fruktoz taşıyıcısı olarak hareket etme kabiliyetine ilişkin değişken raporlar vardır; yakın zamanda, hiperürisemiye etkileri olan, yüksek afiniteli bir ürat taşıyıcısı olduğu rapor edilmiştir (Caulfield et al., 2008). Yüksek kapasiteli bir ürat taşıyıcısı olarak hareket etme yeteneğinin, kısmen heksoz şekerlerle değişimi sağlamasından kaynaklandığı öne sürülmüştür (Augustin, 2010; Caulfield et al., 2008). Bu gruptaki son taşıyıcı olan GLUT 11, öncelikle plazma zarında lokalizedir ve kalp, plasenta, böbrek, iskelet kası, yağ dokusu ve pankreas dahil ancak bunlarla sınırlı olmamak üzere çeşitli doku hücrelerinde bulunabilir (Augustin, 2010; McBrayer et al., 2012). Bugüne kadar üç izoform tanımlanmıştır: GLUT 11A, GLUT 11B ve GLUT 11C ve diğer GLUT'lara kıyasla fruktoz ve glukoz için nispeten düşük afiniteye sahip oldukları bilinmektedir (Augustin, 2010; McBrayer et al., 2012).

Glukoz Taşıyıcı Sınıf III:

GLUT 3 grubunun kanserdeki rolü daha az karakterize edilmiştir. GLUT 6 ağırlıklı olarak beyin, dalak ve beyaz kan hücresinde bulunur (Augustin, 2010). Bir malignitede GLUT 6 aşırı ekspresyonuna ilişkin tek rapor, trizomi 12 ile ilişkili kronik lenfositik lösemide bulundu ve bu aşırı ekspresyonun anlamlı olmadığı belirlendi (Porpaczy et al., 2009). GLUT 8 rutin olarak testis, adrenal bez, karaciğer, dalak ve akciğerde eksprese edilir. Ancak son zamanlarda multipl miyelomda da aşırı eksprese edildiği bildirilmiştir (Augustin, 2010; McBrayer et al., 2012). GLUT 12'nin prostat ve meme kanseri hücre dizilerinin perinükleer bölgesinde ve plazma zarında lokalize olduğu bulunmuştur. Ayrıca kalp, ince bağırsak ve iskelet kasında da ifade edilmiştir (Augustin, 2010; Macheda et al., 2005). GLUT 10 ve GLUT 13 (HMIT) henüz spesifik kanser hücrelerinde/hatlarında karakterize edilmemiştir (Augustin, 2010; Macheda et al., 2005).



Şekil 1: Hücre zarındaki kolaylaştırıcı glukoz taşıyıcı proteinlerin oryantasyonunun modelleri. Transmembran alanları (TM) 1 ila 12 olarak etiketlenmiştir. Glukozilasyon (N) bölgeleri gösterilmiştir. Korunmuş alanlar ve amino asitler de dahildir. Sınıf I taşıyıcılar için, glikoz taşıma kanalını oluşturması önerilen TM'ler, gradyan gölgeleme ile vurgulanır ve heksoz substratları ve GLUT inhibitörü sitokalasin B ile etkileşime giren bölgeler belirtilir (Macheda et al., 2005).

Kanserde Glukoz Metabolizması:

Malign hücreler metabolizmayı hızlandırır ve ATP üretimi için gereksinimleri arttırır. İlk olarak Warburg tarafından kanser hücrelerinin yüksek oranda aerobik glukolize sahip olduğu gözlemlendi (Warburg, 1956). Aerobik glukoliz, piruvatı laktata dönüştüren yüksek laktat dehidrojenaz seviyeleri nedeniyle kanser hücrelerinde laktat birikmesine neden olabilir (Shim et al., 1997). Laktat dehidrojenaz, gelişmiş anaerobik glukolize izin vererek, hipoksik bir ortamda hücre büyümesi için önemli olabilir (Shim et al., 1997). Malign hücrelerde ve dokularda glukolizde yer alan enzimlerin aktivitesinde artış gözlenmiştir (Hennipman et al., 1987). Ayrıca, hekzokinaz ve diğer glukolitik enzimlerin aktiviteleri, metastazlarda primer göğüs tümörlerinden daha yüksektir, bu da glukoliz ve tümör ilerlemesi arasında bir ilişki olduğunu düşündürür (Hennipman et al., 1987). Laktat dehidrogenaz aktivitesinin seviyesi, lenfoma, lösemi ve kolon kanseri için prognostik bir belirteç olarak yaygın bir şekilde kullanılmaktadır (Schwartz, 1992). Enerji üretimine ek olarak, kanser hücrelerinde daha yüksek oranlarda glukolitik akış, nükleotitlerin, yeni hücre zarları için fosfolipidlerin ve hücre bölünmesi sırasında gerekli olan diğer bileşenlerin biyosentezine yol açan öncü moleküllerin artan üretimi için de gereklidir (Newsholme & Board, 1991). Pentoz fosfat yolu, Ribonükleik asit (RNA) ve Deoksirübo nükleik asit (DNA) sentezinde kullanılmak üzere riboz-5-fosfat üretmek için glukoz-6-fosfat kullanır. Pentoz fosfat yolu enzimleri glukoz-6-fosfat dehidrojenaz ve 6-fosfoglukonat dehidrogenaz aktivitelerinin insan servikal karsinomlarında ve sıçan gliomalarında ve birkaç kanser hücre dizisinde normal hücrelere kıyasla daha yüksek olduğu bildirilmiştir (Duţu et al., 1980). Başka bir çalışma, glukoz-6-fosfat dehidrojenaz aktivitesinin, normal dokuya kıyasla habis göğüs dokusunda arttığını, ancak kanser içeren göğüslerden alınan morfolojik olarak normal dokuda da arttığını göstermektedir (McDermott 1990). Bu bulgu, metabolik değişikliklerin meme kanserinde morfolojik değişikliklerden önce gelebileceğini düşündürmektedir. Laktat dehidrogenaz ve pentoz fosfat yolu enzimlerinin artan aktiviteleri, mitokondriye girmek için mevcut piruvat miktarının azalmasına neden olarak trikarboksilik asit döngüsü ve Adenozin trifosfat (ATP) üretimi ile

düşük bir oksidasyon oranına yol açar (Board et al., 1990). Yüksek enerji gereksinimleriyle birleşen düşük ATP üretim hızı, glukoliz ihtiyacının ve dolayısıyla glukoz alımının artmasına neden olur (Board et al., 1990).

Kanser Tedavilerinde Glukoz Taşıyıcıları:

Erken evre hastalık, ilerlemiş primer veya metastatik tümörlerin tespiti, bir ilacın başlangıcını belirlemek, hastalık gelişimini, tedavi etkinliğini veya direncini takip etmek için esastır. Mamogramlar için X-ray görüntüleme, bilgisayarlı tomografi taraması (CT taraması) veya pozitron emisyon tomografisi (PET) taraması gibi birçok invazif olmayan teknik, tümör hacimleri, anatomisi, konumu, işlevi veya metabolizması hakkında yararlı bilgiler sağlamak için geliştirilmiştir. Metabolik görüntüleme PET taraması, tümörlerin daha yüksek glukoz alımına ve glukoliz oranına dayanır. Radyoaktif olarak işaretlenmiş glukoz analoğu 2-Deoksi-2-[florin-18] floro-D-glukoz (18F-FDG) kullanır (Fass, 2008; Zhu et al., 2011). Bu radyo izleyici, GLUT'lar yoluyla hücre zarlarını geçer, daha sonra hekzokinazlar tarafından FDG-6fosfata fosforile edilir, ancak daha fazla metabolize edilemez. Bunun bir sonucu olarak, sitoplazmada birikerek artan bir hücre izleme faaliyeti ortaya çıkarır (Plathow & Weber, 2008). PET, tümör metabolizmasını izlemek için merkezi bir klinik metodoloji olmasına rağmen, bu tekniğin duyarlılığı kanser türlerine göre değişir (Kim et al., 2017; Wuest et al., 2018; Zhu et al., 2011). Bu heterojenite özellikle GLUT1 veya GLUT3 tümör ekspresyonu ile ilişkilendirilmiştir, çünkü 18F-FDG, glukoz taşıyıcıları ve özellikle bu iki uniporter için vüksek bir afiniteve sahiptir (Kim et al., 2017). GLUTI ekspresyonu ile 18F-FDG alımı arasında pozitif bir korelasyon gerçekten de servikal kanser, timik epitelyal tümörler, primer gastrik lenfoma (PGL) ve ayrıca metastatik pulmoner tümörlerde gösterilmiştir (Kaira et al., 2010; Kaira et al., 2011; Watanabe et al., 2013; Yen et al., 2004). GLUT3 ekspresyonu ve 18F -FDG birikimi, primer merkezi sinir sistemi lenfomasında (PCNSL) bağlantılıdır (Takahashi et al., 2014). Aksine, kolorektal adenokarsinomda GLUT1 ekspresyonu, 18F-FDG ile korele değildir. Bu sınırlamalar, glukoz dışında kullanılabilecek alternatif karbon kaynakları ile de açıklanabilir. Örneğin, in vivo deneyler, laktatın akciğer tümörlerinde baskın bir karbon yakıtı olarak kullanılabileceğini veya glutaminin pankreas kanserinde Krebs döngüsüne önemli ölçüde katkıda bulunduğunu göstermiştir (Faubert et al., 2017; Hong & Lim, 2012; Hui et al., 2017).

Pek çok kanser türü başlangıçta kemoterapiye duyarlı olsa da, direnç kaçınılmaz olarak ilaç inhibisyonunu, yıkımını veya hücre ihracatını destekleyen metabolik değişiklikler de dahil olmak üzere çok çeşitli mekanizmalar aracılığıyla ortaya çıkar (Housman et al., 2014). Kanser hücrelerinin tedaviye direnç göstermesini sağlayan farklı olasılıklar arasında glukoz taşıyıcılarının rol aldığı bildirilmektedir. Örnek olarak, glioblastoma tedavisinde kullanılan bevacizumab adı verilen antianjiyojenik Vasküler endotelyal büyüme faktörü (VEGF)-nötralize edici antikor sınırlı bir yanıt süresine sahiptir. Bevacizumab'a yanıt veren dirençli hastadan türetilen tümör ksenogreftlerini karşılaştıran yakın tarihli bir çalışma, ilaca dirençli tümörlerde düşük glukoz koşullarında daha yüksek glukoz alımı, glukoliz ve sağkalımı tanımladı. Fenotipler, *GLUT3* aşırı ekspresyonu üzerine tekrar özetlenmiştir. Buna göre, *GLUT3*, bevacizumab'a dirençli ve hassas tümörlerde yukarı regüle edilmiştir (Kuang et al., 2017). Glukoz taşıyıcı ekspresyonu ile tümör anjiyogenezi arasındaki başka bir bağlantı, immünohistokimya kullanılarak *GLUT1*, *GLUT3* ve *GLUT4* ekspresyonunun VEGF'ninkiyle pozitif korelasyon gösterdiğini ortaya koyan yumurtalık karsinomu için kurulmuştur (Tsukioka et al., 2007).

Benzer bir şekilde, radyasyon tedavisi alan hastalarda ilerlemiş servikal skuamöz hücreli karsinomda radyoterapiye yanıtta ve klinik sonuçlarda *GLUT1*'in rolü araştırılmıştır. Radyasyona duyarlı grubun %53'ünde aşırı *GLUT1* ekspresyonu gözlenirken, radyasyona

dirençli grupta yaklaşık %90'a ulaşılmıştır. Ayrıca, tümörlerde yüksek *GLUT1* ekspresyonu olan hastalar, düşük *GLUT1*'e sahip olanlara göre radyoterapiye karşı daha belirgin bir direnç ve daha kısa progresyonsuz sağkalım göstermektedir (Huang et al., 2014). GLUT1'in ayrıca, önceden tedavi edilmiş 40 tümör biyopsisinden immünohistokimya ile oral skuamöz hücreli karsinomda bir radyodirenç belirteci olduğu bulunmuştur (Kunkel et al., 2007). Son olarak, *GLUT1* boyama, insan kanser hücre dizilerinin NCI-60 panelinde kemorezistans ile bir bağlantıyı vurgulanmıştır (Evans et al., 2008). *GLUT*'ların kemo- veya radyo-direncine dahil olduğu temel mekanizmalar büyük ölçüde bilinmemektedir. Bununla birlikte, birkaç çalışma, glukoliz ile anti-apoptotik gen *MCL1* arasında bir bağlantı olduğunu öne sürmektedir, bu sayede glukoliz inhibisyonu, translasyonunu bloke eder (Meynet et al., 2012; Pradelli et al., 2010). Önemli olarak, proapoptotik bir BH3-mimetik bileşik olan ABT-737 ile kombinasyon halinde kullanılan glukoliz inhibisyonu, lenfoma hücrelerinin bu ilaca duyarlılığını arttırır (Meynet et al., 2012).

SONUÇLAR:

GLUT'lar, yetişkin dokularında glukoz taşınmasındaki rolleri açısından kapsamlı bir şekilde incelenmiştir. Kanser ilerlemesindeki işlevleri, birçok araştırmanın güncel konusudur. Bu araştırma çabaları, tümörlerde düzenlenmesi ve düzensizleştirilmesi hakkında temel bilgiler sağlamaya ve antikanser stratejilerinde onları hedeflemenin önemini vurgulamaya devam ediyor ve etmeye devam edecek. Antikanser tedavisi için, onları eksprese eden ve fizyolojik glukoz homeostazı için bunlara ihtiyaç duyan hücrelerde veya dokularda GLUT'ları bloke etmenin potansiyel istenmeyen etkisini dikkate almamız gerekir.

Kanser hücre hatları ile yapılan *in vitro* deneylerden birçok sonuç elde edilmiş olsa da *GLUT* düzenlemesini ve işlevini *in vivo* araştırmak, ideal olarak tümör mikroçevresinin metabolik adaptasyonunu dikkate almak için immünokompetan fare modellerinde kompleks otokton tümörlerin gelişimini incelemek kritik hale gelir. Şu anda, GLUT proteinlerinin kanser hücresi dışındaki etkisi büyük ölçüde keşfedilmeyi beklemektedir. Belirli hücre tiplerinde Cre rekombinaz ekspresyonunu mümkün kılan genetik yaklaşımlar, son Glut koşullu nakavt fareler ve kanser fare modelleri ile birleştiğinde, tümör kütlesinin farklı hücre tiplerinde glukoz taşıyıcılarının önemini aydınlatabilir.

Ele alınması gereken bir diğer konu da GLUT'lerin kimyasal inhibisyonudur. İn vivo kimyasal yaklaşımları kullanan son çalışmalara rağmen, spesifik ve güçlü GLUT inhibitörleri hala eksiktir. Kristal yapıları ve homoloji tabanlı modelleri birleştiren akılcı tasarım yaklaşımları, kimyasal ekranlar için değerli bilgiler üretir. GLUT inhibe edici bileşiklerin keşfi, fonksiyonel karakterizasyonları için yararlı olabilir, ancak aynı zamanda kanserle savaşmak için muhtemelen geleneksel kemoterapiler veya yeni immünoterapilerle kombinasyon halinde kullanılabilecek ilaçların geliştirilmesi için de yararlı olabilir.

KAYNAKÇA:

- Augustin, R. (2010). The protein family of glucose transport facilitators: It's not only about glucose after all. *IUBMB Life*, 62(5), 315-333. https://doi.org/10.1002/iub.315
- Board, M., Humm, S., & Newsholme, E. A. (1990). Maximum activities of key enzymes of glycolysis, glutaminolysis, pentose phosphate pathway and tricarboxylic acid cycle in normal, neoplastic and suppressed cells. *Biochem J*, 265(2), 503-509. https://doi.org/10.1042/bj2650503
- Bonekamp, N. A., Peter, B., Hillen, H. S., Felser, A., Bergbrede, T., Choidas, A., . . . Larsson, N. G. (2020). Small-molecule inhibitors of human mitochondrial DNA transcription. *Nature*, *588*(7839), 712-716. https://doi.org/10.1038/s41586-020-03048-z

- Cardaci, S., Zheng, L., MacKay, G., van den Broek, N. J., MacKenzie, E. D., Nixon, C., . . . Gottlieb, E. (2015). Pyruvate carboxylation enables growth of SDH-deficient cells by supporting aspartate biosynthesis. *Nat Cell Biol*, *17*(10), 1317-1326. https://doi.org/10.1038/ncb3233
- Carvalho, K. C., Cunha, I. W., Rocha, R. M., Ayala, F. R., Cajaíba, M. M., Begnami, M. D., . . . Soares, F. A. (2011). GLUT1 expression in malignant tumors and its use as an immunodiagnostic marker. *Clinics (Sao Paulo)*, 66(6), 965-972. https://doi.org/10.1590/s1807-59322011000600008
- Caulfield, M. J., Munroe, P. B., O'Neill, D., Witkowska, K., Charchar, F. J., Doblado, M., . . . Cheeseman, C. (2008). *SLC2A9* is a high-capacity urate transporter in humans. *PLoS Med*, *5*(10), e197. https://doi.org/10.1371/journal.pmed.0050197
- Cheeseman, C. (2008). GLUT7: a new intestinal facilitated hexose transporter. *American Journal of Physiology-Endocrinology and Metabolism*, 295(2), E238-E241.
- DeBerardinis, R. J., & Chandel, N. S. (2020). We need to talk about the Warburg effect. *Nat Metab*, 2(2), 127-129. https://doi.org/10.1038/s42255-020-0172-2
- Duţu, R., Nedelea, M., Veluda, G., & Burculeţ, V. (1980). Cytoenzymologic investigations on carcinomas of the cervix uteri. *Acta Cytol*, 24(2), 160-166.
- Engelman, J. A., Chen, L., Tan, X., Crosby, K., Guimaraes, A. R., Upadhyay, R., . . . Wong, K. K. (2008). Effective use of PI3K and MEK inhibitors to treat mutant Kras G12D and PIK3CA H1047R murine lung cancers. *Nat Med*, *14*(12), 1351-1356. https://doi.org/10.1038/nm.1890
- Evans, A., Bates, V., Troy, H., Hewitt, S., Holbeck, S., Chung, Y. L., . . . Airley, R. (2008). Glut-1 as a therapeutic target: increased chemoresistance and HIF-1-independent link with cell turnover is revealed through COMPARE analysis and metabolomic studies. *Cancer Chemother Pharmacol*, 61(3), 377-393. https://doi.org/10.1007/s00280-007-0480-1
- Fass, L. (2008). Imaging and cancer: a review. *Mol Oncol*, 2(2), 115-152. https://doi.org/10.1016/j.molonc.2008.04.001
- Faubert, B., Li, K. Y., Cai, L., Hensley, C. T., Kim, J., Zacharias, L. G., . . . DeBerardinis, R. J. (2017). Lactate Metabolism in Human Lung Tumors. *Cell*, *171*(2), 358-371.e359. https://doi.org/10.1016/j.cell.2017.09.019
- Frolova, A. I., & Moley, K. H. (2011). Glucose transporters in the uterus: an analysis of tissue distribution and proposed physiological roles. *Reproduction*, *142*(2), 211-220. https://doi.org/10.1530/rep-11-0114
- Gatenby, R. A., & Gillies, R. J. (2004). Why do cancers have high aerobic glycolysis? *Nat Rev Cancer*, 4(11), 891-899. https://doi.org/10.1038/nrc1478
- Grabellus, F., Nagarajah, J., Bockisch, A., Schmid, K. W., & Sheu, S. Y. (2012). Glucose transporter 1 expression, tumor proliferation, and iodine/glucose uptake in thyroid cancer with emphasis on poorly differentiated thyroid carcinoma. *Clin Nucl Med*, 37(2), 121-127. https://doi.org/10.1097/RLU.0b013e3182393599
- Hennipman, A., Smits, J., van Oirschot, B., van Houwelingen, J. C., Rijksen, G., Neyt, J. P., . . . Staal, G. E. (1987). Glycolytic enzymes in breast cancer, benign breast disease and normal breast tissue. *Tumour Biol*, 8(5), 251-263. https://doi.org/10.1159/000217529
- Hollinshead, K. E. R., Parker, S. J., Eapen, V. V., Encarnacion-Rosado, J., Sohn, A., Oncu, T., . . . Kimmelman, A. C. (2020). Respiratory Supercomplexes Promote Mitochondrial Efficiency and Growth in Severely Hypoxic Pancreatic Cancer. *Cell Rep*, *33*(1), 108231. https://doi.org/10.1016/j.celrep.2020.108231
- Hong, R., & Lim, S. C. (2012). ¹⁸F-fluoro-2-deoxyglucose uptake on PET CT and glucose transporter 1 expression in colorectal adenocarcinoma. *World J Gastroenterol*, *18*(2), 168-174. https://doi.org/10.3748/wjg.v18.i2.168

- Housman, G., Byler, S., Heerboth, S., Lapinska, K., Longacre, M., Snyder, N., & Sarkar, S. (2014). Drug resistance in cancer: an overview. *Cancers (Basel)*, 6(3), 1769-1792. https://doi.org/10.3390/cancers6031769
- Hoxhaj, G., & Manning, B. D. (2020). The PI3K-AKT network at the interface of oncogenic signalling and cancer metabolism. *Nat Rev Cancer*, 20(2), 74-88. https://doi.org/10.1038/s41568-019-0216-7
- Huang, X. Q., Chen, X., Xie, X. X., Zhou, Q., Li, K., Li, S., . . . Su, J. (2014). Co-expression of CD147 and GLUT-1 indicates radiation resistance and poor prognosis in cervical squamous cell carcinoma. *Int J Clin Exp Pathol*, 7(4), 1651-1666.
- Hui, S., Ghergurovich, J. M., Morscher, R. J., Jang, C., Teng, X., Lu, W., . . . Rabinowitz, J. D. (2017). Glucose feeds the TCA cycle via circulating lactate. *Nature*, *551*(7678), 115-118. https://doi.org/10.1038/nature24057
- Hurst, J. H. (2016). William Kaelin, Peter Ratcliffe, and Gregg Semenza receive the 2016 Albert Lasker Basic Medical Research Award. *J Clin Invest*, 126(10), 3628-3638. https://doi.org/10.1172/jci90055
- Jun, Y. J., Jang, S. M., Han, H. L., Lee, K. H., Jang, K. S., & Paik, S. S. (2011). Clinicopathologic significance of GLUT1 expression and its correlation with Apaf-1 in colorectal adenocarcinomas. *World J Gastroenterol*, 17(14), 1866-1873. https://doi.org/10.3748/wjg.v17.i14.1866
- Kaira, K., Endo, M., Abe, M., Nakagawa, K., Ohde, Y., Okumura, T., . . . Nakamura, Y. (2010). Biologic correlation of 2-[18F]-fluoro-2-deoxy-D-glucose uptake on positron emission tomography in thymic epithelial tumors. *Journal of clinical oncology*, 28(23), 3746-3753.
- Kaira, K., Okumura, T., Ohde, Y., Takahashi, T., Murakami, H., Oriuchi, N., . . . Yamamoto, N. (2011). Correlation between 18F-FDG uptake on PET and molecular biology in metastatic pulmonary tumors. *Journal of Nuclear Medicine*, 52(5), 705-711.
- Kawauchi, K., Araki, K., Tobiume, K., & Tanaka, N. (2008). p53 regulates glucose metabolism through an IKK-NF-kappaB pathway and inhibits cell transformation. *Nat Cell Biol*, *10*(5), 611-618. https://doi.org/10.1038/ncb1724
- Kim, Y. H., Jeong, D. C., Pak, K., Han, M. E., Kim, J. Y., Liangwen, L., . . . Oh, S. O. (2017). SLC2A2 (GLUT2) as a novel prognostic factor for hepatocellular carcinoma. Oncotarget, 8(40), 68381-68392. https://doi.org/10.18632/oncotarget.20266
- Krall, A. S., Mullen, P. J., Surjono, F., Momcilovic, M., Schmid, E. W., Halbrook, C. J., . . . Christofk, H. R. (2021). Asparagine couples mitochondrial respiration to ATF4 activity and tumor growth. *Cell Metab*, *33*(5), 1013-1026.e1016. https://doi.org/10.1016/j.cmet.2021.02.001
- Krzeslak, A., Wojcik-Krowiranda, K., Forma, E., Jozwiak, P., Romanowicz, H., Bienkiewicz, A., & Brys, M. (2012). Expression of GLUT1 and GLUT3 glucose transporters in endometrial and breast cancers. *Pathol Oncol Res*, *18*(3), 721-728. https://doi.org/10.1007/s12253-012-9500-5
- Kuang, R., Jahangiri, A., Mascharak, S., Nguyen, A., Chandra, A., Flanigan, P. M., . . . Aghi, M. K. (2017). GLUT3 upregulation promotes metabolic reprogramming associated with antiangiogenic therapy resistance. *JCI Insight*, 2(2), e88815. https://doi.org/10.1172/jci.insight.88815
- Kunkel, M., Moergel, M., Stockinger, M., Jeong, J. H., Fritz, G., Lehr, H. A., & Whiteside, T. L. (2007). Overexpression of GLUT-1 is associated with resistance to radiotherapy and adverse prognosis in squamous cell carcinoma of the oral cavity. *Oral Oncol*, *43*(8), 796-803. https://doi.org/10.1016/j.oraloncology.2006.10.009

- Luo, X. M., Zhou, S. H., & Fan, J. (2010). Glucose transporter-1 as a new therapeutic target in laryngeal carcinoma. *J Int Med Res*, *38*(6), 1885-1892. https://doi.org/10.1177/147323001003800601
- Macheda, M. L., Rogers, S., & Best, J. D. (2005). Molecular and cellular regulation of glucose transporter (GLUT) proteins in cancer. *J Cell Physiol*, 202(3), 654-662. https://doi.org/10.1002/jcp.20166
- Martínez-Reyes, I., Cardona, L. R., Kong, H., Vasan, K., McElroy, G. S., Werner, M., . . . Chandel, N. S. (2020). Mitochondrial ubiquinol oxidation is necessary for tumour growth. *Nature*, *585*(7824), 288-292. https://doi.org/10.1038/s41586-020-2475-6
- McBrayer, S. K., Cheng, J. C., Singhal, S., Krett, N. L., Rosen, S. T., & Shanmugam, M. (2012). Multiple myeloma exhibits novel dependence on GLUT4, GLUT8, and GLUT11: implications for glucose transporter-directed therapy. *Blood*, *119*(20), 4686-4697. https://doi.org/10.1182/blood-2011-09-377846
- McDermott, E. W., Barron, E. T., Smyth, P. P., & O'Higgins, N. J. (1990). Premorphological metabolic changes in human breast carcinogenesis. *Br J Surg*, 77(10), 1179-1182. https://doi.org/10.1002/bjs.1800771029
- Medina, R. A., & Owen, G. I. (2002). Glucose transporters: expression, regulation and cancer. *Biol Res*, *35*(1), 9-26. https://doi.org/10.4067/s0716-97602002000100004
- Medina Villaamil, V., Aparicio Gallego, G., Valbuena Rubira, L., García Campelo, R., Valladares-Ayerbes, M., Grande Pulido, E., . . . Antón Aparicio, L. M. (2011). Fructose transporter GLUT5 expression in clear renal cell carcinoma. *Oncol Rep*, 25(2), 315-323. https://doi.org/10.3892/or.2010.1096
- Meynet, O., Bénéteau, M., Jacquin, M. A., Pradelli, L. A., Cornille, A., Carles, M., & Ricci, J. E. (2012). Glycolysis inhibition targets Mcl-1 to restore sensitivity of lymphoma cells to ABT-737-induced apoptosis. *Leukemia*, 26(5), 1145-1147. https://doi.org/10.1038/leu.2011.327
- Newsholme, E. A., & Board, M. (1991). Application of metabolic-control logic to fuel utilization and its significance in tumor cells. *Adv Enzyme Regul*, *31*, 225-246. https://doi.org/10.1016/0065-2571(91)90015-e
- Plathow, C., & Weber, W. A. (2008). Tumor cell metabolism imaging. *J Nucl Med*, 49 Suppl 2, 43s-63s. https://doi.org/10.2967/jnumed.107.045930
- Porpaczy, E., Bilban, M., Heinze, G., Gruber, M., Vanura, K., Schwarzinger, I., . . . Jaeger, U. (2009). Gene expression signature of chronic lymphocytic leukaemia with Trisomy 12. *Eur J Clin Invest*, *39*(7), 568-575. https://doi.org/10.1111/j.1365-2362.2009.02146.x
- Pradelli, L. A., Bénéteau, M., Chauvin, C., Jacquin, M. A., Marchetti, S., Muñoz-Pinedo, C., Ricci, J. E. (2010). Glycolysis inhibition sensitizes tumor cells to death receptors-induced apoptosis by AMP kinase activation leading to Mcl-1 block in translation. *Oncogene*, 29(11), 1641-1652. https://doi.org/10.1038/onc.2009.448
- Reinicke, K., Sotomayor, P., Cisterna, P., Delgado, C., Nualart, F., & Godoy, A. (2012). Cellular distribution of Glut-1 and Glut-5 in benign and malignant human prostate tissue. *J Cell Biochem*, 113(2), 553-562. https://doi.org/10.1002/jcb.23379
- Sabatini, D. M. (2017). Twenty-five years of mTOR: Uncovering the link from nutrients to growth. *Proc Natl Acad Sci U S A*, *114*(45), 11818-11825. https://doi.org/10.1073/pnas.1716173114
- Schwartz, M. K. (1992). Enzymes as prognostic markers and therapeutic indicators in patients with cancer. *Clin Chim Acta*, 206(1-2), 77-82. https://doi.org/10.1016/0009-8981(92)90008-e
- Shim, H., Dolde, C., Lewis, B. C., Wu, C. S., Dang, G., Jungmann, R. A., . . . Dang, C. V. (1997). c-Myc transactivation of LDH-A: implications for tumor metabolism and

- growth. *Proc Natl Acad Sci U S A*, *94*(13), 6658-6663. https://doi.org/10.1073/pnas.94.13.6658
- Takahashi, Y., Akahane, T., Yamamoto, D., Nakamura, H., Sawa, H., Nitta, K., . . . Kamada, H. (2014). Correlation between positron emission tomography findings and glucose transporter 1, 3 and L-type amino acid transporter 1 mRNA expression in primary central nervous system lymphomas. *Mol Clin Oncol*, 2(4), 525-529. https://doi.org/10.3892/mco.2014.287
- Tarn, C., Skorobogatko, Y. V., Taguchi, T., Eisenberg, B., von Mehren, M., & Godwin, A. K. (2006). Therapeutic effect of imatinib in gastrointestinal stromal tumors: AKT signaling dependent and independent mechanisms. *Cancer Res*, 66(10), 5477-5486. https://doi.org/10.1158/0008-5472.Can-05-3906
- Tsukioka, M., Matsumoto, Y., Noriyuki, M., Yoshida, C., Nobeyama, H., Yoshida, H., . . . Ishiko, O. (2007). Expression of glucose transporters in epithelial ovarian carcinoma: correlation with clinical characteristics and tumor angiogenesis. *Oncol Rep*, 18(2), 361-367.
- Vander Heiden, M. G., Cantley, L. C., & Thompson, C. B. (2009). Understanding the Warburg effect: the metabolic requirements of cell proliferation. *Science*, *324*(5930), 1029-1033. https://doi.org/10.1126/science.1160809
- Vasan, K., Werner, M., & Chandel, N. S. (2020). Mitochondrial Metabolism as a Target for Cancer Therapy. *Cell Metab*, 32(3), 341-352. https://doi.org/10.1016/j.cmet.2020.06.019
- Warburg, O. (1956). On the origin of cancer cells. *Science*, *123*(3191), 309-314. https://doi.org/10.1126/science.123.3191.309
- Watanabe, M., Naraba, H., Sakyo, T., & Kitagawa, T. (2010). DNA damage-induced modulation of GLUT3 expression is mediated through p53-independent extracellular signal-regulated kinase signaling in HeLa cells. *Mol Cancer Res*, 8(11), 1547-1557. https://doi.org/10.1158/1541-7786.Mcr-10-0011
- Watanabe, Y., Suefuji, H., Hirose, Y., Kaida, H., Suzuki, G., Uozumi, J., . . . Hayabuchi, N. (2013). 18F-FDG uptake in primary gastric malignant lymphoma correlates with glucose transporter 1 expression and histologic malignant potential. *Int J Hematol*, 97(1), 43-49. https://doi.org/10.1007/s12185-012-1225-4
- Wuest, M., Hamann, I., Bouvet, V., Glubrecht, D., Marshall, A., Trayner, B., . . . Wuest, F. (2018). Molecular Imaging of GLUT1 and GLUT5 in Breast Cancer: A Multitracer Positron Emission Tomography Imaging Study in Mice. *Mol Pharmacol*, *93*(2), 79-89. https://doi.org/10.1124/mol.117.110007
- Wuest, M., Trayner, B. J., Grant, T. N., Jans, H.-S., Mercer, J. R., Murray, D., . . . Cheeseman, C. I. (2011). Radiopharmacological evaluation of 6-deoxy-6-[18F] fluoro-D-fructose as a radiotracer for PET imaging of GLUT5 in breast cancer. *Nuclear medicine and biology*, 38(4), 461-475.
- Yen, T. C., See, L. C., Lai, C. H., Yah-Huei, C. W., Ng, K. K., Ma, S. Y., . . . Hsueh, S. (2004). 18F-FDG uptake in squamous cell carcinoma of the cervix is correlated with glucose transporter 1 expression. *J Nucl Med*, 45(1), 22-29.
- Zhu, A., Lee, D., & Shim, H. (2011). Metabolic positron emission tomography imaging in cancer detection and therapy response. *Semin Oncol*, *38*(1), 55-69. https://doi.org/10.1053/j.seminoncol.2010.11.012

THE MOLECULAR MECHANISM OF CANCER METASTASIS

KANSER METASTAZININ MOLEKÜLER MEKANİZMASI

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ÖZET

Metastaz, kansere bağlı ölümlerin en fazlasından sorumlu olan kanserin ayırt edici özelliğidir. Metastatik tümörler erken dönemde belirginleşir ve dünya çapında kansere bağlı ölümlerin başlıca nedenlerinden biridir. Metastaz genleri, ortaklaşa istilaya ve ankrajdan bağımsızlığa neden olan hedef bulma reseptörlerini, bunların ligandlarını ve hücre dışı matrisi bozan proteinazları kodlar. Bağışıklık sistemi hücrelerinin yuvalarına fizyolojik olarak aracılık eden, gelişimsel olarak temel olmayan stres tepkisi genleridir. Metastatik potansiyel, bu genlerin anormal ekspresyonu veya eklenmesiyle kanser hücrelerine kazandırılır. Kanser metastazı, birincil kanser hücrelerinin lenfatik veya kan damarları yoluyla uzak bölgelere istila ettiği süreçtir. Kanser hücrelerinin ya lenfatik ya da kan damarları yoluyla ya da her ikisi yoluyla yayıldığı moleküler mekanizmalar tam olarak belirlenmemekle birlikte bu konu üzerinde çalışmalar hala devam etmektedir. Yıllar geçtikçe metastatik sürecin verimsizliğini açıklamaya çalışmak için birçok hipotez geliştirildi, ancak bu teorilerin hiçbiri mevcut biyolojik ve klinik gözlemleri tam olarak açıklamıyor. Metastazı teşvik eden mekanizmaların sıkı bir sekilde düzenlenmesi ve buna paralel olarak kaçınan inhibitör mekanizmalar metastazın şiddetine ve bölgesine katkıda bulunur. Tümör hücresi kaderinin bireysel bir varlık olarak ve ayrıca farklı teşvik edici faktörler ve ilişkili moleküler mekanizmalarla kombinasyon halinde kapsamlı bir şekilde anlaşılması önümüzdeki yıllarda beklenmektedir. Bu, bilim adamlarının hedefe yönelik kanser tedavileri için tasarım stratejilerini tasvir etmelerini sağlayacaktır. Kanser biyolojisi araştırmalarının sürekli gelişimi ve metastaz araştırmalarında yeni paradigmaların ortaya çıkışı, bu yayılma sürecinin bazı moleküler temellerini ortaya çıkarmıştır. Metastaz, kanser hücreleri ve mikroçevreleri arasındaki çeşitli etkileşimlerin, bu hücrelerin programlanmış davranışlarını aşmasına izin veren değişiklikler sağladığı evrimsel bir sürecin son ürünüdür. Böylece tümör hücreleri yeni doku habitatlarında çoğalır ve gelişir ve sonuçta organ işlev bozukluğuna ve ölüme neden olur. Metastaza dahil olan birçok moleküler faktörü ve süreci anlamak, kanser metastazını önlemek ve tedavi etmek için etkili, hedefe yönelik yaklasımların gelismesine olanak sağlamaktadır. İstilacı tümör hücresi, hedef bölgeye giderken diğer proteinler ve hücrelerle etkileşime girer. Bu etkileşimlerin tanınması, metastatik hücrenin hareketliliğini ve plastisitesini yöneten bazı biyolojik ilkelerinin anlaşılmasını geliştirdi. Tümör mikroçevresi ile iletişim, istilacı kanser hücrelerinin stromal zorlukların üstesinden gelmesine, yerleşmesine ve kolonize olmasına izin verir.

Kanser hücrelerinin bu özellikleri, tümör hücresinin kendisinde ve mikroçevresindeki genetik ve epigenetik modifikasyonlar tarafından yönlendirilir. Metastaza dahil olan moleküler ve genetik kavramların ve süreçlerin daha derinden anlaşılması, başarılı müdahaleler için açık terapötik yöntemler geliştirmek için oldukça önem taşımaktadır.

Anahtar Kelimeler: Kanser Metastazı; Epitelyal-Mezenkimal Dönüşüm; İnvazyon; Ekstravazasyon

ABSTRACT

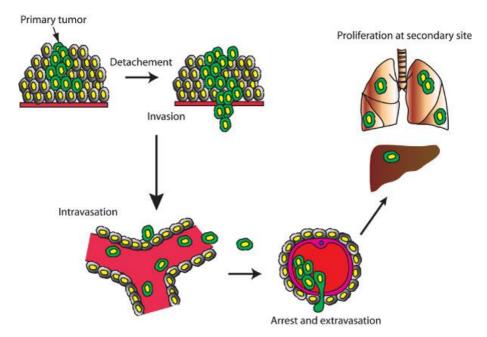
Metastasis is the hallmark of cancer, responsible for the greatest number of cancer-related deaths. Early detection of metastatic tumors, which are one of the main causes of cancerrelated mortality globally. Metastasis genes encode target-finding receptors, their ligands, and proteinases that degrade the extracellular matrix, causing joint invasion and anchorage independence. These stress response genes, which are physiological mediators of immune system cell nests, are developmentally non-essential. Aberrant expression or splicing of these genes gives cancer cells the ability to spread. The process by which initial cancer cells spread to distant areas through lymphatic or blood arteries is known as cancer metastasis. Studies on this topic are still underway, despite the fact that the molecular mechanisms by which cancer cells move through lymphatic or blood vessels, or both, have not yet been fully elucidated. Over the years, a number of theories have been created to try to explain why the metastatic process is ineffective, but none of these theories entirely explains the present biological and clinical facts. The extent and location of metastasis are influenced by the strict regulation of the mechanisms encouraging metastasis and the corresponding inhibitory processes. In the upcoming years, it is anticipated that a thorough understanding of tumor cell destiny as an independent entity, as well as in combination with other stimulating stimuli and associated molecular pathways, will be achieved. This will make it possible for researchers to outline design plans for focused cancer therapies. Some of the molecular underpinnings of this diffusion process have been disclosed by the ongoing advancement of cancer biology research and the creation of new paradigms in metastasis research. The process by which cancer cells interact with their surroundings to bring about modifications that enable these cells to deviate from their preprogrammed activity results in metastasis. As a result, tumor cells multiply and grow in new tissue environments, ultimately leading to organ malfunction and death. The development of efficient, focused strategies to prevent and cure cancer metastasis is made possible by an understanding of the numerous biological variables and processes involved in metastasis. During its route to the target site, the invasive tumor cell engages in interactions with other proteins and cells. Understanding some of the basic principles that control the motility and flexibility of the metastatic cell has improved as a result of the recognition of these interactions. To overcome stromal obstacles, settle, and colonize, invasive cancer cells must communicate with the tumor microenvironment. The microenvironment and the tumor cell's own genetic and epigenetic alterations are what control these characteristics of cancer cells. To create clear therapeutic modalities for effective interventions, it is essential to have a deeper grasp of the molecular and genetic concepts and processes involved in metastasis.

Keywords: Cancer metastasis; Epithelial-mesenchymal transition; Invasion; Extravasation

GİRİS

Metastaz, normal hücrelerin kontrolsüz çoğalan, bağışıklık sisteminden kaçan, programlanmış hücre ölümüne (apoptoz) dirençli hale gelen, anjiyogenezi uyaran, istilacı potansiyel kazanan, kan dolaşımında hayatta kalan ve kanserli büyümeler oluşturan onkojenik hücrelere dönüştüğü dinamik, çok yönlü bir süreçtir (Şek. 1) (Hanahan & Weinberg, 2011). Metastatik kanser için ilk tedavi yöntemi, etkili olabilen sistemik kemoterapidir, ancak hastalar genellikle organ yetmezliği ve yüksek enfeksiyon oranları gibi ciddi yan etkilerden muzdariptir (Dillekås et al., 2019).

Kanseri etkili bir şekilde hedef alan yeni tedavilerin geliştirilmesindeki en büyük engel, metastatik süreci anlamamamızdır. Kanser ilerlemesi sırasında epitelyal-mezenkimal geçiş (EMT), epitelyal-mezenkimal plastisite (EMP) ve bağışıklık sistemi modülasyonu gibi konuların daha sağlam bir şekilde anlaşılması, daha etkili kanser tedavisinin yeni bir çağını başlatabilir (Castaneda et al., 2022)



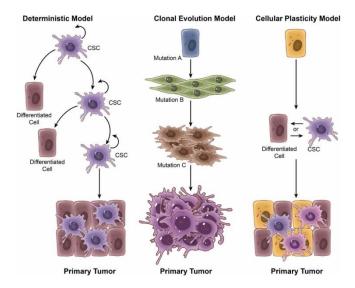
Şekil.1 Metastatik süreç. Metastazın ilk adımları, primer tümörün proliferasyonunu ve bitişik dokular ve bazal membranlardan invazyonu gerektirir. Bu süreç, tek tek tümör hücreleri birincil tümör kütlesinden ayrıldığında ve kan veya lenf yoluyla uzak bir hedef organa taşındığında, tümör kan damarlarını veya lenfatik kanalları istila edene kadar devam eder. Daha sonra, tümör hücreleri uzak organ içindeki küçük damarlarda durur, çevreleyen dokuya ekstravazasyon yapar ve ikincil bölgede çoğalır. Tüm bu adımlar, tümör hücreleri apoptotik sinyallerden ve konakçı bağışıklık tepkilerinden kaçınırken ve hayatta kalırken gerçekleştirilmelidir (Liotta, 1989).

Metastaz, kanserin klinik yönetimi için büyük önem taşır çünkü kanser ölümlerinin çoğu birincil tümörden ziyade yayılmış hastalıkla ilişkilidir (Liotta, 1989). Kanser hastalarında sekonder tümör prevalansına rağmen, metastaz son derece verimsiz bir süreçtir. Uzak bir bölgeyi başarılı bir şekilde kolonize etmek için, bir kanser hücresi kaskadın tüm adımlarını tamamlamalıdır.

Metastatik süreçteki pek çok adımın metastatik verimsizliğe katkıda bulunduğu düşünülse de bu süreci tam olarak anlamamamız, bazı kilit düzenleyici noktaların farkında olduğumuzu ancak tümünün farkında olmadığımızı gösteriyor. (Hunter et al., 2008). Örneğin, damar içi hücrelerin hemodinamik kuvvetler ve parçalama ile yıkımının, metastatik verimsizliğin ana kaynağı olduğu düşünülmüştür (Weiss et al., 1992). Bununla birlikte, son kanıtlar bunun her zaman böyle olmayabileceğini ve kan dolaşımındaki hücrelerin kılcal yataklarda tutulduğunu ve yüksek etkinlikle damar dışına çıktığını ve ikincil bölgelerde uzun süre uykuda kaldığını göstermektedir (Luzzi et al., 1998).

1.Primer Tümör

Kansere kimyasal karsinojenez, viral enfeksiyonlar, epigenetik değişiklikler ve somatik mutasyonlar dahil olmak üzere çeşitli faktörler neden olur (Alexandrov et al., 2013; Sell, 2010). İki farklı model, normal hücrelerin kanser hücrelerine dönüşümü hakkındaki mevcut anlayışımızı bilgilendirmektedir (Şek. 2). Deterministik modelin savunucuları, somatik kök hücrelerin somatik mutasyonlar yoluyla dönüşümünün, kendini yenileme yeteneklerine sahip tümör hücrelerinin ayrı bir alt popülasyonunu oluşturduğunu varsayar; Bu hücreler kanser kök hücreleri (KKH) olarak bilinir (Barker et al., 2007; Singh et al., 2004).



Şekil 2. Tümör başlatma modelleri. Deterministik modelde (solda), KHK'ler hiyerarşik yapının tepesidir. Kendini yenileyebilen csc'lerin daha az tümörijenik farklılaşmış hücreler ürettiği varsayılmaktadır. Klonal evrim modelinde (ortada), tümör hücrelerine normal hücrelere göre üreme avantajları sağlamak için mutasyonlar veya epigenetik modifikasyonlar birikir. Hücresel plastisite modeli (sağda), csc'lerin orijin hücreleri olmadığını varsayar; bunun yerine, plastisite, heterojen bir primer tümörle sonuçlanan KKH'ler veya farklılaşmış hücreler olabilen normal hücrelerin bir özelliğidir (Castaneda et al., 2022).

Onkojenlerdeki ve tümör baskılayıcı genlerdeki mutasyonlar, kontrolsüz çoğalmaya ve hücrelerin büyümesine yol açar. Onkogenlerdeki mutasyonların sadece heterozigot olması gerekir ve onkojenin bir kopyasındaki mutasyon dönüşüm için yeterlidir (Griffiths et al., 2000). Onkojenlerin etkilerinin aksine, tümör baskılayıcılar kontrolsüz çoğalmayı dizginleme işlevi görür; p53'ü kodlayan gen, en iyi karakterize edilen tümör baskılayıcı genlerden biridir (Griffiths et al., 2000). P53, DNA hasarı üzerine stabilize edilir ve hasarlı DNA'nın replikasyonunu önlemek için hücre döngüsü durmasına neden olur. P53 mutasyona

uğradığında, DNA hasarı meydana geldiğinde ne apoptoz ne de hücre döngüsü durması indüklenir, bu da anormal hücre döngüsü ilerlemesine ve kontrolsüz çoğalmaya yol açar (Griffiths et al., 2000). Dış stresin, besin eksikliklerinin ve oksijen eksikliklerinin, yerleşik bir birincil tümörden hücrelerin göçünü uyardığı varsayılmıştır. Bununla birlikte, *HER2*+ meme kanserinde, son kanıtlar, kanser hücrelerinin, birincil tümör elle tutulur hale gelmeden önce bile yayıldığını ve dolaşımdaki kanser hücrelerinin, tümör büyümesinin ikincil bölgelerini tohumlayabildiğini göstermektedir (Harper et al., 2016).

2.Anjiyogenez

Kanser hücrelerinin primer tümörden diğer bölgelere yayılmasının ana yolu anjiyogenezdir (Castaneda et al., 2022). Tümörde yeni oluşan kan damarları hatalı biçimlendirilmiş, hiperplastiktir, aşırı dallanma içerir ve oldukça geçirgen ve sızdırıcıdır, bu da tümör hücrelerinin birincil bölgeden kaçmasına izin verir (Fukumura & Jain, 2008; Weidner et al., 1991). Primer tümörlerde, besinlerin ve oksijenin optimal olmayan perfüzyonu vardır, bu da tümör içinde hipoksik ve asidik bölgelere ve yüksek interstisyel basınca neden olur (Bao et al., 2006; Shweiki et al., 1992; Zhong et al., 1999). Sızdıran vaskülatür ayrıca bağışıklık hücrelerinin düzgün çalışmasını engeller ve sistemik kemoterapi alan hastalarda kemoterapötik ilaçların tümöre taşınmasını bozar (Maeda, 2001). Anjiyojenik anahtar kapalıyken primer tümörler küçük kalır ve lokalize olur. Anjiyojenik süreç, ilk tümör oluşumundan aylar veya yıllar sonra aktive edilebilir ve tümör büyümesinin yenilenmesine, tümör hücrelerinin sürekli replikasyonuna ve kanser hücrelerinin tümörden ikincil bölgelere yayılmasına yol açar (Bielenberg & Zetter, 2015; Carmeliet & Jain, 2000; Folkman, 2002; Tonini et al., 2003). Vasküler endotel büyüme faktörü-C (VEGF-C) veya Vasküler endotel büyüme faktörü-D (VEGF-D)'nin aşırı ekspresyonu, kanser hücresi yayılmasını meditasyon yapan tümörle ilişkili lenfatik damarların büyümesini destekler (Mandriota et al., 2001). Bu lenfatik damarlar, lenf düğümlerinde bulunan kemokin ligand 21 (CCL21) yoluyla tümöre doğru dendritik hücreler toplayarak immün baskılayıcı bir ortam yaratır (Karaman & Detmar, 2014).

3. Epitelyal-mezenkimal dönüşüm

Anjiyogenez sırasında, tüm kanser hücreleri vaskülatüre girme ve hayatta kalma yeteneğine sahip değildir. Başarılı bir şekilde metastaz yapmak için tümör hücrelerinin istilacı ve kök hücre benzeri özellikler kazanması gerekir (Hanahan & Weinberg, 2011). Kanser hücreleri, EMT'nin gelişim programını ele geçirerek bu süreci gerçekleştirir (Cano et al., 2000; Mani et al., 2007; Yang et al., 2004). EMT aktivasyonu, epitel hücrelerinin apikal-bazal polaritelerini ve hücre-hücre kavşaklarını kaybetmelerine ve mezenkimal hücrelerin özellikleri olan istilacı ve göç kabiliyetleri kazanmalarına neden olur (Lamouille et al., 2014). Epitel durumundaki hücreler, sıkı, yapışık ve boşluk kavşakları yoluyla hücre-hücre etkileşimleri oluşturur (Oka et al., 1993; Tunggal et al., 2005). EMT uygulanan bir hücre popülasyonunda, aynı anda hem epitelyal hem de mezenkimal belirteçleri eksprese eden hücreler tespit edilir. Bu sözde hibrit E / M hücreleri, E-kadherin ve N-kadherin aracılı bağlılık yoluyla hücre-hücre etkileşimleri oluşturabilir, ancak bu etkileşimler epitel durumundakinden önemli ölçüde daha zayıftır (Mrozik et al., 2018a). Metastazın birincil itici güçleri olan daha mezenkimal özelliklere sahip hücreler, göçü ve invazyonu kolaylaştıran aktin ve vimentin içeren hücre iskeletlerine sahiptir (Lamouille et al., 2014).

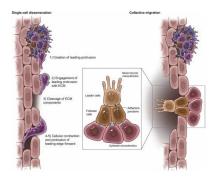
EMT, Forkhead box protein 2 (FOXC2), Twist, Snail, Slug, Çinko parmak E-kutu-bağlama homeobox 1/2 (ZEB1/2) ve Goosecoid dahil olmak üzere çoklu transkripsiyon faktörleri tarafından düzenlenir (Hollier et al., 2013; Mani et al., 2007; Taube et al., 2010; Vasaikar et al., 2021; Yang et al., 2004). Bu transkripsiyon faktörleri, Nörojenik lokus çentik homolog proteini (NOTCH), Wingless and Int-1 (Wnt), glikojen sentaz kinaz-3 beta (GSK3β) ve

Transforme edici büyüme faktör-beta'nın (TGFβ) aracılık ettiği yollar da dahil olmak üzere çeşitli sinyal yollarını aktive eder ve DNA replikasyonunu, bağışıklık tepkisini ve kanser hücrelerinin istilacı ve göçmen yeteneklerini etkiler (Deshmukh et al., 2021; Kwon et al., 2016; Puisieux et al., 2014; Werden et al., 2016; Zhang et al., 2016; Zheng & Kang, 2014).

EMP, hücrelerin epitelyal ve mezenkimal durumlar arasında dönüşüm yapma yeteneği olarak tanımlanır (Hanahan & Weinberg, 2011; Kröger et al., 2019). Bu plastisite, bir mezenkimal durumun edinilmesinin göç ve invazyon için önemli olduğu, ancak metastatik tohumlamanın mezenkimal-epitel geçişi (MET) olarak bilinen bir fenomende bir epitel fenotipine geri dönüş gerektirdiği için kanser metastazı için kritiktir (Fischer et al., 2015). EMP'li hücrelerin mikro ortamdaki değişikliklere uyum sağlamak için EMT'ye maruz kalabileceği veya karşılanabileceği görülmektedir (Alix-Panabières et al., 2017; Liu et al., 2014; Pastushenko et al., 2018). EMP'li hücrelerin, EMT spektrumunun her iki ucundaki hücrelere göre daha yüksek tümör başlatma ve metastatik potansiyele sahip olduğu da varsayılmaktadır (Alix-Panabières et al., 2017; Soundararajan et al., 2015).

4. Invazyon

Primer tümör hücrelerinin kan dolaşımına girmesi, tek hücreli yayılma veya toplu göç yoluyla gerçekleşebilir. Her invazyon türünde yer alan hücreler spesifik morfolojik özelliklere sahiptir ve iki invazyon türünün moleküler mekanizmaları farklıdır (Yu et al., 2013). Hem tek hücreli yayılma hem de toplu göç, morfolojideki değişiklikleri ve göç yollarını oluşturmak için dokunun yeniden şekillenmesini içerir (Krakhmal et al., 2015). Tek hücreli yayılma beş adımı içerir (Şek. 3). Birincisi, önde gelen bir çıkıntı oluşturan hücre iskeletinin polarizasyonudur. İkinci adım, hücre yüzeyinde kümeler oluşturmak için önde gelen çıkıntının hücre dışı matris (ECM) ile hücre içi mekanik sinyallemeye hücre dışı yapışmayı birleştirmek ve kuvvet üretmektir. Üçüncü adım, ECM bileşenlerinin bölünmesiyle sonuçlanan ön kenarın arkasındaki hücre yüzeyi proteazlarının aktivasyonudur. Dördüncü adımda, aktomiyozin hücre iskeleti yoluyla üretilen gerilim, hücresel kasılma ile sonuçlanır. Son olarak, arka kenarda vapısma bağları kopar ve bu da kanser hücrelerinin ileri hareketine neden olur (Chen et al., 2014). Tek hücreli yayılımın merkezinde, göçle ilgili streslerle başa çıkabilen sağlam bir hücre iskeleti bulunur. EMT sırasında kazanılan mezenkimal ara filament vimentin, basınç ve kayma gerilmesine karşı koruma sağlayan elastik bir ağ oluşturarak göçmen bir hücrenin strese karsı direncini güçlendirir (Hu et al., 2019; Kidd et al., 2014; Mendez et al., 2014). Nükleer membranla ilişkili ara filament lamin ayrıca mekanik strese karşı direnç sağlar. Laminler hemen hemen tüm yetişkin memeli hücrelerinde eksprese edilir ve invazyon sırasında nükleer parçalanmayı önler (Harada et al., 2014).



Şekil 3. Kanser ilerlemesi sırasında invazyon türleri. Kanser hücrelerinin primer tümöre bitişik kan damarlarına girmesi, tek hücreli yayılma (solda) veya toplu göç (sağda) yoluyla gerçekleşebilir. Tek hücreli yayılma, çıkıntıdan sonra mezenkimal özellikler kazanan

uyarlanabilir tek hücreleri içerir. Toplu göçün ana invazyon türü olduğuna inanılıyor. Toplu göç sırasında, bir hücre kümesi bir kan damarına girer. Ön kenar mezenkimal özelliklere sahip hücreler içerir ve takip eden hücreler epitel özelliklerine sahiptir (Castaneda et al., 2022).

Toplu göçte, yayılan hücreler, E-kadherin, N-kadherin ve *CD44* gibi adezyon molekülleri ile birbirine bağlanır (Liu et al., 2019; Mrozik et al., 2018b; Padmanaban et al., 2019; Wolf et al., 2020; Yang et al., 2019). Toplu göç, tek hücreli yayılmaya göre daha yüksek invazif ve metastatik potansiyel ile sonuçlanır (Aiello et al., 2018; Hegerfeldt et al., 2002). Toplu göç sırasında, lider hücre ile takipçi hücreler arasında gen ekspresyonu, morfolojisi ve fonksiyonunda belirgin bir fark vardır (Şek. 3) (Tambe et al., 2011). Lider hücreler, ECM'nin yeniden şekillenmesinde önemli bir rol oynar ve takip eden hücrelerden daha yüksek konsantrasyonlarda harici sinyallere maruz kalır (Bianco et al., 2007; Janssens et al., 2010). Lider hücreler, kimyasal ve mekanik sinyalleri ileten ve hücre iskeletinin yeniden düzenlenmesine, yapısal yeniden düzenlenmesine ve hücre kolektifinin morfolojik polarizasyonuna yardımcı olan integrin-β1 gibi integrinler yoluyla ECM ile temas eder (Rørth, 2009). ECM yeniden şekillenmesi, tümör hücresi göçünün anahtarıdır ve matrisin birikmesi, matris liflerinin yeniden hizalanması ve büyüme faktörlerinin lider hücreler tarafından salgılanması, istilaya yardımcı olan mekanik strese neden olur (Lintz et al., 2017).

5.Intravazasyon

İki tür intravazasyon vardır: aktif ve pasif (Bockhorn et al., 2007). Pasif intravazasyonda çoğu hücre ölür veya apoptoza uğrar (Bockhorn et al., 2007). Bu hücrelerin, tümörlerin hipoksik ortamı ve sızdıran vaskülatürü nedeniyle azalan besin kaynağı nedeniyle döküldüğüne inanılmaktadır (Bockhorn et al., 2007; Krzyszczyk et al., 2018). Aktif intravazasyon sırasında hücreler, kemotaksis süreci boyunca besin ve büyüme faktörü gradyanları boyunca bir kan damarına doğru göç eder (Roussos et al., 2011). Bu hücreler ECM'yi ve bazal membranı sindirir ve aktif olarak bir kan damarına intravazasyon yapar (Bockhorn et al., 2007). Dolaşımda, bu kanser hücreleri trombositlerle birleşerek tümör hücrelerinin kesme kuvvetine dayanmasını sağlar (Follain et al., 2020; Strilic & Offermanns, 2017). Bu dolaşımdaki tümör hücreleri içindeki EMT indüksiyonu, ara filamentlerin bu saf kuvvete dayanacak şekilde yeniden düzenlenmesine izin verir (Xin et al., 2020).

6. Ekstravazasyon

Metastatik lezyonlar oluşturmak için kanser hücrelerinin, ikincil bölgedeki endotel hücrelerine yapışmayı, endotel bariyerinin modülasyonunu ve altta yatan dokuya transendotel göçünü içeren zorlu ekstravazasyon sürecinden geçmesi gerekir (Wang et al., 2019). Baskın ekstravazasyon şekli, tümör hücrelerinin iki endotel hücresi arasında göç ettiği paraselüler göçtür (Wang et al., 2019). Bu işlem sırasında, selektinler, kadherinler ve integrinler dahil olmak üzere birçok ligand ve reseptör, tümör hücresi ile endotel hücreleri arasındaki yapışmaya katkıda bulunur (Nieminen et al., 2006; Teo et al., 2012). Ek olarak, ekstravazasyon, trombositler, Miyeloid türevli baskılayıcı hücreler (MDSC) ve Tümör-ilişkili makrofajlar (TAM) dahil olmak üzere tümör hücreleri ile kan hücreleri arasındaki etkileşime dayanır (Wang et al., 2019). Trombositler, Transforme edici büyüme faktör-beta1 (TGFβ1) ve granül türevli Adenozin trifosfat'ı (ATP) serbest bırakarak, endotel kavşaklarını modüle ederek ve tümör hücresi trans-endotel göçünü teşvik ederek invazif bir mezenkimal fenotipi indükler (Labelle et al., 2011; Stanger & Kahn, 2013; Wang et al., 2019). Miyeloid hücreler, vasküler geçirgenliği artırmak için Vasküler endotel büyüme faktörü'nü (VEGF) de serbest bırakan ekiplerde Vasküler hücre adezyon proteini 1 (VCAM1) ve Vasküler adezyon protein 1'in (VAP1) yukarı regülasyonunu indükler (Qian et al., 2009). Kanser hücreleri ayrıca mezenkimal özellikler kazandıktan sonra bazal yüzeylerinde invadopodia oluştururlar; Bu

yapılar çıkıntılı ve yapışkandır ve endotel bariyerini yıkmak için MMP-9 ve MMP-2 gibi matris metaloproteinazları serbest bırakır (Jacob, 2015; Leong et al., 2014).

SONUC

Metastaz, birden çok adımın sıralı olarak tamamlanmasını gerektiren karmaşık bir süreçtir. Tüm adımların ön koşulu, özel adaptasyonlar elde etmek için bir hücre alt kümesinin dönüştürülmesidir. Bu alt popülasyonlar, birincil tümör içinde zaten mevcut olabilir veya nesiller boyu mutasyonlardan sonra gelişebilir. İntravazasyon verimsiz bir süreçtir ve çoğu tümörü birincil konumlarıyla sınırlar. Bununla birlikte, bir kez intravaze edildiğinde, tümörler dolaşımda başarılı bir şekilde hayatta kalır ve verimli bir şekilde damar dışına çıkar. Kanser hücrelerinin nerede metastaz yaptığı, kemokinler, sitokinler ve büyüme faktörlerini içeren spesifik mekanizmaların yanı sıra spesifik olmayan dolaşım modelleri ve kılcal yakalama ile belirlenir. Bu, bazı onkojenlerin tümör hücrelerine yalnızca istilacı özellikler kazandırmakla kalmayıp aynı zamanda kendi kendini yenileme potansiyellerini artırma olasılığını da artırır. Bu tür yeteneklerin, yayılmış bir tümör hücresinin kendini kurması ve metastaz olarak büyümesi için çok önemli olması muhtemeldir. Metastatik kaskadın anlaşılmasındaki daha fazla ilerleme şüphesiz bize metastazı engellemek için klinik olarak ilgili ipuçları sunacaktır.

KAYNAKÇA

- Aiello, N. M., Maddipati, R., Norgard, R. J., Balli, D., Li, J., Yuan, S., Yamazoe, T., Black, T., Sahmoud, A., Furth, E. E., Bar-Sagi, D., & Stanger, B. Z. (2018). EMT Subtype Influences Epithelial Plasticity and Mode of Cell Migration [Article]. *Developmental Cell*, 45(6), 681-695.e684. https://doi.org/10.1016/j.devcel.2018.05.027
- Alexandrov, L. B., Nik-Zainal, S., Wedge, D. C., Aparicio, S. A., Behjati, S., Biankin, A. V., Bignell, G. R., Bolli, N., Borg, A., & Børresen-Dale, A.-L. (2013). Signatures of mutational processes in human cancer. *Nature*, 500(7463), 415-421.
- Alix-Panabières, C., Mader, S., & Pantel, K. (2017). Epithelial-mesenchymal plasticity in circulating tumor cells. *Journal of Molecular Medicine*, 95, 133-142.
- Bao, S., Wu, Q., Sathornsumetee, S., Hao, Y., Li, Z., Hjelmeland, A. B., Shi, Q., McLendon, R. E., Bigner, D. D., & Rich, J. N. (2006). Stem cell–like glioma cells promote tumor angiogenesis through vascular endothelial growth factor. *Cancer Research*, *66*(16), 7843-7848.
- Barker, N., Van Es, J. H., Kuipers, J., Kujala, P., Van Den Born, M., Cozijnsen, M., Haegebarth, A., Korving, J., Begthel, H., & Peters, P. J. (2007). Identification of stem cells in small intestine and colon by marker gene Lgr5. *Nature*, 449(7165), 1003-1007.
- Bianco, A., Poukkula, M., Cliffe, A., Mathieu, J., Luque, C. M., Fulga, T. A., & Rørth, P. (2007). Two distinct modes of guidance signalling during collective migration of border cells [Article]. *Nature*, 448(7151), 362-365. https://doi.org/10.1038/nature05965
- Bielenberg, D. R., & Zetter, B. R. (2015). The contribution of angiogenesis to the process of metastasis. *The Cancer Journal*, 21(4), 267-273.
- Bockhorn, M., Jain, R. K., & Munn, L. L. (2007). Active versus passive mechanisms in metastasis: do cancer cells crawl into vessels, or are they pushed? [Note]. *Lancet Oncology*, 8(5), 444-448. https://doi.org/10.1016/S1470-2045(07)70140-7
- Cano, A., Pérez-Moreno, M. A., Rodrigo, I., Locascio, A., Blanco, M. J., del Barrio, M. G., Portillo, F., & Nieto, M. A. (2000). The transcription factor snail controls epithelial—

- mesenchymal transitions by repressing E-cadherin expression. *Nature cell biology*, 2(2), 76-83.
- Carmeliet, P., & Jain, R. K. (2000). Angiogenesis in cancer and other diseases. *Nature*, 407(6801), 249-257.
- Castaneda, M., den Hollander, P., Kuburich, N. A., Rosen, J. M., & Mani, S. A. (2022). Mechanisms of cancer metastasis. *Semin Cancer Biol*, 87, 17-31. https://doi.org/10.1016/j.semcancer.2022.10.006
- Chen, M.-S., Peng, P.-W., Liou, B.-C., Kuo, H.-C., Ou, K.-L., & Yang, T.-S. (2014). Single-molecule manipulation and detection platform for studying cancer cell chemotaxis. *Journal of Polymer Engineering*, 34(3), 259-265. https://doi.org/doi:10.1515/polyeng-2013-0217
- Deshmukh, A. P., Vasaikar, S. V., Tomczak, K., Tripathi, S., Den Hollander, P., Arslan, E., Chakraborty, P., Soundararajan, R., Jolly, M. K., & Rai, K. (2021). Identification of EMT signaling cross-talk and gene regulatory networks by single-cell RNA sequencing. *Proceedings of the National Academy of Sciences*, 118(19), e2102050118.
- Dillekås, H., Rogers, M. S., & Straume, O. (2019). Are 90% of deaths from cancer caused by metastases? *Cancer medicine*, 8(12), 5574-5576.
- Fischer, K. R., Durrans, A., Lee, S., Sheng, J., Li, F., Wong, S. T., Choi, H., El Rayes, T., Ryu, S., & Troeger, J. (2015). Epithelial-to-mesenchymal transition is not required for lung metastasis but contributes to chemoresistance. *Nature*, *527*(7579), 472-476.
- Folkman, J. (2002). Role of angiogenesis in tumor growth and metastasis. Seminars in oncology,
- Follain, G., Herrmann, D., Harlepp, S., Hyenne, V., Osmani, N., Warren, S. C., Timpson, P., & Goetz, J. G. (2020). Fluids and their mechanics in tumour transit: shaping metastasis [Review]. *Nature Reviews Cancer*, 20(2), 107-124. https://doi.org/10.1038/s41568-019-0221-x
- Fukumura, D., & Jain, R. K. (2008). Imaging angiogenesis and the microenvironment. *Apmis*, 116(7-8), 695-715.
- Griffiths, A., Miller, J., Suzuki, D., Lewontin, R., & Gelbart, W. (2000). Cancer: the genetics of aberrant cell control. *An Introduction to Genetic Analysis*.
- Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer: the next generation. *cell*, 144(5), 646-674.
- Harada, T., Swift, J., Irianto, J., Shin, J.-W., Spinler, K. R., Athirasala, A., Diegmiller, R., Dingal, P. C. D. P., Ivanovska, I. L., & Discher, D. E. (2014). Nuclear lamin stiffness is a barrier to 3D migration, but softness can limit survival. *Journal of Cell Biology*, 204(5), 669-682. https://doi.org/10.1083/jcb.201308029
- Harper, K. L., Sosa, M. S., Entenberg, D., Hosseini, H., Cheung, J. F., Nobre, R., Avivar-Valderas, A., Nagi, C., Girnius, N., & Davis, R. J. (2016). Mechanism of early dissemination and metastasis in Her2+ mammary cancer. *Nature*, *540*(7634), 588-592.
- Hegerfeldt, Y., Tusch, M., Bröcker, E. B., & Friedl, P. (2002). Collective cell movement in primary melanoma explants: Plasticity of cell-cell interaction, β1-integrin function, and migration strategies [Article]. *Cancer Research*, 62(7), 2125-2130. https://www.scopus.com/inward/record.uri?eid=2-s2.0-0036532136&partnerID=40&md5=8a2e4874025e54026923d8e85d6b7284
- Hollier, B. G., Tinnirello, A. A., Werden, S. J., Evans, K. W., Taube, J. H., Sarkar, T. R., Sphyris, N., Shariati, M., Kumar, S. V., & Battula, V. L. (2013). FOXC2 Expression Links Epithelial–Mesenchymal Transition and Stem Cell Properties in Breast CancerFOXC2 in EMT and Cancer Stem Cells. *Cancer Research*, 73(6), 1981-1992.
- Hu, J., Li, Y., Hao, Y., Zheng, T., Gupta, S. K., Parada, G. A., Wu, H., Lin, S., Wang, S., Zhao, X., Goldman, R. D., Cai, S., & Guo, M. (2019). High stretchability, strength,

- and toughness of living cells enabled by hyperelastic vimentin intermediate filaments. *Proceedings of the National Academy of Sciences*, *116*(35), 17175-17180. https://doi.org/doi.10.1073/pnas.1903890116
- Hunter, K. W., Crawford, N. P., & Alsarraj, J. (2008). Mechanisms of metastasis. *Breast Cancer Res*, 10 Suppl 1(Suppl 1), S2. https://doi.org/10.1186/bcr1988
- Jacob, T. (2015). Diving modifications for post-polio survivors: Three case studies [Article]. *Palaestra*, 29(2), 1. https://www.scopus.com/inward/record.uri?eid=2-s2.0-85074512757&partnerID=40&md5=78a498da2ab29ea3316dc486e11e6f0b
- Janssens, K., Sung, H. H., & Rørth, P. (2010). Direct detection of guidance receptor activity during border cell migration [Article]. *Proceedings of the National Academy of Sciences of the United States of America*, 107(16), 7323-7328. https://doi.org/10.1073/pnas.0915075107
- Karaman, S., & Detmar, M. (2014). Mechanisms of lymphatic metastasis. *The Journal of clinical investigation*, 124(3), 922-928.
- Kidd, M. E., Shumaker, D. K., & Ridge, K. M. (2014). The role of vimentin intermediate filaments in the progression of lung cancer. *Am J Respir Cell Mol Biol*, *50*(1), 1-6. https://doi.org/10.1165/rcmb.2013-0314TR
- Krakhmal, N. V., Zavyalova, M. V., Denisov, E. V., Vtorushin, S. V., & Perelmuter, V. M. (2015). Cancer invasion: Patterns and mechanisms [Review]. *Acta Naturae*, 7(2), 17-28. https://doi.org/10.32607/20758251-2015-7-2-17-28
- Kröger, C., Afeyan, A., Mraz, J., Eaton, E. N., Reinhardt, F., Khodor, Y. L., Thiru, P., Bierie, B., Ye, X., & Burge, C. B. (2019). Acquisition of a hybrid E/M state is essential for tumorigenicity of basal breast cancer cells. *Proceedings of the National Academy of Sciences*, 116(15), 7353-7362.
- Krzyszczyk, P., Acevedo, A., Davidoff, E. J., Timmins, L. M., Marrero-Berrios, I., Patel, M., White, C., Lowe, C., Sherba, J. J., Hartmanshenn, C., O'Neill, K. M., Balter, M. L., Fritz, Z. R., Androulakis, I. P., Schloss, R. S., & Yarmush, M. L. (2018). The growing role of precision and personalized medicine for cancer treatment. *TECHNOLOGY*, *06*(03n04), 79-100. https://doi.org/10.1142/s2339547818300020
- Kwon, O.-J., Zhang, L., Wang, J., Su, Q., Feng, Q., Zhang, X. H., Mani, S. A., Paulter, R., Creighton, C. J., & Ittmann, M. M. (2016). Notch promotes tumor metastasis in a prostate-specific Pten-null mouse model. *The Journal of clinical investigation*, *126*(7), 2626-2641.
- Labelle, M., Begum, S., & Hynes, R. (2011). Direct Signaling between Platelets and Cancer Cells Induces an Epithelial-Mesenchymal-Like Transition and Promotes Metastasis [Article]. *Cancer Cell*, 20(5), 576-590. https://doi.org/10.1016/j.ccr.2011.09.009
- Lamouille, S., Xu, J., & Derynck, R. (2014). Molecular mechanisms of epithelial—mesenchymal transition. *Nature reviews Molecular cell biology*, *15*(3), 178-196.
- Leong, H. S., Robertson, A. E., Stoletov, K., Leith, S. J., Chin, C. A., Chien, A. E., Hague, M., Ablack, A., Carmine-Simmen, K., McPherson, V. A., Postenka, C., Turley, E. A., Courtneidge, S. A., Chambers, A. F., & Lewis, J. D. (2014). Invadopodia Are Required for Cancer Cell Extravasation and Are a Therapeutic Target for Metastasis [Article]. *Cell Reports*, 8(5), 1558-1570. https://doi.org/10.1016/j.celrep.2014.07.050
- Lintz, M., Muñoz, A., & Reinhart-King, C. A. (2017). The Mechanics of Single Cell and Collective Migration of Tumor Cells. *Journal of Biomechanical Engineering*, *139*(2). https://doi.org/10.1115/1.4035121
- Liotta, L. (1989). Principles of molecular cell biology of cancer; Cancer metastases. *Cancer Principles and Practice of Oncology*., 98-115.
- Liu, S., Cong, Y., Wang, D., Sun, Y., Deng, L., Liu, Y., Martin-Trevino, R., Shang, L., McDermott, S. P., & Landis, M. D. (2014). Breast cancer stem cells transition between

- epithelial and mesenchymal states reflective of their normal counterparts. *Stem cell reports*, 2(1), 78-91.
- Liu, X., Taftaf, R., Kawaguchi, M., Chang, Y.-F., Chen, W., Entenberg, D., Zhang, Y., Gerratana, L., Huang, S., Patel, D. B., Tsui, E., Adorno-Cruz, V., Chirieleison, S. M., Cao, Y., Harney, A. S., Patel, S., Patsialou, A., Shen, Y., Avril, S., . . . Liu, H. (2019). Homophilic CD44 Interactions Mediate Tumor Cell Aggregation and Polyclonal Metastasis in Patient-Derived Breast Cancer Models. *Cancer Discovery*, *9*(1), 96-113. https://doi.org/10.1158/2159-8290.Cd-18-0065
- Luzzi, K. J., MacDonald, I. C., Schmidt, E. E., Kerkvliet, N., Morris, V. L., Chambers, A. F., & Groom, A. C. (1998). Multistep nature of metastatic inefficiency: dormancy of solitary cells after successful extravasation and limited survival of early micrometastases. *Am J Pathol*, *153*(3), 865-873. https://doi.org/10.1016/s0002-9440(10)65628-3
- Maeda, H. (2001). The enhanced permeability and retention (EPR) effect in tumor vasculature: the key role of tumor-sepective macromolecular drug targeting. *Adv Enzyme Regul*, 41, 189-207.
- Mandriota, S. J., Jussila, L., Jeltsch, M., Compagni, A., Baetens, D., Prevo, R., Banerji, S., Huarte, J., Montesano, R., & Jackson, D. G. (2001). Vascular endothelial growth factor-C-mediated lymphangiogenesis promotes tumour metastasis. *The EMBO journal*, 20(4), 672-682.
- Mani, S. A., Yang, J., Brooks, M., Schwaninger, G., Zhou, A., Miura, N., Kutok, J. L., Hartwell, K., Richardson, A. L., & Weinberg, R. A. (2007). Mesenchyme Forkhead 1 (FOXC2) plays a key role in metastasis and is associated with aggressive basal-like breast cancers. *Proceedings of the National Academy of Sciences*, 104(24), 10069-10074.
- Mendez, M. G., Restle, D., & Janmey, P. A. (2014). Vimentin Enhances Cell Elastic Behavior and Protects against Compressive Stress. *Biophysical Journal*, *107*(2), 314-323. https://doi.org/https://doi.org/10.1016/j.bpj.2014.04.050
- Mrozik, K. M., Blaschuk, O. W., Cheong, C. M., Zannettino, A. C. W., & Vandyke, K. (2018a). N-cadherin in cancer metastasis, its emerging role in haematological malignancies and potential as a therapeutic target in cancer. *BMC cancer*, 18(1), 1-16.
- Mrozik, K. M., Blaschuk, O. W., Cheong, C. M., Zannettino, A. C. W., & Vandyke, K. (2018b). N-cadherin in cancer metastasis, its emerging role in haematological malignancies and potential as a therapeutic target in cancer. *BMC cancer*, *18*(1), 939. https://doi.org/10.1186/s12885-018-4845-0
- Nieminen, M., Henttinen, T., Merinen, M., Marttila-Ichihara, F., Eriksson, J. E., & Jalkanen, S. (2006). Vimentin function in lymphocyte adhesion and transcellular migration [Article]. *Nature cell biology*, 8(2), 156-162. https://doi.org/10.1038/ncb1355
- Oka, H., Shiozaki, H., Kobayashi, K., Inoue, M., Tahara, H., Kobayashi, T., Takatsuka, Y., Matsuyoshi, N., Hirano, S., & Takeichi, M. (1993). Expression of E-cadherin cell adhesion molecules in human breast cancer tissues and its relationship to metastasis. *Cancer Research*, *53*(7), 1696-1701.
- Padmanaban, V., Krol, I., Suhail, Y., Szczerba, B. M., Aceto, N., Bader, J. S., & Ewald, A. J. (2019). E-cadherin is required for metastasis in multiple models of breast cancer. *Nature*, *573*(7774), 439-444. https://doi.org/10.1038/s41586-019-1526-3
- Pastushenko, I., Brisebarre, A., Sifrim, A., Fioramonti, M., Revenco, T., Boumahdi, S., Van Keymeulen, A., Brown, D., Moers, V., & Lemaire, S. (2018). Identification of the tumour transition states occurring during EMT. *Nature*, *556*(7702), 463-468.
- Puisieux, A., Brabletz, T., & Caramel, J. (2014). Oncogenic roles of EMT-inducing transcription factors. *Nature cell biology*, *16*(6), 488-494.

- Qian, B., Deng, Y., Im, J. H., Muschel, R. J., Zou, Y., Li, J., Lang, R. A., & Pollard, J. W. (2009). A Distinct Macrophage Population Mediates Metastatic Breast Cancer Cell Extravasation, Establishment and Growth. *PLOS ONE*, *4*(8), e6562. https://doi.org/10.1371/journal.pone.0006562
- Rørth, P. (2009). Collective cell migration [Review]. *Annual Review of Cell and Developmental Biology*, 25, 407-429. https://doi.org/10.1146/annurev.cellbio.042308.113231
- Roussos, E. T., Condeelis, J. S., & Patsialou, A. (2011). Chemotaxis in cancer. *Nature Reviews Cancer*, 11(8), 573-587. https://doi.org/10.1038/nrc3078
- Sell, S. (2010). On the stem cell origin of cancer. *The American journal of pathology*, 176(6), 2584-2594.
- Shweiki, D., Itin, A., Soffer, D., & Keshet, E. (1992). Vascular endothelial growth factor induced by hypoxia may mediate hypoxia-initiated angiogenesis. *Nature*, *359*(6398), 843-845.
- Singh, S. K., Hawkins, C., Clarke, I. D., Squire, J. A., Bayani, J., Hide, T., Henkelman, R. M., Cusimano, M. D., & Dirks, P. B. (2004). Identification of human brain tumour initiating cells. *Nature*, *432*(7015), 396-401.
- Soundararajan, R., Paranjape, A. N., Barsan, V., Chang, J. T., & Mani, S. A. (2015). A novel embryonic plasticity gene signature that predicts metastatic competence and clinical outcome [Article]. *Scientific Reports*, *5*, Article 11766. https://doi.org/10.1038/srep11766
- Stanger, B. Z., & Kahn, M. L. (2013). Platelets and Tumor Cells: A New Form of Border Control [Short survey]. *Cancer Cell*, 24(1), 9-11. https://doi.org/10.1016/j.ccr.2013.06.009
- Strilic, B., & Offermanns, S. (2017). Intravascular Survival and Extravasation of Tumor Cells [Review]. *Cancer Cell*, 32(3), 282-293. https://doi.org/10.1016/j.ccell.2017.07.001
- Tambe, D. T., Corey Hardin, C., Angelini, T. E., Rajendran, K., Park, C. Y., Serra-Picamal, X., Zhou, E. H., Zaman, M. H., Butler, J. P., Weitz, D. A., Fredberg, J. J., & Trepat, X. (2011). Collective cell guidance by cooperative intercellular forces [Article]. *Nature Materials*, 10(6), 469-475. https://doi.org/10.1038/nmat3025
- Taube, J. H., Herschkowitz, J. I., Komurov, K., Zhou, A. Y., Gupta, S., Yang, J., Hartwell, K., Onder, T. T., Gupta, P. B., & Evans, K. W. (2010). Core epithelial-to-mesenchymal transition interactome gene-expression signature is associated with claudin-low and metaplastic breast cancer subtypes. *Proceedings of the National Academy of Sciences*, 107(35), 15449-15454.
- Teo, G. S. L., Ankrum, J. A., Martinelli, R., Boetto, S. E., Simms, K., Sciuto, T. E., Dvorak, A. M., Karp, J. M., & Carman, C. V. (2012). Mesenchymal stem cells transmigrate between and directly through tumor necrosis factor-α-activated endothelial cells via both leukocyte-like and novel mechanisms [Article]. *Stem Cells*, *30*(11), 2472-2486. https://doi.org/10.1002/stem.1198
- Tonini, T., Rossi, F., & Claudio, P. P. (2003). Molecular basis of angiogenesis and cancer. *Oncogene*, 22(42), 6549-6556.
- Tunggal, J. A., Helfrich, I., Schmitz, A., Schwarz, H., Günzel, D., Fromm, M., Kemler, R., Krieg, T., & Niessen, C. M. (2005). E-cadherin is essential for in vivo epidermal barrier function by regulating tight junctions. *The EMBO journal*, 24(6), 1146-1156.
- Vasaikar, S. V., Deshmukh, A. P., den Hollander, P., Addanki, S., Kuburich, N. A., Kudaravalli, S., Joseph, R., Chang, J. T., Soundararajan, R., & Mani, S. A. (2021). EMTome: A resource for pan-cancer analysis of epithelial-mesenchymal transition genes and signatures. *British journal of cancer*, *124*(1), 259-269.

- Wang, J., Li, D., Cang, H., & Guo, B. (2019). Crosstalk between cancer and immune cells: Role of tumor-associated macrophages in the tumor microenvironment [Review]. *Cancer medicine*, 8(10), 4709-4721. https://doi.org/10.1002/cam4.2327
- Weidner, N., Semple, J. P., Welch, W. R., & Folkman, J. (1991). Tumor angiogenesis and metastasis—correlation in invasive breast carcinoma. *New England Journal of Medicine*, 324(1), 1-8.
- Weiss, L., Nannmark, U., Johansson, B. R., & Bagge, U. (1992). Lethal deformation of cancer cells in the microcirculation: a potential rate regulator of hematogenous metastasis. *Int J Cancer*, 50(1), 103-107. https://doi.org/10.1002/ijc.2910500121
- Werden, S., Sphyris, N., Sarkar, T. R., Paranjape, A., LaBaff, A., Taube, J., Hollier, B., Ramirez-Peña, E., Soundararajan, R., & Den Hollander, P. (2016). Phosphorylation of serine 367 of FOXC2 by p38 regulates ZEB1 and breast cancer metastasis, without impacting primary tumor growth. *Oncogene*, 35(46), 5977-5988.
- Wolf, K. J., Shukla, P., Springer, K., Lee, S., Coombes, J. D., Choy, C. J., Kenny, S. J., Xu, K., & Kumar, S. (2020). A mode of cell adhesion and migration facilitated by CD44-dependent microtentacles. *Proceedings of the National Academy of Sciences*, *117*(21), 11432-11443. https://doi.org/doi:10.1073/pnas.1914294117
- Xin, Y., Li, K., Yang, M., & Tan, Y. (2020). Fluid shear stress induces emt of circulating tumor cells via jnk signaling in favor of their survival during hematogenous dissemination [Article]. *International Journal of Molecular Sciences*, 21(21), 1-16, Article 8115. https://doi.org/10.3390/ijms21218115
- Yang, C., Cao, M., Liu, Y., He, Y., Du, Y., Zhang, G., & Gao, F. (2019). Inducible formation of leader cells driven by CD44 switching gives rise to collective invasion and metastases in luminal breast carcinomas. *Oncogene*, *38*(46), 7113-7132. https://doi.org/10.1038/s41388-019-0899-y
- Yang, J., Mani, S. A., Donaher, J. L., Ramaswamy, S., Itzykson, R. A., Come, C., Savagner, P., Gitelman, I., Richardson, A., & Weinberg, R. A. (2004). Twist, a master regulator of morphogenesis, plays an essential role in tumor metastasis. *cell*, *117*(7), 927-939.
- Yu, M., Bardia, A., Wittner, B. S., Stott, S. L., Smas, M. E., Ting, D. T., Isakoff, S. J., Ciciliano, J. C., Wells, M. N., Shah, A. M., Concannon, K. F., Donaldson, M. C., Sequist, L. V., Brachtel, E., Sgroi, D., Baselga, J., Ramaswamy, S., Toner, M., Haber, D. A., & Maheswaran, S. (2013). Circulating Breast Tumor Cells Exhibit Dynamic Changes in Epithelial and Mesenchymal Composition. *Science*, 339(6119), 580-584. https://doi.org/doi:10.1126/science.1228522
- Zhang, J., Tian, X.-J., & Xing, J. (2016). Signal transduction pathways of EMT induced by TGF-β, SHH, and WNT and their crosstalks. *Journal of clinical medicine*, *5*(4), 41.
- Zheng, H., & Kang, Y. (2014). Multilayer control of the EMT master regulators. *Oncogene*, 33(14), 1755-1763.
- Zhong, H., De Marzo, A. M., Laughner, E., Lim, M., Hilton, D. A., Zagzag, D., Buechler, P., Isaacs, W. B., Semenza, G. L., & Simons, J. W. (1999). Overexpression of hypoxia-inducible factor 1α in common human cancers and their metastases. *Cancer Research*, 59(22), 5830-5835.

LYMPHOCYTE LEVEL AT DIAGNOSIS IN HODGKIN LYMPHOMA: COULD IT BE AN INDICATOR OF THE STAGE AT INITIAL DIAGNOSIS?

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INTRODUCTION

Hodgkin lymphoma (HL), formerly called Hodgkin's disease, is a rare monoclonal lymphoid hematologic malignancy with high cure rates [1]. As a result of the studies, this disease has been divided into two different subgroups: Classical Hodgkin lymphoma (cHL) and nodular lymphocyte-predominant Hodgkin lymphoma (NLP-HL). The current gold standard for advanced stage risk stratification in HL is the International Prognostic Score (IPS) [2]. Despite the existence of standard risk classification systems and effective treatment approaches, 34% to 37% of advanced stage HLs relapse or progress [3]. Therefore, for the sake of prognosis and early prediction of the stage, it is necessary to develop new easily usable parameters. Many studies have been conducted with the goal of determining the prognosis and estimation of the stage of this type of lymphoma consisting of different morphological features. In summary, from studies on tumor microenvironment and host immunity, it can be said that changes in lymphocyte ratio and subtypes constitute a new research subject. At this point, absolute monocyte count (AMC), absolute lymphocyte count (ALC) are shown as prognostic factors [4–6]. Similarly, we see that the developed parameters such as neutrophil-lymphocyte ratio are also used in determining prognosis [7]. Main aim in

present study was to show the relationship between initial lymphocyte count and stage and to examine their effects on prognosis. The initial lymphocyte count which is proven in advanced stage patients, could be an important factor in terms of showing the prognosis also in the early stage.

Material and method

In this study, 190 patients diagnosed with HL between January 2010 and September 2020 were included. HL subtypes (NSHL, MCHL, LDHL, LRHL, NLP-HL), diagnosis stages, presence of bulky or mediastinal mass, lymphadenopathy areas (cervical, thoracic, abdomen, pelvis), as well as demographic data of patients such as age and gender were recorded. It was aimed to obtain a cut-off in the statistical analysis performed in order to reveal the relationship between lymphocyte level and stage, which is the main hypothesis of the study.

Results

Of the 190 patients evaluated, 77 were female (40,5%), and 113 were male (59,5%). When evaluated, in terms of histological subtype, it was seen that 133 patients (70%) were diagnosed with NSHL. When mortality and affecting factors were examined, it was seen that only high leukocyte count at initial diagnosis and advanced age were associated with

mortality. To obtain a cut-off in terms of lymphocyte level and stage relationship, which is the hypothesis of our study; a value of $2380 / \text{mm}^3$ and below was found to be associated with stage 3-4 disease with a sensitivity of 86,44% and a specificity of 33,3% (AUC: 0,613 (0,539-0,682), p < 0,007)

Discussion

The histological distinguishing feature of cHL is that Reed Sternberg cells form approximately 2% of the environment alongside the other tumor microenvironment. Studies have shown that the background known as the tumor microenvironment has a significant effect on prognosis [8]. Tumor-infiltrating lymphocytes and tumor-infiltrating macrophages are reported to be prognostic factors for survival in patients [8–10]. It has long been known that the initial lymphocyte count has a prognostic role in cHL, and lymphopenia (<600 cells / mm3 or <8% of leukocytes) is also associated with adverse survival outcome [5, 9]. In this study, it was aimed to reveal the factors affecting prognosis, response and progression in the Hodgkin group and create a new field in terms of scoring at the time of diagnosis by revealing the relationship between lymphocyte count at the time of diagnosis and stage.

The current approach to HL should be a personalized treatment. Many patients with HL can be treated with standard therapy and therefore they are at risk of potential long-term complications. The factors that determine patients with a low or high risk of relapse will therefore be most useful in optimising treatment based on the patient's expected clinical outcome to avoid over-treatment of some patients and under-treatment of others. Prognostic factors for early-stage HL have been identified and include the presence of a large mediastinal mass, an increased sedimentation rate, involvement of multiple nodal sites, extranodal involvement, age of 50 years, or massive splenic disease [11]. A different prognostic scoring system has been developed for advanced stage HL by the International Prognostic Factor Project [2]. As a result of this study, seven variables were defined: being over 45 years of age,

presence of stage IV disease, being male , leukocyte count \geq 15,000, lymphocyte count $<\!600$, albumin $<\!4,\!0$ g / dL and hemoglobin $<\!10,\!5$ g / dL . The 5-year PFS is 42% in patients with five or more factors, while the 5-year PFS is 84% in patients without negative prognostic factors.

Keywords: Hodgkin lymphoma, lymphocyte, stage, prognosis

References

- 1. Amraee, A., Evazi, M. R., Shakeri, M., Roozbeh, N., Ghazanfarpour, M., Ghorbani, M., Ansari, J., & Darvish, L. (2019). Efficacy of nivolumab as checkpoint inhibitor drug on survival rate of patients with relapsed/refractory classical Hodgkin lymphoma: a meta-analysis of prospective clinical study. *Clinical & translational oncology: official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico*, 21(8), 1093–1103.
- 2. Hasenclever, D., & Diehl, V. (1998). A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. *The New England journal of medicine*, *339*(21), 1506–1514.

- 3. Koh, Y. W., Kang, H. J., Park, C., Yoon, D. H., Kim, S., Suh, C., Kim, J. E., Kim, C. W., & Huh, J. (2012). Prognostic significance of the ratio of absolute neutrophil count to absolute lymphocyte count in classic Hodgkin lymphoma. *American journal of clinical pathology*, 138(6), 846–854.
- 4. Seshadri, T., Pintilie, M., Keating, A., Crump, M., & Kuruvilla, J. (2008). The relationship between absolute lymphocyte count with PFS in patients with Hodgkin's lymphoma undergoing autologous hematopoietic cell transplant. *Bone marrow transplantation*, 42(1), 29–34.
- 5. Tadmor, T., Bari, A., Marcheselli, L., Sacchi, S., Aviv, A., Baldini, L., Gobbi, P. G., Pozzi, S., Ferri, P., Cox, M. C., Cascavilla, N., Iannitto, E., Federico, M., & Polliack, A. (2015). Absolute Monocyte Count and Lymphocyte-Monocyte Ratio Predict Outcome in Nodular Sclerosis Hodgkin Lymphoma: Evaluation Based on Data From 1450 Patients. *Mayo Clinic proceedings*, 90(6), 756–764.
- 6. Quail, D. F., & Joyce, J. A. (2013). Microenvironmental regulation of tumor progression and metastasis. *Nature medicine*, *19*(11), 1423–1437.
- 7. Troppan, K., Deutsch, A., Gerger, A., Stojakovic, T., Beham-Schmid, C., Wenzl, K., Neumeister, P., & Pichler, M. (2014). The derived neutrophil to lymphocyte ratio is an independent prognostic factor in patients with diffuse large B-cell lymphoma. *British journal of cancer*, 110(2), 369–374.
- 8. Steidl, C., Lee, T., Shah, S. P., Farinha, P., Han, G., Nayar, T., Delaney, A., Jones, S. J., Iqbal, J., Weisenburger, D. D., Bast, M. A., Rosenwald, A., Muller-Hermelink, H. K., Rimsza, L. M., Campo, E., Delabie, J., Braziel, R. M., Cook, J. R., Tubbs, R. R., Jaffe, E. S., ... Gascoyne, R. D. (2010). Tumor-associated macrophages and survival in classic Hodgkin's lymphoma. *The New England journal of medicine*, *362*(10), 875–885.

- 9. Schreck, S., Friebel, D., Buettner, M., Distel, L., Grabenbauer, G., Young, L. S., & Niedobitek, G. (2009). Prognostic impact of tumour-infiltrating Th2 and regulatory T cells in classical Hodgkin lymphoma. *Hematological oncology*, 27(1), 31–39.
- 10. Koh, Y. W., Kang, H. J., Park, C., Yoon, D. H., Kim, S., Suh, C., Kim, J. E., Kim, C. W., & Huh, J. (2012). Prognostic significance of the ratio of absolute neutrophil count to absolute lymphocyte count in classic Hodgkin lymphoma. *American journal of clinical pathology*, 138(6), 846–854.
- 11. Ansell S. M. (2020). Hodgkin lymphoma: A 2020 update on diagnosis, risk-stratification, and management. *American journal of hematology*, 95(8), 978–989.

COMPARATIVE ANALYSIS OF NEW OPPORTUNITES FOR PHARMACOTHERAPY OF NON-SPECIFIC

ULCERATIVE COLITS AND WAYS TO IMPROVE ITS PERFORMANCE EVALUATION

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ABSTRACT

The aim of our study was to improve outcomes by improving complex therapy in patients with non-specific ulcerative colitis.

Materials and methods: From 2008 to 2022, there were 261 patients diagnosed with non-specific ulcerative colitis under our control, of whom 171 were women and 90 were men. The age of the patients ranged from 16 to 68. 58 patients had total colitis, 84 patients had leftsided lesions, 119 patients had proctitis and proctosigmoiditis. In the complex treatment of these patients, anti-inflammatory drugs - aminosalicylates - sulfasalazine or salofalk, corticosteroids; immunodepressants were used. Salofalk was used as a suppository during proctitis, as a microenema in left-sided lesions, and in general form as a tablet. Metipred was used during complex therapy as a corticosteroid. Hydrocortisone is prescribed in the form of rectal drops or microenemas in the case of distal localized lesions and I-II degree lesions. 6mercaptopurine and azathioprine were mainly used in the complex therapy of immunodepressants. Elimination of the acute phase and remission was achieved in the majority of patients who received this treatment regimen. In 11 patients with left-sided ulcerative colitis, emergency surgery, subtotal resection of the colon and colostomy were performed due to perforation of the large intestine. From 6 months to 2 years after surgery, the preserved part of the large intestine was rehabilitated with candles and microenemas, topical mesalazine, metronidazole, and hormones such as intestinal antiseptics. Then, in the second stage of the operation, an operation to restore intestinal permeability was performed with the cancellation of the colostomy. Acute toxic dilatation was observed in 13 patients with left-sided ulcerative colitis. In 7 patients with toxic dilatation, the condition was stabilized with conservative therapy, and in the other 6 patients, because conservative therapy did not work, surgery was performed - subtotal resection of the large intestine, ileostomy was performed. Hormones, local mesalazine, metronidazole, suppositories and intestinal antiseptics in the form of microenemas were injected into the preserved part of the large intestine in these patients between 6 months and 2 years after the operation. Then, in the second stage of the operation, an operation to restore intestinal permeability was performed by canceling the ileostomy. In 6 patients with total colitis, conservative treatment did not work, stools were bloody and mucous 14-16 times a day, the disease was aggravated by pseudopolyposis, radical surgery was performed. From 6 months to 2 years postoperatively, patients were treated conservatively, mainly with hydrocortisone as rectal drops and microenemas, according to the above effect. As a result, the process in the rectum was completely canceled and the patients underwent an operation to restore intestinal permeability by closing the ileostomy. Against the background of treatment, favorable results were obtained in 100% of patients with proctitis.

Conclusion: According to our observations, complex therapy with anti-inflammatory aminosalicylates sulfosalazine or salofalk, corticosteroids and immunodepressants in patients with non-specific ulcerative colitis was a favorable method that led to rapid activation of patients, quick elimination of the acute period, early discharge from the hospital and a significant reduction of relapses, complications and during the surgery performed on time allows patients to get a positive result. Positive results are achieved in 70-80% of cases after the operation. Annual preventive examination is recommended.

Key words: ulcerative colitis, toxic dilatation, surgical treatment

USE OF OILSEEDS BY-PRODUCTS IN AQUA-FEEDS

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ABSTRACT

In the current talk will discuss about the use of conventional and non-conventional plant byproducts in aqua-feeds to promote the sustainable production of multiple fish species in aquaculture. The development of sustainable protein sources to substitute fish meal in aquafeeds is critical to the continued growth and intensification of aquaculture productivity. Fish feed plays an important role in the growth of the aquaculture industry. Fishmeal (FM) has been employed as the principal protein element in aquaculture because of its beneficial essential amino acids, high digestibility, and palatability. Fishmeal prices are expected to rise by 20% between now and 2030 because of rising demand and increased output. This requires the search for better FM alternatives for long term aqua-feed production. In this light, much efforts have been conducted to seek the sustainable supplies of protein sources to substitute FM. Good nutrition in production systems is essential to economically produce a healthy, high product the first consideration for formulation of feed is the quality of the feed ingredients. Use of plant protein source in the feed industry has been in practice for various advantages such as sustainability, availability, cost effectiveness etc. Because of their high protein content, excellent amino acid profile, low cost, and year-round availability, they are commonly utilized as a cost-effective alternative to high-quality fish meal in diets for many aquaculture fish species. Moringa oleifera leaf meal, Moringa oleifera seed meal, Canola meal, Sunflower meal, and Cottonseed meal have all been studied extensively. Different supplements, such as enzymes, probiotics, organic acids, and Nano-particles, are also given to fish meals in addition to plant by-products. All of these factors help fish species enhance their growth, nutrient digestibility, and body composition.

Keywords: plant by-products, replacement, feed formulation, cost effective, environment friendly

IMPACT OF HEAVY METALS CONTENT FOUND IN IRRIGATED RED PEPPER IN CHALLAWA INDUSTRIAL AREA

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ABSTRACT

Wastewater from Challawa industrial area were used for irrigation purpose, red pepper were sample and used to determine the presence of heavy metal content and their concentrations in the sample. The sample were collected and prepared using standard analytical procedures. The concentration of red pepper was determined using atomic absorption Spectroscopy (AAS). The mean concentration ug/g obtained from the analysis was found to be pb 12.82, Cd 2.02, Cu 2.99, Zn 3.67 and Cr 7.96. The results indicated that significant amount of Pb, Cd and Cr are beyond permissible limit whereas Cu and Zn concentration are within the permissible limit. There is health risk in taking excess amount of those heavy metals in higher concentration above permissible limit.

Keywords: Red pepper, AAS, Heavy metal, Waste water, Permissible limit.

PREPARATION AND EVALUATION OF TOPICAL PREPARATION OF EULALIOPSIS BINATA EXTRACT

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ABSTRACT

Now a days, human race suffer from number of health problems like respiratory obstruction, arthritis, heart disease, stroke, diabetes etc. and the major cause of all diseases is the poor diet, lack of exercise and formation of free radical etc. However by improving the life style can easily get rid from majority of diseases for example use of antioxidant in diet can easily avoid the formation of free radicals and Reactive oxygen species (ROS) that are able to bind with almost all cell/tissue, causing damage that result in various degenerative diseases. Scientific study revealed that the plant are the rich source of antioxidants and human race used plants since time immemorial to treat illness. *Eulaliopsis binata* (sabai grass or Chinese alpine rush), is a perennial plant belonging to the grass family that is grown in many Asian countries and most commonly used to make rope, feeder material for plants etc in India, but apart from this it also possess the antimicrobial, anti-inflammatory and wound healing activities. For its better pharmacological effect homogeneous, semi-solid or viscous preparations that possess a relatively fluid consistency and are intended for external application to the skin. Research stated that the topical preparation gain attention of researchers, from the past few decades. In this study we prepared the cream of aqueous extract from the leaf of Eulaliopsis binata and evaluate its different analyzing parameters.

Key Words: Eulaliopsis binate, Topical preparation, Cream, Antimicrobial, Antioxidants

NOVEL CRYOPROTECTANTS AND THEIR EFFECTS ON DECREASING GLYCEROL CONCENTRATION DURING CRYOPRESEVVATION

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ABSTRACT

Cryoprotectants are extensive supplements that added on extender to reduce ice-crystal formation during freeze-thawing process. In the field of theriogenology and obstetrics, we cryopreserve the sperm to control transmission of various bacterial or viral micro-organisms. On the other hand, cryopreservation is useful to store and transfer high-producer genes in farm animals. Two type of cryoprotectants use in extender including non-permeating and permeating. Permeating cryoprotectants entering the sperm and replacing with intracellular water and thus cellular dehydration occur. Polyethylene glycol, glycerol and DMSO are kind of permeating cryoprotectants that use extremely on sperm cryopreservation in both human and animals. Second type of cryoprotectants are permeating cryoprotectants such as polysaccharides, polyaminoacids and disaccharides that reduce the freezing temperature of extender and thus reduce extracellular ice formation. Novel cryoprotectants that use in field of sperm cryopreservation are carboxymethyl cellulose, trehalose, platelet-rich plasma, polyvinylpyrrolidone and cyclodextrins. Recent studies demonstrated that adding variable concentration of novel cryoprotectants on extender can reduce DNA fragmentation index (DFI), reactive oxygen species (ROS). Furthermore, plasma membrane integrity (PMI) and sperm parameters significantly enhance with adding these novel cryoprotectants. Moreover, some investigations showed that with adding different cryoprotectants before freeze-thawing process in extender simultaneously with glycerol, we can manipulate on exact concentration of glycerol that proved previously on studies. Glycerol have adverse effect on sperm during cryopreservation of sperm and can damage on sperm during freeze-thawing process that named croyoinjury. Some studies proved that when other supplements as carboxymethyl cellulose and trehalose added on extender, we can reduce the concentration of glycerol on extender and replace it with novel non-permeating cryoprotectants. Reduction of glycerol concentration from 6% to 4%(v/v) is suitable for sperm and enhance all sperm parameters such as progressive motility, viability and etc.

keywords: Cryoprotectants, cryodamage, extender, sperm.

HYDROXYMETHYL-P-TOLUENESULFONAMIDE AS AN ANTIOXIDANT ADDITIVE TO DIESEL FUELS

ГИДРОКСИМЕТИЛ-П-ТОЛУОЛСУЛЬФОНАМИД В КАЧЕСТВЕ АНТИОКИСЛИТЕЛЬНОЙ ПРИСАДКИ К ДИЗЕЛЬНЫМ ТОПЛИВАМ

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АННОТАЦИЯ

В связи с развитием машиностроения потребность в антиокислительных присадках к топливам растет из года в год, это связано с тем, что при неполном сгорании топлив в моторах и двигателях в процессе их эксплуатации ухудшается коэффициэнт полезного действия, что приводит к образованию осадков, забивающих топливные фильтры и форсунки двигателей.

Авторы данной работы предложили новое соединение гидроксиметил-птолуолсульфонамид в качестве антиокислительной присадки к дизельным топливам, формулы:

Соединение получено взаимодействием п-толуолсульфонамида с параформом в щелочной среде по нижеследующей схеме:

$$\begin{array}{c|c} \mathsf{CH_3} & \mathsf{CH_3} \\ \hline \\ \mathsf{SO_2NH_2} & \mathsf{SO_2NHCH_2OH} \end{array}$$

Исследование антиокислительных свойств, проводились в сравнении известной антиокислительной присадки ионол, формулы:

$$(CH_3)_3C$$
 $C(CH_3)_3$ CH_3

Результаты исследования показали, что антиокислительные свойства гидроксиметил-птолуолсульфонамида значительно превосходят антиокислительные свойства ионола. Это можно объяснить наличием в синтезированном соединении гидроксильных, амидных и ароматических групп.

Гидроксиметил-п-толуолсульфонамид может быть рекомендован в качестве антиокислительной присадки к дизельным топливам.

Ключевые слова: антиокислительные присадки, толуолсульфонамид, дизельное топливо

ABSTRACT

In connection with the development of the engineering industry, the demand for antioxidant additives to fuels is growing from year to year, this is due to the fact that with incomplete combustion of fuels in motors and engines during their operation, the efficiency deteriorates, which leads to the formation of precipitation that clogs the fuel filters and nozzles of engines.

The authors of this work proposed a new compound, hydroxymethyl-p-toluenesulfonamide, as an antioxidant additive to diesel fuels, with the formula:

The compound was obtained by the interaction of p-toluenesulfonamide with paraform in an alkaline medium according to the following scheme:

$$CH_3$$
 $+ CH_2O$
 KOH
 SO_2NH_2
 SO_2NHCH_2OH

The study of antioxidant properties was carried out by comparing the known antioxidant additive ionol, formula:

$$(CH_3)_3C$$
 $C(CH_3)_3$ CH_3

The results of the study showed that the antioxidant properties of hydroxymethyl-p-toluenesulfonamide are much superior to the antioxidant properties of ionol. This can be explained by the presence of hydroxyl, amide, and aromatic groups in the synthesized compound.

Hydroxymethyl-p-toluenesulfonamide can be recommended as an antioxidant additive for fuels.

Keywords: antioxidant additives, toluenesulfonamides, diesel fuel

DETERMINATION OF THE INFLUENCE OF STRUCTURE, SIZE OF WORKING NESTS AND THEIR FORAGING ON THE DEVELOPMENT OF FIELD MOUSE IN SOWN AREAS

ƏKİN SAHƏLƏRİNDƏ İŞLƏK YUVALARIN QURLUŞUNUN, ÖLÇÜLƏRİNİN, ONLARIN QİDA YIĞIMININ ÇÖL SIÇANLARININ İNKİŞAFINA TƏSİRİNİN MÜƏYYƏN EDİLMƏSİ

ОПРЕДЕЛЕНИЕ ВЛИЯНИЯ СТРОЕНИЯ, РАЗМЕРОВ РАБОЧИХ ГНЕЗД И ИХ КОРМОВОГО СБОРА НА РАЗВИТИЕ ПОЛЕВОЙ МЫШИ НА ПОСЕВНЫХ ПЛОЩАДЯХ

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XÜLASƏ

Kənd təsərrüfatı bitkilərinə daha çox zərər vuran zərərvericilərdən biri də gəmiricilərin əsas nümayəndələrindən olan adi çöl siçanıdır (Misrotus socialis pall). Azərbaycan faunasının tərkibində 8 fəsilə və 19 cinsə daxil olan 37 növ gəmirici yayılmışdır. Çöl siçanlarına qarşı mübarizə tədbirlərinin hazırlanmasında işlək yuvaların quruluşunun, ölçülərinin, onların sayının öyrənilməsinin böyük əhəmiyyəti vardır. Məqalədə bunlarla yanaşı yuvalarda qida yığımının və digər göstəricilərin çöl siçanlarının inkişafına təsiri şərh edilmişdir.

Ilk dəfə olaraq Azərbaycanın Mil-Qarabağ bölgəsində 2021-2022-ci illərdə müxtəlif əkin sahələrində çöl siçanlarının inkişafına təsir edən amillərdən asılı olaraq yuvaların ölçüləri (eni və hündürlüyü) və yuvalarda toplanmış yem ehtiyyatının mühüm əhəmiyyətinin olması müəyyən edilmişdir. Eyni zamanda tədqiqatlar zamanı çöl siçanlarının yuvalarının dərinliyi ilin mövsümləri üzrə dəyişməsidə müəyyən edilmişdir.

Müşahidələrdən və ölçmələrdən məlum olur ki, çöl siçanlarının yuvalarının dərinliyi müxtəlif olur. Ən dayaz yuvaların dərinliyi 5-10 sm-ə qədər, buğda, arpa əkin sahələrində şumlamadan asılı olaraq 20-25 sm, nadir hallarda isə daha dərin olmuşdur.

Tədqiqatlar zamanı işlək yuvaların eni və hündürlüklərin nisbətən böyük olması həmin yuvalarda daha çox miqdarda yem ehtiyyatının olmasına təsadüf edilmişdir. Qeyid etmək lazımdır ki, işlək yuvaların ölçülərinin dəyişməsinə müvafiq olaraq daha çox yem ehtiyyatına əsasən payız mövsümündə rast gəlinmişdir. Beləki,taxıl əkinlərində payizda işlək yuvalarda yem ehtiyyatının miqdarı 236,3-250,4 qram, yonca sahələrində 241,3-258,4 qram, meyvə və üzümlüklərdə isə daha çox 243,2-264,3 qrama bərabər olmuşdur.

Tədqiqatlardan belə nəticəyə gəlmək mümkündür ki, işlək yuvaların ölçülərinin böyüklüyü çöl siçanlarının bu yuvalarda xüsusiilə də meyvə və üzüzümlüklərdə təsadüf edilən işlək yuvalada daha çox miqdarda yem ehtiyyatının toplanmaları üçün əlverişli olmuşdur. Bu isə işlək yuvaların ölçülərinin böyüklüyü və yuvalarda yem ehtiyyatının bolluğunun çöl siçanlarının bu yuvalarda artıb çoxalmaları üçün əlverişli şəraitin olması zəruriyyətini yaradır.

Açar sözlər: əkin sahələri, çöl siçanları, yuvaların quruluşu, gəmiricilər

АБСТРАКТНЫЙ

Полевая мышь (Misrotus socialis pall), один из основных представителей грызунов, является одним из вредителей, наносящих наибольший ущерб сельскохозяйственным культурам. Животный мир Азербайджана включает 37 видов грызунов, принадлежащих к 8 семействам и 19 родам. Изучение строения, размеров и количества функциональных гнезд имеет большое значение при подготовке мероприятий по борьбе с полевыми мышами. Кроме них, в статье описано влияние сбора пищи в гнездах и других показателей на развитие полевых мышей.

Впервые в Миль-Карабахском районе Азербайджана в 2021-2022 годах было установлено, что размеры гнезд (ширина и высота) и собранный в гнездах кормовой запас имеют значение в зависимости от факторов, влияющих на развитие полевых мышей. В то же время в ходе исследований установлено, что глубина гнезд полевых мышей изменяется в зависимости от времени года.

Из наблюдений и измерений известно, что глубина гнезд полевых мышей неодинакова. Глубина самых мелких гнезд была до 5-10 см, 20-25 см была в зависимости от вспашки на пшеничном и ячменном полях, редко бывало и глубже.

В ходе исследований было выявлено, что относительно большая ширина и высота рабочих гнезд совпадали с наличием в них больших запасов корма. Следует отметить, что изменения размеров рабочих гнезд были обнаружены в осенний сезон в зависимости от кормовой базы. Так, количество кормовых запасов в рабочих гнездах осенью на зерновых культурах составило 236,3-250,4 грамма, на полях люцерны - 241,3-258,4 грамма, а на плодовых и виноградниках - 243,2-264,3 грамма.

Из исследований можно сделать вывод, что размер рабочих гнезд был благоприятным для того, чтобы полевые мыши собирали в этих гнездах больше запасов пищи, особенно в рабочих гнездах, обнаруженных во фруктовых и виноградных садах. Это приводит к благоприятным условиям для роста и размножения полевых мышей в этих гнездах из-за больших размеров рабочих гнезд и обилии кормовой базы в гнездах.

Ключевые слова: посевные площади, полевые мыши, устройство гнезд, грызуны.

ABSTRACT

The field mouse (Misrotus socialis pall), one of the main representatives of rodents, is one of the most damaging pests to crops. The animal world of Azerbaijan includes 37 species of rodents belonging to 8 families and 19 genera. The study of the structure, size and number of functional nests is very important for the preparation of measures to control field mice. In addition to these, the paper describes the effect of nest collection and other indicators on the development of field mice.

For the first time in the Mil-Karabakh region of Azerbaijan in 2021-2022, the size of nests (width and height) and the amount of food collected in the nests were found to be relevant to the factors influencing the development of field mice. At the same time, studies have found that the depth of field mouse nests varies with the time of year.

From observations and measurements, we know that the depth of field mouse nests varies. The depth of the shallowest nests was up to 5-10 cm, 20-25 cm depending on ploughing in wheat and barley fields, rarely deeper.

Studies showed that the relatively large width and height of the working nests coincided with the presence of large fodder reserves in the nests. It should be noted that variation in working nest size was found during the autumn season depending on the food availability. For example, the number of forage nests in autumn in grain crops was 236.3-250.4 grams, in alfalfa fields, 241.3-258.4 grams, and in fruit and vineyards, 243.2-264.3 grams.

We may conclude from the research that the size of the worker nests was favourable for field mice to collect more food reserves in these nests, especially in the worker nests found in orchards and vineyards. This leads to favourable conditions for the growth and reproduction of field mice in these nests due to the large size of the working nests and the abundance of food in the nests.

Key words: sowing area, field mouse, nesting, rodents.

GROWTH VARIATION IN FOREST TREE SPECIES IN AFFORESTATION OF GRADONI TERRACING

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ABSTRACT

The study was carried out to contribute forestry practices in an afforestation area established by gradoni terracing of Taurus cedar also called Cedar of Lebanon (*Cedrus libani* A.Rich.), Anatolian black pine [*Pinus nigra* Arnold. subsp. *pallasiana* (Lamb.) Holmboe] and Crimean juniper (*Juniperus excelsa* M. Bieb. *excelsa*) in southern part of Turkiye in 2007. The species *C. libani* (0.4 million ha), *P. nigra* (4.3) and *J. excelsa* (1.5) occupy at 6.2 million ha which of 26.8% total forest area of Turkiye. However, 42% of total forest area of Turkiye is unproductive or also called degraded forest. It was 25% in *C. libani*, 33% in *P. nigra* and 73% in *J. excelsa*. Afforestation practices included many stages is main tool in conversion of degraded forest to productive forest.

Tree height and diameter at base were measured in thirty individuals chosen randomly in each species at end of growth period of 2022. The species were compared by linear model of analysis of variance for the characteristics. Tree height and diameter at base were related by correlation analysis for each species.

Anatolian black pine had the highest diameter at base (11.96 cm), while tree height was the highest in Taurus cedar (3.55 m). There were also large differences among individuals within species for the characteristics. Individual tree heights were ranged from 1.95 m to 5.50 m in *C. libani*, from 1.87 to 4.05 in *P. nigra*, from 1.85 to 3.24 in *J. excels*, while, diameter at base varied between 1.95 and 5.20 cm in *C. libani*, between 7.50 and 15.38 cm in *P. nigra*, and between 6.08 and 11.38 cm in *J. excels* for individual trees.

Species showed significant ($p \le 0.01$) differences for tree height and diameter at base according to results of analysis of variance. There were positive and significant ($p \le 0.05$) relations between the characteristics in all the species. According to results of correlation analysis phenotypic correlation coefficients (r_p) were 0.919 in *C. libani*, 0.618 in *P. nigra* and 0.507 in *J. excels*.

Results of the study were discussed based on plantation forestry and other forestry practices in the species.

Keywords: Growth, Plantation, Silviculture, Seedling, Variation.

EFFECT OF TERRACING ON GROWTH OF TAURUS CEDAR (CEDRUS LIBANI): A CASE STUDY FROM ISPARTA DISTRICT

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ABSTRACT

Taurus cedar (*Cedrus libani* A. Rich.) is a key species used in Turkish plantation forestry widely. Soil treatment also known soil preparation has play important role in biological and economical success of the plantation forestry together with other biotic and a-biotic factors such as climatic, edaphic and geographic characteristics.

In this case study, growth performances of Taurus cedar were compared between soil preparation by terracing and control treatment (mean un-preparation) based on tree height and diameter at base of sampled 35 trees of each treatment in plantation areas established at Isparta district from southern part of Turkiye in 2008.

Terracing preparation had higher tree height (211.6 cm) to control (178.9 cm) opposite to diameter at base (6.46 cm and 7.73 cm), while individual trees showed large difference for the characteristics within treatment. Tree height had higher variation than diameter in both treatments.

The treatments showed similar (p>0.05) growth performances for the characteristics performed by analysis of variance. Positive and significant $(p\le0.01)$ phenotypic relations (r) between tree height and diameter at base in terracing (r=.699) and control (r=.559) treatments, and also pooled treatments (r=.314).

Present case study was carried out by one year data and limited area. New studies should be carried out by different characteristics such as survival, diameter at breast height, and locations to give accurate conclusions.

Keywords: Diameter, Forest, Height, Soil, Survival.

INTRODUCTION

Taurus cedar also known Cedar of Lebanon (*Cedrus libani* A. Rich.) is used plantation forestry widely (Ayan *et al.*, 2017) because of social-cultural importance and commercial wood product of the species, although limited natural distribution (0.4 million ha) in Taurus mountains at southern Turkiye (OGM, 2022). Many biotic and a-biotic factors such as climatic, edaphic and geographic characteristics and treatments such as soil treatment/soil preparation or its different methods, watering, fertilization could play important roles in success of the plantation forestry practices.

In this case study, plantation areas prepared by terracing and control (mean un-preparation in the paper) were compared by tree height and diameter at base to contribute plantation forestry of the species.

MATERIAL AND METHODS

Two plantation areas of Taurus cedar were sampled soil preparation by terracing and control (mean un-preparation) treatments established at Isparta district from southern part of Turkiye in 2008 (Table 1, Figure 1). The plantations were close to each other. We assumed climatic and epahic conditions, provenance of the seedlings, seedling type and planting foresters were similar in the areas.

Table 1. Some details of the plantation areas.

Treatments	Latitude Longitude		Altitude	Slope	Aspect	Spacing
	(N)	(E)	(m)	(%)		(m)
Terracing	37°51′647″	30°29′2932″	1122	25-30	West	3x1.5
Control	37°51′818″	30°28′792″	1062	30-35	South	2x1.5





Fig. 1. Terracing (left side) and control areas.

Growth data (Tree height-**TH** and diameter at base- \mathbf{D}_0) was collected from 35 individual trees sampled randomly from each treatment at end of growth period of 2022.

The treatments were compared for the tree height and diameter at base by following linear ANOVA model at SPSS (SPSS, 2011):

$$Y_{ij} = \mu + P_i + e_{ij} \tag{1}$$

Where Y_{ij} is the observation from the j^{th} tree of the i^{th} treatment, μ is overall mean, P_i is the random effect of the i^{th} treatment, and e_{ij} is random error.

Tree height and diameter at base was related by Pearson's phenotypic correlation analysis at SPSS (SPSS, 2011).

RESULTS AND DISCUSSION

Terracing preparation had higher tree height (211.6 cm) performance than control treatment (178.9 cm), while control treatment (7.73 cm) showed higher diameter at base performance than terracing treatment (6.46 cm) (Table 2, Figure 2). It could be said that annual increments were 0.15 m for TH and 0.0046 m for D_0 in terracing, while they were 0.12 m and 0.0046 m in control, respectively (Table 2). Averages of tree height and diameter at base were found 9.0 m and 0.27 m in 30 years plantation of the species at southern Turkiye (Kartal and Bilir, 2022). They were reported 3.55 m and 9.05 cm in 15 years plantations established by terracing by Yazıcı and Bilir (2023). Averages of tree height and diameter at base were reported 2.01 m and 0.32 m in 9 years common plantation of the species (Bilir, 2004). However there could be many biotic and a-biotic factors such as climatic, edaphic and geographic characteristics could be effective on the performances. For instance, significant

effect of soil preparation or soil properties on growth performance of afforestation practices was reported by Göl and Yel (2016) and Yazıcı and Turan (2016). The results emphasized importance of location and plantation practices, and evaluation of age of plantations. Averages of tree height and diameter at base were found 43 cm, 116 cm and 201 cm for tree height; 10.7 mm, 22.0 mm and 32.3 mm for diameter at base in a plantation of the species at 3, 6 and 9 years (Bilir, 2004). Boydak (1996) emphasized importance of age in growth performance of the species.

Tree height had higher variation than diameter based on coefficient of variation in both treatments. It was found 17.6% for tree height and 11.4% for diameter at base for pooled treatments (Table 2). The result could be used in forestry practices such as forest tending in the species.

Control Terracing Total TH (cm) TH (cm) TH (cm) \mathbf{D}_{0} (cm) \mathbf{D}_0 (cm) \mathbf{D}_0 (cm) 211.6 5.73 178.9 6.46 195.3 6.09 Averages Ranges 135-310 3.90-7.45 135-245 4.47-8.34 135-310 3.90-8.34 CV% 14.8 11.4 16.0 15.2 17.6 11.4

Table 2. Averages, ranges and coefficient of variation (CV) for the characteristics.

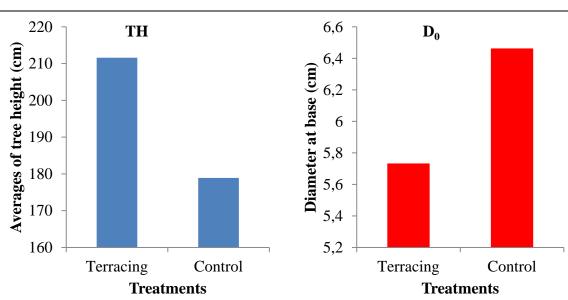


Fig. 2. Averages of the characteristics.

Individual growth performances were varied between 135 cm and 310 cm for TH, and between and 3.90 cm and 7.45 cm for D_0 in terracing and ranged from 135 cm to 245 cm for TH, and ranged 4.47 cm to 8.34 cm for D_0 in control (Table 2, Figure 3). It could be a guide for future practices such as forest tending. Similar individual variations were also found for the characteristics in the species (i.e., Bilir, 2004; Özel, 2018; Kartal and Bilir, 2022; Yazıcı

and Bilir, 2023). It indicated large genetic diversity in the species, and importance of selection in forestry practices. The results showed importance of seed sources and individuals in seed source for seed harvesting.

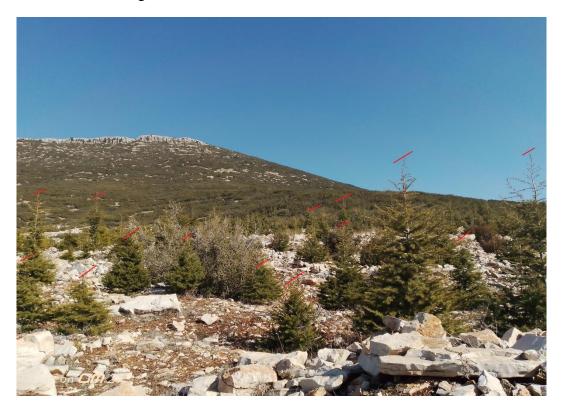


Fig. 3. Individual height variation in terracing.

Terracing and control showed similar (p>0.05) growth performances for the characteristics based on results of analysis of variance (Table 3). However, the case study was carried out by limited data collected from two areas.

Table 3. Results of analysis of variance for the characteristics of the species.

variation	df	Mean Square	F	P value
Between Groups	2	34	1011.246	.751
Within Groups	87	35	1346.371	
Total	89	69		
Between Groups	2	34	.590	.617
Within Groups	87	35	.955	
Total	89	69		
	Between Groups Within Groups Total Between Groups Within Groups	Between Groups Within Groups Total Between Groups Within Groups 47	Between 2 34 Within 87 35 Total 89 69 Between 2 34 Within Groups 2 34 Within 87 35	Between Groups 2 34 1011.246 Within Groups 87 35 1346.371 Total 89 69 Between Groups 2 34 .590 Within Groups 87 35 .955

There were positive and significant ($p \le 0.01$) phenotypic relations (r) between tree height and diameter at base in terracing (r=.699) and control (r=.559) (Figure 4). Similar results were also reported in early studies of the species (i.e., Bilir, 2004; Özel, 2018; Ertugrul and Bilir, 2020; Kartal and Bilir, 2022; Yazıcı and Bilir, 2023). The results could be used for future studies in the species.

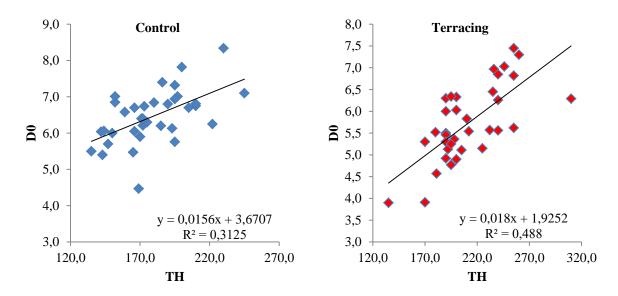


Fig. 4. Relations between tree height and diameter at base in treatments.

CONLCUSIONS

Results of the study could be used in forestry practices. However, the present case study was carried out by one year data and limited area of Taurus cedar. New studies should be carried out by different characteristics such as survival, number of branches, diameter at breast height, and locations of different species to give accurate conclusions.

REFERENCES

Ayan, S., Yer, E.N., Gulseven, O. (2017). Evaluation of Taurus cedar (*Cedrus libani* A. Rich.) afforestation areas in Turkey in terms of climate type. *Journal of Forestry Faculty of Artvin Coruh University*, 18:152-161.

Bilir, N. (2004). Phenotypic age-age correlations for height, diameter and volume in *Cedrus libani* A. Rich. *Journal of Forestry Faculty of Suleyman Demirel University*, A(1):12-18.

Boydak, M. (1996). Ecology, silviculture and conservation of Taurus cedar (*Cedrus libani* A. Rich.). Ministry of Forestry press, No:12, Ankara.

- Ertuğrul, G.S., Bilir N. (2020). Evaluation on natural regenerations in Kütahya-Simav district of Anatolian black pine. *Artvin Coruh University Journal of Forestry Faculty*, 21(1), 75-81.
- Göl, C., Yel, S. (2016). Assessing the effects of different soil preparation methods on sampling growth in afforestation studies. *Turkish Journal of Forestry*, 17(2): 125-131.
- Kartal, R., Bilir, N. (2022). Evaluation of Ehrami black pine plantations in Isparta district: 30th year results. *Bartın University International Journal of Natural and Applied Sciences*, 5:10-17.
- OGM. (2022). Forestry Statistics-2021. www.ogm.gov.tr. Turkiye, Ankara (Date of access: 15.07.2022).
- Özel, S. (2018). Silvicultural evaluation of plantations in Isparta-Yalvaç district. Graduate School of Natural and Applied Science, Suleyman Demirel University, PhD. Thesis, Isparta.
- SPSS. (2011). IBM SPSS Statistics for Windows, Version 20.0., NY: IBM Corp.
- Yazıcı, N., Bilir, N. (2023). Growth variation in forest tree species in afforestation of gradoni terracing. 4th Latin American Scientific Research Congresses, Rio de Janeiro, 13-15 March, (in press).
- Yazıcı, N., Turan, A. (2016). Effect of forestry afforestation on some soil properties: A case study from Turkey. *Fresenius Environmental Bulletin*, 25(7): 2509-2513.

GROWTH VARIATION IN FOREST TREE SPECIES IN AFFORESTATION OF GRADONI TERRACING

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ABSTRACT

The study was carried out to contribute forestry practices in an afforestation area established by gradoni terracing of Taurus cedar also called Cedar of Lebanon (*Cedrus libani* A.Rich.), Anatolian black pine [*Pinus nigra* Arnold. subsp. *pallasiana* (Lamb.) Holmboe] and Crimean juniper (*Juniperus excelsa* M. Bieb. *excelsa*) in southern part of Turkiye in 2007. The species *C. libani* (0.4 million ha), *P. nigra* (4.3) and *J. excelsa* (1.5) occupy at 6.2 million ha which of 26.8% total forest area of Turkiye. However, 42% of total forest area of Turkiye is unproductive or also called degraded forest. It was 25% in *C. libani*, 33% in *P. nigra* and 73% in *J. excelsa*. Afforestation practices included many stages is main tool in conversion of degraded forest to productive forest.

Tree height and diameter at base were measured in thirty individuals chosen randomly in each species at end of growth period of 2022. The species were compared by linear model of analysis of variance for the characteristics. Tree height and diameter at base were related by correlation analysis for each species.

Anatolian black pine had the highest diameter at base (11.96 cm), while tree height was the highest in Taurus cedar (3.55 m). There were also large differences among individuals within species for the characteristics. Individual tree heights were ranged from 1.95 m to 5.50 m in *C. libani*, from 1.87 to 4.05 in *P. nigra*, from 1.85 to 3.24 in *J. excels*, while, diameter at base varied between 1.95 and 5.20 cm in *C. libani*, between 7.50 and 15.38 cm in *P. nigra*, and between 6.08 and 11.38 cm in *J. excels* for individual trees.

Species showed significant ($p \le 0.01$) differences for tree height and diameter at base according to results of analysis of variance. There were positive and significant ($p \le 0.05$) relations between the characteristics in all the species. According to results of correlation analysis phenotypic correlation coefficients (r_p) were 0.919 in *C. libani*, 0.618 in *P. nigra* and 0.507 in *J. excels*.

Results of the study were discussed based on plantation forestry and other forestry practices in the species.

Keywords: Growth, Plantation, Silviculture, Seedling, Variation.

INTRODUCTION

Taurus cedar also called Cedar of Lebanon (*Cedrus libani* A.Rich.), Anatolian black pine [*Pinus nigra* Arnold. subsp. *pallasiana* (Lamb.) Holmboe] and Crimean juniper (*Juniperus excelsa* M. Bieb. *excelsa*) are important forest tree species because of their large natural distributions in different ecological conditions. They cover 26.8% total forest area which is 23.1 million ha of Turkiye. However, about 42% of the species and Turkey are degraded/unproductive forest area (Table 1, OGM, 2022).

Table 1. Forest area of the species and Turkey

Species	Productive (ha)	Degraded (ha)	Total (million ha)
C. libani	0.3 (75%)	0.1 (25%)	0.4
P. nigra	2.9 (67%)	1.4 (33%)	4.3
J. excelsa	0.4 (27%)	1.1 (73%)	1.5
Turkey	13.5 (52%)	9.6 (42%)	23.1

Afforestation practices are main tools in conversion of degraded forest to productive forest. The practices are many stages from seed collection, seedling production, planting, soil preparation to forest tending. Soil preparation has play important role in successful afforestation. For instance, Göl and Yel (2016) indicated importance of soil preparation method in Anatolian black pine plantation. Gradoni terracing is one of the soil preparation methods in afforestation practices. It could be also seen as an environmental factor in the practices. In this study, growth variation in three tree species in an afforestation established by gradoni terracing were examined based on tree height and diameter at base to contribute afforestation and other forestry practices of the species.

MATERIAL AND METHODS

Tree height (TH), diameter at base (D_0) data was collected from a afforestation area (37°52'930" N latitude, 30°30'157" E Longitude, 968 m asl.) established by gradoni terracing soil preparing method in southern part of Turkiye in 2007 (Figure 1).

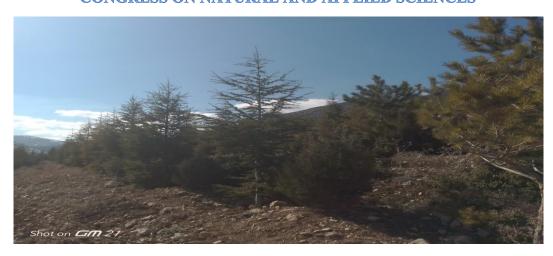


Fig. 1. Studied afforestation area

Thirty individuals of Taurus cedar, Anatolian black pine and Crimean juniper were sampled randomly from each species at the same area to collect tree height (**TH**) and diameter at base ($\mathbf{D_0}$) data at end of growth period of 2022.

Collected data was performed by one-way analysis of variance to compare the species for the characteristics at SPSS (SPSS, 2011).

Phenotypic correlations (r_p) between tree height (TH) and diameter at base in the species were estimated by (Falconer (1989).

RESULTS AND DISCUSSION

Averages, ranges and standard deviation of tree height and diameter at base for the species were given in Table 2. Average of diameter at base was the highest in Anatolian black pine (*Pinus nigra*) (11.96 cm), while tree height was the highest in Taurus cedar (*Cedrus libani*) (3.55 m) (Table 2, Figure 2).

Table 2. Averages, minimum, maximum and standard deviation for the characteristics in the species.

	C. libani		P. nigra		J. excelsa	
	TH (m)*	D_0 (cm)	$\mathbf{TH}(\mathbf{m})$	$D_0 (\text{cm})$	TH(m)	$D_0 (\text{cm})$
Averages	3.55°	9.05a	2.73 ^b	11.96 ^b	2.32 ^a	8.31a
Minimum	1.95	5.96	1.87	7.50	1.85	6.08
Maximum	5.50	15.33	4.05	15.38	3.25	11.38
St. deviation	2.36	.91	.60	2.59	.38	1.33

^{*;} Same letters are not significantly (p>0.01) different among the species.

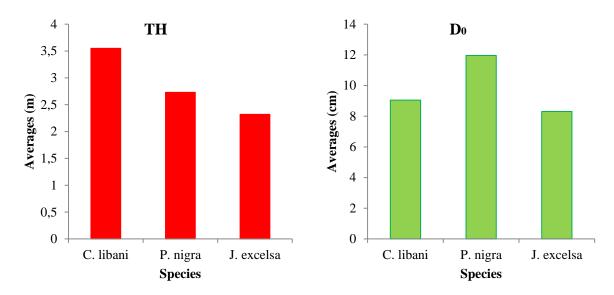


Fig. 2. Averages of the characteristics for the species

Averages were 9 m in *C. libani* and 12.3 m in *P. nigra* of tree height, and 27.2 cm in *C. libani* and 40.9 cm in *P. nigra* of diameter at base in an afforestation area from southern Turkiye (Kartal and Bilir, 2022). Annual increments of *C. libani*, *P. nigra* and *J. excelsa* were 0.24 m, 0.18 m and 0.15 m for tree height, and 0.30 cm, 0.80 cm and 0.55 cm in the species, respectively (Table 2). The increments of *C. libani* and *P. nigra* were reported 0.30 m and 0.41 m for tree height, and 0.91 cm and 1.36 cm for diameter at base in the species in a thirty year afforestation, respectively (Kartal and Bilir, 2022). Similar higher performances of *P. nigra* to *C. libani* were also reported by Özel (2018). The results indicated importance of species, location and age in afforestation practices.

Individual trees showed also large differences within species for the characteristics. Individual tree heights were ranged from 1.95 m to 5.50 m in *C. libani*, from 1.87 to 4.05 in *P. nigra*, and from 1.85 to 3.24 in *J. excelsa*. It was between 1.95 and 5.20 cm in *C. libani*, between 7.50 and 15.38 cm in *P. nigra*, and between 6.08 and 11.38 cm in *J. excels* for diameter at base (Table 2, Figure 3). Similar variations among individuals were also found for tree height and diameter at base in *C. libani* and *P. nigra* (Kartal and Bilir, 2022; Özel, 2018), and reproductions of *P. nigra* (Ertugrul and Bilir, 2020).

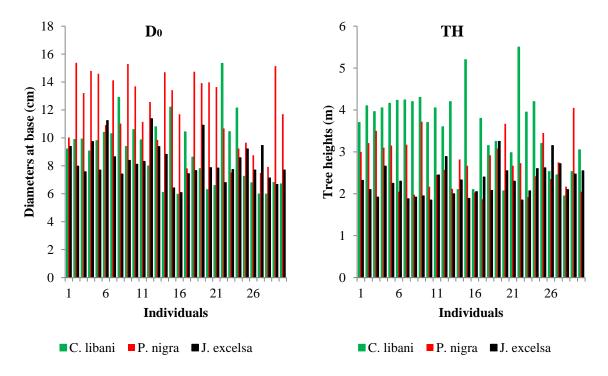


Fig. 3. Individual tree height and diameter at base in the species

According to results of analysis of variance showed significant ($p \le 0.01$) differences among the species for tree height and diameter at base (Table3). The results were well accordance between *C. libani* and *P. nigra* for tree height and diameter at base in (Kartal and Bilir, 2022; Özel, 2018). The species were more homogenous for diameter at base than tree height according to Duncan's multiple range' test (Duncan, 1955) (Table 2). The results emphasized importance of tree species and characteristics in afforestation and forestry practices.

Table 3. Results of analysis of variance for the characteristics of the species

Characteristics	Source of variation	df	Mean Square	F	P value
\mathbf{D}_0	Between Groups	2	111.378	23.815	.000
	Within Groups	87	4.677		
	Total	89			
TH	Between Groups	2	11.851	26.663	.000
	Within Groups	87	.444		
	Total	89			

Positive and significant ($p \le 0.05$) phenotypic relations between tree height and diameter at base in *C. libani* ($r_p = .919$), *P. nigra* ($r_p = .618$) and *J. excelsa* ($r_p = .507$) according to results of correlation analysis (Figure 4). Similar findings were reported in plantation areas of *C. libani* and *P. nigra* (Kartal and Bilir, 2022; Özel, 2018), and reproductions of *P. nigra* (Ertugrul and Bilir, 2020). The results could be used forestry practices such as forest tending, and future studies in the species.

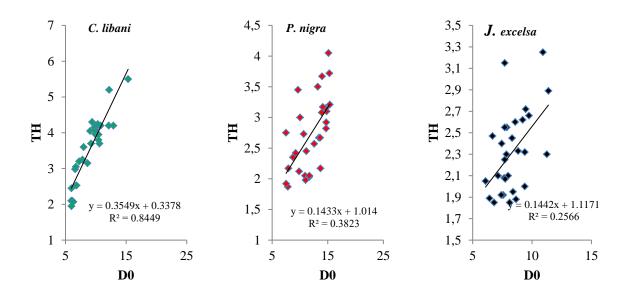


Fig. 4. Relations between tree height and diameter at base in the species

CONLCUSIONS

Results of the study showed importance of selection of tree species in afforestation practices. Relations between the characteristics could be a tool for future studies in the species. The study was carried out in an afforestation area of the species by one year data and limited characteristics. Future studies could be carried out in different locations, species, soil preparation methods, and characteristics such as survival.

REFERENCES

Duncan, DB. (1955) Multiple range and multiple F-test. *Biometrics*, 11,1-5.

Ertuğrul, G.S., Bilir N. (2020). Evaluation on natural regenerations in Kütahya-Simav district of Anatolian black pine. *Artvin Coruh University Journal of Forestry Faculty*, 21(1), 75-81.

Falconer, D.S. (1989). Introduction to Quantitative Genetics. 3rd Edition, Longman Scientific and Technical, New York.

Göl, C., Yel, S. (2016). Assessing the effects of different soil preparation methods on sampling growth in afforestation studies. *Turkish Journal of Forestry*, 17(2): 125-131.

- Kartal, R., Bilir, N. (2022). Evaluation of Ehrami black pine plantations in Isparta district: 30th year results. *Bartın University International Journal of Natural and Applied Sciences*, 5:10-17.
- OGM. (2022). Forestry Statistics-2021. www.ogm.gov.tr. Turkiye, Ankara (Date of access: 15.07.2022).
- Özel, S. (2018). Silvicultural evaluation of plantations in Isparta-Yalvaç district. Graduate School of Natural and Applied Science, Suleyman Demirel University, PhD. Thesis, Isparta.
- SPSS. (2011). IBM SPSS Statistics for Windows, Version 20.0., NY: IBM Corp.

ARONIA AND ANTHOCYANINS

ARONYA VE ANTOSİYANİNLER

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ÖZET

Antosiyaninler, bitkiler alemindeki en yaygın doğal pigmentlerden biridir. Bitkisel besinlerin kırmızıdan mora kadar değişen renklerinden sorumlu olan ve insan sağlığına olumlu etkisi olan suda çözünür pigmentlerdir. pH ve sıcaklık değişimlerine karşı çok hassastırlar. Antosiyaninler, polifenoller grubuna ait flavonoid maddelerdir. Çoğu meyve, sebze ve çeşitli içeceklerde (meyve suyu, bira, şarap ve kahve) yaklaşık 7.000 farklı flavonoid bulunur. Her bitki türü, kırmızıdan maviye bir dizi renk sergileyen, dolayısıyla meyve ve sebzelerin renklerini taşıyan karakteristik bir antosiyanin pigmentine sahiptir. Antosiyaninler doğada Oglikozitler seklinde bulunurlar, bunların aglikonlarına (sakkarit olmayan kısım) antosiyanidinler denir. En yaygın antosiyanidinler, siyanidin, delfinidin, peonidin, malvidin, pelargonidin ve petunidindir. Antosiyaninlerin insan sağlığı üzerindeki yararlı etkileri 16. yüzyıldan beri bilinmektedir. Antosiyaninler, antiinflamatuar, antikanser, antimikrobiyal, antiobezite ve antidiyabetik etkilerinin yanı sıra kardiyovasküler hastalıklar üzerinde koruyucu etkilere sahiptir. Aronya (Aronia melanocarpa), yüksek fenolik bileşik içeriği, antioksidan özellikleri ve sağlık üzerindeki olumlu etkisi nedeniyle son yıllarda tüketiciler tarafından tercih edilen bir meyve türüdür. Aronia, içindeki antosiyaninler toplam polifenollerin yaklaşık %25'ini oluşturur. Antosiyanin miktarının %64'ünü siyanidin-3-galaktosid ve %29'unu siyanidin-3-arabinosid oluşturmaktadır. Ayrıca, eser miktarda pelargonidin 3-O-galaktozid ve pelargonidin arabinosid tespit edilmiştir. Antosiyaninler ise meyvenin hem kabuğunda hem de etinde bulunmaktadır. Meyvenin olgunlaşma sırasındaki antosiyanin konsantrasyonu, rengi ve görsel çekiciliği artırır. Bu derlemede aronya meyvesinindeki antosiyaninler ve sağlık üzerine olan etkilerine ilişkin araştırma sonuçları sunulmuştur.

Anahtar Kelimeler: Aronya, Polifenol, Sağlık

ABSTRACT

One of the most prevalent naturally occurring pigments in the plant kingdom is anthocyanin.

These are water-soluble pigments that give plant meals their colors, which range from red to

purple, and they are beneficial to human health. They are extremely sensitive to changes in

temperature and pH. Anthocyanins are flavonoid compounds that fall under the category of

polyphenols. Most fruits, vegetables, and diverse drinks include one of the approximately

7,000 distinct flavonoids (e.g., juice, beer, wine, and coffee). Each plant species has a

distinctive anthocyanin pigment that displays a spectrum of colors from red to blue, giving

fruits and vegetables their distinct hues. In nature, anthocyanins appear as O-glycosides; their

aglycones (non-saccharide parts) are known as anthocyanidins. Cyanidine, delphinidine,

peonidine, malvidine, pelargonidine, and petunidine are the most prevalent anthocyanidins.

Since the 16th century, anthocyanins have been associated with improved human health. Due

to its high phenolic component content, antioxidant qualities, and advantageous effects on

health, aronia (Aronia melanocarpa) has become a popular fruit type in recent years. Aronia

contains roughly 25% of the total amount of polyphenols in anthocyanins. Cyanidin-3-

galactoside makes up 64% of the anthocyanin content, whereas cyanidin-3-arabinoside makes

up 29%. Furthermore, pelargonidin 3-O-galactoside and pelargonidin arabinoside in trace

levels were found. The fruit's surface and flesh are both covered in anthocyanins. Fruit's

anthocyanin concentration grows as it ripens, giving it more color and aesthetic appeal.

Research findings on the anthocyanins in aronia fruit and their impact on health are discussed

in this review.

Key Words: Aronia, Polyphenols, Health

73

EVALUTION OF ATOMIC PROPERTIES FOR LI-LIKE IONS SYSTEMS USING HARTREE-FOCK AND CONFIGURATION INTERACTION METHODS

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ABSTRACT

In this study, we investigated the effect of electron correlation for three-electrons systems ,on the K-shell , $KL(^1S)$ -shells (singlet states) and $KL(^3S)$ -shells (triplet states) in the ground state of Li-like ions (Li atom, Be $^+$ ion, B $^{+2}$ ion, and C $^{+3}$ ion). Among the atomic properties, are the inter-particle distribution function $f(r_{12})$ for the Hartree-Fock (HF) and configuration interaction (CI) wave function approximations. The one-particle radial density distribution function D(r) expected values for the two techniques and ($< r_1^n >$, $< r_{12}^n >$) where n is an integer number from -2 to 2, the standard deviation Δr_i and Δr_{12} . The properties of the energies expectation values, repulsion potential energy < Vee >, attractive potential energy < Ven >, total potential energy <V>, kinetic energy <T> and total energy <E>. In conclusion increasing the atomic number leads to an increase in all studied

energies by increasing the amount of ionization of the studied elements with both

approximations, and it was found that the CI is the closest to the practical values, because it

takes into account the neglected electronic bonding by the HF method. Finally, the equations

have been programmed in Mathematics 2015 and all calculations have been calculated in

atomic units.

Keywords: singlet states, triplet states, repulsion, Hartree, Mathematic

75

DESIGN AND MODEL OF AN INDUCTIVE WIRELESS POWER TRANSFER SYSTEM FOR ELECTRIC VEHICLES

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ABSTRACT

Wireless power transfer (WPT) systems has become very important in recent years. WPT is used in many areas. In this study, an inductive wireless power transfer (IWPT) system was designed for electric vehicles. The shape of the primary and secondary coils is circular and their radius is 25 cm. The operating frequency of the system is 20 KHz and the applied voltage is 100 volts. The effect of the distance between the primary and secondary coils on the efficiency of the system was investigated by generating a 3D Maxwell model of the system. The distance between the primary and secondary coils was modified as 10, 15, 20 and 25 cm and the coupling coefficient, mutual inductance, input power, output power and efficiency of the system were investigated in each case. As a result, it was observed that the coupling coefficient, the common inductance, and the efficiency of the system are inversely proportional with the distance between the coils. When the distance between the coils was 10 cm, the efficiency of the system was 84.21%. As the distance between the coils increases, the system efficiency decreases and when the distance between the coils is 25 cm, the system efficiency becomes 71.07%.

Keywords: Wireless power transfer, contactless power transfer, inductive power transfer.

ELECTRICAL AND STRUCTURAL CHARACTERIZATION OF PBS THIN FILMS PRODUCED BY SPRAY METHOD

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ABSTRACT

Lead sulfide is a semiconductor materiel used in diverse executions. They exhibit excellent special features for diverse executions such as LEDs, IR detectors and lasers, solar energy frameworks, optical fibers, window coverings through to the selective sensitivity of Pb⁺² ions. Owing to the wide exciton and effective Bohr radius (18 nm) of cubic crystalline PbS, its absorption from the infrared (IR) to the visible region is quite effective. Due to the quantum limitations of the carriers, it has also strengthened the non-linear optical feature, which can be used as an optical code in optical equipments.

In this research, PbS films were turned out on glass substrates heated at 150 °C using the spray method. Depending on the 1, 2 and 3 spray numbers of the films, the grain sizes, dislocation intensites, crystallization numbers per unit area and lattice strains were found to be 16.57 nm, 14.66 nm, 13.73 nm; 3.64×10^{-3} line/nm², 4.65×10^{-3} line/nm², 5.30×10^{-3} line/nm²; 18.66×10^{-2} (1/nm²), 80.01×10^{-2} (1/nm²), 114.30×10^{-2} (1/nm²); 7.91×10^{-3} , 9.52×10^{-3} and 9.21×10^{-3} , respectively. The electrical resistivity values were calculated with the four-point probe method. Depending on the number of 1, 2 and 3 sprays, the electrical resistivity values were calculated as 8.20×10^{-6} Ω cm, 4.20×10^{-6} Ω cm and 2.48×10^{-6} Ω cm, respectively.

Keywords: PbS, Thin film, spray method, electrical resistivity, lattice strain, grain size, dislocation density

INTRODUCTION

If electronic and optoelectronic devices have perfect crystal structures, their performance is also quite good (Yücel & Yücel, 2022; Pawar et al., 2011). However, the growth of crystals requires a complicated production operate with up procurement expenditures due to ultravacuum technologies such as MOCVD and MBE (Brahlek et al., 2018; Qin et al., 2022). On the other hand, semiconductor thin films synthesized with falling expenditure, facile and industrial scale production have significant advantages (Jung et al., 2015; Qin et al., 2022). However, due to a large scale of irregularly structured states such as grain boundary defects, they usually occur in polycrystalline structures (Hirth, 1974; Choi et al., 2009). Eventually, the far-scale array and periodic potential zone of polycrystalline thin films seriously impair photonic and electrical properties (Najmaei et al., 2014). It is therefore important to understand purposeful scholarly and tech problems on how to enhance crystal grade to achieve brilliant electronic and optoelectronic properties.

Colloidal PbS quantum dots (Ellingson et al., 2005) have majority carriers due to sufficient multi-exciton generation and high state density (Nair et al., 2008; Pijpers et al., 2009). With its striking photonic and optoelectronic special features such as direct narrow band structure (0.4 eV) (Wu et al., 2019; Miller et al., 2016), PbS is very interesting as a short wave infrared semiconductor at room temperature. In addition, it has technological importance in many areas such as infrared detectors (Liu et al., 2009; Kim et al., 2020), solar cells (Günes et al., 2007; Zhao et al., 2010), gas sensors (Fu, 2009), diode lasers Ralston et al., 1974). Latterly, PbS thin films have been put out by diverse practices incorporating chemical bath deposition and sequential ionic thickness suction and reactions (Patil et al., 2006; Puišo et al., 2003; Preobrajenski & Chasse, 1999). However, electronic conduction attributions of thin films in chemical synthesis technics deteriorate due to inappropriate chemical pollution from organic reagents. However, despite single-crystalline PbS thin films have been prospered with MBE Preobrajenski & Chasse, 1999), they are quite expensive and complex. In addition, PbS thin films can be produced with distinct production mechanisms such as chemical bath deposition (CBD) (Bai et al., 2017; Liu et al., 2019), spray pyrolysis (Salah et al., 2005; Sarica & Bilgin, 2017), electrodeposition (Ikhioya et al., 2018), evaporation (Cheragizade et al., 2014), sputtering (Guozheng et al., 2014). Therefore, low-cost, clean and convenient synthesis technologies for preparing PbS thin films with high crystal quality remain fascinating.

In this work, PbS films were fabricated on glass substrates heated at 150 °C using the spray method. Depending on the 1, 2 and 3 spray numbers of the films, the grain sizes, dislocation densities, crystallization numbers per unit area, lattice strains and electrical resistivity values were investigated.

EXPERIMENTAL PROCEDURE

In 2 separate beakers, 1.044 g of PbNO₃ and 0.648 g of NaOH were dissolved in 10 ml of distilled water for 10 minutes with the help of a magnetic stirrer. Then, the contents of these two beakers were mixed in a 50 ml beaker and the blend was allowed to become homogeneous for 10 minutes. Again in a separate beaker, 0.73 g of thiourea was dissolved in 10 ml of distilled water with a magnetic stirrer for 10 minutes and added to the solution in a 50 ml beaker. The solution was stirred on a magnetic stirrer for about 10 min until the colorway of the dissolution changed to dark gray. When the glass substrates placed on the heater are at 150 °C, The films were deposited with air gas by adjusting to be 10 cm the length between the substrate and the nozzle at a right angle to the surface for spraying amount of 1, 2 and 3. In this method, parameters such as the temperature of the substrate, the amount of spraying and the thickness of the film affect the quality of the film.

The structured qualities of the PbS thin films were explored by XRD and the surface morphologies were analyzed by FESEM. The thickness of the films was evaluated with the Mitutoya Surftest Ver2.00 device. Electrical resistivity values were computed from current-voltage (I-V) estimates in the range of -0.3 to 0.7 volts with Keithley 2400 sourcemeter and Keithley 2100/220 Multimeter in dark environment at room temperature by taking 1 mm between contacts.

RESULTS AND DISCUSSION

XRD diffraction figures of PbS thin films for spray amount 1, 2 and 3 are given in Figure 1. Since it is sprayed with air gas, there is also a low-intensity PbSO₄ structure inside the structure. The strongest peak is observed at 30.17° (2 0 0) (PDF Card No.: 00-002-0699) in the cubic structured orientation. Average grain sizes (D) were calculated over the strongest peak with Scherrer's equation (Eq.1).

$$D = \frac{0.9\lambda}{\beta \cos \theta} \tag{1}$$

Where λ , θ , β are the wavelength of used X-ray, Bragg angle and angular line width at half-maximum intensity in radians, respectively. The dislocation density (δ) was calculated by (Eq.2).

$$\delta = \frac{1}{D^2} \tag{2}$$

The number of crystals per unit area (N) is obtained by using (Eq.3).

$$N = \frac{t}{D^3} \tag{3}$$

where t represents the thickness of the film.

Lattice Strain (ε) is calculated with (Eq.4).

$$\varepsilon = \frac{\beta \cot \theta}{4} \tag{4}$$

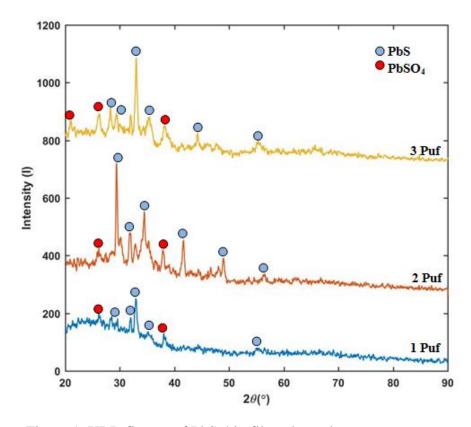


Figure 1. XRD figures of PbS thin films depend on spray amount.

Depending on the 1, 2 and 3 spray numbers of the films, the grain sizes, dislocation intensties, crystallization numbers per unit area and lattice strains were ascertained to be 16.57 nm, 14.66 nm, 13.73 nm; 3.64x10⁻³ line/nm², 4.65x10⁻³ line/nm², 5.30x10⁻³ line/nm²; 18.66x10⁻² (1/nm²), 80.01x10⁻² (1/nm²), 114.30x10⁻² (1/nm²); 7.91x10⁻³, 9.52 x10⁻³ and 9.21 x10⁻³, respectively. The values obtained in this study are quite compatible with the PbS thin films fabricated by the spray pyrolysis tech by Chandekar et al. (Chandekar et al., 2022).

Depending on the 1, 2 and 3 spray numbers of the films, FESEM images are given in Figure 2. Accordingly, the films for 1 and 2 sprays show a very dense and homogeneous surface morphology. For 3 spray, the dislocation density increased and gaps were formed in places.

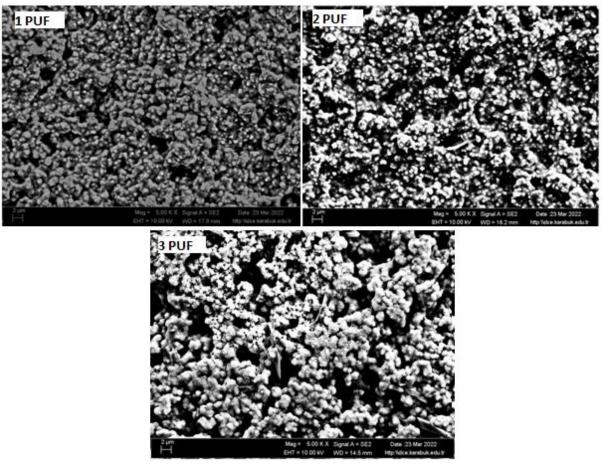


Figure 2. FESEM images of PbS thin films.

The electrical resistivity values were obtained with the four-point probe method and (Eq. 5).

$$\rho = \frac{\pi t}{\ln 2} (\frac{V}{I}) \tag{5}$$

Here, V, I and t demonstrate the potential difference, current and film thickness, respectively. In order to calculate the electrical resistivity values, the film thicknesses's were computed with the Mitutoya Surftest Ver2.00 device. The film thicknesses were measured as 849 nm, 2521 nm and 2960 nm for 1, 2 and 3 sprays, respectively. As the number of sprays increased, the film thickness also increased, as depicted in Figure 3. The current-voltage (I-V) graphs of the films are given in Figure 4. Depending on the number of 1, 2 and 3 sprays, and the

electrical resistivity valueswere calculated as $8.20 \times 10^{-6}~\Omega$ cm, $4.20~\times 10^{-6}~\Omega$ cm and $2.48~\times 10^{-6}~\Omega$ cm, respectively. As the film thickness increases, the electrical resistivity values decrease and the electrical conductivity increases.

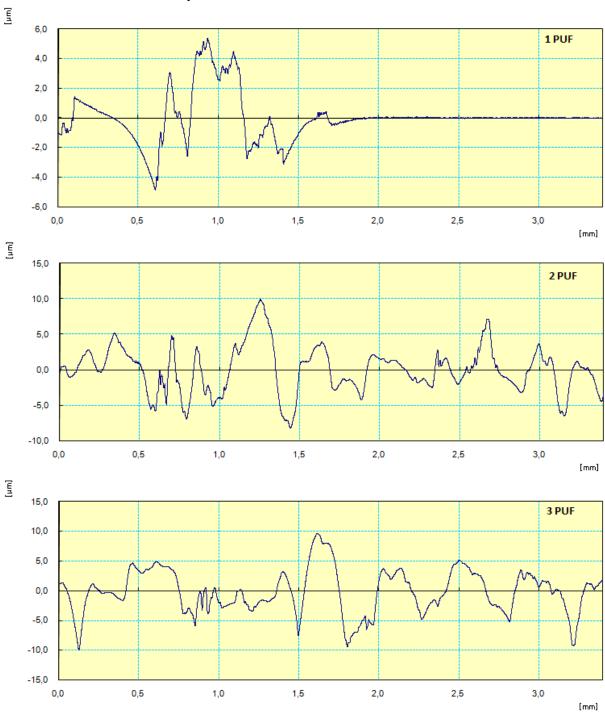


Figure 3. Film thicknesses of PbS thin films for 1, 2 and 3 sprays.

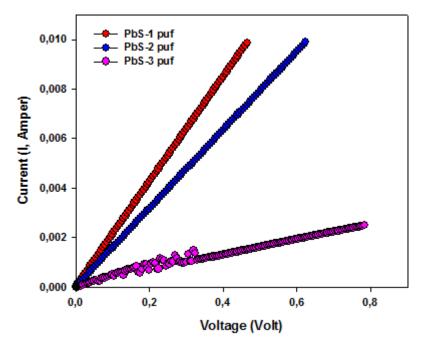


Figure 4. I-V curves of PbS thin films for 1, 2 and 3 sprays.

CONCLUSION

In this work, PbS thin films were produced depending on the amount of spray. It has been found that the increment in film thickness depending on the topological surfaces of the prepared films affects the structural and electrical properties. Increasing the number of sprays triggered the formation of more disorder structures. These microstructural irregularities led to the excitation of microstrains, resulting in an increase and a decrease in grain size. With the increase of film thickness, it showed typical semiconductor properties and its electrical conductivity increased. The increase in electrical conductivity with film thicknesses contributed little to the scattering of carriers from the surface and grain boundaries of the film. The resulting PbS thin films can be used in solar energy collectors, selective surface devices, IR and near-IR detectors, and optoelectronic devices.

REFERENCES

Bai, R., Kumar, D., Chaudhary, S., & Pandya, D. K. (2017). Highly crystalline p-PbS thin films with tunable optical and hole transport parameters by chemical bath deposition. Acta Materialia, 131, 11-21.

Brahlek, M., Gupta, A. S., Lapano, J., Roth, J., Zhang, H. T., Zhang, L., ... & Engel-Herbert, R. (2018). Frontiers in the growth of complex oxide thin films: past, present, and future of hybrid MBE. Advanced Functional Materials, 28(9), 1702772.

Chandekar, K. V., Alkallas, F. H., Trabelsi, A. B. G., Shkir, M., Hakami, J., Khan, A., ... & AlFaify, S. (2022). Improved linear and nonlinear optical properties of PbS thin films synthesized by spray pyrolysis technique for optoelectronics: An effect of Gd3+ doping concentrations. Physica B: Condensed Matter, 641, 414099.

- Cheragizade, M., Yousefi, R., Jamali-Sheini, F., Mahmoudian, M. R., Sa, A., & Huang, N. M. (2014). Synthesis and characterization of PbS mesostructures as an IR detector grown by hydrogen-assisted thermal evaporation. Materials science in semiconductor processing, 26, 704-709.
- Choi, J., Jeong, H. K., Snyder, M. A., Stoeger, J. A., Masel, R. I., & Tsapatsis, M. (2009). Grain boundary defect elimination in a zeolite membrane by rapid thermal processing. Science, 325(5940), 590-593.
- Ellingson, R. J., Beard, M. C., Johnson, J. C., Yu, P., Micic, O. I., Nozik, A. J., ... & Efros, A. L. (2005). Highly efficient multiple exciton generation in colloidal PbSe and PbS quantum dots. Nano letters, 5(5), 865-871.
- Fu, T. (2009). Research on gas-sensing properties of lead sulfide-based sensor for detection of NO2 and NH3 at room temperature. Sensors and Actuators B: Chemical, 140(1), 116-121.
- Guozheng, M., Binshi, X., Haidou, W., Shuying, C., & Zhiguo, X. (2014). Excellent vacuum tribological properties of Pb/PbS film deposited by Rf magnetron sputtering and ion sulfurizing. ACS Applied Materials & Interfaces, 6(1), 532-538.
- Günes, S., Fritz, K. P., Neugebauer, H., Sariciftci, N. S., Kumar, S., & Scholes, G. D. (2007). Hybrid solar cells using PbS nanoparticles. Solar Energy Materials and Solar Cells, 91(5), 420-423.
- Hirth, J. P. (1974). Defect structures in grain boundaries. Acta Metallurgica, 22(8), 1023-1031.
- Ikhioya, I., Ehika, S., & Ijabor, B. (2018). Influence of deposition potential on lead sulphide (PbS) thin film using electrodeposition technique. Asian. J. Chem. Sci.[Online], 3(4), 1-8.
- Jung, C., Kim, S. M., Moon, H., Han, G., Kwon, J., Hong, Y. K., ... & Park, J. (2015). Highly crystalline CVD-grown multilayer MoSe2 thin film transistor for fast photodetector. Scientific reports, 5(1), 15313.
- Kim, J., Ampadu, E. K., Oh, E., Choi, H., Ahn, H. Y., Cho, S. H., ... & Byun, J. Y. (2020). Photocurrent spectra for above and below bandgap energies from photovoltaic PbS infrared detectors with graphene transparent electrodes. Current Applied Physics, 20(3), 445-450.
- Liu, M., Zhan, Q., Li, W., Li, R., He, Q., & Wang, Y. (2019). Effect of Zn doping concentration on optical band gap of PbS thin films. Journal of Alloys and Compounds, 792, 1000-1007.
- Liu, Z., Kim, J. H., Fernandes, G. E., & Xu, J. (2009). Room temperature photocurrent response of PbS/InP heterojunction. Applied Physics Letters, 95(23), 231113.
- Miller, E. M., Kroupa, D. M., Zhang, J., Schulz, P., Marshall, A. R., Kahn, A., ... & Van De Lagemaat, J. (2016). Revisiting the valence and conduction band size dependence of PbS quantum dot thin films. ACS nano, 10(3), 3302-3311.

- Nair, G., Geyer, S. M., Chang, L. Y., & Bawendi, M. G. (2008). Carrier multiplication yields in PbS and PbSe nanocrystals measured by transient photoluminescence. Physical Review B, 78(12), 125325.
- Najmaei, S., Amani, M., Chin, M. L., Liu, Z., Birdwell, A. G., O'Regan, T. P., ... & Lou, J. (2014). Electrical transport properties of polycrystalline monolayer molybdenum disulfide. ACS nano, 8(8), 7930-7937.
- Qin, L., Wu, S., Wang, J. G., Li, Q., Yuan, C., Wang, Z., ... & Wang, Q. (2022). Enhancement of infrared response speed via modulating crystallinity of highly-oriented PbS polycrystalline thin films. Infrared Physics & Technology, 121, 104033.
- Salah, H. B. H., Bouzouita, H., & Rezig, B. (2005). Preparation and characterization of tin sulphide thin films by a spray pyrolysis technique. Thin Solid Films, 480, 439-442.
- Sarica, E., & Bilgin, V. (2017). Effect of Pb: S molar ratio in precursor solution on the properties of lead sulphide thin films by ultrasonic spray pyrolysis. Materials Science in Semiconductor Processing, 71, 42-49.
- Patil, R. S., Pathan, H. M., Gujar, T. P., & Lokhande, C. D. (2006). Characterization of chemically deposited nanocrystalline PbS thin films. Journal of materials science, 41, 5723-5725.
- Pawar, S. M., Pawar, B. S., Kim, J. H., Joo, O. S., & Lokhande, C. D. (2011). Recent status of chemical bath deposited metal chalcogenide and metal oxide thin films. Current Applied Physics, 11(2), 117-161.
- Pijpers, J. J. H., Ulbricht, R., Tielrooij, K. J., Osherov, A., Golan, Y., Delerue, C., ... & Bonn, M. (2009). Assessment of carrier-multiplication efficiency in bulk PbSe and PbS. Nature Physics, 5(11), 811-814.
- Preobrajenski, A. B., & Chasse, T. (1999). Epitaxial growth and interface structure of PbS on InP (110). Applied surface science, 142(1-4), 394-399.
- Puišo, J., Lindroos, S., Tamulevičius, S., Leskelä, M., & Snitka, V. (2003). Growth of ultra thin PbS films by SILAR technique. Thin Solid Films, 428(1-2), 223-226.
- Ralston, R. W., Walpole, J. N., Calawa, A. R., Harman, T. C., & McVittie, J. P. (1974). High cw output power in stripe-geometry PbS diode lasers. Journal of Applied Physics, 45(3), 1323-1325.
- Wu, X., Kim, M., Qu, H., & Wang, Y. (2019). Single-defect spectroscopy in the shortwave infrared. Nature Communications, 10(1), 2672.
- Yücel, E., & Yücel, Y. (2022). Deposition of PbS thin films using a continuous flow reactor: Comparison of the modified technique with conventional methods in the coating of PbS thin film on the substrate. Journal of the Indian Chemical Society, 99(10), 100706.
- Zhao, N., Osedach, T. P., Chang, L. Y., Geyer, S. M., Wanger, D., Binda, M. T., ... & Bulovic, V. (2010). Colloidal PbS quantum dot solar cells with high fill factor. ACS nano, 4(7), 3743-3752.

PbS SUPERCAPACITOR ELECTRODE STRUCTURES

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ABSTRACT

Developments in today's electronics world are directly related with advances in semiconductor material technologies. Electronic circuit elements produced using semiconductors have become a basic need in every aspect of human life. Semiconductor circuit elements are used in communication, medicine, informatics, automotive, transportation, military and many other fields. Systems realized using semiconductor; it has advantages such as being light, small, low error rate, economical and high efficiency.

In this study, PbS thin film electrode systems were obtained depending on the number of sprays on the substrates heated at 150 °C. The surface morphologies of these structures were determined by FESEM, compositional analyzes was determined by EDX mapping, and crystal structures were determined by XRD. Specific capacitance values (Cs) are measured the help of Keithley 2400 sourcemeter and 2100/220 Keithley multimeter using in-plane time-dependent I-V method with 10 mV/s, 25 mV/s, 50 mV/s and 100 mV/s scanning rates in the range of 0 to 1 volts for 1, 2 and 3 sprays. Accordingly, the amount of mass coated for 1, 2 and 3 sprays was weighed as 2.27×10^{-3} g, 13.5×10^{-3} g and 23×10^{-3} g, respectively. It is seen that the Cs valuations decline with increasing scanning rate and the quantity of plating mass. Cs valuations were obtained as 923 F/g, 725 F/g and 524 F/g, respectively, at the least scanning rate 10 mV/s for 1, 2 and 3 times spraying.

Key Words: Lead sulfide, Thin-film, Supercapacitor Electrode, Specific Capacitance

INTRODUCTION

Chalcogenites are materiels including one or more chalcogen elements. It is from the oxygen group in the 16th column of the periodic table. It contains the elements oxygen, sulfur, selenium, tellurium and polonium (O, S, Se, Te and Po). They have 6 valence electrons and are -2 valences (Chopra&Kaur, 1983; George, 1992; Rossnagel, 2003; Pickart, 1970). This group of elements exhibits metal properties as their atomic number scale up. Oxygen and sulfur are nonmetals, selenium and tellurium are metalloids, and polonium is a metal. The bonding distinctives of these elements are latitude to the metal properties. These elements are

covalently bonded materiels and can have amorphose or crystalline structure. They are basic semiconductors with a band gap of 1-2 eV dependant their components. Although chalcogenides have potential disadvantages for some applications, they are potent and have significant advantages for printing structures in fibers. Also, they are glassy semiconductors with interesting electrical properties. Metal chalcogenide semiconductors play an assets role as absorber layer for thin-film photovoltaic equipments, so the scholarly committee is interested in optoelectronic and energy devices because of their multifunctional properties (Putley & Arthur, 1951). Among the IV-VI compound semiconductors, PbS has an FCC cubic rock salt crystal structure. PbS is an essential semiconductor with a direct narrow band structure and a Bohr radius of 18 nm with an energy band gap of about 0.4 eV at 300 K (Smith, 2002; Bunshah, 1994; Ibragimova et al., 2018; Karazhanov et al., 2000). They exhibit striking features making them appropriate for a variety of applications as LEDs, IR detectors and lasers, solar power regulations, optical fibers, window coverings (Ni et al., 2004; Peterson & Krauss, 2006).

Flexibility and size are enabled in design devices for specific applications. This thin-film practice is even more essential in today's solid-state industrial, CDs, disk drives, and optical device industrials. Thin film technology consisting of metal oxides, metal chalcogenides and transition metal oxides is important in semiconductor research fields and coating applications (Sahadevan et al., 2022). Different storage techniques including chemical bath deposition (CBD), spray pyrolysis, electrodeposition, evaporation and sputtering (Uhler & Helz, 1984; Salah et al., 2005; Sharon et al., 1997; Kumar et al., 2003; Martinet al., 1982) have been used to fabricate PbS thin films. In this work, the spray method was used because of its low cost, suitable for large area coatings, low functional temperature and easy usability of the devices.

EXPERIMENTAL SECTION

In 10 ml distilled water, 0.01 Molar PbNO₃ and 0.15 Molar NaOH were dissolved in 2 separate beakers with the help of a magnetic stirrer for 10 minutes. Then, the contents of these two beakers were stirred in a 50 ml beaker and the blend was allowed to become homogeneous for 10 minutes. In a separate beaker, 0.05 Molar thiourea [(NH₂)₂CS] was dissolved in 10 ml of ultra pure water with a magnetic stirrer for 10 minutes and added to the dissolution in the 50 ml beaker. The dissolution was mixed on a magnetic stirrer for approximately 10 min till the color of the dissolution changed to dark gray. When the glass substrates placed on the heater are at 150 °C, The films were deposited with air gas by adjusting to be 10 cm the length between the substrate and the nozzle at a right angle to the surface for spraying amount of 1, 2 and 3.

The surface morphologies of these structures were imaged by FESEM, compositional analyzes was determined by EDX mapping, and crystal structures were obtained by XRD. Specific capacitance values are measured the help of Keithley 2400 sourcemeter and 2100/220 Keithley multimeter using in-plane time-dependent I-V method with 10 mV/s, 25 mV/s, 50 mV/s and 100 mV/s scanning rates in the range of 0 to 1 volts for 1, 2 and 3 sprays.

RESULTS AND DISCUSSION

Depending on the 1, 2 and 3 spray amounts of the films, XRD patterns are given in Figure 1 and structural parameters are given in Table 1.

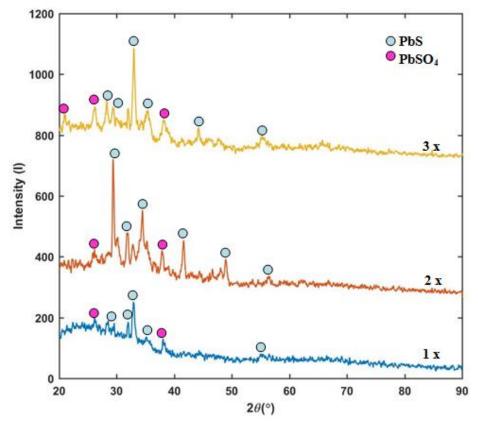


Figure 1. XRD patterns of PbS thin films depend on spray amount.

Table 1. Crystal Parameters of PbS thin films.

Crystal	Diffraction	Miller Index	Distance Plane		
Structures	Angle 2θ (°)	(hkl)	d (Å)		
	26,03	(111)	3.420		
5 4	30.17	(200)	2.960		
PbS (PDF Card No.: 00-002- 0699)	43.47	(220)	2.080		
0 G	50.98	(311)	1.790		
59 59 596	53.55	(222)	1.710		
75	20.83	(011)	4.260		
t Card 0- 867)	26.75	(210)	3.330		
2 년 00 08 0	37.44	(212)	2.400		
PbSO4 (PDF Card No.: 00- 001-0867)					

Accordingly, the films for 1 and 2 sputtering show a very dense and homogeneous surface morphology (Figure 2). There are no cracks on the film surfaces. They have small spherical shapes. There are gaps in the intermediate regions of the film for 3 sprays. Since the grain sizes of the films are small, composition analyzes were performed with EDX mapping on a black background and are depicted in Figure 3.

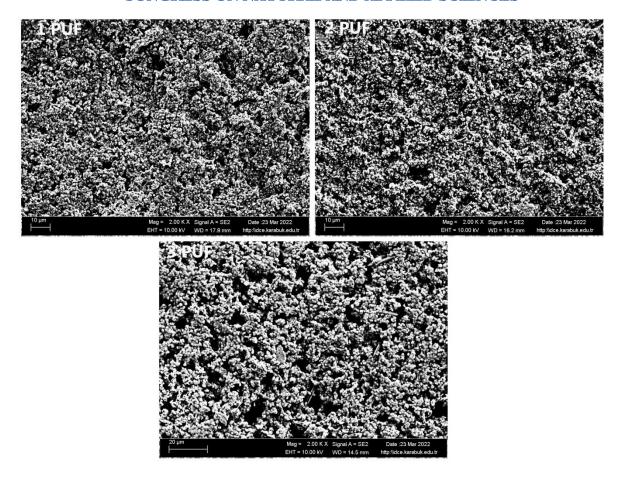
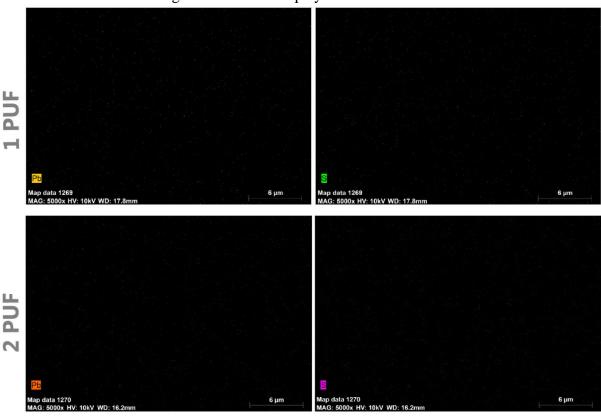


Figure 2. FESEM displays of PbS thin films.



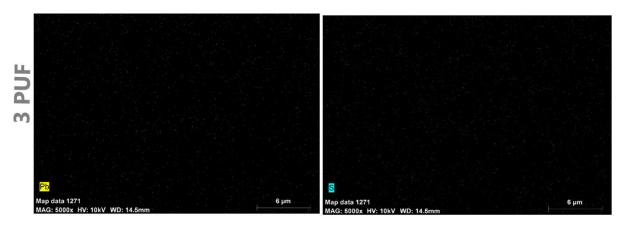


Figure 3. EDX mappings of PbS thin films depends on spray amount.

The substrates were weighed with a precision balance before and after the films were coated, and the quantity of plating mass was determined. Cs valuations are measured the help of Keithley 2400 sourcemeter and 2100/220 Keithley multimeter using in-plane time-dependent I-V modus with 10, 25, 50 and 100 mV/s scanning between 0 - 1 volts for 1, 2 and 3 sprays by

Kickstart program. Whole evaluations were acquired at room temp and in the dark. The specific capacitance values were calculated with the help of Eq.1 by using the amount of coated mass.

$$C_{S} = \frac{I}{m \cdot \frac{dV}{dt}} \tag{1}$$

where C_S is capacitance (F/g), I is current (A), m is quantity of coated film (g). Accordingly, the amount of mass coated for 1, 2 and 3 sprays was weighed as 2.27x10⁻³ g, 13.5x10⁻³ g and 23x10⁻³ g, respectively. For 1, 2 and 3 times spraying, the cyclic voltammetry curves depending on the scanning rates and the variance of the Cs are given in Figures 4 and 5, respectively. It is observed that the Cs valuations decline with increasing scanning rate and the quantity of plating mass. Cs valuations were obtained as 923 F/g, 725 F/g and 524 F/g, respectively, at the least scanning rate 10 mV/s for 1, 2 and 3 times spraying. Durga et al. (Durga et al., 2018) found specific capacitance values between 248.48 F/g and 41.4 F/g for PbS supercapacitor electrodes synthesized on Ni foam by chemical bath deposition method, which is also consistent with the values obtained in this study.

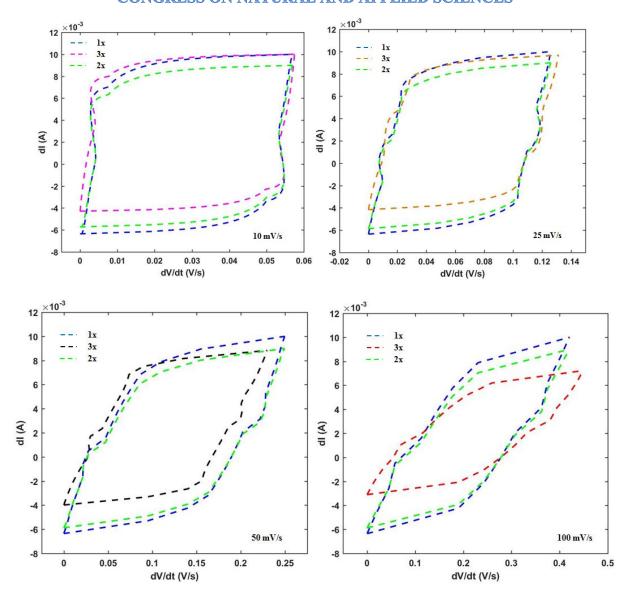


Figure 4. Cyclic voltammetry curves of PbS thin film electrode structures depend on scanning rate.

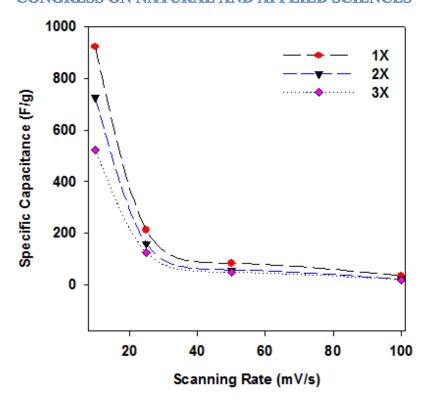


Figure 5. Specific capacitance curves of PbS thin film electrode structures depend on scanning rate.

Table 2. Specific capacitance values for PbS thin film electrode structures.

	Scan Rate (mV/s)	C, Specific Capacitance (F/g)
1 PUF	10	923
	25	211
	50	82.3
	100	33.9
	Scan Rate	C, Specific Capacitance
	(mV/s)	(\mathbf{F}/\mathbf{g})
E	10	725
2 PUF	25	159
	50	56.9
	100	20.2
	Scan Rate	C, Specific Capacitance
	(mV/s)	(F / g)
E	10	524
3 PUF	25	123
	50	47.8
	100	19.7

CONCLUSION

In this study, PbS thin film electrode samples were fabricated by spray method, which is easy, inexpensive, does not require much equipment and suitable for large-scale coatings, depending on the amount of spray on glass substrates at 150 °C. Surface morphologies appear quite dense and homogeneous. A small amount of PbSO₄ crystal structures were also formed due to the production with air. With the increase of the spray number, the amount of coated mass increased and with the increase of the scanning speed, the specific capacitance values decreased because only the surface charges were active. Due to the high carrier density of the PbS chalcogenite structure, high performance supercapacitors with low cost, low toxicity, environmentally friendly, appropriate size and morphology can be obtained and improved with additives.

REFERENCES

Bunshah, R. F. (Ed.). (1994). Handbook of deposition technologies for films and coatings: science, technology, and applications. William Andrew.

Chopra, K. L., & Kaur, I. (1983). Microelectronic Applications. Thin Film Device Applications, 129-170.

George, J. (1992). Preparation of thin films. CRC Press.

- Ibragimova, R., Ganchenkova, M., Karazhanov, S., & Marstein, E. S. (2018). First-principles study of SnS electronic properties using LDA, PBE and HSE06 functionals. Philosophical Magazine, 98(8), 710-726.
- Kanaka Durga, I., Srinivasa Rao, S., Ahn, J. W., Park, T. Y., Jin-Soo, B., Ho, C. I., ... & Kim, H. J. (2018). Dice-like nanostructure of a CuS@ PbS composite for high-performance supercapacitor electrode applications. Energies, 11(7), 1624.
- Kumar, S., Sharma, T. P., Zulfequar, M., & Husain, M. (2003). Characterization of vacuum evaporated PbS thin films. Physica B: Condensed Matter, 325, 8-16.
- Karazhanov, S. Z., Zhang, Y., Mascarenhas, A., & Deb, S. (2000). The effect of excitons on CdTe solar cells. Journal of Applied Physics, 87(12), 8786-8792.
- Martin, P. J., Netterfield, R. P., & Sainty, W. G. (1982). Spectrally selective PbS films produced by ion beam sputtering. Thin Solid Films, 87(3), 203-206.
- Ni, Y., Liu, H., Wang, F., Liang, Y., Hong, J., Ma, X., & Xu, Z. (2004). PbS crystals with clover-like structure: Preparation, characterization, optical properties and influencing factors. Crystal Research and Technology: Journal of Experimental and Industrial Crystallography, 39(3), 200-206.
- Peterson, J. J., & Krauss, T. D. (2006). Fluorescence spectroscopy of single lead sulfide quantum dots. Nano letters, 6(3), 510-514.
- Pickart, S. J. (1970). Physical properties of sulfide materials. Mineral. Soc. Amer. Spec. Rop, 3, 145-153.
- Putley, E. H., & Arthur, J. B. (1951). Lead Sulphide-An Intrinsic Semiconductor. Proceedings of the Physical Society. Section B, 64(7), 616.
- Rossnagel, S. M. (2003). Thin film deposition with physical vapor deposition and related technologies. Journal of Vacuum Science & Technology A: Vacuum, Surfaces, and Films, 21(5), S74-S87.
- Sahadevan, J., Muthu, S. E., Kulathuraan, K., Arumugam, S., Kim, I., Pratha, G. B. S., & Sivaprakash, P. (2022). Structural, morphology and optical properties of PbS (Lead Sulfide) thin film. Materials Today: Proceedings, 64, 1849-1853.
- Salah, H. B. H., Bouzouita, H., & Rezig, B. (2005). Preparation and characterization of tin sulphide thin films by a spray pyrolysis technique. Thin Solid Films, 480, 439-442.
- Sharon, M., Ramaiah, K. S., Kumar, M., Neumann-Spallart, M., & Levy-Clement, C. (1997). Electrodeposition of lead sulphide in acidic medium. Journal of Electroanalytical Chemistry, 436(1-2), 49-52.
- Smith, H. M. (2002). High performance pigments. Germany, 127-308.
- Uhler, A. D., & Helz, G. R. (1984). Precipitation of PbS from solutions containing EDTA. Journal of crystal growth, 66(2), 401-411.

EXPERIMENTAL INVESTIGATION OF THE EFFECT OF DIFFERENT DIAMETER CYLINDER USED IN HYDRO-PNEUMATIC SUSPENSION SYSTEM ON THE STRUCTURE

HİDRO-PNÖMATİK SÜSPANSİYON SİSTEMİNDE KULLANILAN FARKLI ÇAPLARDAKİ SİLİNDİRİN YAPI ÜZERİNDEKİ ETKİSİNİN DENEYSEL İNCELENMESİ

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ABSTRACT

The subject of this study is the hydro-pneumatic suspension (HPS) system, which has been widely encountered in recent years, especially in high-tonnage construction equipment. In the paper, the features and capabilities of the hydro-pneumatic suspension test unit that we manufacture are explained. This unit represents one fourth of a vehicle or a construction machine, based on the quarter vehicle model, which is especially encountered in comfort analyzes in vehicle dynamics. For the test unit, experiments were carried out for three different cylinders with different piston diameters, and a parametric infrastructure was created for the selection of the most suitable suspension system elements to be used in the systems according to the relevant parameters. The road data to be used as the disruptive input of the system were collected from the work machine and given to the system as displacement, and the outputs were examined. In this way, it is ensured that the correct disruptive inputs that will directly affect the structure are applied. According to the results obtained, the vertical movements of the structure were examined and the most sensitive valve and cylinder selection was made.

Keywords: Hydro-pneumatic suspension, Quarter Car, Design, Testing, Modeling.

ÖZET

Bu çalışmanın konusu, özellikle yüksek tonajlı iş makinalarında son yıllarda yaygın olarak karşımıza çıkan hidro-pnömatik süspansiyon (HPS) sistemidir. Bildiride imalatını gerçekleştirdiğimiz hidro-pnömatik süspansiyon test ünitesinin özellikleri ve kabiliyetleri anlatılmıştır. Bu ünite taşıt dinamiğinde konfor analizlerinde özellikle karşımıza çıkan çeyrek taşıt modeli temel alınarak bir aracın ya da iş makinasının dörtte birini temsil etmektedir. Test ünitesi için farklı piston çaplarına sahip üç farklı silindir için deneyler yapılmış olup ilgili parametrelere göre sistemlerde kullanılması en uygun süspansiyon sistem elemanlarının seçimine yönelik ve parametrik bir altyapı oluşturulmuştur. Sistemin bozucu girdisi olarak kullanılacak yol verileri iş makinası üzerinden toplanarak sisteme deplasman olarak verilerek çıktılar incelenmiştir. Bu sayede doğrudan yapı üzerine etki edecek doğru bozucu girdilerin uygulanması sağlanmıştır. Elde edilen sonuçlara göre yapının düşeydeki hareketleri incelenerek en hassas valf ve silindir seçimi yapılmıştır.

Anahtar Kelimeler: Hidro-pnömatik süspansiyon, Çeyrek Taşıt, Tasarım, Test, Modelleme.

ANALYSIS OF TOOL WEAR AND SURFACE ROUGHNESS VALUES IN THE MACHINING OF STAINLESS STEEL MATERIALS

PASLANMAZ ÇELİK MALZEMELERİN İŞLENMESİNDE TAKIM AŞINMASI VE YÜZEY PÜRÜZLÜLÜĞÜ DEĞERLERİNİN ANALİZİ

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ÖZET

Talaşlı imalat yüksek boyutsal hassasiyete sahip parçaların üretilmesi için kullanılan temel yöntemlerden biridir. Bu yöntemde, kesici takım iş parçası üzerinden talaş kaldırırken sürekli olarak aşınmaktadır. Kesici takımlar açısından aşınma kontrol edilmesi gereken en önemli konulardan biridir. Kesici takımın mümkün olan en ekonomik şekilde kullanılırken üretkenliğin korunması üretim sürecinin sağlıklı olması açısından bir gerekliliktir. Bu nedenle takım ömrünün izlenmesi gerek endüstriyel gerek bilimsel en önemli araştırma konularından biridir. Bu çalışmada işlenmesi zor malzeme sınıfında yer alan paslanmaz çelik malzemeler üzerinde işlenebilirlik deneyleri gerçekleştirilmiştir. Deneylerde 150 m/dk sabit kesme hızı, 0,1 mm ilerleme hızı ve 0,8 mm kesme derinliği kullanılmış, takım ömrü ve yüzey pürüzlülüğü değişimi analiz edilmiştir. Deneylerde, 31. dakikanın sonunda takım ömrünün tamamlandığı anlaşılmıştır. Ayrıca takım yüzeyinde belirgin çentik aşınması ve talas yapısması da gözlenmiştir. Bunların yanında yüzey pürüzlülüğünün takım asınmasına bağlı olarak kötüleştiği tespit edilmiştir. Ayrıca birçok pasoda talaş sarma tespit edildiğinden yüzey kötüleşmesi de görülmüştür. Bununla birlikte kesici takımın aşınmasına bağlı olarak kimi pasolarda talaş sarma görülmediğinden yüzey kalitesi diğer pasolara kıyasla daha iyi sonuçlanmıştır.

Anahtar Kelimeler: Talaşlı imalat, Paslanmaz çelik, Takım ömrü, Yüzey pürüzlülüğü

EXTENTED ABSTRACT

Machining is one of the essential methods used to produce parts with high dimensional accuracy. With this method, the cutting tool continually wears while removing chips from the workpiece. The main cause of tool wear is the friction between the cutting tool and the workpiece and the various wear mechanisms that occur due to this friction. The main cause of tool wear is the friction between the cutting tool and the workpiece and the various wear mechanisms that occur due to this friction. Wear in cutting tools is affected by many factors, such as workpiece material, cutting tool material, and cutting conditions. In terms of cutting tools, wear is one of the most vital matters to be controlled. Maintaining productivity while

using the cutting tool in the most economical way possible is a necessity for a stable production process. For this reason, monitoring tool life is one of the most crucial research topics, both industrially and scientifically. In this study, machinability tests were carried out on stainless steel materials, which are difficult-to-cut materials. In the experiments, the change in tool life and surface roughness was analyzed using a constant cutting speed of 150 m/min, a feed rate of 0.1 mm, and a depth of cut of 0.8 mm. Tool wear measurements were performed using a toolmaker's microscope. After each pass, the cutting tool was examined, and the amount of wear was determined. Surface roughness measurements were taken from the workpiece surface five times at the end of each pass. Tool wear analyses were concluded with the flank wear value reaching the limit value of 300 µm. In the experiments, it was understood that the tool life was completed at the end of the 31st minute due to flank wear. Significant notch wear and built-up-edge formation were also observed on the tool surface. The crater wear expected to be observed was not detected. It can be claimed that the reason for this is the cooling of the cutting tool and workpiece at the end of each pass due to measuring and the crater wear not developing sufficiently due to cooling. Besides, it was determined that the surface roughness deteriorated due to tool wear. In addition, surface deterioration was also observed because of chip wrapping in many passes. However, wear on the cutting tool caused no chip wrapping in some passes, and the surface quality was better than others. In addition, it was determined that the surface roughness of the workpiece slightly improved before the end of the tool's life.

Keywords: Machining, Stainless steel, Tool life, Surface roughness

GIRIŞ

Talaşlı imalat gerek yüksek boyutsal doğruluk sunması gerekse istenen iş parçası geometrilerinin elde edilebilmesi nedeniyle önde gelen imalat yöntemlerinden biridir. Ayrıca talaşlı imalat ile çok düşük yüzey pürüzlülük değerlerine ulaşmak mümkündür. Bu nedenle imalat yöntemleri arasında öne çıkan bu yöntemin kullanım alanı sürekli olarak artmaktadır [1]. Talaşlı imalat ile birçok farklı malzeme türü kullanılarak farklı makine parçalarının imalatı mümkündür. Bununla birlikte bazı malzemeler sahip oldukları niteliklerden dolayı talaşlı imalata nispeten uygun değildir. Talaşlı imalat esnasında kesici takım ile iş parçası sürekli temas halindedir ve bu temas alanında yüksek sıcaklıklar meydana gelir. Paslanmaz çelikler düşük ısıl iletkenlikleri nedeniyle kesme esnasında oluşan ısının kesici takımdan uzaklaşmasına yardım edemezler. Bu nedenle ısı takım ucunda sürekli olarak birikir ve erken takım aşınması gerçekleşir. Bunun sonucunda takım ekonomik değerini hızlıca kaybederken işlenen parçanın yüzey pürüzlülük değerleri ise sürekli bozulur [2-3]. Genel olarak çelik içeresinde %12'den fazla Cr bulunması durumunda paslanmaz çelik elde edilmektedir. Paslanmaz celik malzemeler temel olarak dört sınıfta incelenebilir. 1. Ferritik 2. Martenzitik 3. Östenitik ve 4. Dubleks (Ferritik-Östenitik). Bu sınıflar arasında işlenebilirlik açısından en zorlu malzeme Dubleks (Ferritik-Östenitik) paslanmaz çeliklerdir. Bu durumun belirli sebepleri vardır. Bunların başında düşük ısıl iletkenlik ve deformasyon sertleşmesi gelmektedir [2].

Rashid ve diğerleri yapmış oldukları çalışmada [4] takım aşınması ve işlenen malzemelerin yüzey pürüzlülüğü üzerine araştırmalar yapmışlardır. Bu araştırmalarda AISI 4340 malzeme üzerinde tornalama işlemi gerçekleştirilmiş ve düşük ilerleme değerlerinde kesici takım uç aşınmasının arttığını tespit etmişlerdir. Santhanakumar ve diğerleri maraging çeliğinin tornalaması ile ilgili yapmış oldukları çalışmada [5] optimum işleme şartlarının gerek takım aşınması gerekse yüzey pürüzlülüğü değerlerini ciddi şekilde iyileştirebileceğini

ortaya koymuştur. Böylelikle Ra değerini 0,8 µm seviyesinden 0,4 µm seviyesine ve serbest yüzey aşınma değerini 0,0445 mm değerinden 0,0234 mm değerine düşürmüşlerdir. Araújo ve diğerleri [6] çalışmalarında yüzey pürüzlülüğü ve takım aşınmasının etkilerini incelemişlerdir. Bu incelemelerde kesme sırasında ortaya çıkan ısının oldukça önemli olduğunu ve soğutma sıvısı kullanarak bu ısının düşürülmesinin önemini vurgulamışlardır. Böylelikle gerek yüzey pürüzlülüğü gerekse takım aşınmasının ciddi şekilde düşürdüğünü ileri sürmüşlerdir. Demir ve Adıyaman [7] takım yanaşma açısının takım aşınması üzerindeki etkilerini incelemiştir. Ayrıca işlenen malzemelerin yüzey pürüzlülüğü değerlerini de irdelemişlerdir. Araştırmacılar kesme şartlarının optimizasyonunun uygun olmaması durumunda kesici takımların ciddi şekilde aşındığını ortaya koymuşlardır. Bununla birlikte yüzey pürüzlülüğü değerlerinin de takım asınmasına bağlı olarak bozulduğunu vurgulamıslardır. Chen ve diğerleri [8] paslanmaz çelik malzemelerin farklı kesme hızı, ilerleme değeri ve kesme derinliği parametreleri altında işlenebilirliklerini incelemiştir. Yapılan incelemelerde takım aşınması ve yüzey pürüzlülüğü değerleri analiz edilmiştir. Zamana bağlı olarak 6., 12. ve 18. dakikalarda yapılan analizlerde takımın önce hızlıca aşınma gösterdiği sonrasında aşınmanın sabit bir hızla ilerlediği ve 18. dakikada ciddi takım aşınmasının gözlendiğini vurgulamıştır. Bu aşınmaya bağlı olarak yüzey pürüzlülüğü değerlerinin 1,4 µm değerinden 19,4 µm değerine kadar kötüleştiğini tespit etmişlerdir. Fox-Rabinovich ve diğerleri [9] takma uçlu (insert) kesici takımlar ile yaptıkları tornalama deneylerinde CVD ve PVD kaplamalarının etkilerini araştırmışlardır. Özellikle yığma kenar oluşumu temelli olarak yaptıkları takım ömrü çalışmalarında kaplamanın takım ömrü üzerinde belirgin etkisi olduğunu ileri sürmüşlerdir. Bu araştırmada kimi kesme şartlarında 8 kat daha az yığma kenar oluşumu meydana geldiğini tespit etmişlerdir. Ayrıca yan yüzey aşınmasında ise CVD kaplamalarda çok daha az aşınma gözlemişlerdir. Parsi ve diğerleri [10] çalışmalarında süper-dubleks paslanmaz çeliklerin işlenebilirliğini incelemiştir. Farklı kesme hızları ile yapılan deneylerde kaplamasız, AlTiN ve AlCrN kaplamaları takımlarda takım asınma miktarının değisimi ve yüzey pürüzlülüğünde olusan değisimi araştırmışlardır. Sonuç olarak kaplamasız takımların gerek yüzey pürüzlülüğü gerekse takım ömrü açısından daha başarısız sonuçlar ürettiği anlaşılmıştır. Bununla birlikte kaplamalı takımların ise birbirine yakın sonuçlar elde ettiği gözlenmiştir.

Bu çalışmada talaşlı imalat açısından zorlayıcı niteliklere sahip olan AISI 4462 (X2CrNiMoN2253) dubleks paslanmaz çelik malzeme üzerinde takım aşınması analizi yapılmıştır. Ayrıca işlenen parçanın yüzey pürüzlülüğündeki değişimin takım aşınmasına bağlı olarak nasıl değiştiği araştırılmıştır.

2. Materyal ve Metot

2.1. Materyal

Bu çalışmada işlenmesi zor malzeme sınıfında yer alan AISI 4462 (X2CrNiMoN2253) dubleks paslanmaz çelik malzemeler üzerinde takım ömrü ve yüzey pürüzlülüğü analizleri gerçekleştirilmiştir. AISI 4462 dubleks paslanmaz çeliğe ait ASTM E1086 standartlarına göre kimyasal kompozisyon Tablo 1.'de mekanik özellikler ise Tablo 2.'de sunulmuştur.

Tablo 1. AISI 4462 dubleks paslanmaz çeliğe ait kimyasal kompozisyon (%)

				r					J (· -)
Element	C	Si	Mn	P	S	Cr	Mo	Ni	N
Ağırlıkça %	0,015	0,50	1,40	0,029	0,004	22,69	3,11	4,84	0,1690

Tablo 2. AISI 4462 dubleks paslanmaz çeliğe ait mekanik özellikler

Mekanik özellik	Akma dayanımı	Çekme dayanımı	Uzama	Sertlik
	(MPa)	(MPa)	(%)	(HBW)
Değer	488	692	47	218

Kesme deneyleri Korloy marka PTGNR2020K16 kater ve TNMG160404-HA (Grade PC9030) kesici uç (insert) ile gerçekleştirilmiştir. Deneyler Hasan Ferdi Turgutlu Teknoloji Fakültesinde Makine Mühendisliği bölümünde bulunan Goodway GLS-1500M CNC torna tezgahı ile gerçekleştirilmiştir. Yüzey pürüzlülüğü ölçümü için Mahr M300 terminali ve Mahr Marsurf RD18 ölçüm cihazı kullanılmıştır. CNC Torna tezgahı üzerinde iş parçasını sökmeden yüzey pürüzlülüğü ölçümü yapılabilmesi amacıyla CNC Torna tezgahının parça yakalayıcı kısmına bir fikstür yerleştirilmiştir. Ölçümler bluetooth destekli Mahr Marsurf RD18 ölçüm cihazı ile yapılıp, sonuçlar Mahr M300 terminalinden alınmıştır. Yüzey pürüzlülüğü ölçümleri ISO 4288 standarttı temel alınarak gerçekleştirilmiştir. Takım aşınmasının ölçümü için Mahr MM200 takımcı mikroskobu kullanılmıştır. Bu mikroskoba M-Shot MD30 kamera ile aküple edilerek ölçüm fotoğraflarının dijital ortama nakledilmesi sağlanmıştır (Şekil 1.).

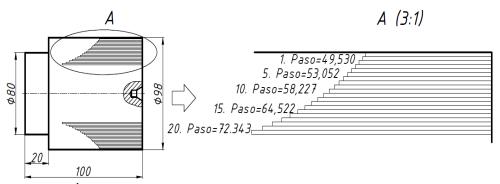


Şekil 1. Takım aşınması ölçüm sisteminin hazırlanması

AISI 4462 (X2CrNiMoN2253) paslanmaz çelik malzemeler üzerinde gerçekleştirilen takım aşınması deneyleri ISO 3685'e göre belirlenmiştir. ISO 3685 torna tezgâhı gibi tezgahlarda kullanılan tek noktalı kesici takımların aşınma değerlerinin tespitinde kullanılan temel standarttır. Deneylerde 0,8 mm talaş derinliği ve kesici takım üreticisi tarafından önerilen 150 m/dk kesme hızı kullanılmıştır. Deneyler kesme uzunluğu, kesici takım ömrü açısından 1 dakikalık kesme süresine denk gelecek şekilde gerçekleştirilmiştir. Bu nedenle deneylerde belirlenen kesme hızı için farklı kesme uzunlukları oluşmaktadır. Kesme uzunluğunun tespiti için Eşitlik 1'de görülen formül kullanılmıştır.

$$l = \frac{Tx f x 1000 x V}{\pi x d}$$
 (Eşitlik 1)

Eşitlik 1'e göre 1 dakikalık kesme ömrüne karşılık gelen kesme uzunluğu doğrudan iş parçası çapına bağlıdır. İş parçaları Ø100 mm ölçüsünde temin edilmiştir. Ancak malzeme yüzeyinde istenmeyen düzensizlikler olabileceği düşünülerek iş parçası üzerinden 2 mm talaş kaldırılarak malzeme çapı Ø98 mm'ye düşürülmüştür. Eşitlik 1'te görülen hesaplama her çap değeri için ayrı ayrı hesaplanmış ve hesaplanan kesme uzunluğuna göre kesme işlemi yapılmıştır. Çap değeri düştükçe kesme uzunluğunun arttığı görülmektedir. Şekil 2'de bu durum görselleştirilmiştir.



Şekil 2. İşlenen çap değerine bağlı olarak kesme uzunluğunun değişimi

Şekil 2.'de görülen bu durum teknik olarak birbirini takip eden pasolar arasındaki farkın ikinci bir takım ile temizlenmesi gerekliliğini ortaya koymaktadır. Bu sebeple her işlenen paso sonrası ikinci bir takım ile birbirini takip eden pasolar arasındaki fark temizlenmiştir. Şekil 3.'te sırasıyla yapılan bütün işlemler görülmektedir.



Kesici takımını aşınmış kabul edilebilmesi için ISO 3685'e göre temel olarak üç kriter ileri sürülebilir.

- Yan yüzey aşınması düzenli ise $VB_B = 0.3$ mm olduğunda takım aşınmış kabul edilmektedir.
- Yan yüzey aşınmasının düzenli olmaması durumunda ise $VB_{max} = 0.6$ mm olduğunda takım aşınmış kabul edilmektedir.
- Krater aşınması olması durumunda KT = 0.06 + 0.3f değerinden büyük bir aşınma takım ömrünün tamamladığını göstermektedir.

ISO 3685'te belirtilen aşınma durumlarına bağlı olarak Şekil 3.'te görülen işlemler her bir paso için ayrı ayrı gerçekleştirilmiştir. Her paso sonrası yapılan takım aşınması ölçümleri sonunda ISO 3685'te belirtilen şartlardan birinin oluştuğu gözlenmesi durumunda deneyler durdurulmuş ve takım ömrünün tamamlandığı kabul edilmiştir. Gerçekleştirilen talaşlı imalat ve yüzey pürüzlülük ölçümleri Şekil 4.'de görülmektedir.





Şekil 4. Talaşlı imalat işlemleri ve yüzey pürüzlülüğü ölçümü

Kesici takım aşınmasının incelenmesi amacıyla kesici takımın üzerine koyulabileceği ve farklı açılarda görüntü alınabilecek bir fikstür tasarlanmıştır (Şekil 5.). Takımcı mikroskobu tablasına yerleştirilen bu fikstür kullanılarak toplam altı adet görüntü alınması mümkündür. Bunlarda beş adedi 10°, 30°, 45°, 90° ve F (Yan yüzey aşınması-Flank wear) kısımlarıdır. Fikstür üzerinde 90° ölçüm bölümü hem kesici uç üst yüzeyinin incelenmesi amacıyla hem de kesici takımı dik yerleştirerek burun aşınması kontrolü için kullanılmıştır. Böylelikle her paso sonunda toplam altı adet görüntü analiz edilmiştir. Kesici takımı aşınma ölçümleri ise Şekil 5'te görülmektedir.

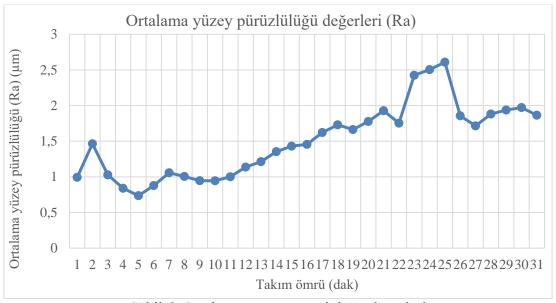


Şekil 5. Takım aşınmasının kontrolü için kullanılan fikstür ve ölçüm sistemi

3. Sonuçlar

3.1. Yüzey Pürüzlülüğü Ölçüm Sonuçları

Talaşlı imalat ile her bir dakikalık takım ömrü sonunda iş parçası tezgahtan sökülmeden yüzey pürüzlülüğü ölçümleri gerçekleştirilmiş ve ortalama yüzey pürüzlülüğü değerleri (Ra) tespit edilmiştir. Bu amaçla tezgâh üzerinde 72° (360°/5=72°) derece ile tüm yüzeyden elde edilen beş adet yüzey pürüzlülüğü ölçümünün ortalaması alınarak Şekil 6. elde edilmiştir.

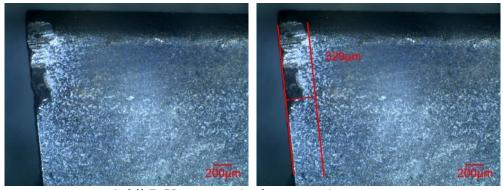


Şekil 6. Ortalama yüzey pürüzlülüğü değerleri

Ortalama yüzey pürüzlülüğü değerlerinin takım aşınmasına bağlı değişimi Şekil 6'da görülmektedir. Talaşlı imalat deneyleri ve yüzey pürüzlülüğü ölçümleri takım ömrü tamamlana kadar devam edilmiştir. Yapılan deneylerde takım ömrü 31. dakikada tamamlanmış bu nedenle 31 adet ortalama yüzey pürüzlülüğü verisi ölçülmüştür. Takım aşınması zamana bağlı olarak arttığından kesici uç zaman içeresinde kesme kenarlarını kaybetmektedir. Bunun sonucu olarak yüzey pürüzlülüğünde kötüleşme beklenebilir [11]. Yapılan deneyler de bu durum görülmekle birlikte zamana bağlı olarak kötüleşen yüzey pürüzlülüğü oldukça belirgindir. Kötüleşen yüzey pürüzlülüğü belirgin olmakla birlikte son 4-5 pasoda önceki pasolara kıyasla yüzey pürüzlülük değerlerinde iyileşme görülmüştür.

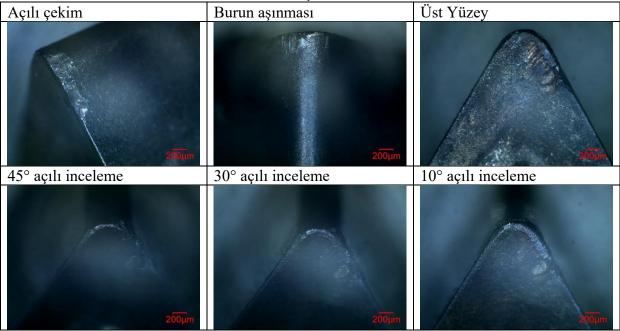
3.2. Takımcı Mikroskobu ile Takım Aşınması Ölçüm Sonuçları

Takım aşınması ölçümlerinde farklı açılardan görüntüler elde edilmiş (Şekil 7) ve ölçümler yapılmıştır. Takımcı mikroskobu ile elde edilen görüntüler Tablo 4.'de sunulmuştur.



Şekil 7. Yan yüzey (serbest yüzey) aşınması

Tablo 4. Takım aşınmasının incelenmesi



Takımcı mikroskobu kullanılarak elde edilen 10°, 30°, 45°, 90° ve F (Yan yüzey aşınması-Flank wear) görüntüleri ile takım aşınması takip edilmiştir. Bununla birlikte 30° ve 45° açı ile alınan görüntülerin takım aşınmasının kontrolü için kullanılabilecek durumda olmadığı görülmektedir. Takımcı mikroskobuna aküple edilen M-Shot MD30 kamera ile elde edilerek bilgisayar ortamına aktarılan görüntüler Digital image anlaysis yazılımı kullanılarak değerlendirilmiştir. Yazılım ile elde edilen aşınma değerlerinin zamana bağlı olarak değişimi Şekil 8.'te görülmektedir.



Şekil 8. Takımcı mikroskobu ile alınan görüntüler

Şekil 8'de görülen aşınma değerleri incelenmiştir. Takım aşınması önce hızlıca belli bir düzeye gelmiş ardından sabit bir eğimle artış göstermiş ve son olarak hızlıca artmıştır. Bu kesme şartlarında 31. dakika sonunda takım ömrünü tamamlamış ve ISO 3685'te belirtilen 0,3 mm (300 µm) takım aşınmasına ulaşılmıştır. Aşınma öncelikle hızla gerçekleşmiş, ardından sabit bir şekilde artmaya başlamış ve takım ömrü sonlarına doğru hızlıca artan

takım aşınması tespit edilmiştir. Literatür çalışmalarında da Letot ve arkadaşları [11] ve Derani ve arkadaşları [12] benzer şekilde takım ömrünün sonuna doğru hızlıca gelişen bir aşınma tespit etmişlerdir [11-12].

Takım aşınma türlerinin nerdeyse tamamına bu çalışmada rastlanmıştır. Yan yüzey aşınması, burun aşınması ve yığma kenar oluşumu belirgin şekilde tespit edilmiştir. Takım ömrü ISO 3685'e göre yan yüzey aşınmasına bağlı olarak tamamlanmıştır. Pekşen ve arkadaşları [12] yaptıkları çalışmada belirgin yan yüzey aşınması tespit etmişlerdir. Benzer şekilde Patil ve arkadaşları da belirgin yan yüzey aşınması tespit etmişlerdir [13]. Bununla birlikte literatürde sıklıkla görülen krater aşınması belirgin olarak görülememiştir. Pekşen [12] yan yüzey aşınmasının yanında belirgin krater aşınması tespit etmiştir. Benzer şekilde Wu ve arkadaşları da belirgin krater aşınması ile karşılaşmıştır [14]. Literatürde görülen krater aşınmasının mevcut deney şartlarında belirgin olmaması ısı girdisi ile ilişkilendirilebilir. Paslanmaz çelikler düşük ısıl iletkenliğe sahiptir. Bu nedenle ısı, kesici takımda birikerek krater aşınmasını hızlandırır. Bununla birlikte mevcut deney şartlarında her paso sonrası kesici takımın sökülmesi ve gerekli ölçümlerin yapılması hem iş parçasının soğumasına hem de kesici takımın soğumasına neden olmuştur. Kuru işlem şartlarında beklenen krater aşınmasının meydana gelmemesi ölçümler esnasında takımın ve iş parçasının soğumasına bağlanabilir.

Kesici takımlar genel olarak aşındıkça kesme özellikleri kötüleşmekte ve talaşlı imalatta daha kötü yüzey kalitelerine neden olmaktadırlar. Bu durumu Demir ve Zülküf vurgulamıştır [15]. Bu çalışmada da genel olarak takım aşınması arttıkça yüzey kalitesi kötüleşmiştir. Bununla birlikte ilginç bir şekilde son pasolarda yüzey kalitesinin önceki pasolara kıyasla iyileştiği görülmektedir. Bazı literatür kaynakları da benzer durumları rapor etmektedirler. Örneğin Derani ve arkadaşları [11] ile Akhavan ve arkadaşları [16] bu durumlar karşılaşmıştır. Takım ömrünün son kısımlarında işlenen parçasının yüzey kalitesinin iyileştiğini ortaya koymuşlarıdır [11,16].

6. Sonuç ve Öneriler

Talaşlı imalat çok iyi yüzey kalitesi ve yüksek boyutsal doğruluk sunabilmesi nedeniyle diğer imalat yöntemlerinin önüne çıkan hassas ve kontrolü zor bir yöntemdir. Bu çalışmada işlenmesi zor malzeme sınıfında yer alan AISI 4462 (X2CrNiMoN2253) dubleks paslanmaz çelik malzeme üzerinde takım ömrü ve yüzey pürüzlülüğü deneyleri yapılmıştır. Bu kapsamda AISI 4462 malzemeler 150 m/dk kesme hızı ile talaşlı imalat işlemine tabi tutulmuştur. Kesici takımın bir dakikalık kesme süresine denk gelen kesme mesafesi kadar kullanılmasını takiben kesici takım üzerinde aşınma değerleri ve işlenen parçanın yüzey pürüzlülük değerleri ölçülmüştür. Bu işlemler sonucunda aşağıda belirtilen sonuçlar ortaya çıkmıştır.

Kesici takım üzerinde belirgin yan yüzey aşınması ana aşınma türü olarak öne çıkmıştır. Takım ömrü ISO 3685 standartına göre yan yüzey aşınmasının 0,3 mm (300 μ m) değerine 31. dakika sonunda ulaşması ile tamamlanmıştır. Ayrıca çentik aşınması ve yığma kenar oluşumu da gözlenmiştir. Bununla birlikte görülmesi beklenen krater aşınmasına rastlanmamıştır.

Kesici takım aşınmasına bağlı olarak yüzey pürüzlülüğü değerlerinde kötüleşme tespit edilmiştir. Yapılan deneylerde daha kontrollü şartlar altında ve daha uzun süre ile aşınma gözlendiğinden yüzey pürüzlülüğü değerlerinde görülen bozulma daha belirgin olmuştur. Bununla birlikte takım ömrünü tamamlamak üzereyken iş parçalarının yüzey pürüzlülük değerlerinde bir miktar iyileşme tespit edilmiştir.

Talaşlı imalat birçok faktörden etkilenen karmaşık bir süreç olduğundan bundan sonraki çalışmalarda bu çalışmadan farklı olarak bazı konuların araştırılması mümkündür. Deneyler kuru işleme şartlarında gerçekleştirilmiştir. Aynı çalışmanın ıslak çalışma şartları yanında minimum miktarda yağlama ve vortex tüp ile soğutma gibi şartlar altında denenmesi ilgi çekici olabilir. Paslanmaz çelik malzemelerde meydana gelen deformasyon sertleşmesinin talaşlı imalat sonrası durumunun takip edilmesi önemli bir veri kaynağı olabilir. Ayrıca artan takım aşınmasına bağlı olarak kesme kuvvetlerinin ölçülmesi veya sonlu elemanlar metodu ile modellenmesi de yapılabilecek çalışmalar arasındadır.

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KAYNAKLAR

- [1] Groover, Mikell P. Fundamentals of Modern Manufacturing: Materials, Processes, and Systems, John Wiley & Sons, Amerika Birleşik Devletleri, 2020, 816 s.
- [2] ÇAKIR, M.C. Modern Talaşlı İmalatın Esasları (Modern Metal Cutting), Nobel Yayın-Dağıtım, Ankara, Türkiye, 2006, 308 s.
- [3] Ortner, H.M., Ettmayer P., and Kolaska H. The history of the technological progress of hardmetals. International Journal of Refractory Metals and Hard Materials 2014, 44: 148-159.
- [4] Rashid, W. B., Goel, S., Davim, J. P., & Joshi, S. N. Parametric design optimization of hard turning of AISI 4340 steel (69 HRC). The International Journal of Advanced Manufacturing Technology, 2016, 82(1), 451-462.
- [5] Santhanakumar, M., Adalarasan, R., Siddharth, S., & Velayudham, A. An investigation on surface finish and flank wear in hard machining of solution treated and aged 18% Ni maraging steel. Journal of the Brazilian Society of Mechanical Sciences and Engineering, 2017, 39(6), 2071-2084.
- [6] Araújo, R. P., Rolim, T. L., Oliveira, C. A., Moura, A. E., & Silva, J. C. A. Analysis of the surface roughness and cutting tool wear using a vapor compression assisted cooling system to cool the cutting fluid in turning operation. Journal of Manufacturing Processes, 2019, 44, 38-46.
- [7] Demir, Z., & Adiyaman, O. Investigation of influence of approach angle and chip slenderness ratio on vibration, chip formation and surface quality in turning of AISI 1050 steel. Journal of the Brazilian Society of Mechanical Sciences and Engineering, 2019, 41(10), 1-15.
- [8] Chen, J., Wang, Y., Zhang, Y., Yang, S., & Zhang, X. Investigation on tool wear mechanism during dry cutting 304 stainless steel. Manufacturing Technology, 2000, 20(1), 36-44.

- [9] Fox-Rabinovich, G., Gershman, I. S., Yamamoto, K., Dosbaeva, J., & Veldhuis, S. Effect of the adaptive response on the wear behavior of pvd and cvd coated cutting tools during machining with built up edge formation. Nanomaterials, 2020, 10(12), 2489.
- [10] Parsi, P. K., Kotha, R. S., Routhu, T., Pandey, S., & Dwivedy, M. Machinability evaluation of coated carbide inserts in turning of super-duplex stainless steel. SN Applied Sciences, 2020, 2(11), 1-19.
- [11] Letot, C., Serra, R., Dossevi, M., & Dehombreux, P. Cutting tools reliability and residual life prediction from degradation indicators in turning process. The International Journal of Advanced Manufacturing Technology, 2016, 86(1), 495-506.
- [12] Derani, M. N., Ratnam, M. M., & Nasir, R. M. Improved measure of workpiece surface deterioration during turning using non-contact vision method. Precision Engineering, 2021, 68, 273-284.
- [13] Pekşen, H., & Kalyon, A. Optimization and measurement of flank wear and surface roughness via Taguchi based grey relational analysis. Materials and Manufacturing Processes, 2021, 36(16), 1865-1874.
- [14] Patil, P., & Karande, P. (2022). Experimental Investigations and Optimization of Machining Parameters in CNC Turning of SS304 Using Coolant at 0°C. Journal of Manufacturing and Materials Processing, 2022, 6(6), 128.
- [15] Wu, J., He, L., Wu, Y., Zhou, C., Zou, Z., Zhan, G., & Zhang, X. Enhancing Wear Resistance and Cutting Performance of a Long-Life Micro-Groove Tool in Turning AISI 201. Coatings, 2021, 11(12), 1515.
- [16] Demir, Z., & Adiyaman, O. Investigation of influence of approach angle and chip slenderness ratio on vibration, chip formation and surface quality in turning of AISI 1050 steel. Journal of the Brazilian Society of Mechanical Sciences and Engineering, 2019, 41(10), 1-15.
- [17] Niaki, F. A., & Mears, L. (2017). A comprehensive study on the effects of tool wear on surface roughness, dimensional integrity and residual stress in turning IN718 hard-to-machine alloy. Journal of Manufacturing Processes, 2017, 30, 268-280.

MODELING IMPEDANCE CONTROL WITH LIMITED INTERACTION POWER FOR A 2R PLANAR ROBOT ARM

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ABSTRACT

Impedance control is a widely used concept in robotics to regulate the interaction between a robot and its environment in tasks such as pushing, polishing, cleaning, and grinding. The impedance controller regulates the dynamic relationship between the robot and the environment. The force applied by the robot to the environment depends on the position of the robot arm endpoint and the corresponding impedance. The interaction force directly affects the energy consumed by the robot, impacting the torques in the joints. This fact makes it imperative to control the interaction between the robot and the environment. However, in certain scenarios, the interaction power of the robot may be limited due to constraints such as actuator saturation, limited energy supply, or safety concerns. In these situations, it becomes crucial to model impedance control with limited interaction power to achieve effective and safe robot behavior. This study presents a detailed analysis of impedance control with limited interaction power, with a focus on developing an analytical model that accurately captures the dynamic behavior of the system while considering constraints on interaction power. The proposed model provides a framework for designing control strategies that can achieve desired behavior while satisfying the limitations. To optimize the impedance controller parameters, the Bees Algorithm is used. Following the optimization process, a model for interaction power limitation was developed, resulting in limited interaction power consumption for each joint. The effectiveness of the proposed model is demonstrated through simulations, showing successful control of the interaction between the robot and its environment with limited interaction power. Numerical and graphical results of the study are presented.

Keywords: Energy consumption, input trajectory functions, 2R planar robot arm, optimum impedance control, controller design, The Bees Algorithm.

1. INTRODUCTION

The field of robotics has seen remarkable advancements in recent years, with robots being deployed across a wide range of industries, from manufacturing and healthcare to agriculture and space exploration. As robots are increasingly integrated into various applications, it becomes critical to ensure that they can interact safely and effectively with their environment. Impedance control has emerged as a popular concept in robotics to regulate this interaction, allowing robots to perform tasks such as pushing, polishing, cleaning, and grinding with high precision [1, 2]. To ensure the safety of both the robot and other entities in contact, it is essential to control the interaction between the robot and the environment.

In impedance control, the robot's endpoint is considered as a virtual spring-mass-damper system, and the controller regulates the dynamic relationship between the robot and the environment by adjusting the impedance of this system [3-6]. The impedance controller acts as an intermediary between the robot and its environment, enabling the robot to exert the desired force while also sensing the force feedback from the environment. This feedback is essential in ensuring that the robot can adapt to changes in the environment and maintain stable interactions [7]. The input trajectory function used in impedance control is also important in determining the interaction distance, interaction force, joint torques, and energy consumption of the robot [8].

However, in some scenarios, the interaction power of the robot may be limited due to various constraints, such as actuator saturation, limited energy supply, or safety concerns. In such cases, developing models for impedance control with limited interaction power becomes crucial to achieving safe and effective robot behavior.

Optimization algorithms are divided into two as global optimization algorithms and local search algorithms [9]. Global optimization algorithms such as Genetic Algorithm [10, 11], Particle Swarm Optimization [12] and The Bees Algorithm [13-16] focus on searching across the entire space. Local search algorithms such as Hooke-Jeeves [17] and Newton Raphson [18] focus on searching in local areas.

This study aims to provide a detailed analysis of impedance control under such conditions,

with a focus on developing an analytical model that accurately captures the dynamic behavior of the system while considering limitations on interaction power. The proposed model offers a framework for designing control strategies that can achieve the desired behavior while satisfying the constraints. Additionally, the study uses the Bees Algorithm to optimize the impedance controller parameters [7], and a model for interaction power limitation is developed, resulting in limited interaction power consumption for each joint.

The effectiveness of the proposed model is demonstrated through simulations, showing successful control of the interaction between the robot and its environment with limited interaction power. The numerical and graphical results of the study provide valuable insights for optimizing impedance controller parameters and developing control strategies for safe and effective robot behavior. Overall, this study contributes to the development of robotic systems that can operate safely and effectively in real-world environments with constrained interaction power.

2. MATHEMATICAL MODEL

The robotic arm examined in this study is a planar 2 degree-of-freedom (DOF) manipulator that consists of two revolute joints. The arm's physical structure comprises two links, each having a distinct mass denoted by m_1 and , m_2 as shown in Figure 1.

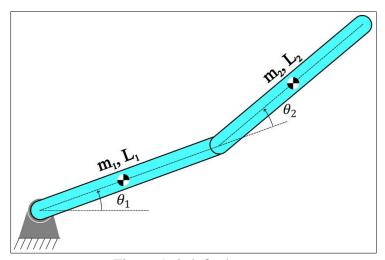


Figure 1. 2 dof robot arm

To establish the mathematical model for the planar 2R robot manipulator, it is necessary to determine the position of the center of mass relative to the joint angles. The relationship

between the center of mass position of the robot's two linkages, characterized by their respective masses m_1 and m_2 , and the joint angles is described by Equation (1).

$$\begin{split} \bar{x}_1 &= \frac{L_1}{2} \cos \theta_1 \\ \bar{y}_1 &= \frac{L_1}{2} \cos \theta_2 \\ \bar{x}_2 &= L_1 \cos \theta_1 + \frac{L_2}{2} \cos(\theta_1 + \theta_2) \\ \bar{y}_2 &= L_1 \sin \theta_1 + \frac{L_2}{2} \sin(\theta_1 + \theta_2) \end{split} \tag{1}$$

To determine the mass moments of inertia of the linkages rotating around their respective centers of mass, the expression $I = \frac{1}{12} \text{mL}^2$ is utilized. The kinetic energy of the system, denoted by T, is expressed by Equation (2), while the potential energy, represented by V, is described by Equation (3).

$$T = \frac{1}{2}m_1(\dot{x}_1^2 + \dot{y}_1^2) + \frac{1}{2}I_1\dot{\theta}_1^2 + \frac{1}{2}m_2(\dot{x}_2^2 + \dot{y}_2^2) + \frac{1}{2}I_2(\dot{\theta}_1 + \dot{\theta}_2)^2$$
 (2)

$$V = m_1 g \dot{\bar{y}}_1 + m_2 g \dot{\bar{y}}_2 \tag{3}$$

The equation of motion for the system can be derived by applying the Euler-Lagrangian equation. The Lagrangian expression for the system is given by Equation (4).

$$L = T - V \tag{4}$$

The equation for the joint torques can be derived from the Lagrangian expression, resulting in Equation (5).

$$\tau_i = \frac{d}{dt} \left(\frac{\partial L}{\partial \dot{\theta}_i} \right) - \frac{\partial L}{\partial \theta_i} \tag{5}$$

In order to obtain the values for the torques τ_1 and τ_2 , the equation of motion was calculated and is represented by Equation (6).

$$\tau_{1} = \left(\frac{1}{3}m_{1}L_{1}^{2} + m_{2}\left(L_{1}^{2} + \frac{1}{3}L_{2}^{2} + L_{1}L_{2}\cos(\theta_{2})\right)\right)\ddot{\theta}_{1} + m_{2}L_{2}\left(L_{1}\cos(\theta_{2}) + \frac{2}{3}L_{2}\right)\ddot{\theta}_{2} \\
- m_{2}L_{1}L_{2}\sin(\theta_{2})\left(\dot{\theta}_{1}\dot{\theta}_{2} + \frac{1}{2}\dot{\theta}_{2}^{2}\right) + \frac{1}{2}(m_{1} + 2m_{2})gL_{1}\cos(\theta_{1}) \\
+ \frac{1}{2}m_{2}gL_{2}\cos(\theta_{1} + \theta_{2}) \\
\tau_{2} = \frac{1}{2}m_{2}L_{2}\left(L_{1}\cos(\theta_{2}) + \frac{2}{3}L_{2}\right)\ddot{\theta}_{1} + \frac{1}{2}m_{2}L_{1}L_{2}\sin(\theta_{2})\dot{\theta}_{1}^{2} + \frac{1}{3}m_{2}L_{2}^{2}\dot{\theta}_{2}^{2} \\
+ \frac{1}{2}m_{2}gL_{2}\cos(\theta_{1} + \theta_{2})$$
(6)

3. IMPLEMENTATION OF IMPEDANCE CONTROL

In order to implement impedance control, several steps must be taken, as depicted in Figure 2. The first step is to compute the forward kinematics and inverse dynamics equations for the desired interaction point of the robot, which is based on the joint angles. The next step is to determine the difference between the position derived from forward kinematics and the target position, which is then transformed into an interaction force by multiplying it with the spring constant and damping coefficients. This interaction force is then multiplied with the transpose of the Jacobian matrix, which results in torques at the joints. The torques computed from the inverse dynamics equations are then combined with these torques to derive the final torque that is sent to the robot, thereby providing control over the robot's interactions with its environment.

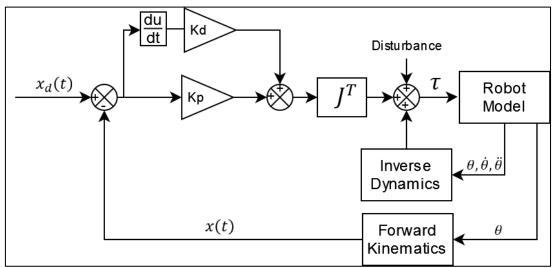


Figure 2. Impedance control schematics

The interaction force generated using PID control can be expressed mathematically in

Equation (7). The equation represents the feedback control loop used to minimize the error between the desired and actual position of the robot manipulator. The proportional gain (k), integral gain (i), and derivative gain (b) are tuning parameters that determine the strength of the response to error, the rate at which the error is corrected, and the rate of change of the error, respectively. The error signal is obtained by subtracting the current position of the manipulator from the desired position, and the integral and derivative terms are obtained by integrating and differentiating the error signal over time, respectively. The resulting interaction force is then multiplied by the transpose of the Jacobian matrix to compute the joint torques required to achieve the desired interaction force.

$$F_{int} = k \begin{bmatrix} x_{2d} - x_2 \\ y_{2d} - y_2 \end{bmatrix} + b \begin{bmatrix} \dot{x}_{2d} - \dot{x}_2 \\ \dot{y}_{2d} - \dot{y}_2 \end{bmatrix} + i \int \begin{bmatrix} x_{2d} - x_2 \\ y_{2d} - y_2 \end{bmatrix} dt$$
 (7)

The target position of the robot's endpoint, denoted by x_{2d} and y_{2d} , is compared to the actual position of the endpoint, represented by x_2 and y_2 . The equation that describes the position of the endpoint of the robot can be expressed mathematically as given in Equation (8).

$$x_2 = L_1 \cos \theta_1 + L_2 \cos(\theta_1 + \theta_2)$$

$$y_2 = L_1 \sin \theta_1 + L_2 \sin(\theta_1 + \theta_2)$$
(8)

The conversion of the interaction force represented in Equation (7) into torques necessitates the multiplication by the Jacobian matrix of the endpoint of the robot. The Jacobian matrix of the system is mathematically expressed as Equation (9).

$$J = \begin{bmatrix} \frac{dx_2}{d\theta_1} & \frac{dx_2}{d\theta_2} \\ \frac{dy_2}{d\theta_1} & \frac{dy_2}{d\theta_2} \end{bmatrix}$$

$$J = \begin{bmatrix} -L_1 \sin(\theta_1) - L_2 \sin(\theta_1 + \theta_2) & -L_2 \sin(\theta_1 + \theta_2) \\ L_1 \cos(\theta_1) + L_2 \cos(\theta_1 + \theta_2) & L_2 \cos(\theta_1 + \theta_2) \end{bmatrix}$$
(9)

The impedance torques, obtained by multiplying the interaction forces with the transpose of the Jacobian matrix, are mathematically represented as Equation (10).

$$\tau_{e} = J^{T} F_{int}$$

$$\tau_{e} = \begin{bmatrix} -F_{x}(L_{1} \sin(\theta_{1}) + L_{2} \sin(\theta_{1} + \theta_{2})) + F_{y}(L_{1} \cos(\theta_{1}) + L_{2} \cos(\theta_{1} + \theta_{2})) \\ -F_{x} L_{2} \sin(\theta_{1} + \theta_{2}) + F_{y} L_{2} \cos(\theta_{1} + \theta_{2}) \end{bmatrix}$$
(10)

In Equation (10), the x component of the F_{int} force is represented as F_x while the y component is denoted as F_y . The final torques required for controlling the robot are obtained by summing the dynamic torques computed using Equation (6) with the impedance torques derived from Equation (10). The combined torques thus obtained are then transmitted to the robot, allowing the system to achieve the desired position and impedance control.

4. NUMERICAL APPLICATION

 $L_1 = L_2 = 1$ and $m_1 = m_2 = 5 \, kg$. According to the scenario, the movement of the robot's endpoint is sequential, starting from point 1, then moving to points 2, 3, 4, and eventually returning to point 1, as shown in Figure 3. Throughout the movement of the endpoint, the interaction power is constrained to a maximum of 0.25 Watts.

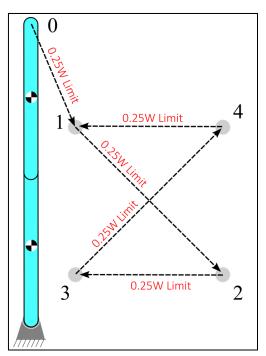


Figure 3. Numeric application view

Based on a previous study [8], the sinusoidal function was identified as the most energy-efficient function among seven different functions. Therefore, in this study, the sinusoidal function expressed in Equation (11) was chosen as the trajectory function for the robot's endpoint.

$$f_{6} = \begin{cases} h_{0} & \text{, } t < t_{0} \\ h_{0} + (h_{1} - h_{0}) \frac{\sin(\pi(t_{m} - 0.5)) + 1}{2} & \text{, } t_{0} \le t \le t_{1} \\ h_{1} & \text{, } t > t_{1} \end{cases}$$
(11)

The desired motion trajectory is defined by the initial desired position, h_0 , at time t_0 , and the final desired position, h_1 , at time t_1 . To enable scaling of the time interval $[t_0, t_1]$ to the range [0,1], a scaled time parameter, t_m , is introduced, as shown in Equation (12).

$$t_m = \frac{t - t_0}{t_1 - t_0} \tag{12}$$

The objective function utilized to optimize the coefficients k, b, and i in Equation (7) is defined as Equation (13).

$$f_{obj} = \int_{t_1}^{t_2} (x_{2d} - x_2)^2 + (y_{2d} - y_2)^2$$
 (13)

The objective function used for optimization of the coefficients k, b, and i in Equation (7) is established by squaring the distance between the target and actual position, also known as the distance error. The objective of minimizing this function is to reduce the distance error and bring the actual position closer to the target position. The optimization results are shown in Table 1.

Table 1. The results of The Bees Algorithm

	nitial iditio	ns	Initial Objective Function	The Bees Algorithm Result		rithm	Resulting Objective Function
k	b	i		k	b	i	
25	3	0	5.19	249.83	49.92	11.09	0.01

The requested interaction power of each joint is determined by the product of the angular velocity ω_i and the impedance torque τ_e , as expressed in Equation (14). However, in order to limit the interaction power, τ_e is modified as τ_{eL} and shown in Equation (15).

$$P_r = \omega \cdot \tau_{\rho} \tag{14}$$

 τ_{eL} is modified in order to saturate the interaction power and is shown in (15). P_L is the power limit target and is selected in this example as 0.25 W, P_r is the requested power.

$$\tau_{eL} = \min\left(\frac{P_L}{|P_{r1}|}, \frac{P_L}{|P_{r2}|}, 1\right) \cdot \tau_e \tag{15}$$

3. RESULTS AND DISCUSSION

Figure 4 shows the comparison of endpoint locations with and without limited interaction power. Although the limited interaction power leads to an increase in the positioning error between the points, the positional error at the points is as low as that without any limitation.

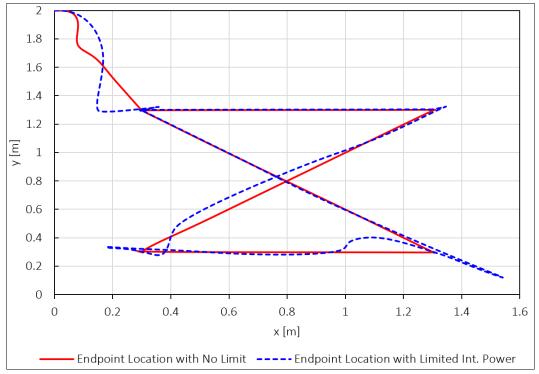


Figure 4. Endpoint location comparison between limited and unlimited interaction power

In the limited power interaction mode, the interaction torques may increase at some points due to the increasing positional error. This effect can be observed in Figure 5. However, in the starting position, the interaction torques are higher in the unlimited power interaction mode compared to the limited power interaction mode.

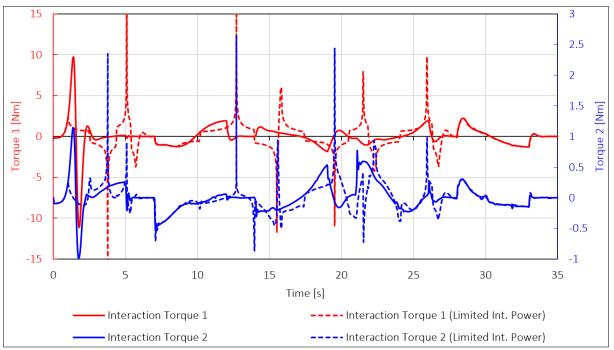


Figure 5. Interaction torque comparison between limited and unlimited interaction power

At the starting position, the angular velocities in the unlimited power interaction mode are higher than those in the limited interaction power mode. However, in later seconds, the angular velocities are higher in the limited interaction power mode. This trend can be observed from the angular velocity graph shown in Figure 6.

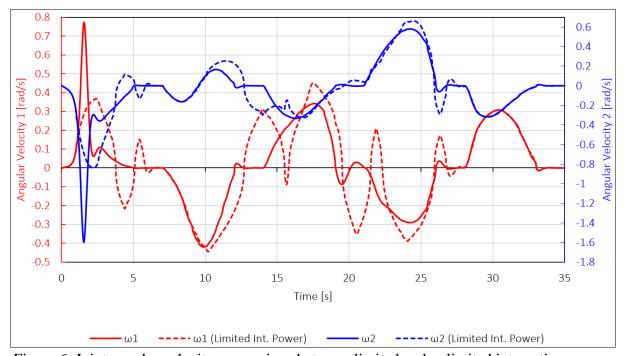


Figure 6. Joint angular velocity comparison between limited and unlimited interaction power

In the unlimited interaction power mode, the interaction powers are observed to reach up to 6 W. However, in the limited interaction power mode, the interaction power is limited to 0.25 W as expected, as shown in Figure 7.

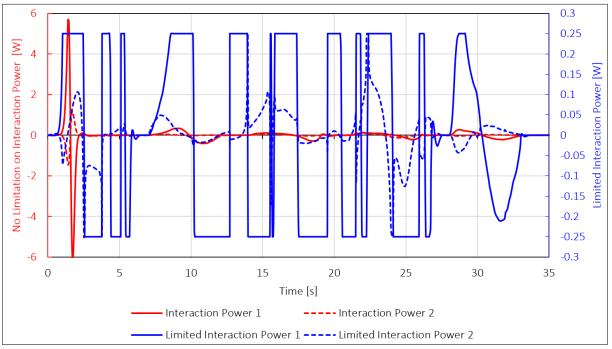


Figure 7. Interaction power comparison between limited and unlimited interaction power

Table 2 presents the interaction energy consumption in both the unlimited and limited interaction power modes. The results show that the interaction power consumption was increased by 1.62% in the limited interaction power mode compared to the unlimited interaction power mode.

Table 2. Interaction energy consumptions

	Interaction Energy	Interaction Energy	Total	
Interaction	Consumption of	Consumption of	Interaction	Change
Power Mode	Joint 1 [J]	Joint 2 [J]	Energy [J]	Ratio
Unlimited	5.97	1.46	7.43	0%
Limited	6.42	1.13	7.55	+1.62%

CONCLUSIONS

In conclusion, this study presented a control method for a robotic arm to optimize the interaction power consumption while achieving precise positioning. The use of a sinusoidal trajectory function and an objective function based on minimizing the distance error led to a

significant reduction in the interaction power consumption. The limitation of interaction power to 0.25 W resulted in some increase in the positioning error between points, however the positional errors at the desired scenario points were still low. The study also showed that limiting the interaction power led to lower interaction torques and angular velocities compared to unlimited interaction power mode. However, the interaction power consumption was increased by 1.62% in the limited interaction power mode. Overall, the findings of this study demonstrate the effectiveness of the proposed control method in optimizing interaction power consumption while maintaining precision in robotic arm positioning.

As the results of this study have shown, the limited interaction power consumption method can be a promising approach for reducing power consumption peaks in industrial robots. Therefore, future studies could investigate the application of this method to larger and more complex industrial robots, as well as explore the potential benefits of combining this method with other power-saving techniques. Additionally, further research could also investigate the effect of different trajectory functions and optimization algorithms on the performance of the limited interaction power consumption method.

REFERENCES

- [1] Bicchi, A., Kumar, V., 2000, *Robotic grasping and contact: A review*, Proc. Proceedings 2000 ICRA. Millennium conference. IEEE international conference on robotics and automation. Symposia proceedings (Cat. No. 00CH37065), IEEE, pp. 348-353.
- [2] Pliego-Jiménez, J., Arteaga-Pérez, M. A., 2015, Adaptive position/force control for robot manipulators in contact with a rigid surface with uncertain parameters, European Journal of Control, 22(pp. 1-12.
- [3] Hogan, N., 1984, *Impedance control: An approach to manipulation*, Proc. 1984 American control conference, IEEE, pp. 304-313.
- [4] Hogan, N., 1984, *Impedance control of industrial robots*, Robotics and computer-integrated manufacturing, 1(1), pp. 97-113.
- [5] Hogan, N., 1987, *Stable execution of contact tasks using impedance control*, Proc. Proceedings. 1987 IEEE International Conference on Robotics and Automation, IEEE, pp. 1047-1054.
- [6] Kumar, C., Mukherjee, A., Dasgupta, A., 1993, A Study on Interaction Control through Passive Degrees of Freedom: Stability and Adaptation of Impedance Variation, IETE Journal of Education, 34(1), pp. 1-20.
- [7] Erdemir, A., Kalyoncu, M., 2023, *Optimal Impedance Control of A 2R Planar Robot Manipulator*, Mas 17th International European Conference on Mathematics, Engineering, Natural & Medical Sciences, Cairo, Egypt, pp. 82-92.

- [8] Erdemir, A., Kalyoncu, M., 2023, Comparison of Energy Consumptions of Input Trajectory Functions in Impedance Controlled 2R Planar Robot Manipulator, International Euroasia Congress on Scientific Researches and Recent Trends 10, Baku, Azerbaijan, pp. 312-325.
- [9] Erdemir, A., Kalyoncu, M., 2019, *Optimization of a Multi-Axle Steered Heavy Vehicle Steering Mechanism by using the Bees Algorithm and the Hooke-Jeeves Algorithms Simultaneously*, International Symposium on Automotive Science And Technology (ISASTECH 2019), Ankara/Turkey, pp. 613-622.
- [10] Lau, T. L., 1999, Guided genetic algorithm, pp. v, 166 leaves.
- [11] Ortmann, M., Weber, W., 2001, *Multi-criterion optimization of robot trajectories with evolutionary strategies*, Proc. Proceedings of the 2001 Genetic and Evolutionary Computation Conference. Late-Breaking Papers, Morgan Kaufmann San Francisco, CA, pp. 310-316.
- [12] Wang, D., Tan, D., Liu, L., 2018, *Particle swarm optimization algorithm: an overview*, Soft computing, 22(2), pp. 387-408.
- [13] Pham, D., Kalyoncu, M., 2009, *Optimisation of a fuzzy logic controller for a flexible single-link robot arm using the Bees Algorithm*, Proc. 2009 7th IEEE International Conference on Industrial Informatics, IEEE, pp. 475-480.
- [14] Erdemir, A., Kalyoncu, M., 2015, *Bir Ağır Vasıtanın Çok Akslı Direksiyon Mekanizmasının Arı Algoritması Kullanılarak Optimizasyonu*, Uluslararası Katılımlı 17. Makina Teorisi Sempozyumu UMTS 2015, pp. 421-426.
- [15] Pham, D. T., Koç, E., Kalyoncu, M., Tınkır, M., 2008, *Hierarchical PID controller design for a flexible link robot manipulator using the bees algorithm*, Proceedings of 6th International Symposium on Intelligent Manufacturing Systems, Sakarya, Turkey, pp. 757-765.
- [16] Erdemir, A., Alver, V., Kalyoncu, M., 2022, *Arı Algoritması Kullanılarak Önden Dümenlemeli Bir Aracın Dümenleme Mekanizmasının Optimizasyonu*, International Aegean Conferences on Innovation Technologies & Engineering 6, İzmir, Türkiye, pp. 50-59.
- [17] Hooke, R., Jeeves, T. A., 1961, "Direct Search" Solution of Numerical and Statistical Problems, Journal of the ACM (JACM), 8(2), pp. 212-229.
- [18] Ypma, T. J., 1995, *Historical development of the Newton–Raphson method*, SIAM review, 37(4), pp. 531-551.

DEVELOPMENT OF FLAME RETARDANT PA6 AND PA66 COMPOSITES ACCORDING TO RAILWAYS EN 45545-2 STANDARD

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ÖZET

Yanma geciktiricili polimer karışımları, mühendislik plastikleri içerisinde önemini gittikçe arttıran malzeme sınıfıdır. Yangın gibi insan hayatı için tehlikeli afet durumlarında, plastiklerin yangın karşısındaki davranışı, verdiği reaksiyon, büyüme hızı çevresinde bulunan insanların hayatına doğrudan etki edebilen durumlardır. Plastiklerin maruz kalabilecekleri her türlü yangın tehlikesine karşı bariyer olma, durdurma veya yavaşlatma gibi karakteristikleri insan hayatının ve çevrenin korunmasına yardımcı olabilecek unsurlardır. Plastiklerin geciktiricilik yanmaya karsı direncleri, vanma davranısları cesitli normlarla belirlenebilmektedir. Bu normlar içerisinde en bilineni UL Sertifikasyon Kurumunca belirtilmiş UL-94 testidir. Bu test malzemenin yanma karakteristiğini V0, V1, V2 ve HB olarak sınıflamaktadır. Bu sınıflamalar içerisinde V0 karakteristiği alev geciktiriciliği en yüksek olan sınıfı, HB ise en düşük olan sınıfı belirtmektedir. Çeşitli kullanım alanlarında bu ve bunun gibi sınıflandırmalar doğru malzeme seçimi konusunda karar verilmesini sağlamaktadır. Toplu taşıma araçlarında ise UL'in dışında Avrupa Standartları Kurumu'nca belirlenmiş olan EN 45545-2 standardı bulunmaktadır. Bu standart özellikle demiryolları gibi yanmazlık sınıfı ürünlerin tasıma vasıtalarında ne tür hangi parçalarda kullanılabileceğini belirleyen standarttır. Bu kapsamda malzemelerin yangına karşı direnci, yanma reaksiyonu sırasında salınan duman toksikliği gibi yolcular için hayati önem taşıyan malzeme davranışlarını sınıflandırmaktadır. Bu çalışmada, EN 45545-2 standardınca belirlenmiş olan farklı kullanım alanlarında kullanılmak üzere geliştirilmiş olan polyamit 6 ve polyamit 66 kompozitleri geliştirilmiştir. Çalışmada her iki polimer türü de cam elyaf takviyeli (%25, %30, %35) demiryollarında kullanıma uygun olacak şekilde halojensiz alev geciktirici bileşenler ile üretilmiştir. Yanma geciktiricili katkılar farklı oranlarda (%16-22) formülasyona dahil edilmiştir. Kullanılan katkılar demiryollarında kullanıma uygun olacak şekilde düşük toksisiteye sahip bileşiklerden seçilmiştir. Geliştirilen kompozitlerin yanma davranışları dikey yanmazlık (UL-94), kızgın tel tutuşma sıcaklığı (IEC 60695-2-13), kızgın tel yanma indeksi (IEC 60695-2-12), yatay yanmazlık (FMVSS 302), Limit Oksijen Indeksi (LOI), duman salınımı (EN ISO 5659-2), toksisite değeri (EN ISO 17094) EN 45545 standardında belirtilmiş olan konektör parçalarında kullanıma uygunluğunun belirlenebilmesi icin test edilmistir. EN 45545-2 standardınca belirlenen testler LAPI bağımsız laboratuvar şirketi tarafında test edilmiş ve tehlike seviyesi (HL) sınıflandırılmıştır. Aynı zamanda kompozitlerin fiziksel ve mekaniksel özellikleri; yoğunluk (ISO 1183), çekme-kopma özellikleri (ISO 527-2), çentiksiz ve çentiksiz darbe dayanım özellikleri (ISO 179/1eA, ISO 179/1eU), ısıl deformasyon sıcaklığı (HDT) testleriyle incelenmiştir. Çalışma kapsamında kompozitlerin nihai olarak kullanılacağı parça tasarımları üzerinde kızgın tel tutuşma sıcaklığı testi yapılarak malzemenin kullanımı uygunluğu doğrudan gözlemlenmiştir. Sonuç olarak, EPLAMID 6 GX0 30 ve EPLAMID 66 GX0 30 ürünleri için EN 45545 standardına uygun olarak HL3 seviyesinde R22, R23 ve R24 ihtiyaç setlerine uygunluk sertifikası alınmıştır.

ABSTRACT

Flame retardant polymer composites are a class of materials that are becoming increasingly important in engineering plastics. In disasters that are dangerous for human life such as fire, the behavior of plastics against fire, their reaction, and growth rate are situations that can directly affect the lives of people around them. Characteristics of plastics such as being a barrier, stopping or slowing down all kinds of fire hazards they may be exposed to are elements that can help protect human life and the environment. The fire resistance and fire retardancy behavior of plastics can be determined by various norms. The most well-known among these norms is the UL-94 test specified by the UL Certification Authority. This test classifies the flammability characteristics of the material as V0, V1, V2 and HB. Among these classifications, the V0 characteristic indicates the class with the highest flame retardancy, and HB indicates the class with the lowest. This and similar classifications in various fields of use enable the decision on the suitable material selection. In public transportation vehicles, apart from UL, there is the EN 45545-2 standard, which is determined by the European Standards Institution. This standard is the standard that determines what kind of flammability class products can be used in which parts, especially in public transport vehicles such as railways. In this context, it classifies material behaviors that are vital for passengers, such as the resistance of materials to fire and the toxicity of smoke released during the combustion reaction. In this study, polyamide 6 and polyamide 66 composites, which were developed to be used in different usage areas determined by the EN 45545-2 standard, were developed. In the study, both polymer types were produced with glass fiber reinforced (25%, 30%, 35%) and halogen-free flame retardant components suitable for use in railways. The additives with fire retardant were included in the formulation at different rates (16-22%). The additives used were selected from compounds with low toxicity to be suitable for use in railways. Combustion behavior of the developed composites, vertical flammability (UL-94), glow wire ignition temperature (IEC 60695-2-13), glow wire flammability index (IEC 60695-2-12), horizontal flammability (FMVSS 302), Limit Oxygen Index (LOI)), smoke emission (EN ISO 5659-2), and toxicity value (EN ISO 17094) has been tested to determine its suitability for use in connector parts specified in EN 45545 standard. The tests determined by the EN 45545-2 standard have been tested by an independent laboratory company LAPI and have been classified as hazard level (HL). At the same time, the physical and mechanical properties of composites; Density (ISO 1183), tensile properties (ISO 527-2), notched and unnotched impact strength properties (ISO 179/1eA, ISO 179/1eU), heat deflection temperature (HDT) tests were investigated. Within the scope of the study, the use of the material was directly observed by performing the glow wire ignition temperature test on the part designs where the composites will be used at the end. As a result, for EPLAMID 6 GX0 30 and EPLAMID 66 GX0 30 products, conformity certificates were obtained for the R22, R23 and R24 requirement sets at the HL3 level in accordance with the EN 45545 standard.

FINITE ELEMENT ANALYSIS BASED DEFORMATION ANALYSIS OF A SPESIFIC UNI-AXIAL COMPRESSION TEST SET-TO FOR DETERMINATION OF CIRCLIP LIMIT FORCE

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ABSTRACT

Unlike the conventional uni-axial tensile test, some extra fixtures and/or apparatus are needed in case of component-based verification studies. For instance, aiming to determine the max. bearing force of a circlip which runs for a transmission shaft, some complex mechanical set-up should be constructed. Furthermore, these extra apparatus create new challenges in terms of mechanical testing as like (i) due to high payloads some elastic deformations and/or deflections may take place during the test (ii) aforementioned deflections could bring up reasonable amount of controversial forces which eliminates the uni-axial loading scenario. Owing to those facts, necessary theoretical and/or numerical analysis should be performed beforehand to assure the precision of the mechanical test. This contribution was devoted to FEA based analysis of such a specific compression test set-up. Linear elastic analysis was conducted and the studied test design was modified until the desired max. deflection amount was satisfied.

Keywords: Uni-axial compression test, deflection, circlip

THE IMPORTANCE OF PHYSICAL ACTIVITY IN IMPROVING PUBLIC HEALTH

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ANNOTATION:

This article discusses the importance and value of exercise in promoting public health.

We all know that regular exercise creates a healthy image for our children and youth.

Heals their will so that they grow up to be brave and courageous people, able to bravely overcome various trials and tribulations.creates a solid foundation. The most important thing is that we are children who are friends with sports. Does not join completely alien and harmful currents.

In order to form an immune system against the disease in Uzbekistan by involving all segments of the population in regular physical education and sports, on October 30, 2020, President Shavkat Mirziyoyev issued Decree No. PF-6099 "On the large-scale introduction of a healthy lifestyle". lifestyle and the public Decree No. PQ-4063 of December 18, 2018 on Measures for the Further Development of Sports and Support for the Prevention of Noncommunicable Diseases, Healthy Lifestyles and Physical Activity of the Population. In accordance with the Decree "On measures to increase the level of industrial gymnastics" in state institutions and organizations during the working day. In order to ensure the implementation of the specified resolution and resolution, from January 1, 2021, the position of "Sports Promoter" was introduced in state bodies and organizations.

The role of a sports promoter is to organize the performance of industrial gymnastics by employees depending on working conditions. For this, special breaks are included in working hours.

The main task of a sports promoter is to organize a "Health Day", which provides for the participation of employees in physical culture and mass events at least once a week, as well as regular sports competitions and other physical education events among employees. calculated.

Production gymnastic exercises are performed for 5-10 minutes during the day, taking into account the peculiarities of the work process.

Industrial gymnastics is a set of exercises performed during the working day in order to improve health and increase productivity.

Health is also a balanced unit of biological, mental, physical states and labor activity of the human body. Health is happiness for everyone.

A healthy lifestyle is a cultural, physical development of a person, a cocktail to increase productivity and creative activity. The main components of a healthy lifestyle are effective work, personal hygiene, giving up bad habits, proper nutrition at the appointed time, physical activity, regular physical activity.

Physical training is systematized with exercises and mass sports through exercise or physical activity at the level of physical maturity, the body's ability to withstand the adverse effects of the external environment and diseases, an adequate attitude to the requirements of life, life activity is understood.

In secondary schools, the health and performance of students is improved and strengthened on the basis of the correct organization of student behavior, which allows students of schools, academic lyceums and vocational colleges to study every day. reform requirements and covers rehabilitation work. The provision of these health-related activities, combined with classroom activities, ensures a high level of physical activity for students. This significantly reduces the fatigue of students and increases the effectiveness of educational activities.

The content of physical education, its means and age, gender, health status and physical training of participants Depending on the application, methods of application are developed separately.

Notably, it is widely used. Among them - health-improving physical training, applied means and methods.

Physical exercise has a positive effect on the human body and pay attention to the design features of the above was found. That is why physical education is so straightforward. It is worth dwelling on the concept. According to the great scientist Abu

Ali ibn Sino, the famous Russian scientist M.I. Sarkisov Sornzi and talented Uzbek scientist T.S. Usmonkhodzhaeva, the treatment of physically weak, sick children and adults with the help of physical exercises, as well as a variety of exercises used in the physical development of healthy people, therapeutic methods of their use are understood as physical culture.

From this comes content and meaning, which only heals. institutions, not just hospitals. but first of all, the whole family, kindergartens, schools, residences, recreation and amusement parks, sports facilities organization of mass physical culture and sports events

reveals the essence of physical therapy.

In general, the physical and mental activity of people engaged in physical activity are exercises that ensure working capacity, various games, excursions, etc. promotes good health.

Only special exercises are used to ensure the physical fitness and skills of civil servants. without it, physical culture is used effectively and purposefully. This, in turn, promotes health and is an expression of developmental properties.

Healthy physical activity in different people different in their health, gender, physical condition by layers and categories training and interest in exercises and beliefs. The corresponding designation was noted above. Healing physical full understanding and assimilation of the benefits and essence of education some artists who received home conditions in the morning, in the afternoon 2-3 times in the process of work, again after work in sports facilities or the habit of training in fitness centers. It should be noted that Some people pass in the morning at least 5-6 km or more, running distances, some of which are different means (dumbbells, springs, elastic bands, etc.). Self 14 and some healthy football fans 1-2 times a day with peers and peers (in the workplace and in the community) to play football. A group of people from different areas (business) or neighborhood) to form teams (teams) and play football, argue like a competition (lay something in the middle) is possible) has become a habit in many places.

Remedial activities include:

- 1) Traditional sports events sports festivals that are attended by all citizens, which has become a national tradition in the primary grades. New Year sports events; Sports event dedicated to Women's Day on March 8; Sports event dedicated to the holiday "Navruz" on March 21 and others.
- 2) Non-traditional activities, events held during the year on the basis of the annual calendar plan of the educational institution.
- 3) Daily wellness activities, morning physical training, exercise, pre-workout gymnastics, long break games, extended hours.

In a word, sports competitions of various forms, content, goals and objectives are aimed at increasing the physical fitness of the population, the formation of physical fitness, as well as increasing their interest in sports, the importance of physical culture and sports for human life. , sociocultural, educational - consciously leads to a conscious understanding of one's place in education and other areas.

Among the recreational activities held in an educational institution are physical education classes, classes in sports sections, sports competitions and sports holidays, as well as mass tourism.

Keywords: health improving gymnastics, sports promoter, health, healthy lifestyle, industrial gymnastics.

ROLE OF APOPTOSIS AND PROLIFERATION OF VASCULAR WALL CELLS IN ATHEROGENESIS

Aigul Myrzabayeva

ABSTRACT

Target. The aim of the work is to study the features of cell death and their proliferation in the wall of human arteries against the background of the development of immune inflammation during atherogenesis.

Scientific novelty. The scientific article discusses the stages of atherogenesis, indicates the mechanism of action of apoptosis and its role in atherogenesis. Also in the scientific article there is information and the study of promising agents in the pharmacotherapy of apoptosis in the treatment of human vascular atherosclerosis.

- It has been established that apoptosis of endothelial cells, caused by the action of macrophages, is a trigger mechanism for the rupture of atherosclerotic plaque.
- -The aim of the work is to study the features of cell death and their proliferation in the wall of human arteries against the background of the development of immune inflammation during atherogenesis.
- -The scientific article shows the results of a study by a group of scientists led by M.D. Rekhter, who studied atherosclerotic plaques, where, as a result, the topographic patterns of the distribution of proliferating cells depending on their type were determined.
- -The role of apoptosis in the physiological processes of the body and the ways in which apoptosis is involved in the aging process are also described.

Conclusions. The work is of theoretical importance for deciphering the mechanisms of development of immune inflammation during atherogenesis. The results of this work can be used to study the pathogenesis of atherosclerosis and be taken into account in the development of new approaches to the treatment of this disease aimed at regulating the kinetics of arterial wall cells.

Key words: Apoptosis. Atherogenesis. Aging.

THE RELATIONSHIP OF NEUTROPHIL-LYMPHOCYTE RATIO AND PROGNOSIS IN COVID-19 PATIENTS

COVID-19 HASTALARINDA NÖTROFİL LENFOSİT ORANININ PROGNOZ İLE İLİŞKİSİ

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ÖZET

COVID-19'un sebep olduğu hastalık, ortaya çıktığından bu yana, tüm dünyayı etkisi altına almıştır. Başlangıçta, virüsün yapabileceği hasar ve şiddetini tahmin etmek güç olsa da yapılan çalışmalarla ve klinik tecrübelerle, prognoz belirteci olabilecek tetkiklerin incelendiği çalışmalar ön plana çıkmıştır. Bunlardan belki de en önemlisi, basit ve hızlı bir test olan, hemogram tahlilindeki nötrofil lenfosit oranı ile hastalığın şiddetini öngören çalışmalardır. Bu çalışmada; hastaların hastaneye başvuru anındaki hemogram tahlili ile prognoz ilişkisi incelenmeye çalışılmıştır.

Bu çalışmaya; Mart 2020-Aralık 2021 tarihleri arasında, COVID polikliniğine başvuran ve PCR + ya da COVID pnömonisi ile uyumlu sonuçlar elde edilen hastaların hemogram tahlilleri incelenmiştir. Hastalar; hastanedeki sonlanıma göre ex olan ya da taburcu olan olmak üzere 2 gruba yarılmıştır. Çalışmaya dahil olan tüm hastaların yaş ortalaması 60±14,5 idi. Ex olan grupta yaş ortalaması (71,6±9,4), pnömoni şiddeti oranı diğer gruba göre daha yüksekti. Ayrıca ex olan grupta; nötrofil sayısı daha yüksek, lenfosit sayısı daha düşük ölçüldü. Hastaneye başvurusundaki nötrofil-lenfosit oranı yüksek, pnömoni şiddeti ağır olan ve yaşlı popülasyonun prognozunun kötü seyrettiği gözlenmiştir.

Bu çalışmadan çıkan sonuçlara göre; hastaların nötrofil-lenfosit oranı prognoz belirteci olarak kullanılabilir.

Anahtar Kelimeler: COVID-19, Nötrofil Lenfosit Oranı, Prognoz, Pnömoni

ABSTRACT

The disease caused by COVID-19 has affected the whole world since its emergence. Although it was difficult to predict the damage and severity of the virus at the beginning, studies that examined the tests that could be prognostic markers came to the fore with the studies and clinical experience. The most important of these are the studies that predict the severity of the disease with the neutrophil-lymphocyte ratio in the hemogram analysis, which is a simple and rapid test. In this study, the relationship between the hemogram analysis of the patients at the time of admission to the hospital and the prognosis was tried to be examined.

In this study, between March 2020 and December 2021, the hemogram analysis of the patients who applied to the COVID outpatient clinic and whose results were compatible with PCR + or COVID pneumonia was examined. The patients, according to the outcome in the hospital, were divided into 2 groups, ex or discharged. The mean age of all patients included in the study was 60 ± 14.5 years. The mean age (71.6 ± 9.4) and pneumonia severity rate were higher in the ex-group than in the other group. In addition, in the ex-group, the neutrophil count was higher, and the lymphocyte count was lower. It was observed that the poor prognosis of the elderly population with a high neutrophil-lymphocyte ratio and severe pneumonia.

According to the results of this study, the neutrophil-lymphocyte ratio of patients can be used as a prognostic indicator.

Keywords: COVID-19, Neutrophil-Lymphocyte Ratio, Prognosis, Pneumonia

MATERNAL IMMUNITY TOLERANCE

MATERNAL İMMUN TOLERANS

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ÖZET

İmmun sistem, kendine ait olan ile olmayanı ayıt etmek için özelleşmiş ve bunu yapmada oldukça ustalaşmış bir sistemdir. Kendinden olmayan antijenleri tespit etmesi durumunda gerekli hücreleri alarma geçirerek en kısa zamanda müdahalede bulunur. Bu sistemin, aslında gerekli ve hayati olmasına karşın gebelik gibi istisnai bir durumda aynı şekilde işlemesi canlılığın başlamadan bitmesine sebep olabilir idi. Bu nedenle yarı-allojenik olan embriyo/fetus gebelik boyunca anne immün sistemi tarafından idare edilmekte ve bu durum maternal immün tolerans olarak nitelendirilmektedir. Bu sistemin, tam olarak anlaşılmamış olmakla birlikte pek çok mekanizmanın katkısıyla gerçekleştiği bilinmektedir. Fakat bu özel tolerans sistemi annenin dış etkenlere karşı verdiği tepkileri değil sadece plasentada ve trofoblast hücreleri ile ilişkili bir sistemdir. Aslında başlangıçta bu özel sistemin nasıl bir mekanizmaya sahip olduğuna dair farklı görüşler ileri sürüldü. Fakat çeşitli sebeplerle biri haric hepsi cürütüldü ve bunun ancak embriyonik/fetal hücrelerin saklanarak anne immun sisteminden saklandığı yani bir immun bariyerin varlığı üzerinde duruldu. Bu saklanma olayına pek çok mekanizma katkıda bulunmaktadır fakat HLA-G denen çözünebilir insan lökosit antijeni en iyi anlaşılabilmiş faktör olarak oldukça önemlidir. HLA-G, trofoblastlar tarafından eksprese edilir ve sitotoksik T ve Natural Killer (NK) hücrelerinin aktivasyonunu engelleyerek işlev gösterir. Ayrıca embriyonun kendisi de salgıladığı maddeler vasıtasıyla uygun ortamı sağlamaya katkıda bulunmaktadır. İmmünsüpresif etkiye sahip olan progesteron hormonu anneye ait olup katkıda bulunan faktörler arasında sayılabilir. Bunlar haricinde de pek çok mekanizma etkilidir. Bu konunun her yönüyle açıklığa kavuşması, düşük durumlarının engellenebilmesi veya yeni tedavi yollarının keşfedilmesini ayrıca organ nakil süreçlerinin daha başarılı sonuçlanmasını sağlayabilir.

Anahtar Kelimeler: Embriyo, Fetüs, HLA-G, Maternal tolerans, Trofoblast

ABSTRACT

The immune system is a system that is specialized to distinguish between what is its own and what is not, and it is quite adept at doing this. If it detects non-self antigens, it alerts the necessary cells and intervenes as soon as possible. Although this system is necessary and vital, in an exceptional situation such as pregnancy, it could have caused life to end before it even started. Therefore, the semi-allogeneic embryo/fetus is managed by the maternal immune system throughout pregnancy and this situation is described as maternal immune tolerance. It is known that this system is realized with the contribution of many mechanisms, although it is not fully understood. However, this special tolerance system is not the mother's response to external factors, but only a system related to the placenta and trophoblast cells. Different views were put forward as to what kind of mechanism this particular system had at the beginning. However, for various reasons, all but one were refuted, and it was emphasized that only embryonic/fetal cells were hidden from the maternal immune system, that is, the existence of an immune barrier. Many mechanisms contribute to this hiding phenomenon, but the soluble human leukocyte antigen called HLA-G is very important as the best-understood factor. HLA-G is expressed by trophoblasts and functions by inhibiting the activation of cytotoxic T and Natural Killer (NK) cells. In addition, the embryo itself contributes to providing the appropriate environment through the substances it secretes. The progesterone hormone, which has an immunosuppressive effect, belongs to the mother and can be counted among the contributing factors. Apart from these, many mechanisms are effective. Clarification of this issue in all aspects may prevent miscarriage cases or discover new treatment methods, as well as provide a more successful result in organ transplantation processes.

Keywords: Embryo, Fetus, HLA-G, Maternal tolerance, Trophoblast

A RARE CASE OF NOVEL MUTATION IN THE KIFBP GENE

KIFBP GENİNDE NOVEL MUTASYON SAPTANAN NADİR BİR OLGU

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ÖZET

Goldberg-Shprintzen sendromu (GOSHS), zihinsel gelişim bozukluğu, mikrosefali ve dismorfik yüz özellikleri ile karakterize otozomal resesif geçisli çoklu konjenital anomali sendromudur. Çoğu hastada ayrıca Hirschsprung hastalığı ve/veya nöral krest hücreleri ve nöronların göçündeki kusurlarla tutarlı olarak beyinde giral anormallikler vardır. Megalokornea veya ürogenital anomaliler gibi diğer özellikler de mevcut olabilir. Goldberg-Shprintzen sendromu Mowat-Wilson sendromu (MOWS; 235730) ile bazı benzerlikler gösterir ancak genetik olarak farklıdır. Bu gendeki defektlere sahip aile bireyleri farklı fenotipler göstermektedir. KIFBP geninde kodlanan KIF-binding protein proteini periferik ve merkezi sinir sistemi gelişimi sırasında aksonal mikrotübüllerin organizasyonu ve aksonal büyüme ve bakım için gerekli olduğu düşünülmektedir. Sunumumuza konu olan 15 yaşında kadın hasta; boy kısalığı, yürüme bozukluğu ve skolyoz şikayetleri ile genetik tanı merkezimize sevk edildi. Hastaya tüm ekzom dizileme (WES) analizi planlandı ve analiz neticesinde elde edilen genetik varyasyonlar in siliko araçların yardımıyla değerlendirildi. Hastada kliniği ile ilişkili olduğu öngörülen KIFBP geni [NM_015634.4] c.979_981del (p.Leu327del) varyasyonu homozigot olarak saptandı. Tespit edilen varyasyon, proteinin fonksiyonel bölgesinde bulunan 327. pozisyondaki lösin amino asidinin silinmesine sebebiyet vermektedir. Saptadığımız varyasyon gnomAD, ClinVar ve PubMed taramalarında varyasyona saptanmadığından novel bir varyasyon olduğu düşünülmektedir. KIFBP'nin KIF-1 binding protein C terminal fonksiyonel domainini etkileyerek hücresel metabolizmayı bozan varyasyonlar, hastalarda farklı fenotipik tutulumlar ortaya çıkarabilmekte ve klinik bulguların șiddetiyle de korelasyon gösterdiği düşünülmektedir. Bu bağlamda çalışmamızın literatüre katkı sağlayacağını düşünmekteyiz. Türkiye, Asya ve Avrupa kıtası arasında geçiş noktası olması ve akraba evliliklerinin herhangi bir Ortadoğu ülkesine benzer olması açısında OR hastalıklara dair verilerin dikkatle değerlendirilmesi ayrıca önem taşımaktadır.

Anahtar Kelimeler: İskelet bozuklukları, WES, Otozomal resesif, Goldberg-Shprintzen megakolon sendromu.

ABSTRACT

Goldberg-Shprintzen syndrome (GOSHS) is an autosomal recessive multiple congenital anomaly syndrome characterized by impaired intellectual development, microcephaly and dysmorphic facial features. Most patients also have Hirschsprung's disease and/or gyral abnormalities of the brain consistent with defects in the migration of neural crest cells and neurons. Other features such as megalocornea or urogenital anomalies may also be present. GOSHS has some similarities with Mowat-Wilson syndrome (MOWS; 235730) but is genetically distinct. Family members with defects in this gene show different phenotypes. The KIF-binding protein protein encoded in the KIFBP gene is thought to be essential for the organization of axonal microtubules and axonal growth and maintenance during peripheral and central nervous system development. A 15-year-old female patient was referred to our genetic diagnosis center with complaints of short stature, gait disturbance and scoliosis. Whole exome sequencing (WES) analysis was planned and genetic variations obtained as a result of the analysis were evaluated with the help of in silico tools. The KIFBP gene [NM_015634.4] c.979_981del (p.Leu327del) variation, which was predicted to be associated with the patient's clinic, was homozygous. The variation causes deletion of the leucine amino acid at position 327 in the functional region of the protein. The variation is considered to be a novel variation as it was not detected in gnomAD, ClinVar and PubMed databases. Variations that disrupt cellular metabolism by affecting the KIF-1 binding protein C terminal functional domain of KIFBP may lead to different phenotypic involvement in patients and are thought to correlate with the severity of clinical findings. In this context, we think that our study will contribute to the literature. The fact that Turkey is located at a transitional point between Asia and Europe, and that consanguineous marriages are similar to any Middle Eastern country, it is also important to carefully evaluate the data on OR diseases.

Keywords: Skeletal abnormalities, WES, Autosomal recessive, Goldberg-Shprintzen megacolon syndrome.

USAGE OF ICP-MS IN BIOLOGICAL SAMPLES

BİYOLOJİK ÖRNEKLERDE ICP-MS KULLANIMI

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ÖZET

ICP-MS olarak bilinen indüktif eşleşmiş plazma-kütle spektroskopisi, temel inorganik bileşiklerden olan eser element, mineral ve ağır metaller gibi periyodik tabloda bulunan birçok elementin analizini yüksek seçicilik ve hassasiyetle yapan spektroskopik bir cihazdır. Biyolojik örneklerde elementlerin analizi klinik ve rutin analizler açısından oldukça önem arz etmektedir. Bunun dışında araştırma ve inceleme konusu olarak da son yıllarda literatüre oldukça katkı sağlayan çalışmalar yapılmaktadır. Biyolojik örneklerde ICP-MS'in çok tercih edilme sebebi çok düşük algılama limitlerinde, birçok elementi aynı anda hızlıca ölçme yeteneğine sahip olmasıdır. Biyolojik örneklerde ICP-MS çok tercih edilmesine rağmen, kullanımında çeşitli zorluklar ortaya çıkmaktadır. Bunlar, az miktardaki örnekte hedef türün düşük derişimlerde bulunması, matriks etkisi, kontaminasyon ve çeşitli girişimlerdir. Bunun haricinde ICP MS ile biyolojik örneklerin analiz edilebilmesi için örneklerin sıvı forma dönüştürülmesi ve organik bileşenlerinin büyük çoğunluğunun uzaklaştırılması şarttır. Bu anlamda numune hazırlık asaması ICP-MS analizlerinde ilk ve en önemli basamaktır. Bu amaçla numune hazırlığında en çok Mikrodalga yakma sistemleri kullanılmaktadır. Farklı tasarımlarda üretilen ICP-MS cihazlarında numunenin direkt olarak cihaza uygulanarak analiz edilmesi biyolojik örneklerde büyük avantaj sağlamaktadır. Yüksek hassasiyeti, aynı anda çok sayıda elementi hızlı bir şekilde analiz edebilme yeteneğiyle de rutin klinik analizlerde ve toksikolojide çok tercih edilen ICP-MS, güçlü ve analitik bir cihazdır. Son yıllarda birçok hastalık ve patolojik durumlarda ICP-MS cihazı ile yapılan araştırmalar hız kazanmıştır.

Anahtar Kelimeler: ICP-MS, biyolojik örnekler, eser element

ABSTRACT

Inductively coupled plasma-mass spectroscopy, known as ICP-MS, is a spectroscopic device that analyzes many elements in the dream table, such as trace elements, minerals and heavy metals, which are basic inorganic things, with high selectivity and sensitivity. Materials collected from living things such as humans, animals, plants, fungi, bacteria, and model organisms constitute biological sample groups. These materials include; body fluids, tissue,

cells and many other components. Researchers need specific types of biological samples to perform their work and advance medicine. The analysis of elements in biological samples is very important in terms of clinical and routine analysis. Apart from this, studies that have contributed to the literature in recent years have been carried out as a research and examination subject. The reason why ICP-MS is highly preferred in biological samples is that it has the ability to quickly measure many elements simultaneously, at very low detection limits. Although ICP-MS is highly preferred in biological samples, various difficulties arise in its use. These are low concentrations of the target species in a small amount of samples, matrix effect, contamination and various interferences. The most common is the contamination that may occur during sampling and storage. The materials used in the sample collection stage should be carefully selected to avoid elemental contamination and should be plastic. Plastic materials used in sample preparation and collection should be washed with 2% nitric acid. Samples can be stored for a long time at +4-8 °C with pre-treatment, convert to solution and acidification processes. Apart from this, in order to analyze biological samples with ICP MS, it is necessary to convert the samples into liquid form and remove the majority of their organic components. Biological samples cause matrix effect due to their organic components and high salt content. Digestion of the organic part, dilution up to a certain rate, is effective in reducing matrix interactions. In this sense, sample preparation is the first and most important step in ICP-MS analysis. For this purpose, microwave combustion systems are mostly used in sample preparation. Analyzing the sample by applying the sample directly to the device in ICP-MS devices produced in different designs provides a great advantage in biological samples. ICP-MS, which is highly preferred in routine clinical analyzes and toxicology, is a powerful and analytical device with its high sensitivity and ability to quickly analyze many elements at the same time. In recent years, research with the ICP-MS device has gained momentum in many diseases and pathological conditions.

Key Words: ICP-MS, biological samples, trace elements

GİRİŞ

Canlı organizmalarda birçok biyokimyasal sürecin yürütülmesinde temel inorganik bileşiklerden olan mineraller ve eser elementlerden faydalanılır (Frausto da Silva JJR, 2001). Biyolojik örneklerin, yaş ağırlığının %1'inden daha az olan elementlere eser element denilmektedir (Bowen, 1988). Eser elementler yaşamsal döngü homeastazındaki rolleri, eksiklikleri veya aşırılıkları sebebiyle çeşitli hastalıklara sebep olabilmektedir ve bu nedenle son yıllarda sıkça araştırılmaya başlanmıştır (Fraga, 2005). Örneğin bu eser elementlerden Çinko (Zn), bakır (Cu) ve Mangan (Mn) birçok enzimin kofaktörleridir ve ayrıca antioksidan olarak işlev görürler (H, 2010). Demir (Fe), santral sinir sisteminin fonksiyonları ve yapısı için hayati önem taşımakla kalmayıp, oksijen transferinin de en önemli kofaktörüdür (JM, 2001). Kobalt (Co), yağ aside metabolizması ve folat için ihtiyaç duyulan B12 vitamini ile bütünleşmiş şekilde bulunmaktadır. Kadmiyum (Cd) çevresel ve mesleki maruziyetlerle birikim gösteren toksik elementlerdendir. Kurşun(Pb) ise, inflamasyona sebep olan, oksidatif stresi tetikleyen, nitrik oksit üretimini azaltan ağır metaldir (Chen PC, 2013). Selenyum (Se),

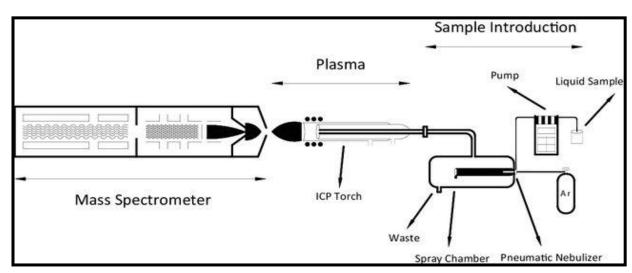
hastalık durumlarında bağışıklık sisteminde rol alır ve hücre zarlarını oksidatif hasardan korur (U,T 2008).

Biyomedikal alanda, eser elementlerin canlılardaki rolleri ve toksik etkilerini araştırmaya yönelik pek çok araştırma yapılmaktadır. Bu anlamda eser elementlerin incelendiği materyaller ise, kan, doku, saç, diş, tırnak, idrar ve çok çeşitli vücut sıvılarını içermektedir. Ancak, biyolojik örnekler matris girişimleri, kontaminasyon, düşük analit ve numune miktarları sebebiyle analiz edilirken güçlük yaşanmaktadır (Tunç, 2006). Bu yüzden biyolojik örneklerde eser element içeriklerini belirleyebilmek ve doğru bilgiye ulaşmak için, uygulanması kesinleşmiş yöntemlerinin kullanılması mecburidir (Ivanenko, 2011).

Biyolojik örneklerde farklı teknik, seçicilik ve hassasiyetle element analizi yapan çeşitli spektroskopik cihazlar vardır. Çoğunlukla, atomik absorpsiyon spektrometresi (AAS), indüktif eşleşmiş plazma atomik emisyon spektrometresi (ICP-AES) aynı zamanda indüksiyonla birleşmiş plazma optik emisyon spektroskopisi (ICP-OES) olarak da bilinir, Xray floresan analizi (XFA veya XRF) ve indüktif eşleşmiş plazma kütle spektrometrisi (ICP-MS) kullanılmaktadır. Nadir olarak da Sıyırma voltametresi (SVA) ve nötronaktivasyon analizi (NAA) kullanılmaktadır (Ivanenko, 2011). Biyolojik örneklerde eser element tayini için bu cihazlardan en çok ICP-MS kullanılmaktadır. Sebebi yüksek hassasiyet ve çoklu element analizine imkân sunmasıdır.

1.ICP-MS Cihazının Genel Özellikleri ve Bileşenleri

İndüktif eşleşmiş plazma-kütle spektrometresi (ICP-MS), biyolojik örnekler başta olmak üzere birçok numunenin çok düşük konsantrasyonlarda (μg/L, ng/L), birçok elementin aynı anda analiz edilmesini sağlayan gelişmiş analitik bir yöntemdir. Yöntemin ana prensibi, çözelti halindeki örneğin, argon gazı ile plazmaya gönderilmesi ve burada yüksek sıcaklıkta (8000-10000 Kelvin) iyonlaştırılan elementlerin kütle/yük (m/z) oranına göre de kütle spektrometre (MS) ünitesinde tespit edilmesine dayanmaktadır (Bahadır, 2020).



Şekil-1: ICP-MS ana bileşenler şeması (Kashani, 2010).

Günümüzde farklı dizaynlarda ICP-MS cihazları bulunsa da, birçoğunun ana bileşenleri aynıdır ayrı bir ünitesi olmadıkça sadece S1V1 örneklerin analizini gerçekleştirebilmektedirler. Örneğin sprey odası, nebulizatör, plazma torcu, dedektör tüm ICP-MS cihazlarında ortak bileşenlerdir. Sıvı numune peristaltik pompa aracılığıyla sisleştirilmek üzere nebulizatöre gönderilir. Numune burada argon gazı ile aerosol şeklinde sprey odasına püskürtülür. Numune aerosolü quartz torch bölümünden plazmaya ulaşır. Ouartz torc RF sarmalı denen, yüksek radyo frekansı olusturan bakır bobinler içinden geçmektedir. Bu yüksek manyetik alandaki voltajlı kıvılcım ve torch içinden geçen argon gazı molekülleri carpısmaktadır ve yüksek sıcaklıkta plazma olusmaktadır böylelikle tüm elementler iyonlaşmaktadır. Pozitif yüklü iyonlar nikel cone lardan geçerek iyon lensine ulaşır. İyonlar kütle detektörüne girmeden önce girişim yapan iyonların uzaklaştırılması amacıyla çarpıştırma hücresinde inert bir gaz olan helyum veya hidrojen ile çarpıştırılarak uzaklaştırılır. Ardından kütle analizöründe iyonlar kütle/yük oranına göre ayrılır, sadece kararlı iyonlar detektöre iletilirler (Tunç, 2006).

1.1. ICP-MS kullanımının avantajları

ICP-MS, mükemmel duyarlılığı, seçiciliği ve izotop belirleme potansiyeli ile eser element analizlerinde önemli bir yer etmiştir. Çok sayıda elementi eş zamanlı olarak hızlı bir şekilde tayin edebilmektedir. Cihaz tasarımına göre, tek enjeksiyonla belirlediğiniz kadar (örneğin 1-5) okuma yapabilmektedir. Oto örnekleme ünitesi sayesinde, çok sayıda örneği hızlı bir şekilde enjekte ederek analiz edebilmektedir. Girişim yapan türleri uzaklaştırmak adına inert gazlar ile çarpıştırma ve girişim engelleme özelliğine sahiptir (Zoorob, 1998).

1.2. ICP MS kullanımının dezavantajları

- ✓ Nispeten yüksek sermaye maliyeti
- ✓ Yüksek operatör deneyim gereksinimi
- ✓ Toplam Cözünmüs Katılar < 0.2% (TDS)
- ✓ Matriks girişimleri
- ✓ İzobarik girişimler
- ✓ Sapma/belirsizlik
- ✓ Nispeten yüksek işletme maliyetleri
- ✓ Daha yüksek konsantrasyonlar için "çok hassas" olabilir (Tyler, 1995).

1.3. ICP-MS kullanımında girişimler

ICP-MS'de spektral ve spektral olmayan iki tür girişim söz konusudur. Spektral girişimlerde plazmadaki hedef tür iyonunun m/z oranı ile iyonik türün m/z oranının çakışmasıyla oluşur. Spektral olmayan girişimler ise matriksten kaynaklanmaktadır. Yoğun sinyal sebebi ile atom kütlesinin baskılanması ile oluşur. Matriks etkisinin oluşumunu 500-1000 mg/mL den çok olan girişimsel türlerin derişimi sebep olmaktadır.

1. Spektral Girişimler:

- ✓ Elementel izobarik girişimler
- ✓ Çift yüklü türler
- ✓ Çok Atomlu Girişimler
- ✓ Artık Müdahaleleri

2. Spektral Olmayan Girişimler:

- ✓ Matris
- ✓ Boşluk yükü etkisi
- √ Fiziksel

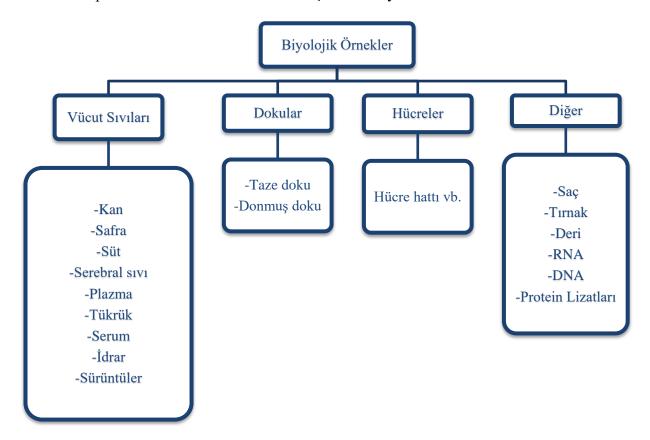
3. Diğer

- ✓ Bellek etkisi
- ✓ Kirlilik problemleri (Balaram, 2021).

2. Biyolojik Örneklerin ICP-MS'de Analizi

İnsan, hayvan, bitki, mantar, bakteri ve model organizmalar gibi canlılardan toplanan materyaller biyolojik numune gruplarını oluşturur. Bu materyaller; vücut sıvıları, doku, hücreler ve diğer birçok bileşeni kapsamaktadır. Araştırmacılar, çalışmalarını gerçekleştirmek ve tıbbı ilerletmek için belirli türde biyolojik örneklere ihtiyaç duyarlar.

Biyolojik örneklerin elementel analizi oldukça meşakkatlıdır. Biyolojik örneklerin düşük hacim ve analit içeriklerinden dolayı, elementel analizlerinden sağlıklı sonuç alabilmek için örneklerin toplanması ve analize hazırlanması işlemleri büyük önem arz etmektedir.



Şekil-2: Biyolojik örnek sınıflaması

2.1. Biyolojik Örneklerin Toplanması

Uygulanan yöntemden bağımsız olarak, biyolojik örneklerin analizinin en genel sorunu, numune alımı ve saklama sırasında oluşabilecek olan kirliliklerdir. Kan örneklerinin toplanmasını ele alacak olursak, ilk aşamada kan alımı için kullanılan enjektörlerde Al, Cr, Ni ve Zn kontaminasyonu riski vardır. Bunun önüne geçmek için plastik venöz kanül kullanımı tavsiye edilmektedir (Orbelis, 2008). Alınan kanın hemolizli olması da ayrıca serumdaki Fe, Cu, Zn, Pb, Rb, Mn ve Mg konsantrasyonlarını arttırdığından bu aşama da oldukça dikkatli olunmalıdır (Bertram, 1992). Kan alındıktan sonra saklanacak tüplerde oldukça önemlidir. Antikoagülan içeren tüplerin numuneyi kontamine etme riski de oldukça yüksektir (Ivanov, 2009). Bu nedenle lacivert kapaklı eser element tüpleri ile Fe, Zn, Cu, Hg, Pb gibi eser elementlerin tayininde kullanılmaktadır. Pıhtı aktivatörü olarak, K₂Edta ya da Naheparin içermektedir. Eser element analizine kullanılan bu tüplerde Na ve K analizi uygun olmaz.



Şekil-2: Eser element Analiz Tüpü

Doku vb diğer numunelerin toplanmasında da benzer kontaminasyonlar söz konusudur. Dokulardan kesit alınırken kullanılan bisturi, sonrasında saklanacakları kapların temiz ve elementel girişime sebep olmaması önemlidir.

Toplanan numunelerin ön işlem aşamalarında kullanılan teflon tüpler, pipet uçları, enjeksiyon tüplerinin temizliği de elementel analiz aşamalarında oldukça önemlidir.

2.2. Biyolojik Örneklerin Analize Hazırlanması

Biyolojik numunelerin karmaşık matris bileşimi (organik bileşenler, yüksek tuz içeriği gibi) çoğunlukla numune hazırlama aşamasının analiz prosedüründen çıkarılmasına izin vermez. Uygulanan yöntemlerin seçiciliğine bağlı olarak numune hazırlama, basit numune seyreltmesinden numunenin termal veya mikrodalga parçalanması gibi adımlar izlenebilir. Numunenin organik kısmının parçalanması, belli bir orana kadar seyreltme matriks etkileşimlerinin azaltılmasında etkilidir. (Ivanenko, 2011). Bununla birlikte, biyolojik dokuların ICP-MS ile analizi için, katı numunenin ayrışma prosedürü ve numunenin ICP'ye eklenmesinden önce bunun homojen bir sıvı faza dönüştürülmesi genellikle gereklidir. Analiz öncesinde numuneler genellikle asit ortamında parçalanır. Açık veya kapalı kaplarda yaş yakma metotları, mikrodalga destekli asitli parçalama ile çeşitli numunelerde başarılı olmasına rağmen mikrodalga sistemlerinin birkaç dezavantajı da vardır. En önemlisi çoklu

numunelerde kullanımı kısıtlıdır, sebebi ise mikrodalga rotorlarının her döngüde sınırlı olan örnek kapasitesidir. Bir diğeri ise, kullanılan kaplarda kalan kirliliklerin birkaç kez temizleme döngüsüne tabii tutulması gerekliliğidir (Batista, 2009). Bu yüzden az zaman ve emekle daha çok örneğin ön hazırlığı arzu edilir bir durumdur.

Bunlar dışında, cihaz tasarımlarına göre değişkenlik gösteren birçok metot bulunmaktadır. Bazı cihazlarda numunenin direk enjekte edildiği aparatlar mevcutken (Sussulini, 2017), bazı cihazlar için farklı kimyasallar ile muamele sonrası enjeksiyona imkân sağlayan metotlar ve tasarımlar mümkündür (Batista, 2009).

2.3.Sonuç

ICP-MS de biyolojik örneklerin analiz edilmesi son yıllarda kapsamlı bir şekilde kullanılmaktadır. Özellikle kan ve idrarda seviyeleri artan elementlerin kronik ve akut maruziyetlerini belirlemek adına oldukça faydalıdır. ICP-MS de çoklu ve tekli elementlerin özellikle klinik toksikoloji ve rutin analizlerde kullanımı hayati önem taşımaktadır (Goullé, 2014).

Biyolojik örneklerde elementel analize imkân sağlayan güçlü, analitik bir cihazdır.

- ✓ Oldukça hassastır
- ✓ Çok sayıda elementin tek seferde eş zamanlı tayiniyle toksikolojik vakalarda hızlı sonuç sağlamaktadır.
- ✓ Gruplara göre yöntem uygulanabilirliği çok iyidir.
- ✓ Donanım ve yazılımında düzeltme denklemlerinin kullanımıyla hassasiyet ve özgüllüğü de artırmaktadır.

Kavnakca

- Bahadır, Z. (2020). Atık Su Örneklerinde Bazı Ağır Metallerin İndüktif Eşleşmiş Plazma Kütle Spektrometresi ile (ICP-MS) Tayini. *Journal of Anatolian Environmental and Animal Sciences*, 56-60.
- Batista, B. L. (2009). Determination of trace elements in biological samples by inductively coupled plasma mass spectrometry with tetramethylammonium hydroxide. *plasma mass spectrometry with tetramethylammonium hydroxide*, 23-29.
- Balaram, V. (2021). Strategies to overcome interferences in elemental and isotopic geochemical analysis by quadrupole inductively coupled plasma mass spectrometry: A critical evaluation of the recent developments. . *Rapid Communications in Mass Spectrometry*.
- Bertram, H. (1992). Spurenelemente: Analytik, Okotoxikologische und Medizinisch. *Klinische Bedeutung, Muenchen: Wien, Baltimore, Urban und Schwarzen berg.*
- Bowen, H. J. (1988). Trace elements in biological samples. (Vol. 8, pp. 1-17). Elsevier. Bowen içinde, *In Techniques and Instrumentation in Analytical Chemistry* (s. 1-17). England: elsevier.
- Chen PC, e. a. (2013). Blood trace minerals concentrations and oxidative stress in patients with obstructive sleep apnea. *J Nutr Health Aging*, 639-644.

- Fraga, C. G. (2005). Relevance, essentiality and toxicity of trace elements in human health. . *Molecular aspects of medicine*, 235-244.
- Frausto da Silva JJR, W. R. (2001). *The biological chemistry of the elements*. Oxford: Oxford University Press.
- Goullé, J. P. (2014). Current role of ICP–MS in clinical toxicology and forensic toxicology: a metallic profile. *Bioanalysis*, 2245-2259.
- H, V. e. (2010). Alterations of plasma magnesium, copper, zinc, iron and selenium concentrations and some related erythrocyte antioxidant enzyme activities in patients with Alzheimer's disease. *J Trace Elem Med Biol*, 169-173.
- Ivanenko, N. B. (2011). Determination of trace elements in biological fluids . *Journal of analytical chemistry*, 784-799.
- Ivanov, V. M. (2009). Toksikologicheskaya khimiya. Metabolizm i analiz toksikantov (Toxicological Chemistry: Toxicant Metabolism and Analysis), A textbook for higher schools, Kaletina, NI, Ed. 206: Journal of Analytical Chemistry.
- JM, O. (2001). Trace elements and DNA damage. Biochem Soc Trans, 354-357.
- Kashani, A. &. (2010). Aerosol characterization of concentric pneumatic nebulizer used in inductively coupled plasma-Mass spectrometry (icp-ms). *Atomization and Sprays*, 415-433.
- Orbelis, D. K. (2008). Biolog icheskaya rol' makro i mikroelementov u cheloveka i zhivotnykh (Biological Role of Macro and Microele ments in Human and Animals). *St. Petersburg: Nauka*.
- Sussulini, A. B. (2017). Laser ablation ICP-MS: Application in biomedical research. . *Mass spectrometry reviews*, 47-57.
- Tunç, M. (2006). Biyolojik sıvılarda bazı eser elementlerin tayini ve metot geliştirme. Yıldız Teknik Üniversitesi, Fen Bilimleri Enstitüsü.
- Tyler, G. &. (1995). ICP-OES, ICP-MS and AAS Techniques Compared. *ICP Optical Emission Spectroscopy Technical Note*, 5
- U.T. (2008). Selenium: its role as antioxidant in human health. Environ Health, 102-108.
- Zoorob, G. K. (1998). ICP-MS for elemental speciation studies. *Microchimica Acta*, 145-168.

INVESTIGATION OF THE BLOOD MICROBIOME PROFILE

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ABSTRACT

The blood that flows continuously through our veins performs a multitude of functions that are essential for our survival. This extensive circulatory system facilitates oxygen delivery as well as nutrient transport, prevents infection, and distributes heat throughout our body. Human blood consists of ~54.3% plasma, ~45% red blood cells (erythrocytes), ~0.7% white blood cells, and platelets. The human microbiome includes a wide range of bacterial, archaeal, viral, and fungal microbial taxa. Since human blood is thought to be completely sterile consisting only of blood cells, platelets, and plasma, the detection of microbes in the blood has consistently been interpreted as an indicator of infection. However, although the human

blood microbiome is a controversial topic, there is growing evidence for its existence. While the origins, identities, and functions of these microorganisms remain to be elucidated, there is increasing knowledge on bloodborne microbial phylogeny. The discovery of the human microbiome has been greatly facilitated by the emergence of Next Generation Sequencing (NGS) and whole metagenome shotgun sequencing (WMGS) as new techniques to study microbial genetic material present in different human body parts. The application of innovative analytical technologies such as 16S rRNA-targeted metagenomic sequencing has provided increasingly robust evidence for the existence of a human blood microbiome. Here we underline that many pathogens can survive in blood. Given the growing number of studies investigating whether the presence of foreign invaders in human blood is not associated with infection or a diseased condition, we explore the characteristics of a healthy human blood microbiome.

Keywords: Blood microbiome, bacterial infection, bloodstream

IN VITRO CULTURE MODELS IN LATENT TUBERCULOSIS INFECTION

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ABSTRACT

Tuberculosis (TB), one of the ancient diseases, infects about 10 million people every year. One out of every four people in the world carries a live TB bacillus in their body but does not show any symptoms of the disease. These individuals represent latent TB infection. Latent TB infection is one of the biggest obstacles to the eradication of the disease. Because individuals with latent TB are the largest reservoir of active TB cases. In individuals infected with TB bacillus, the immune system tries to control the infection by keeping the bacilli in a compact immune system cell cluster, mostly macrophages, called granulomas. If the granuloma cannot be preserved due to the disorders in the immune system, the TB bacillus is released and the infection progresses to active TB disease. It is assumed that the replication of bacilli within the granuloma continues at a low level, metabolic activities are minimally regulated, gene expression changes and there is phenotypic drug tolerance. The environment in granuloma has a different profile, including hypoxia, nutrient deprivation, limited carbon sources, high concentration of nitric oxide, and low pH. It is thought that these environmental conditions are the transition of the bacillus to the dormant phase. It is necessary to elucidate

the mechanisms by which bacilli return to a dormant state and active growth for the control of TB infection. For this reason, several in vitro models have been developed that mimic conditions within the granuloma. Wayne's hypoxia model, Loebel's nutrient limitation model, nitric oxide model, and multiple stress model are some of them. All models contribute to the laboratory modeling of latent infection and understanding the mechanism of infection by imitating the stress conditions in the granuloma in a closed tube in a culture medium.

Keywords: Mycobacterium tuberculosis, latent infection, dormancy models, granulomas

INVESTIGATION OF THE USABILITY OF THE HIGHWAY SURFACE DRAINAGE SYSTEM AS A PRECIPITATION WATER HARVESTING SYSTEM

KARAYOLLARI YÜZEY DRENAJ SİSTEMİNİN YAĞIŞ SUYU TOPLAMA SİSTEMİ OLARAK KULLANILABİLİRLİĞİNİN İNCELENMESİ

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ABSTRACT

Highways are travelable roadways that are utilized by modern cultures to preserve their way of life. They are used for transportation inside and between cities. Rainfall coming to the roof is collected by rainwater collection systems to be used as irrigation or drinking water. Systems for managing rainwater are frequently used to protect the security of roadways. Accordingly, systems that serve two related but distinct goals can be merged. In this context, this study is a preliminary study on the usability and conversion potential of the highway precipitation drainage system as a snow water and rainwater harvesting system. For this, a study area has been determined. The length of the surface precipitation drainage channels of the asphalt road is 2000 m (left side) and 2900 m (right side), and the total length is 4900 m. In addition, there are anti-erosion stone walls. The total amount of equivalent snow water that comes with snow for the period between January 26 and February 2, 2023, has been calculated as 377300 m³. On February 2, 14635 m³ of snow water was harvested. In addition, it can be said that the water quality is fairly excellent since a water quality of less than 50 ppm is achieved. It has been observed that the studied region has a serious potential for a rainwater harvest however, the drainage system needs to be rearranged due to structural defects and water leaks in the current situation. Asphalt roads, which are only used for transportation, may be used to meet energy and water needs, save resources in a way that will meet the needs of future generations, and create products utilizing diverse processes to add value.

Keywords: Highway surface drainage system, rainwater harvesting, usability, sustainability.

ÖZET

Otoyollar, modern kültürler tarafından yaşam tarzlarını korumak için kullanılan seyahat edilebilir yollardır. Onlar, şehir içi ve şehirlerarası ulaşım için kullanılırlar. Çatıya gelen yağış, sulama veya içme suyu olarak kullanılmak üzere yağmur suyu toplama sistemleri tarafından toplanır. Yağmur suyunu yönetmeye yönelik sistemler, yolların güvenliğini korumak için sıklıkla kullanılmaktadır. Buna göre, birbiriyle ilişkili ancak farklı iki amaca hizmet eden sistemler birleştirilebilir. Bu bağlamda bu çalışma, karayolu yağış drenaj sisteminin kar suyu ve yağmur suyu toplama sistemi olarak kullanılabilirliği ve dönüşüm potansiyeli üzerine bir ön çalışmadır. Bunun için bir çalışma alanı belirlenmiştir. Asfalt yolun yüzey yağış drenaj kanallarının uzunluğu 2000 m (sol taraf) ve 2900 m (sağ taraf) olup, toplam uzunluk 4900 m'dir. Ayrıca, erozyon önleyici tas duvarlar mevcuttur. 26 Ocak – 2 Subat 2023 tarihleri arasında karla birlikte gelen toplam eşdeğer kar suyu miktarı 377300 m³ olarak hesaplanmıştır. 2 Şubat 2023 tarihinde 14635 m³ kar suyu hasadı yapılmıştır. Ayrıca, 50 ppm'in altında bir su kalitesi elde edildiğinden su kalitesinin oldukça iyi olduğu söylenebilir. İncelenen bölgenin yağmur suyu hasadı için ciddi bir potansiyele sahip olduğu görülmüştür ancak mevcut durumdaki yapısal bozukluklar ve su kaçakları nedeniyle drenaj sisteminin yeniden düzenlenmesi gerekmektedir. Sadece ulaşım için kullanılan asfalt yollar, enerji ve su ihtiyacını karşılamak, gelecek nesillerin ihtiyaçlarını karşılayacak şekilde kaynak tasarrufu sağlamak ve farklı süreçler kullanılarak değer katan ürünler oluşturmak için kullanılabilir.

Anahtar Kelimeler: Karayolu yüzey drenaj sistemi, yağmur suyu hasadı, kullanılabilirlik, sürdürülebilirlik.

Nomenclature

 $A_{road,channel}$ rainwater collection area, m²

 C_r runoff (loss) coefficient

RWH yearly amount of harvestable rainwater from the road and channel, m³

 RW_{tot} total annual rainfall, m

Tiw total amount of incoming water, m³
Tcw total amount of collecting water, m³

1. Introduction

Highways are roads that are used for transportation in and between cities and can be traveled, which today's societies use to maintain their lives. Asphalt roads, which are only utilized for transportation, may be utilized to fulfill energy demands, conserve them in a way that will satisfy future generations' needs, and create energy using various means to add more value. With these ideas in mind, the idea of using energy for energy generation without endangering the design of roadways but with new industrial equipment has emerged. On the other hand, innovative ideas for asphalt roads are being developed. These can be categorized as road concepts, along with the production of hot water and air, electricity generation (using piezoelectric generators, PV panels, thermoelectric modules, pyroelectric), energy storage (using phase-changing material-PCM, aquifer thermal energy storage, batteries), and self-heating using frost and icing prevention systems (Şevik, 2016; Şevik, 2021).

Precipitation is any kind of vapor condensation in atmospheric water clouds that rises to the earth's surface because of the clouds' gravitational attraction. Rain, sleet, snow, ice pellets, graupel, drizzle, and hail are the main forms of precipitation. The topic may be divided into two categories: drainage systems and rainwater collection systems. Water and poor drainage on the road surface reduce the strength of the pavement and sub-base, causing premature asphalt road distress, which leads to driving problems and road structural failures. Inadequate drainage causes problems such as traffic safety (aquaplaning and icing), and low bearing capacity in sub-floor and road structures that cause erosion and permanent deformation. Therefore, drainage systems need to be well-organized. Such situations can cause accidents, disrupt traffic flow, and interrupt normal life. In addition, drainage systems need to be wellorganized or require good maintenance. The service life of the pavement can be enhanced by 50% if the water is immediately removed from the asphalt road (Rokade et al., 2012). Thus, to guarantee the structural integrity of the flexible pavements, an efficient drainage system should also be built for the drainage of precipitation water during road building. On the other hand, as in a study conducted by Kayhanian et al. (2019) and stated to have an important role in stormwater flow management, it is also possible to apply permeable pavement on highways. Surface concrete drainage systems are typically selected because they are inexpensive, simple to build, and maintain. As opposed to level terrain, sloping land allows for much easier water evacuation using the surface concrete drainage system since it has the necessary bearing capacity to evacuate the flow.

Rainwater collection systems are generally applied to roofs to collect water from roofs, thus

saving water by using them in toilets, gardens, etc. According to Ghisi et al. (2009), using rainwater at gas stations can result in potable water savings of up to 33% and water savings of up to 57%. Kaya (2020) evaluated the rainwater potential of the roofs of the buildings in the Izmit district, Turkey, and calculated the rainwater utilization rate for 2017 as 33.27%. On the other hand, there are systems where rainwater is collected over PV panel arrays in solar PV power plants (Aktaş et al., 2021; Şevik and Aktaş, 2022). Şevik and Aktaş, (2022) established a system consisting of rainwater collection channels, pump-hydrophore installation, and tanks with a capacity of 25 m³ in the facility area for rainwater harvesting in the PV plant. They also installed a drip irrigation system for an orchard that is located higher than the PV plant. They reported that the potential for collecting rainwater from a small portion (288 m²) of the PV power plant is approximately 118 m³/year. In addition, they stated that the harvesting system would reach 1646 m³/year when applied to the entire PV power plant.

Drainage and rainwater harvesting systems can be used together to both manage water and recycle water for use in agriculture. The objectives of this research are to a) evaluate the current state of the drainage network in the existing highway, b) assess the system's capacity to serve its purposes, c) identify the drainage system's water harvesting potential, d) determine whether the drainage system can be converted to a precipitation harvesting system, and e) evaluate the water collection capacity when used as a precipitation harvesting system.

2. Material and Method

2.1. Multiple Use Opportunities of Highways

Even though there is now a limited quantity of energy produced on highways, studies are being done to satisfy these demands and increase the value of highways, which is currently only utilized for travel and freight movement. However, for a variety of reasons, some of these studies are unable to get past the concept, proposal, and idea stages. The following is a list of some of the techniques utilized or aimed at for energy production on highways (Şevik, 2021).

- a) Electricity generation with wind turbines
 - Electric power generation with conventional wind turbines
 - Electricity generation with modified wind turbines
- b) Electric energy production with biomass
- c) Electricity generation by waves and tides
- d) Electric power generation with mixed biofuels
- e) Renewable energy-assisted electric vehicle charging stations

- f) Renewable energy-assisted vehicle hydrogen charging stations
- g) Generating a small amount of electrical energy using the thermoelectric effect
- h) Generating a small amount of electrical energy by vibration capture technology
- i) Generating a small amount of electrical energy using the piezoelectric effect.
- j) Heat and electrical energy production with solar energy
 - Electric power generation with PV panels for warning signs and street lighting
 - Generation of electrical energy with solar noise-canceling barriers
 - Electricity generation with solar-powered road panel
 - Heat energy generation with asphalt road solar collector

Some systems collect roof-borne rainwater for use as a utility or drinking water. In addition, rainwater management systems, which are often employed to maintain the safety of highways, are also utilized. Therefore, similar systems serving two different purposes can be combined. Thus, a win-win situation occurs and sustainable water management can be realized.

2.2. Current working area

The size of the drain depends on a variety of factors, including the frequency and amount of rainfall, the width and profile of the highway, the porosity of the backfill, and the hydraulic conductivity of the subgrade soil (Ozioma, 2022). The computation of the drainage system for water discharge is not present in this analysis, though, as it only examines the current roadway and drainage system. A double asphalt road with a length of 3350 m has just been constructed on sloping terrain. The double asphalt road passing through the studied area is slightly curved and the level difference is 135 m. While the starting altitude of the road is 971 m, the ending altitude is 1106 m. The study location is located in an area with 422.7 mm of annual precipitation.

In this study, highway, and roadway are defined as follows;

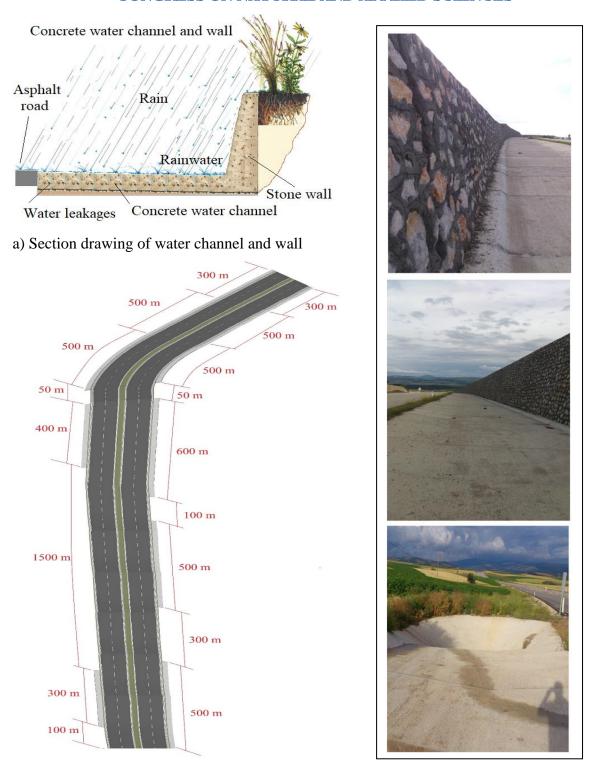
Highway=2*Roadway, and Roadway= Margin+Shoulder+carriage way+Shoulder+Margin

2.3. Existing surface concrete precipitation drainage system

It has open-concept concrete precipitation drainage channels on both sides of the existing double road and in the middle of the roundtrip roads. Although the length of the double asphalt road passing through the studied area is 3350 m, the water channels were not built integrally on both sides of the road. Surface precipitation drainage channels and erosion prevention barriers with a total length of 2000 m are located on the left side of the asphalt road. On the right side of the asphalt road, there is a similar structure with a total length of

2900 m. In general, the surface concrete discharge system can be inclined, V-shaped, U-shaped, trapezoidal, rectangular, or square, and the channels can be lined with mass concrete or reinforced concrete. In the current location, a "V"-shaped concrete structure, divides the roundtrip roads. On the right and left of the double asphalt road, there are surface concrete discharge channels of certain lengths and intermittently organized. Fig. 1 shows the double asphalt road precipitation drainage system. Fig 1a shows the section drawing of the water channel and wall. Fig 1b shows the photos of the concrete channel drainage system and the entire workspace.

According to Fig. 1, on the left side of the asphalt road, there are surface precipitation drainage channels and erosion prevention walls, consisting of five parts and a total length of 2000 m. To the right side of the asphalt road, there are surface precipitation drainage channels and erosion prevention walls, consisting of six parts and a total length of 2900 m. Accordingly, the entire length of the drainage line is approximately 4900 m. The section of approximately 2*250 m has a slight slope. Other sections have a pretty slope. The anti-erosion stonewalls have a slope of 8%, and the channels have an inclination of 6% in the direction of the stone wall.



b) Photos of the concrete water channel drainage system and the entire workspace Fig. 1. Double asphalt road precipitation drainage system

The precipitation intensity (PI) of the area is measured by measurement equipment. Weather data are obtained from weather studies of the nearest meteorological station.

$$PI = PD/t \tag{1}$$

where *PD* is precipitation depth in mm, *t* is precipitation duration in min.

The inflow volume (V_i) of the water entering the channel is

$$V_i = l_o.PI.A \tag{2}$$

 l_o is the coefficient representing water losses.

The outflow volume (V_0) of the water entering the channel is

$$V_0 = l_e. V_i \tag{3}$$

 l_e is coefficient representing water leakages.

The annual amount of rainwater that can be harvested can be estimated from meteorological information. The volume of daily rainwater harvesting is calculated from the daily rainfall amount by multiplying the area with the rainfall amount and deducting the water losses.

The yearly amount of harvestable rainwater (RWH) from road and channels can be calculated as follow;

$$RWH = RW_{tot}A_{road,channel}C_r \tag{4}$$

3. Result and discussion

In the province where the work area is located, the annual precipitation amount, which has been measured and determined for many years, is approximately 422.7 mm. The highest monthly rainfall was in May (62.2 mm), and the lowest was in August (15.2 mm). Fig. 3 shows the meteorological data between January 26 and February 2, 2023. Snowfall amounts were 3.1 mm on 29 January 2023, 1 mm on 31 January, and 8.8 mm on 1 February.

Snow water harvesting was carried out on the day after a snowfall. Fig. 4 shows the snow water harvesting on February 2, 2023. While there was more snow in the shaded areas, there was less snow in the sun-exposed areas. Photos without snow were taken in the afternoon. A conversion from snow to snow water is made to calculate the water coming into the drainage system being studied. This may be called the equivalent snow water or snow-to-rain conversion. The formula used for snow-to-rain conversion is as follows

Rainfall
$$[mm]$$
 = snow depth $[mm]$ *rain-to-snow ratio (5)

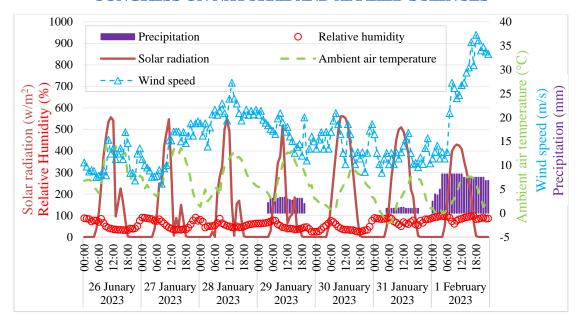


Fig. 3. The meteorological data between January 26 and February 1, 2023.



Fig. 4. Snow water harvesting on February 2, 2023

Fig. 5 shows the total amount of water in terms of snow water coming into the drainage system studied. It also shows the amount of water collected from that drainage system. In

other words, Fig. 5 shows the total amount of water collected (m³) and the total amount of incoming water (m³). The total amount of incoming equivalent snow water has been calculated as 377300 m³. The amount of equivalent snow water obtained from the melting snow on February 2, 2023, is 14635 m³. There has collected very little water in comparison to the amount of snow. Even so, it is possible to gather the majority of the accumulated snow.

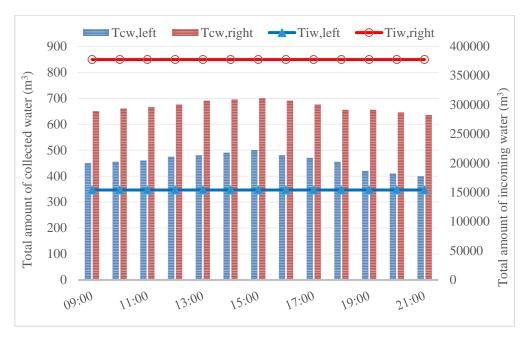


Fig. 5. The amount of water harvested from the workspace, February 2, 2023 (Tiw: the total amount of incoming water, and Tcw: the total amount of collecting water)

With the snowfall on 6-7 February, the capacity to harvest water roughly doubled, but a small amount of water could be collected owing to the negative ambient air temperatures. The snowstorm on February 6-7 caused a significant amount of snow to accumulate on the water channel and anti-erosion walls, as shown in Fig. 6. In addition, the snow shoveled over the road by the snowplow vehicles was also carried to the channels. This indicates an increase in snow that will turn into water, and thus more water can be collected.

Water quality measurements were conducted when the air temperature rose and the snow melted. Fig. 7 shows the water quality measurements. The water quality was assessed using a TDS meter (range: 0-9990 ppm, accuracy: $\pm 2\%$, measures from 0-999 ppm, with a resolution of 1 ppm). The water quality values between 18 and 39 ppm were measured based on the measurements made at various locations. While low readings were made near snow accumulations, greater readings were recorded towards the channel's terminus. While the tap water in the study area had a value of 369 ppm, the value in its pool was calculated at 384

ppm. Hence, because the water quality is below 50 ppm, it is feasible to declare that an accomplishment has been made. Note that the measurements were performed at 13°C.



Fig. 6. Photographs of snowdrifts on the water channel and anti-erosion walls due to snowfall and snow plowing from the road on February 6-7, 2023.



Fig. 7. The water quality measurements

Instead of using ground or surface water for irrigation, rainwater may be collected and used in certain periods. There is an irrigation dam in the nearby area, where water can be transported

naturally to be used during the agricultural irrigation season. Collected precipitation water can be stored in certain tanks or an irrigation dam. Fig. 8 shows the study area and the delivery of collected water to an agricultural irrigation dam.



Fig. 8. Study area and transmission of collected water to an agricultural irrigation dam

The collected water can be conveyed directly to the irrigation dam or the pools with the drainage system or a modern system can be installed as in Fig. 9. Fig. 9 shows a modern water management system using a storage tank. It will be easy to deliver water to the irrigation dam thanks to this design's ability to improve the quality of the surface water. In this system, the natural flow method can be used as well as the pump can be used.

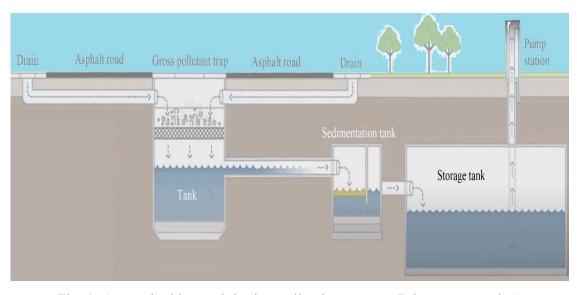


Fig. 9. A sustainable precipitation collection system (It is representative)

4. Conclusion

It has been attempted to ascertain if the highway surface drainage system can be employed as a method for collecting precipitation water in this study. The drainage line's total length is about 4900 m. The total amount of water that comes with snow for the period between January 26 and February 2, 2023, has been calculated as 377300 m³. On February 2, 2023, 14635 m³ of water was harvested by snowmelt. Water quality levels between 18 and 39 ppm were found using measurements made at various locations. It has been observed that the studied region has a serious potential for a rainwater harvest. When the gaps in the drainage line are also arranged, the drainage line can reach a total of 6700 m (3350 m on the right and left). In this case, the water capacity will increase significantly.

In case, the study area is desired to be transformed into a rainwater harvesting system.

- In its current condition, water can be collected, but it needs to be rearranged.
- In the current state of the existing canals, water can be collected but needs to be rearranged.
- A sustainable precipitation collection system can be established, as in Fig. 8.
- The collected water must be conveyed to the dam used for agricultural irrigation by a
 pipeline or water collection pond(s) should be constructed at the lowest position of the
 study area.
- Regular cleaning and maintenance to avoid blockage and guarantee proper flow.
 Maintenance may be carried out once a year, ideally right before the rainy season starts.
- Erosion control should be done at the outlet of the drain and the culvert.
- The drainage line has to be cleared of any obstruction.
- People have to be educated about proper garbage disposal.

The design of highways and highway drainage systems may be better understood with the help of this study. In many countries, proper maintenance of road drainage structures is overlooked on most roads that are more or less intense. When such water collection systems are implemented, better maintenance of water channels can be provided, which increases the safety of the roads.

References

- Aktaş, A., Şevik, S., Aktaş, Ş. (2021). Rainwater harvesting in a 600 kW solar PV power plant. ISPEC 7th Int. Conference on Agriculture, Animal Sciences and Rural Development, 18-19 September 2021, 1116–1124, Muş, Turkey.
- Ghisi, E., Fonseca Tavares D., Rocha, V.L. (2009). Rainwater harvesting in petrol stations in Brasília: Potential for potable water savings and investment feasibility analysis. Resources, Conservation and Recycling, 54 79–85.
- Kayhanian, M., Li, H., Harvey, J.T., Liang, X. (2019). Application of permeable pavements in highways for stormwater runoff management and pollution prevention: California research experiences. International Journal of Transportation Science and Technology, 8(4), 358–372.
- Kaya, M. (2020). Evaluation of the existing solar energy and rainwater potential in the total roof area of buildings: Izmit district example. Advances in Materials Science and Engineering, 8167402, 16 pages.
- Ozioma, O.C. (2022). A Drainage System for Road Construction on Flat Terrain. In (Ed.), Applied Methods in Design and Construction of Bridges, Highways and Roads Theory and Practice. IntechOpen.
- Rokade, S., Agarwal, P.K., Shrivastava, R. (2012). Study on drainage related performance of flexible highway pavements. Int. J. Adv. Eng. Tech., 3(1), 334–337.
- Şevik, S. (2016). Modeling of a multi-functional solar-asphalt energy harvesting and snow-ice prevention system for sustainable superstructures. TÜBAV Sci. J., 9(1), 1–16.
- Şevik, S. (2021). Evaluation of energy production on highways and energy harvest from asphalt roads. 3rd International November 24 Head Teacher Education and Innovative Sciences Symposium, Baku, Azerbaijan, 22–41.
- Şevik, S., Aktaş, A. (2022). Performance enhancing and improvement studies in a 600 kW solar photovoltaic (PV) power plant; manual and natural cleaning, rainwater harvesting and the snow load removal on the PV arrays. Renewable Energy, 181, 490–503.

IN HISTORICAL BUILDINGS DAMAGE CAUSITIVE STRUCTURE PHYSICS FACTORS

TARİHİ YAPILARDA HASARA SEBEP OLAN YAPI FİZİĞİ ETKENLERİ

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ÖZET

Kent ve çevre kimliğine katkı sağlayan, geleneksel ve yöresel yaşam biçimini yansıtan yapılar tarihi ve estetik değer taşımaktadır. Kültürel, sosyal ve ekonomik kayıplara neden olan yapılar geri dönüşü olmayan durumlarla karşı karşıya kalmaktadır. Ayrıca ortam koşullarından etkilenen ve inşaları sırasında yapılan tasarım ve uygulama hatalarından kaynaklanan birçok problemlerinde oluşmasına neden olmuştur. Çalışmanın birinci aşamasında, kültür yapılarımızın nitelikli örneklerini içeren Sakarya ili Taraklı ilçesinde yer alan sivil mimariler yerinde incelenerek fotoğraflarla belgelenmiştir. İkinci aşamada, yapılar üzerinde incelemeler yapılarak yapılarda kullanılan malzeme ve geçirdiği onarımlar hakkında değerlendirmelerde bulunulmuştur. Bu değerlendirmelerden elde edilen verilerin çevresel etkenler, fiziksel ve mekanik etkenler, biyolojik etkenler, yapı fiziği problemleri ve kullanıcı kaynaklı sorunlar olduğu ortaya çıkarılmıştır. Kültür varlıklarımızı etkileyen yapı fiziği problemleri (nem, 181, ses, güneş yangın ve korozyon) yapıların taşıyıcı sistemlerinde geri dönüşü olmayan bozulmalara yol açarak önemli ölçüde tarihi yapıların tahribatına neden olmaktadırlar. Bu çalışmanın amacı; kültür varlıklarımızın gelecek kuşaklara aktarılmasını riske sokmamak için seçilen örneklem alanında karşılaşılan mevcut sorunlar özellikle yapı fiziği problemleri tespit edilmiştir. Bu tespitlerle korunması gerekli yapılara özgün ölçütte önlemlerin alınabilmesi için gelecekte karşılaşılacak benzer olumsuzluklara karşı ışık tutabilecek önerilerde bulunulmustur.

Anahtar Kelimeler: Bozulma, Sivil Mimarlık Örnekleri, Yapı Fiziği Problemleri.

ABSTRACT

Contributing to the city and environmental identity, buildings reflecting traditional and regional life style it has historical and aesthetic value. Structures that cause cultural, social and economic losses are faced with irreversible situations. In addition, it has caused many problems that are affected by environmental conditions and caused by design and application errors made during construction. In the first stage of the study, civil architectures in the Taraklı district of Sakarya province, which contain qualified examples of our cultural structures, were examined on site and documented with photographs. In the second stage, by examining the buildings, evaluations were made about the materials used in the buildings and the repairs they had undergone. It has been revealed that the data obtained from these evaluations are environmental factors, physical and mechanical factors, biological factors, building physics problems and user related problems. Building physics problems (humidity, heat, sound, sun, fire and corrosion) affecting our cultural assets cause irreversible deterioration in the bearing systems of the structures and cause the destruction of historical buildings to a large extent. The aim of this study in order not to risk the transfer of our cultural assets to future generations, the current problems encountered in the selected sample area, especially the problems of building physics, have been identified. With these findings, In order to take measures specific to the structures that need to be protected, Suggestions have been made to shed light on similar negativities to be encountered in the future.

Keywords: Deterioration, Examples of Civil Architecture, Building Physics Problems.

1. INTRODUCTION

Contributing to the city and environmental identity, buildings reflecting traditional and regional life style it has historical and aesthetic value. Structures that cause cultural, social and economic losses are faced with irreversible situations. In addition, it has caused many problems that are affected by environmental conditions and caused by design and application errors made during construction.

The properties of the building materials and the application conditions directly affect the durability of the building. For this reason, mistakes and deficiencies in the production and application processes of the building and building materials cause the structures to be damaged and destroyed over time. In addition to using a suitable material in the building production process, it is necessary to prevent the material from deteriorating over time and not losing its performance.

Buildings are damaged over time due to environmental factors. It is caused by wrong design,

wrong material selection, wrong workmanship and outdoor conditions. Mechanical effects,

heat effects, water and moisture effects, physico-mechanical effects are called building

physics problems. Building physics factors cause damage to the structure over time and

deterioration of human health and comfort conditions.

2. CAUSES OF BUILDING PHYSICS PROBLEMS

2.1. Mechanical Effects

Made up of structures cracks are caused by mechanical effects. Causes such as faulty

workmanship, insufficient material selection, expansion, contraction or vibration of the floor,

deflection of beams, excessive load, wind, snow can cause cracks in structures (Güler, 2010).

2.2. Heat Effects

Heat factors such as heat expansion, frost, sun effect and fire are one of the building physics

problems. Capillary cracks in building materials, stresses arising from the effect of frost cause

physical breakage and fragmentation of materials (Torraca, 1988). The use of materials with

different expansion coefficients in buildings causes deformations in the materials, and the

problems caused by the effect of the sun cause color changes (Yüzer vd., 2000).

2.3. Water and Humidty Effects

The penetration of water into the material is called penetration, and the increase in the volume

of the building material as a result of getting wet is called swelling. Rain water, snow, ice and

ground water cause an increase in moisture within the stone in different ways (Ziyaettin,

2010).

With the effect of the moisture rising from the ground and the salts it carries, flowering occurs

in the building material. Humidity caused by condensation, rain and fog humidity, and

moisture rising from the soil by capillary cause physical and chemical deterioration in the

material (Küçükkaya, 2004).

They occur due to wetting and humidity, atmospheric effects and plumbing failures. Water

and humidity damage the exterior and interior walls, roof coverings, wet floor coverings,

balconies and railings of the buildings.

162

2.4. Physico-Chemical Effects

Corrosion occurs as a result of oxidation of metal or alloy. Physico-chemical effects such as corrosion, sun and inflorescence cause pollution in the structures and chemical and physical deteriorations occur in the materials.

The aim of this study in order not to risk the transfer of our cultural assets to future generations, the current problems encountered in the selected sample area, especially the problems of building physics have been identified.

In the first stage of the study, the civil architectures in the Taraklı district of Sakarya province, which contain qualified examples of our cultural structures, were examined on site and documented with photographs. In the second stage, evaluations were made about the materials used in the buildings and the repairs they had undergone by examining the buildings.

3. EXAMINATION OF BUILDING PHYSICS EFFECTS IN TARAKLI HOMES

3.1. Investigation of mechanical effects

The Taraklı houses, which were chosen as the sample area, were examined and the mechanical effects that caused the building physics factors were examined. As shown Figure 1. Ayşe Sezgin House of bending caused by mechanical effect on the floor covering is given.



Figure 1. Ayşe Sezgin House of bending caused by mechanical effect on the floor covering. As shown Figure 2. and Figure 3. Ayşe Sezgin House of bending caused by mechanical effect on the ceilling covering is given.



Figure 2. Ayşe Sezgin House of bending caused by mechanical effect on the ceilling covering.



Figure 3. Nevzat Akay House of bending caused by mechanical effect on the ceilling covering.

As shown Figure 4. İbrahim Pilavcı House of breaks in balcony railing due to mechanical effect is given.

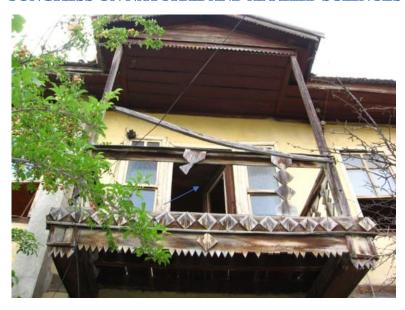


Figure 4. İbrahim Pilavcı House of breaks in balcony railing due to mechanical effect.

3. 2. Investigation of heat effects.

As shown Figure 5. Ayşe Sezgin House of Deteriorations caused by the effect of heat on the exterior of the sturucture is given.



Figure 5. Ayşe Sezgin House of Deteriorations caused by the effect of heat on the exterior of the sturucture.

As shown Figure 6. İbrahim Pilavcı House of deteriorations caused by the effect of heat on the exterior of the sturucture, Figure 7. and Figure 8. Nevzat Akay House of deteriorations caused by the effect of heat on the exterior of the sturucture are given.



Figure 6. İbrahim Pilavcı House of deteriorations caused by the effect of heat on the exterior of the sturucture.



Figure 7. Nevzat Akay House of deteriorations caused by the effect of heat on the exterior of the sturucture.



Figure 8. Nevzat Akay House of deteriorations caused by the effect of heat on the exterior of the sturucture.

3.3. Investigation of the effects of water and humidity

As shown Figure 6. Ayşe Sezgin House of moisture formation on the wall surface due to water and humidity, Figure 10. and Figure 11. Ayşe Sezgin House of deterioration of the wall surface due to water and moisture are given.



Figure 9. Ayşe Sezgin House of moisture formation on the wall surface due to water and humidity.



Figure 10. Ayşe Sezgin House of deterioration of the wall surface due to water and moisture.



Figure 11. Ayşe Sezgin House of deterioration of the wall surface due to water and moisture.

3.4. Investigation of phsico-mechanical effects

As shown Figure 12. Ayşe Sezgin House of crack caused by mechanical action on the wall surface and Figure 13. Ayşe Sezgin House of corrosion induced deterioration in flooring are given.

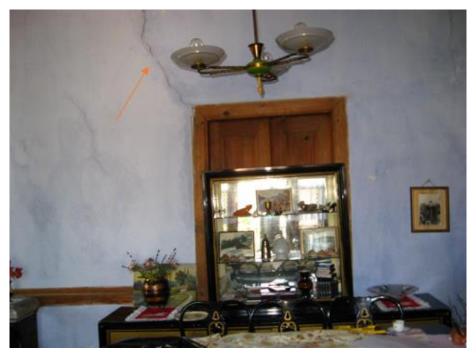


Figure 12. Ayşe Sezgin House of crack caused by mechanical action on the wall surface.



Figure 13. Ayşe Sezgin House of corrosion induced deterioration in flooring.

As shown Figure 14., Figure 15., Figure 16. and Figure 17. İbrahim Pilavcı House of crack caused by mechanical action on the wall surface are given.



Figure 14. İbrahim Pilavcı House of crack caused by mechanical action on the wall surface.

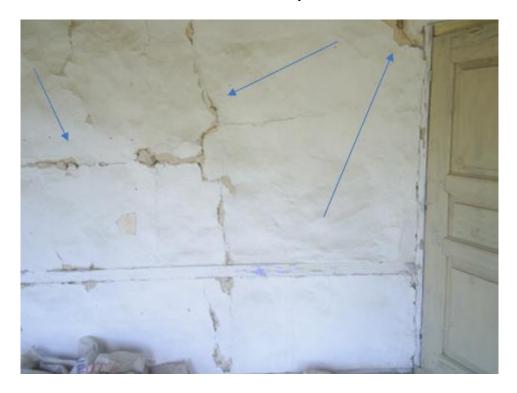


Figure 15. İbrahim Pilavcı House of crack caused by mechanical action on the wall surface.



Figure 16. İbrahim Pilavcı House of crack caused by mechanical action on the wall surface.



Figure 17. İbrahim Pilavcı House of crack caused by mechanical action on the wall surface.

It has been revealed that the data obtained from these evaluations are structure physics problems such as environmental factors, physical and mechanical factors, chemical and biological factors, and user-related problems.

4. RESULT

Building physics problems affecting our cultural assets cause irreversible deterioration in the bearing systems of the structures and cause the destruction of historical buildings to a great extent.

In order to historical buildings be long-lasting, problems arising from building physics problems should be determined. Then, measures should be taken to prevent the original texture of the structures from deteriorating. According to the necessary protection methods, applications should be made with original materials suitable for the environment.

Attention should be paid to material compatibility, correct workmanship and the application of correct construction techniques in structures. Measures should be taken against deterioration caused by thermal factors applying heat insulation material on exterior and interior facades against heat expansion. Water and moisture-related problems should be also prevented by applying waterproofing material to prevent water from entering the structure.

5. REFERENCES

Ahunbay, Z. (1998). Tarihi Cevre Koruma ve Restorasyon, Yapı Yayın, İstanbul.

- AKMAN, M. S., (2000). Yapı Hasarları ve Onarım İlkeleri, TMMOB İnşaat Mühendisler Odası, İstanbul.
- Eser, F., & Yardımlı, S. (2017). Tunceli İli Meşeyolu Köyü Yapılarının Yapı Fiziği Açısından Değerlendirilmesi, Bilim ve Gençlik Dergisi, c.2, v.5, 96-112.
- Günay, R. (2002). *Geleneksel Ahsap Yapılar Sorunları ve Çözüm Yolları*, Birsen Yayınevi, İstanbul, 2002.
- Mihlayanlar, E. (2005). Binalarda Hasra Sebep Olan Yapı Fiziği Etkenler, *Yüksek Lisans Ders Notları*, Edirne.
- Özkan, Ö. (2009). Taraklı Sivil Mimarlık Örnekleri ile Halim Düzgün Evi'nin Proje ve Ali Pektaş Evi'nin Restorasyon Çalışmaları, Yüksek Lisans Tezi, Sakarya Üniversitesi, Fen Bilimleri Enstitüsü, Sakarya.

- Özkan Önür Ö. & Yerli, Ö. (2019). Sivil Mimarlık Örneklerinden Ayşe Sezgin Evi'nin Restorasyonu. Mimarlık, Planlama ve Tasarım Alanında Araştırma Makaleleri, ss.201-219.
- Özkan Önür, Ö., Apay, A. C. & Mutlu, E. (2022). Tarihi Yapılarda Koruma Fatma Sevim Dönmez Evi. *Kültürel Miras Araştırmaları Dergisi*, c.3, v.1, 17–25.
- Güler, H., Sezer Ş., & Ülkü, S. (2010). Binalarda Yapı Fiziği Problemleri: Bursa'da Bir Kamu Kurumu Örneği, *Uludağ Üniversitesi Mühendislik-Mimarlık Fakültesi Dergisi*, c.15, vol. 2, 53-64.
- Küçükkaya A. G. (2004). Taşların Bozulma Nedenleri Koruma Yöntemleri. Birsen Yayınevi.
- Taraklı Belediye Arşivi, 2009.
- Torraca G. (1988). Porrous Building Materials, Science for Architectural Censervation. Iccrom.
- Yüzer, E., Gürdal, E., Ersen, A., Güleç, A, Eyüboğlu R., Eriş, İ., Görür, N., Vardar, M., Suner, F., Mahmutoğlu, Y., & Pehlivanoğlu, C. (2000). *Dolmabahçe Sarayı, Kullanılan Taşların Korunmuşluk Durumlarının ve Ayrışma Nedenlerinin Belirlenmesi*, Koruma ve Onarım Yöntemlerinin Saptanması Projesi Koruma ve Onarım Yöntemlerinin Saptanması Projesi, İstanbul Teknik Üniversitesi Geliştirme Vakfı Araştırma Projesi Raporu, İstanbul.
- Ziyaettin, N. (2010). 'Kimyasal Uygulamalarının Kuzey Kıbrıs Yapı Taşlarının Dürabilitesi Üzerine Etkisi', Doktora Tezi, İstanbul Teknik Üniversitesi Fen Bilimleri Enstitüsü, İstanbul, Türkiye.

SATELLITE MUSEUMS AND ITS IMPACT ON URBAN SPACE

UYDU MÜZELER VE KENTSEL MEKANA ETKİLERİ ÜZERİNE BİR İNCELEME

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ÖZET

Kentler, küreselleşmenin baskın bir akım olarak kentleri biçimlendirdiği 1980 sonrası dönemde birbirleriyle rekabet içerisine girmişlerdir. Bu yarışmacı süreç kentleri kendi, markalarını yaratmaya, olumlu yönlerini öne çıkarmaya yönelik uygulamalar yaparken olumsuzluklarını bertaraf etmeye, tehditleri ortadan kaldıracak ve potansiyellerini maksimum seviyede kullanabilecek stratejiler yaratmaya itmiştir. Her kent daha zengin turist ve yatırımcıyı kentine çekmeyi istemektedir. Özellikle hizmet sektörünün ekonomik pay dağılımındaki artan oranı turistik faaliyetlerden biri olan kültür eksenli küresel hareketliliği de öne çıkarmıştır. Organizasyon ve etkinliklere ev sahipliği yapmak önemsenen bir strateji haline gelmiştir. Bu etkinlikler süreli veya süresiz şeklinde gruplanmaktadır. Müzeler ve özellikle tematik nitelikte olanlar gerek mimarisiyle gerekse sergiledikleri ürünlerle kendileri birer çekim noktası haline gelmişlerdir. Müzeler de nitelik farklı gruplara ayrılmaktadır. Bunların bulundukları kente etkileri bulunmaktadır. Ancak bu çalışma son dönemlerde daha da görünür olan ve dünya çapında da birçok örneklerini gördüğümüz uydu müzelere odaklanmaktadır. Yirmi birinci yüzyılın bu yeni uydu modelinde merkez müzeler sahip oldukları eserleri farklı kent veya ülkedeki uydu müzelere aktarmaktadır. Böylesi bir akışta asıl müzenin bilinirliği artmakta; uydu müzeler ise bulundukları kent parçasında birer öncü proje özelliği ile çevresini dönüşmektedir. Çalışma kentlerin markalaşması bakış açısından başlayarak bir pazarlama stratejisi olarak müzeleri ve uydu müzeleri tanımlamayı ve bu tip yapıların kentsel mekanlar üzerindeki etkilerini kuramsal çerçeve ve dünya örnekleri üzerinden ortaya çıkarmayı amaçlamaktadır.

Anahtar Kelimeler: Müze, Uydu Müze, Turizm, Küreselleşme

ABSTRACT

Cities entered into competition with one another in the post-1980 period, when globalization shaped cities as a dominant trend. This competitive process has pushed cities to create their brands, eliminate their negative aspects, create strategies that will eliminate threats, and use their potential at the maximum level while making practices to highlight their positive aspects. Every city wants to attract richer tourists and investors to its city. In particular, the increasing rate of the service sector in the economic share distribution has also highlighted cultural-oriented global mobility, which is one of the touristic activities. Hosting organizations and events has become an important strategy. These activities are grouped as temporary or indefinite. Museums, especially the thematic ones, have become points of attraction with their architecture and the products they exhibit. Museums are also divided into different groups. These have effects on the city in which they are located. However, this study focuses on satellite museums, which have become more visible in recent years and we see many examples around the world. In this new satellite model of the twenty-first century, central museums transfer their works to satellite museums in different cities or countries. In such a flow, the awareness of the original museum increases; Satellite museums, on the other hand, transform their surroundings with the characteristics of pioneering projects in the part of the city they are located in. The study aims to define museums and satellite museums as a marketing strategy, starting from the point of view of the branding of cities, and to reveal the effects of such structures on urban spaces through a theoretical framework and world examples.

Keywords: Museum, Satellite Museum, Tourism, Globalization

SECURITY VULNERABILITIES IN CLOUD TECHNOLOGY

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ABSTRACT

Cloud technologies have been widely used in recent years with the development of technology. The widespread use of cloud technology makes it attractive for attacks. The most important difference between the attacks that cloud technology is exposed to is that it is accessible to all devices in the same ecosystem. This situation increases the course and amount of attacks. Cyber attacks and their methods are also changing and developing in the cyber world, which is developing more each day. Today, an important part of the attacks that cloud tools are exposed to, the increasing number of users, consists of attacks on users. Social hacking has become very common, especially with the use of social media. Due to the presence of unconscious users, a large number of attacks take place. Cloud services are constantly open to the outside world, which also makes them vulnerable to attack. Cloud service providers are also trying to provide security with two-factor authentication, authentication, and end-to-end encryption to remedy these attacks. In this study, the advantages and disadvantages of cloud technology were also investigated. In this study, detailed research was conducted on the security vulnerabilities of cloud technology.

Keywords: Cloud Technologies, Cloud Technologies Security, Security Vulnerabilities

1. INTRODUCTION

Developments in electronic and communication tools have been at an unprecedented pace in recent years. Every day, new technology or innovation takes its place in our lives. It is also possible for people and devices to communicate with each other, transfer data, and store data in one place, thanks to cloud technology. The fact that data can be stored, transferred to many places simultaneously, and accessible at any time and any hour makes cloud technologies attractive. The development of cloud computing dates back to the 1960s.

Cloud computing is a set of virtual services that ensure that data is stored in another environment, accessible on the internet, that acts with a pay-as-you-go mentality, and allows users to pay only for the service they use (Srinivasamurthy et al., 2013). Cloud technologies are useful and easily accessible technology that enables users to store their data and applications in a remote environment and to make them accessible whenever they want. Ease of administration, configuration, access, and service advantages make it a popular service provider[2]. It provides services for personal or corporate use purposes. In the current age, it can be said that there is no area where there is no internet and communication is not provided. Even the progress in the last few years is much greater than in previous decades. Cloud computing technology has also overtaken classical storage and data transfer activities. These systems are used more frequently in the business world and provide fast and secure data transfer, storage, easy manageability, and ease of access. The intense demand for cloud computing causes the rapid development of this field and various security needs.

Cloud computing has a distributed system architecture with open-source software. The information on the user data and the physical addresses where this data is stored are not shared (Sun, 2020). One of the advantages of cloud computing is that it can be accessed from anywhere in the world and handle various tasks. It can be moved on the cloud through browsers and provides great mobility in the corporate sense. This makes cloud computing products attractive, which also avoids classical storage costs. This study will discuss the security and vulnerabilities of cloud computing products.

2. CLOUD COMPUTING TECHNOLOGIES

It is a technology that has started to be developed since the 1960s and provides services in

areas such as data storage and data transfer. It is a system that allows storing data on the Internet, thus freeing users from physical storage devices and environments and providing access anywhere at any time. Devices in the cloud ecosystem are not physically connected. Remote network servers provide this service. It can also be called the virtualization of data. It is designed to store data securely, manage easily, run applications, and transmit content and services. It can be accessed from any device connected to the internet (Bhajantri and Mujawar, 2019).

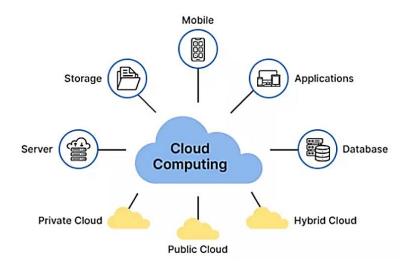


Figure 1. Cloud Computing (Myrasecurity, 2023).

Cloud deployment types are divided into 4 main classes public cloud, private cloud, hybrid cloud, and community cloud. These distribution models emerged as a result of determining individual and institutional needs. It can be perceived as an advantage that it is divided into these distribution types in terms of cost and security. Individuals and organizations have different security needs, and the security of these distribution types differs. Since the number of users using corporate products is more than one, they are always open to security threats. The threat level is increasing, especially when users are unaware of this. Users should be made aware of attack methods and safe use (Goumidi et al., 2020).

2.1. Cloud Deployment Types

2.1.1. Public Cloud

A public cloud is a type of cloud deployment that anyone can use and whose security the service provider determines privacy, profit rate, expenses, and prices. The most popular cloud instances are Google Drive, Amazon, iCloud, Dropbox, Yandex Disk, and One Drive. There

are paid and free versions according to the service provider's approach. For example, Google Drive gives free storage of up to 15GB.

2.1.2. Private Cloud

A private cloud is a service where users provide resources such as data storage and data transfer in their ecosystem. This cloud system is the service the organization provides with its servers. A private cloud is a cloud infrastructure that serves a single organization without outside user access (Mell and Grance, 2011). A private cloud is easier to secure as there is no outside access. Since it is the service the organization provides, it can be more flexible in establishing security. Although it is an open system to the Internet, it can only be accessed by authorized persons, making this system more secure.

2.1.3. Community Cloud

The community cloud deployment type consists of cloud infrastructure as several collaborative entities. Organizations in the ecosystem can access applications and data in the cloud. They have the same security system, reliability, and workspace. Today, government institutions also use the common cloud infrastructure (Mell and Grance, 2011). It uses a central and shared cloud infrastructure and reduces threats such as task and load distribution and security and facilitates the work done in this context. The main purpose of this project is to act on the common interest by working in harmony and security.

2.1.4. Hybrid Cloud

This type of cloud deployment has emerged from a variety of security needs. It works as a combination of private and public clouds. It is the way two or more clouds work together. Clouds are different, but they work in conjunction with each other. This allows the use of multiple placement models (Steven, 2011). This type of cloud creates a resource pool based on a consistent infrastructure. Companies deliver higher performance, efficiency, reliability, and security across all cloud models by using the same tools, environments, rules, and teams.

3. CLOUD TECHNOLOGY ADVANTAGES AND DISADVANTAGES

3.1. Cloud Technology Advantages

Cloud computing has many advantages for personal and corporate use. However, it is more prominent in corporate use. It provides many advantages over the price-performance index. It provides benefits in many aspects, from the energy consumed per unit of time to the costs of the equipment used (Alouffi et al., 2021; But et al., 2020).

- It can make a backup in case the units where it stores the data are damaged, and it can perform backup recovery whenever it wants.
- Since there is common registration and common access in the common cloud system, every user can easily access and make the necessary changes whenever they want. It helps save time and workload.
- Information can be accessed wherever there is an internet connection. It also prevents the problem of dependence on the institution in corporate affairs.
- Instead of using expensive products for information technology management and data storage, it can use as much as it needs and pay for what it uses.

3.2. Cloud Computing Disadvantages

As with any technology product, cloud computing has both advantages and disadvantages (Sputniknews, 2023).

- Since all data is stored on the internet, there will be no access from a place without a strong internet connection. There is no other way to access the cloud.
- Since the supplier company provides cloud computing security and reliability, users can not work on this issue. Due to these attacks, there is always the possibility of cyber-attacks and data being accessed by third parties. For example, in the past years, the iCloud system has been attacked, which has caused many users' data to be stolen.
- The continuous online presence of the cloud system makes it vulnerable to cyberattacks. Even professionals who are good in their field can suffer from security weaknesses due to attacks from time to time.
- Cloud systems can also be costly for small businesses in the short term. This contrasts with the main purpose of cloud technology, the reduction of storage costs.

4. SECURITY VULNERABILITIES OF CLOUD COMPUTING

One of the most fundamental problems of cloud computing is security. Unauthorized persons gain access to the cloud system and may steal data for many reasons, such as working online and occasionally being used by unconscious users. Considering that one of the most practical issues of our time is to have data, this is a great danger in itself. It will also lower the reliability of the cloud system provider if the data is stolen (Rewagad and Pawar, 2013).

Software user interfaces and APIs control cloud systems. Although cloud providers are constantly working to develop interfaces and APIs, these developments also bring security vulnerabilities. It is necessary to close these gaps regularly and continuously, and the system

should be made more secure by constantly updating it. One of the most common problems is password reuse. Passwords previously saved in the system may not be deactivated after changing them. This makes it exploitable by attackers (Tripathi and Abhinav, 2011).

Configurations made to facilitate access and management of information may also cause vulnerabilities in the system. Theft of the password is not a desirable situation as it can be used over many accounts. It can have dire consequences when it comes to data leakage. For example, user data registered to a shopping site called Yemek Sepeti was stolen in recent years. Many users' information, from address information to credit card information, was stolen, and users were victimized in this regard (Tirumala et al., 2015).

Organizations are obliged to comply with rules such as the Personal Data Protection Law. In this regard, it is obliged to limit the data. The theft of information such as credit card information may cause damages that are difficult to compensate users. Many measures can be taken in these matters. Methods such as cryptology software, making data independent from each other, and physical separation can be used.

5. CONCLUSION

In this study, evaluations were made on the importance of the security of cloud computing software, a technology used in almost every field today, and its usage areas are constantly increasing. These technologies have security vulnerabilities due to user and direct network attacks. One of the best ways to minimize this vulnerability is to protect the system with upto-date and constantly updated software. Necessary training should be given to raise awareness of users. There will always be these attacks; data is the most important thing in today's world, and people will make every effort to get it. Although it is difficult to be protected from these attacks, it is not impossible. The development and change of cloud technology will always continue to increase. The more users, the more attractive it will be to attack. In addition to the cloud provider's security measures, the user should also take precautions. As a result, data can be accessed due to the weakness caused by the user. The user and the cloud provider must know their job descriptions well and fulfill their responsibilities within the framework of their responsibilities. Against attacks that may occur during user access, methods such as multi-factor authentication, authentication, and end-toend encryption should be used. The vast majority of data breaches occur because users are caught phishing. Users need to use it in an educated and conscious way.

REFERENCES

Alouffi, B., Hasnain, M., Alharbi, A., Alosaimi, W., Alyami, H., & Ayaz, M. (2021). A systematic literature review on cloud computing security: threats and mitigation strategies. IEEE Access, 9, 57792-57807.

Bhajantri, L. B., & Mujawar, T. (2019, December). A survey of cloud computing security challenges, issues and their countermeasures. In 2019 Third International conference on I-SMAC (IoT in Social, Mobile, Analytics and Cloud)(I-SMAC) (pp. 376-380). IEEE.

Butt, U. A., Mehmood, M., Shah, S. B. H., Amin, R., Shaukat, M. W., Raza, S. M., ... & Piran, M. J. (2020). A review of machine learning algorithms for cloud computing security. Electronics, 9(9), 1379.

Goumidi, H., Aliouat, Z., & Harous, S. (2020). Vehicular cloud computing security: A survey. Arabian Journal for Science and Engineering, 45, 2473-2499.

Mell P. Grance T., The NIST Definition of Cloud Computing, 2009, http://www.wheresmyserver.co.nz/storage/.

Myrasecurity, https://www.myrasecurity.com/en/knowledge-hub/cloud-computing/, accessed date: 12.02.2023.

Rewagad, P., and Pawar, Y. (2013). Use of Digital Signature with Diffie Hellman Key Exchange and AES Encryption Algorithm to Enhance Data Security in Cloud Computing, Communication Systems and Network Technologies (CSNT), pp. 437-439, 2013.

Sputniknews, https://tr.sputniknews.com/20181021/apple-icloud-itunes-bitcoin-turkish-crime-family-kerem-albayrak-hack-fidye-1035764707.html, accessed date: 12.02.2023.

Srinivasamurthy, S., Liu, D., Vasilakos, A., Xiong, N. (2013). Security and Privacy in CloudComputing: A Survey," Parallel&CloudComputing (PCC). London, vol. 2, pp126-149, New York, NY: American V-KingScientific Publishing, 2013.

Steven, A.," When Hybrid Clouds Are A Mixed Blessing." May 2011.

Sun, P. (2020). Security and privacy protection in cloud computing: Discussions and challenges. Journal of Network and Computer Applications, 160, 102642.

Tirumala, S., Sathu, H., and Naidu, V. (2015). Analysis and Prevention of Account Hijacking based INCIDENTS in Cloud Environment, International Conference on Information Technology, pp. 124-129.

Tripathi, A., and Abhinav, M. (2011). "Cloud computing security considerations." Signal Processing, Communications and Computing (ICSPCC), 2011 IEEE International Conference on. IEEE, 2011.

APPLYING UX PRINCIPLES TO FIND PRE-PATTERNS IN HANDHELD AUGMENTED REALITY GAMES

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ABSTRACT

Reality-based interfaces that produce "embodied" game play experiences have recently attracted a lot of attention from the gaming industry and allied research areas. Handheld augmented reality (HAR) is a reality-based interface that superimposes computer-generated imagery (CGI) over a user's view of the actual world. In a HAR environment, players can use their existing physical and social skills to engage with the game system. The application of user experience (UX) design principles to augmented reality (AR) systems has received only a limited amount of research attention. In this study, we look into the potential relevance of such principles to the field of handheld augmented reality game development. The UX design tools such as shadowing, ethnographic research, people and context research, empathy mapping and experience map are used to define the pre-patterns in HAR games.

Participants - We select a sample of 23 gamers of the gaming society Indian Institute of Technology Kanpur. After the sample of 23 gamers we select diverse sample of 27 individuals to dive deep into the UX research.

Keywords - embodied game, handheld augmented reality (HAR), computer generated imagery (CGI), shadowing, experience map, pre-patterns.

MULTIAXIAL NON-PROPORTIONAL RANDOM ANALYSIS OF A TYPICAL HUB STEERING KNUCKLE WITH RESPECT TO IN-SERVICE LOADING EFFECTS ON ITS GEOMETRIC MODEL

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ABSTRACT

In this study, the high-strength-lightweight aluminium alloy A356.0-T6 was applied on Toyota Camry LE vehicle steering knuckle model, which remains a strategic component that serves as the link between axle housing, stub axle, and tie rod. An attempt was made to determine the effect of loading conditions (lateral and multiaxial forces) from multi-translated axis that may result in failure of a steering knuckle during its service life. Also, to determine the various loads and moments on the suspension system which is translated to the steering knuckle in its duty cycle. A 3D model was developed using SolidWorks 2018 version while ANSYS workbench R15.0 (2019 version) was used to conduct static structural analysis. The total force on the knuckle hub acting in the Z direction was determined as 3938.715N, which represented total loads on the four tyre of the car. Steering moment of 5400N.mm at perpendicular distance of 108mm, braking force of 3964.63 N.mm and breaking moment of 277,524.73N.mm were achieved. Solid mesh was selected as the type of mesh while blended curvature based mesh was employed as the type of mesher. Maximum equivalent Von-mises stress of 36.079 MPa, equivalent elastic strain of 0.00018393 mm/mm, maximum principal stress of 44.587 MPa and maximum shear stress of 19.871 MPa were obtained. This led to directional deformation of 0.010135 mm, representing bending along the Z-axis and maximum total deformation of 0.069036 mm. Although maximum safety factor of 15 dominated the model as the best value, an average safety factor of 10 was obtained at that current state, with a minimum safety factor of 2.5 found at the bolt bottom hole. The boundary conditions are safe to be adopted in real life events with insignificant or zero catastrophes.

Keyword: Steering knuckle, Static analysis, Total deformation, Factor of safety, Failure.

1. Introduction

The steering knuckle serves as the link between the axle housing, stub axle, and tie rod. A king pin connects the steering knuckle to the axle housing. It connects to another end towards the tie rod. With the aid of a bearing, the wheel hub is then secured over the knuckle. The steering knuckle's job is to change the tie rod's linear motion into angular motion of the stub axle (Babu et al., 2014). Steering itself is made possible by the steering knuckles, which join the wheel to the suspension system. Although steering knuckles were first used in the 18th century, their popularity has subsequently skyrocketed. On cars, trucks, buses, and other large

and heavy vehicles, you can find them. The suspension system, which enables the vehicle to travel smoothly in different directions, is connected to them, aiding in the steering of the vehicle. The steering knuckle is a component of the car's suspension that is used to turn the wheel. The front wheels, suspension, and steering all come together at the steering knuckles. They offer the attachment places for the tie-rod ends, the spindle and/or hubs that hold the wheels on, the upper and lower control arms or struts and lower arms, and more. The steering knuckles enable the wheels to move both horizontally and vertically in response to steering input and the suspension's response to road imperfections (Li et al; 2022). There are numerous variations of steering knuckles. They have various designs to accommodate various uses and suspension kinds. They can be separated into two categories, though. The other has a spindle, while the first has a hub.

In this research study, a steering knuckle of a Toyota Camry LE saloon car was employed as a study component in this investigation. Weight reduction is a growing concern for the automotive industry. Losing weight will have a significant influence on efforts to cut emissions (greenhouse gases), improve fuel efficiency, and protect the environment. Numerous technical advancements, including those in materials, design and analytical methodologies, fabrication processes, optimization techniques, etc., can lower weight. Throughout its service life, the steering knuckle is subjected to time-varying stresses, which causes fatigue failure. Consequently, an essential component of the product development cycle is its design (Dumbre et al., 2014; Muhamad et al., 2012; Sharma et al., 2014; Kashyzadeh and Farrahi, 2023). Additionally, the need to extend the High-Cycle Fatigue (HCF) life of automobile safety components that experience random, non-proportional multiinput loading is becoming more and more of interest to automotive industry. The steering knuckle experiences the most random stresses from the road and steering, which are applied at multiple spots (i.e., joints of knuckle with lower control arm, steering linkage, and Macpherson strut). Additionally, improper wheel angle adjustment increases the intensity of road stresses. In this regard, earlier research has demonstrated that wheel angles have an impact on the component's service life (Kashyzadeh and Farrahi, 2023; Liu et al., 2023).

Yadav et al. (2016) designed and analysed a steering knuckle component using forged steel EN 47, considering an average vehicle weight of 1240 Kg. The steering knuckle was modelled with Creo (Pro-E) 2.0 while static analysis was carried out using ANSYS workbench 15.0. Maximum total deformation of 0.89651 mm, maximum directional deformation (X-axis) of 0.62675 mm, maximum principal stress of 70.295 MPa, maximum shear stress of 62.111 MPa, Maximum equivalent Von-mises stress of 112.25, maximum equivalent elastic strain of 0.00069023 and maximum shear elastic strain of 0.00080745 were obtained. Apart from the improved yield strength of this material, the mass density (7700 kg/m³) and corrosion properties were some of the possible flaws of the material for steering knuckle application. In a similar study were mild steel and mild steel with nickel composite as well as average vehicle weight of 1240 Kg was used, directional deformation of 0.392, 0.21422 and 0.3534 mm at X, Y and Z-axis, total deformation of 1.8643 mm, equivalent elastic strain of 0.026808, maximum principal elastic strain of 0.021241 and equivalent Vonmises stress of 4467.6 MPa were obtained. However, mass density of the materials was also a setback.

Dusane et al. (2016) conducted analysis on All Terrain Vehicles (ATV) steering knuckle. The CAD model was developed using CATIA V5 while ANSYS 12 was used to perform static on aluminium alloys 6061-T6 steering knuckle frame and EN8 material for the spindle. With mass density of 2700 Kg/m3 and tensile yield strength of 276 MPa, both aluminium 6061-T6 alloy and EN8 were found to be better materials for steering knuckle due to good physical and mechanical properties as well as lightweight.

Kashyzadeh, K. R. (2023) conducted static analysis on a composite steering knuckle, assuming a road condition characterized by roughness and manoeuvres. The in-service driving condition of the vehicle model was simulated using multi-body dynamics (MBD) method, and the imposed loads on connection points of the steering knuckle to different components of the suspension system were extracted considering various maneuvers. CATIA software was used in developing the steering knuckle model by applying coordinate measuring machine (CMM) data. The results revealed that increase in tungsten carbide led to increase in the strength of the steering knuckle under purely axial loads (normal stress criterion) while increase in this substance resulted in a decrease in the strength of the parts subjected to shear loads (shear stress criterion). It was observed that the application of metal matrix composite is not suitable for this super critical component, based on the conditions of the study.

This research seeks to explore for ideas to decipher failure analyses (static analysis) of all kinds that the automotive industry is requesting from manufacturing lines in big quantities with respect to steering knuckles as applicable to Toyota Camry LE saloon car. In other words, a static structural analysis of a typical hub steering knuckle with respect to in-service loading effects on the geometric model, with specific attention on mass density and yield strength of the component material. It makes sense that the steering knuckle would benefit greatly from optimization for either volume or weight. In the same vein, the goal of a static analysis of the steering knuckle is to determine the maximum stresses and deformation that can occur under various conditions, including braking force, load transfer during acceleration and braking, etc. The outcome of will play a critical role in shape optimization which is a unique face sort by manufacturers in the synthesis of such product with enormous functionality and reliability.

2. Materials and Method

Steering Knuckle is an element of the suspension of the automobile that is used for turning and the wheel. The steering knuckles are where the suspension and steering systems and the front wheels converge. They provide the attachment points for the upper and lower control arms or struts and lower arms, the tie-rod ends, and the spindle and/or hubs to which the wheels are mounted. The steering knuckles allow the wheels to move vertically as the suspension reacts to road irregularities and horizontally in response to steering input. The knuckle was modelled in SolidWorks 2018. The steering knuckle shown in Figure 1a was modelled after the Toyota Camry LE saloon car. The aluminium alloy A356.0-T6 assigned to the steering knuckle model had mass density of 2670 kg/m³ as physical property, and tensile strength (ultimate) >= 234 MPa, tensile strength (yield) >= 165 MPa, elongation at break >= 3.5%, shear modulus of 27.2 GPa, shear strength of 143 MPa, tensile modulus of 72.4 GPa and hardness (Brinell) of 70-105 as its mechanical properties. The knuckle was modelled in SolidWorks 2018 and then Analysed by ANSYS R15.0 workbench. This study investigated the hub type steering knuckle. Several multi-translated loads (lateral and multiaxial forces) act on the knuckle in static condition and are illustrated in Figure 1b follows.



Figure 1a: Steering knuckle model knuckle

Figure 1b: Forces acting on the steering

Part assembly drawing of the steering knuckle with dimensions are shown in Figure 2 while mesh visualization of the steering knuckle is presented in Figure 3. The ANSYS workbench mechanical meshing was used with fine relevance centre and slow transition of element, with a total of 116048 nodes and 76870 elements. Solid mesh was selected as the type of mesh while blended curvature based mesh was employed as the type of mesher.

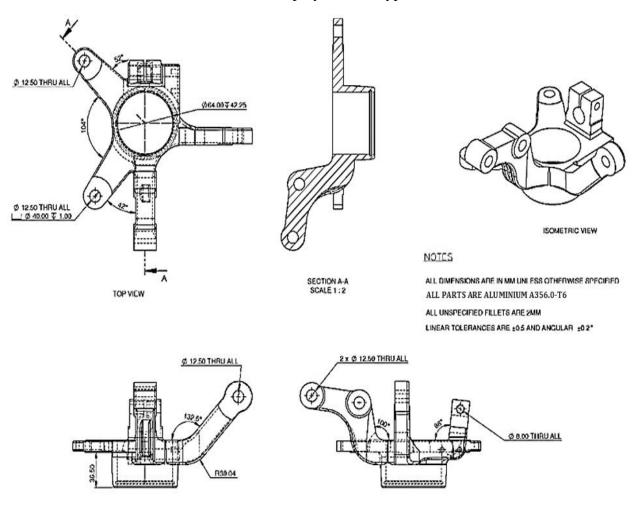


Figure 2: Sketches for steering knuckle with dimensions

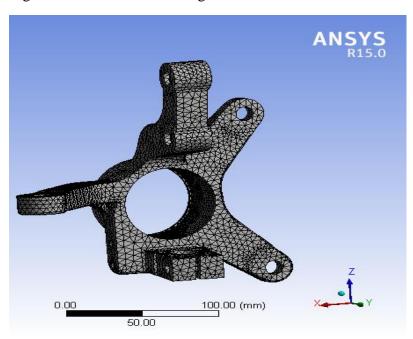


Figure 3: Mesh visualization of the steering knuckle

2.1. Loads/Forces Acting on the Steering Knuckle

There are two major type of loads acting on the steering knuckle which includes tensile and compressive load, and other forms of multi-translated loads (lateral and multiaxial forces). The stress due to these loads can be achieved using the following formulas:

Tensile load
$$(P_t)$$
 = Tensile stress * Area (1)

Compressive stress
$$(P_c)$$
 = Compressive stress * Area (2)

Inertia load is another form of load acting on the steering knuckle which is due to the inertia of moving parts. The inertia load can be derived from the following expression in Equations 3 and 4:

Inertia load
$$(F_a) = \omega^2 R \left[Cos\theta + \frac{R}{L} Cos(2\theta) \right]$$
 (3)

Bending load
$$(F_b) = \frac{\rho AtLsin(\theta + \emptyset)}{2} N$$
 (4)

The force of resistance per unit area, offered by a body against deformation is known as stress. This is given by Equation 5:

Stress
$$(\sigma) = \frac{P}{A}$$
 (5)

Inertia bending load sets up a stress which would be tensile on one side of the steering knuckle and compressive on another side and this changes sign each half revolution (Babu et al., 2014). The bending moment at any section from the small end is given Equation 6:

$$M = \frac{x}{a} \left[1 - \frac{x^2}{L^2} \right] \tag{6}$$

The stress could be computed using the following Equation 7:

$$\sigma_B = \frac{M}{z} \tag{7}$$

$$M = \frac{I}{2.5} \times t \tag{8}$$

$$I = 419 * t^4 \tag{9}$$

The steering knuckle is subject to a number of multi-translated loads (lateral and multiaxial forces) which are highlighted as follows:

- i. Load on Hub Bearing
- ii. Steering Moment
- iii. Braking Force

The analysis attempts to investigate the impact of these forces on the model. A static structural analysis was carried out to determine the impact of the several loads and moments on the knuckle. The model was done on SolidWorks 2018 while the analysis was done on ANSYS 2019 R1.

i. Load on the Hub Bearing

The load on the Hub is the load of the car, evenly distributed into the four tyres. The load model used for the analysis was 1606 Kg assumed to be dead weight of the car, therefore the total weigh on the knuckle hub was given by 1606/4 = 401.5Kg. The total force on the hub was recorded as (This force acted in the Z direction):

 $401.5 \times 9.81 = 3938.715N$.

ii. Steering Moment

A small steering force of 50N is usually required to turn the steering arm. Therefore, the moment from the force is multiplied by the perpendicular distance of 108mm. The moment was calculated as:

 $50 \times 108 = 5400N.mm$

iii. The Braking Force

The Braking force on the wheel was calculated using Equation 10.

$$F = \frac{mv^2}{2D} \tag{10}$$

Where F is the braking force, m is the mass of vehicle =1606Kg, v is the velocity of vehicle (maximum) = 44.44(160Km/h) and D is the braking distance =100m

$$F = \frac{401.5 \times 44.44^2}{2 \times 100} = 3964.63$$

Braking moment = $F \times d = 3964.63 \times 70.04 = 277,524.73N.mm$

Gravity was enabled to take proper account of inertia. The model loads of the steering knuckle under static condition is shown in Figure 4, while load summary of the steering knuckle model is presented in Table 1.

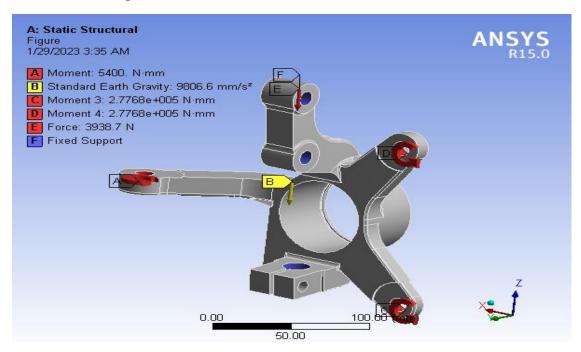


Figure 4: Model loads of the steering knuckle under static condition

Table 1: Load summary of the steering knuckle model

Object Name	Fixed	Steering	Braking Moment	Hub Loading	
_	Support	Moment		_	
State	Fully	Fully Defined	Fully Defined	Fully Defined	
	Defined				
Geometry	3 Faces	1 Face	2 Faces	1 Face	
Type	Fixed	Moment	Moment	Force	
	Support				
Suppressed	No	No	No	No	
Define By		Vector	Vector	Components	
Coordinate System					
X Component					
Y Component					
Z Component				-3938.7N (ramped)	
Magnitude		5400. N·mm	277,524.73		
		(ramped)	N.mm		
			(ramped)		
Direction		Defined	Defined		

3. Results and Discussion

Mechanical failures in automobile are often attributed to wear and tear of two moving parts of a vehicle in contact, poor design or manufacturing defects, lack of proper inspection or maintenance etc (Ikpe et al., 2016a). The analysis of steering knuckle component in this study was done with ANSYS Workbench 15.0. The load applied to the steering knuckle component was determined based on what is obtainable in literature. According to these papers, the average weight of vehicles is assumed to be 1606 kg. This weight is directly applied to all four knuckles, resulting in a weight of 401.5 kg on each wheel. This translates to an average force of 3041.1 N on each wheel, taking into account the acceleration due to gravity. The knuckle is also subject to multi-translated loads (lateral and multiaxial forces) such as braking force, moment, lateral force, and steering force, as well as loads in the X, Y and Z directions. The results of these analyses are presented in Table 2.

Table 2: Results summary of static analysis

Object Name	Equivalent	Total	Equivalent	Maximum										
Object Ivallic	Stress	Deformation	Elastic Strain	Maximum Principal	Shear Stress									
	Sucss	Deformation	Liasue Strain	Stress	Silear Siless									
Scope														
Scoping			ometry Selection	n										
Method			ometry beleetio	11										
Geometry	All Bodies													
Comount		Defini												
J F *	(von-Mises)	Deformation	Elastic Strain	Principal	Maximum Shear Stress									
	Stress			Stress	1									
By Time														
Display Time	<u> </u>													
Calculate	Yes													
Time History														
Suppressed														
Integration Point Results														
Display	Averaged Averaged													
Option														
Average	No		No											
Across														
Bodies														
		Resu		T										
Minimum	1.3995e-004	0. mm	6.0614e-009	-14.045 MPa	8.0273e-005									
	MPa		mm/mm		MPa									
Maximum	36.079 MPa	6.9036e-002	5.0853e-004	45.388 MPa	19.665 MPa									
		mm	mm/mm											
Minimum Value Over Time														
Minimum	1.3995e-004	0. mm	6.0614e-009	-14.045 MPa	8.0273e-005									
7.5	MPa		mm/mm	-14.045 MPa	MPa									
Maximum	1.3995e-004	0. mm	6.0614e-009	8.0273e-005										
	MPa	<u> </u>	mm/mm		MPa									
Maximum Value Over Time														

Minimum	36.079 MPa	6.9036e-002	5.0853e-004	45.388 MPa	19.665 MPa
		mm	mm/mm		
Maximum	36.079 MPa	6.9036e-002	5.0853e-004	45.388 MPa	19.665 MPa
		mm	mm/mm		

Considering the theory of Von-mises failure criterion, material component is said to be in a state of failure if the Von mises stress resulting from the applied force exceeds the material yield strength. However, if the Von-mises stress value is below the material's yield strength, it the material is believed to possess more strength that can accommodate further forces before it finally yields (Ikpe et al., 2016b; Ikpe and Owunna, 2017). This relates to the theory of material elasticity which state that a given material under loading material can accommodate more loads/forces as long as its elastic limit is not exceeded. Considering maximum Vonmises stresses value (36.079 MPa) obtained for the steering knuckle model in this analysis and yield strength (165 MPa) of the Aluminium alloy A356.0-T employed as the steering knuckle material, the equivalent maximum simulated Von-mises stress obtained for the materials is below the yield strength of the A356.0-T materials, which implies that the component may likely not fail under the applied load and condition of the simulation. The equivalent maximum simulated Von-mises stress profile is shown in Figure 5. This led to a total deformation of 0.069033 mm as shown in Figure 6 as well as directional deformation (Bending along the Z-axis) of 0.010135 mm as shown in Figure 7. This implies that said deformation may not have any catastrophic effect on the steering knuckle component, as there is still room to accommodate additional forces/loads before it finally yields or fails.

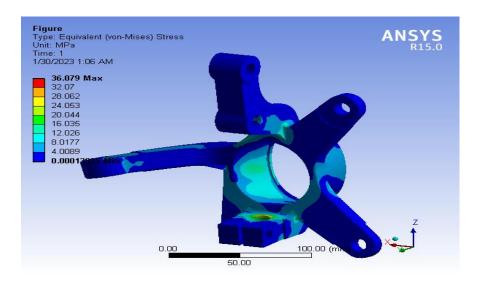


Figure 5: Plot of equivalent Von-mises stress profile

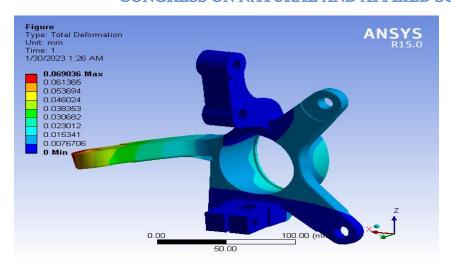


Figure 6: Plot of total deformation profile

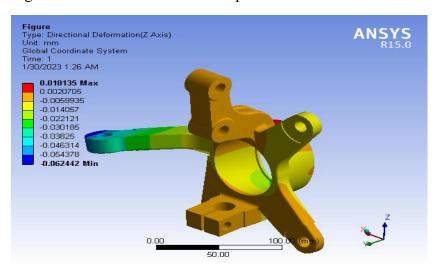


Figure 7: Plot of directional deformation (bending along Z-axis) profile

When the steering knuckle undergoes internal external and external forces due to vibration, steering displacement, temperature, corrosion etc, stress is induced on the material which eventually translates into strain deformation. This is characterized by geometric deformation representing the relative displacement between particles in the material. The said deformation can be considered elongations due to distortion of atoms within the metal lattice, and are dependent on the direction of forces/loads (Etuk et al., 2019). In extreme conditions where the vehicle is exposed to uneven road surfaces characterized by potholes and speed bumps, the steering knuckle may be prone to cyclic loading which induces fluctuating stresses, elastic strains, tensile stresses etc, on the knuckle system that may results in bending deformation and possibly leads to fatigue. The simulated maximum equivalent elastic strain profile is shown in Figure 8. This led to a maximum principal stress ($\sigma > \sigma > \sigma$ 1 2 3) of 44.587 MPa as shown in Figure 9, which are stresses corresponding normal stresses acting on the principal planes of zero shear stress. These planes are perpendicular to the principal directions upon which the principal stresses act.

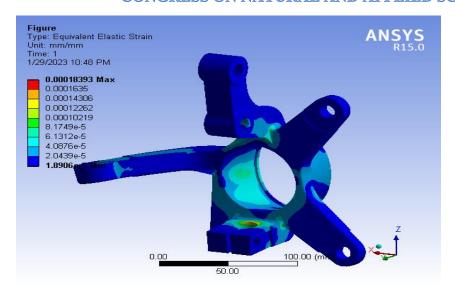


Figure 8: Plot of equivalent elastic strain profile

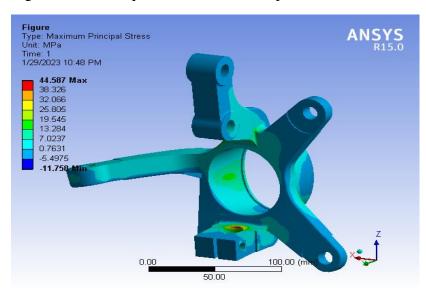


Figure 9: Plot of maximum principal stress profile

Although very insignificant from the beginning, shear stress is induced on the steering knuckle at each corning cycle made by the steering members, and however tends to be significant after the component might have been exposed to thousands and millions of vibrational and frequency cycle, occasioned by the constant exposure to multi-translated loads (lateral and multiaxial forces) acting on the vehicle suspension system. The simulated maximum shear stress profile as shown in Figure 10 was obtained as 19.871 MPa, which is the load/force per unit area that tends to cause deformation of the steering knuckle by slippage along the planes parallel to imposed stresses.

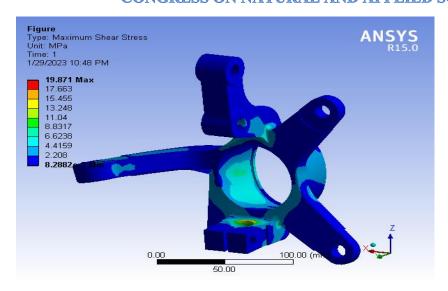


Figure 10: Plot of maximum shear stress profile

Factor of safety plays a vital role in mechanical engineering designs, as users of engineering components oftentimes overload the components beyond their design limit which eventually exposes the component to premature failure during service condition. However, selection of low Factor of Safety (FOS) in engineering design implies that such design may not always meet its design life expectancy due to poor design considerations and low integrity and vice versa (Ikpe and Owunna, 2019). Considering the colour distribution chart on the steering knuckle model shown in Figure 11, royal blue colour is observed to be predominant, followed by lemon colour designated by a value of ten (10) at the mid-section, with little traces of orange colour (with a value of 2.293) at the base. Red colour designated by zero is observed to appear as the least value on the colour profile. Following the colour band on the model, royal blue which has a maximum value of 15 dominates the model, indicating that if FOS of about 15 is selected for the design of a steering knuckle, the final product will have a better quality than when FOS of 10, while steering knuckle designed with FOS of 10 will have a better quality than the same component designed with FOS of 2.293 which happens to be the least on the colour profile in Figure 11. However, it should be noted that a given steering knuckle with higher FOS implies a better quality which comes at a higher cost.

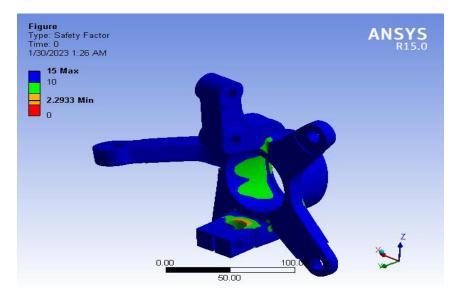


Figure 11: Plot showing factor of safety profile

4. Conclusion

In this study, multiaxial non-proportional random analysis of a typical hub steering knuckle was successfully conducted with respect to in-service loading (lateral and multiaxial loads) effects on the geometric model. The aluminium alloy A356.0-T6 assigned to the steering knuckle model in this study had mass density of 2670 kg/m³ which could provide a reasonable fuel reduction in auto applications. The maximum Von-mises stress was recorded as 36.079 MPa, with maximum principal stress of 45.388 MPa and shear stress of 19.665 MPa. An average FOS of 10 as well as maximum FOS of 15 was obtained in the current state of the analysis. Except at the bottom bolt hole where SOF was just about 2.5. The maximum total deformation of the model is 0.069mm. The directional deformation in the Z-axis indicated the bending of the member under the influence of the applied forces, with maximum bending of 0.06242mm. The maximum Von-mises stress value was observed to be less than the yield strength of Aluminium alloy A356.0-T employed in the analysis, indicating that the steering knuckle model still had the strength to withstand additional forces before yielding. This was due to average value of 10 selected as the FOS which implied that a better material with optimum physical, mechanical and thermal properties was employed which could withstand the in-service loads/forces acting on the steering knuckle during service condition. Moreover, proper boundary conditions well as quality mesh. This was observed to influence the rest of the parameters that were analysed in this study such as the total deformation, directional deformation (bending along Z-axis), equivalent elastic strain, maximum elastic stress as well as the maximum shear stress. Considering the aforementioned findings obtained from this study, the following recommendations could help manufacturers improve the quality of conventional steering knuckle for optimum vehicular performance:

- i. From the colour distribution profiles of the steering knuckle mode, lemon and blue colour represented by a value of 10 and 15 were identified as the average and better FOS. Therefore, manufacturers adopting the analytical conditions presented in this study should aim at a FOS between 10 and 15. On the other hand, while FOS with higher values may incur additional cost, it should be borne in mind that FOS lower than recommended value can compromise the quality and performance of the component during service condition.
- ii. Also, manufacturers should take cognisance of physical, mechanical and thermal properties of materials selected for steering knuckle application, as the longevity of the component even in rough terrains also depend on the material properties.
- iii. Lightweight materials should also be considered for steering knuckle application, as this will provide an ideal fuel saving scenario during service condition of the vehicle.

References

Babu, B., Prabhu, M., Dharmaraj, P. and Sampath, R. (2014) Stress analysis on steering knuckle of the automobile steering system. International Journal of Research in Engineering and Technology, 3(3), 363-366.

Kashyzadeh, K. R. (2023) Failure Strength of Automotive Steering Knuckle Made of Metal Matrix Composite. Applied Mechanics, 4, 210-229.

Li, F., Sun, J., Bao, J., Yang, J., Li, H., Zhong, C., Gao, Y., He, Q., Xie, K. and Li, W. (2022) Failure analysis of truck steering knuckle. Engineering Failure Analysis, 140, 106537.

- Dumbre, P., Mishra, A. K., Aher, V. S., and Kulkarni, S. S. (2014) Structural analysis of steering knuckle forweight reduction, International Journal of Advanced Engineering Research Studies, e-ISSN: 2249-8974, 1-4.
- Babu, B., Prabhu, M., Dharmaraj, P. and Sampath, R. (2014) Stress Analysis on Steering Knuckle of the Automobile Steering System. International Journal of Research in Engineering and Technology, 3(3), 363-368.
- Muhamad, W. M., Sujatmika, E., Hamid, H. and Tarlochan, F. (2012) Design improvement of steering knuckle component using shape optimization. International Journal of Advanced Computer Science, 2(2), 65-69.
- Ikpe, A. E. and Owunna, I. B. (2019) Design of Remotely Controlled Hydraulic Bottle Jack for Automobile Applications. International Journal of Engineering Research and Development, 11(1), 124-134.
- Sharma, M. P., Mevewala, D. S., Joshi, H. and Patel, D. A. (2014) Static analysis of steering knuckle and its shape optimization. Journal of Mechanical and Civil Engineering, e-ISSN: 2278-1684, 34-38.
- Liu, S., Zhang, G. and Wang, A. (2023) Progressive failure mechanism of structuralized cemented slopes. Engineering Failure Analysis, 143, 106939.
- Etuk, E. M., Ikpe, A. E. and Azum, U. A. (2019) Modelling and Analysis of 2-Stage Planetary Gear Train for Modular Horizontal Wind Turbine Application. Journal of Applied Research on Industrial Engineering, 6(4) 268-282
- Kashyzadeh, K. R. and Farrahi, G. H. (2023) Improvement of HCF life of automotive safety components considering a novel design of wheel alignment based on a Hybrid multibody dynamic, finite element, and data mining techniques. Engineering Failure Analysis, 143, 106932.
- Ikpe A. E. and Owunna I. B. (2017) Design of Vehicle Compression Springs for Optimum Performance in their Service Condition. International Journal of Engineering Research in Africa Submitted, 33, 22-34.
- Dusane, S. V., Dipke, M. K. and Kumbhalkar, M. A. (2016) Analysis of Steering Knuckle of All Terrain Vehicles (ATV) Using Finite Element Analysis. IOP Conf. Series: Materials Science and Engineering 149 (2016) 012133.
- Ikpe, A. E., Owunna, I. B., Ebunilo, P. O. and Ikpe, E. E. (2016a) Static Analysis on a Vehicle Tie Rod to Determine the Resulting Buckling Displacement. International Journal of Industrial and Manufacturing Systems Engineering, 1(1), 16-24
- Yadav, S., Mishra, R. K., Ansari, V. and Lal, S. B. (2016) Design and Analysis of Steering Knuckle Component. International Journal of Research and Technology, 5(4), 457-463.
- Ikpe A. E. and Owunna I. B. and Ebunilo, P. O. (2016b) Determining the Accuracy of Finite Element Analysis when Compared to Experimental Approach for Measuring Stress and Strain on a Connecting Rod Subjected to Variable Loads. Journal of Robotics, Computer Vision and Graphics, 1(1), 12-20.

PERFORMANCE ANALYSIS OF SWARM-BASED METAHEURISTIC ALGORITHMS ON CONTINUOUS OPTIMIZATION PROBLEMS

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ABSTRACT

Scientists have drawn creative inspiration from nature for centuries. Swarm intelligence, an essential branch of artificial intelligence, has emerged to simulate the laws of nature and the social behavior of insects or animals. Metaheuristic algorithms are used successfully in wide application areas as they offer potential solutions for complex optimization problems. Metaheuristic algorithms inspired by swarm intelligence have become very popular due to their flexibility and robustness. In recent years, researchers influenced by natural phenomena have proposed many different swarm-based metaheuristic algorithms and applied them to real-world problems in different application fields. In this study, performance analysis of four swarm-based metaheuristic algorithms, namely Harris Hawk Optimization (HHO), Moth Flame Optimization (MFO), Salp Swarm Algorithm (SSA), and Whale Optimization Algorithm (WOA), was performed and the results were comparatively examined. The performances of these algorithms were tested for twelve different benchmark functions in four different types, namely multi-dimension unimodal, fixed-dimension unimodal, multidimension multimodal, and fixed-dimension multimodal. The results obtained for the different benchmark functions were analyzed according to the best value, mean value, and standard deviation values. When the results were evaluated, it was seen that the HHO algorithm obtained more promising results for the selected benchmark functions than the other three algorithms. These algorithms and their many different versions can be effectively applied to solve many search and optimization problems.

Keywords: swarm intelligence, optimization, continuous optimization problem.

NONLINEAR BEHAVIOR OF CIRCULAR SHALLOW ARCHES

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ABSTRACT

One of the important conditions required in order for the structure to carry the external loads safely is the prevention of buckling. Under the influence of compressive loads, it is essential to consider the buckling problem of structural elements, which are thin compared to their length. Otherwise, although the compressive force acting on the structure is safe according to the allowable stress, it may cause the structure to collapse due to buckling. When examining buckling problems, the maximum force that the structure can carry without buckling is investigated, which is called the critical buckling load, thus ensuring that the external forces acting on the structure are less than the critical buckling load, keeping the structure safe. There are two modes of elastic instability, one of them is bifurcation of equilibrium that seeks a solution using the classical buckling theory, and the other is limit equilibrium, which requires snap-through buckling research. These modes depend on the state of the loading and the geometry of the structural element. For example, straight beams subjected to axial compression load exhibit a bifurcation buckling mode, while shallow arches that carry transverse loading mainly by compressive axial forces exhibit a snap-through buckling mode. In the snap-through buckling analysis, pre-buckling deformations are taken into account and the problem is handled as geometrically nonlinear. Shallow arches exhibiting snap-through behavior are frequently used in macro or micro dimensions in various fields of engineering such as civil, mechanical, and aviation.

In this study, the snap through buckling problem of circular shallow arches with pinned support at both ends, under the effect of uniformly distributed vertical load, is investigated within the framework of the Euler Bernoulli beam theory. To solve this problem, firstly, the nonlinear differential equations are converted into nonlinear algebraic equations by using the finite differences method. Then, the nonlinear algebraic equations obtained are solved numerically using the Newton-Raphson method. In the solution of the problem, the effect of the modified slenderness ratio, which is a geometric parameter, on the snap-through buckling behavior should be examined. It is stated that the absence of buckling or the observance of a purely snap-through behavior depends on the values of the modified slenderness ratio. In this study, critical buckling loads are calculated for various values of the modified slenderness ratio of shallow arches.

This study provides insight about the design of the geometry of shallow arches, and contributes to their development through the improvement of knowledge about shallow arches.

Keywords: shallow arch, snap-through buckling, nonlinear equations, modified slenderness ratio

Acknowledgements: This work was supported by Yildiz Technical University Scientific Research Projects Coordination Unit. Project Number: FYL-2022-5167

YIELD RESPONSES OF WHEAT (TRITICUM AESTIVUM L.) TO EXOGENOUS APPLIED MORINGA LEAF EXTRACT (MLE)

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ABSTRACT

Wheat is the staple food in Pakistan which is being consumed by the majority of population on daily basis. In recent years, a decline in wheat production while an upsurgin human population has been identified as serious threat to food security.

Moringa leaf extract (MLE) is one of the recently introduced bio-stimulant to enhance growth, yield and stress tolerance in plants. However, availability, shelf life and handling of

MLE are the hindrances in its adaptability and marketing. A field experiment was conducted to evaluate the efficiency of MLE as bio-stimulant on wheat productivity. Experiment was performed at Agronomy Research Farm, University of Agriculture Faisalabad using Randomized Complete Block Desing (RCBD) with three replicates to allocate the treatments. Data for different parameters was recorded and analyzed at 5% probability of LSD test. Treatments included were (T₁=Control, T₂= Priming with 3% Dry MLE, T₃= Priming with 5% Dry MLE, T₄= Priming with 3% fresh, T₅= Priming with 5% Fresh MLE, T₆=Foliar spray of 3% Dry MLE T₇= Foliar spray of 5% Dry MLE, T₈= Foliar spray of 5% Dry MLE, T₉= Foliar spray of 5% Dry MLE). MLE either fresh or dry performed positively in enhancing the yield of field. Increase in wheat yield was observed in all treatments as compared to control. Highest wheat yield (4680.0 kg h⁻¹) was recorded from treatment where 5% fresh MLE was applied as foliar spray which was 19.54% more as compared to control (3846.7 kg h⁻¹). İn addition, significantly the highest spike length, no. of productive tillers, grains per spike, biological yield, harvesting index, leaf area index, leaf area duration and crop growth rate observed were also increased in comparison to control. It is recommended from the current experiment to use 5% fresh MLE spray on wheat to enhance its production in an economic way.

Keywords: Wheat, MLE, Priming, Foliar application, Spray

EFFECT OF DIFFERENT SEEDING RATE AND HARVESTING INTERVAL ON THE FORAGE YIELD AND QUALITY OF MAIZE (Zea mays L.)

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ABSTRACT

Increasing animal population in Pakistan is exerting pressure on agriculture sector to explore more sources and utilizing them more efficiently to feed the animals.

Livestock in under nurished in the country due to less production potential and poor management practices by the farmers for fodder crops. Maize (Zea mays L.) is an excellent fodder crop because of its rapid growth, succulency, digestibility, outstanding quality and great productive potential. Optimal seed rate and harvesting interval of all fodderes play significant role in quality determination as delayed harvesting results in increased fiber contents with decreasing proteins. Therefore, a field experiment was conducted to investigate the effect of different seeding rates and harvesting interval on the forage yield and quality of maize (Zea mays L.) at Agronomic Research Area, University of Agriculture, Faisalabad during summer season, 2021. The experiment was conducted using Randomized Complete Block Design (RCBD) with factorail arrangement and replicated thrice. The experiment was comprised of two factors; seeding rate and harvesting interval. The treatments of seeding rates used were S₁=80 kg ha⁻¹, S₂=100 kg ha⁻¹ and S₃=120 kg ha⁻¹ while harvesting intervals were H₁=55 days after sowing (DAS), H₂=65 days after sowing and H₃=75 days after sowing. Mazie variety "Pak Afgoi" was sown by hand drill with keeping 30cm row to row distance. Agronomic and quality factors were measured using standard methods and data collected was analyzed statistically using Fisher's analysis of variance technique. Differences in treatment means were compared by using Tukey's test at 5% level of significance. The results showed that seeding rate and harvesting interval significantly effected the agro-qualitative traits of forage maize. The maximum fresh weight per plant, dry weight per plant, fresh forage yield, dry matter percentage, dry matter yield and crude protein were obtained from the treatment where seeding rate of 100 kg ha⁻¹ was used and the crop was harvested at 65 days after sowing.

Keywords: Maize, Seed rate, Harvesting interval, Fodder, Forage

PRODUCTION OF TRANSGENIC EDIBLE BANANA PLANT CONTAIN CT B GENE

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ABSTRACT:

Plant biotechnology was promoted to express the foreign antigen in plant tissues as edible vaccine. Vaccination was the best known and most successful application of immunological principles to human health. ¹Recombinant DNA technology had already radically altered the field of vaccines. They understand better how our body interacts with microbes at the molecular level. Molecular biology also facilitates the development, production and delivery of safe and effective vaccines

In this study, CT-B gene was cloned into plant expression vector. The plasmid PCAMBIA was constructed by inserting the coding region for CT-B from PRK2013 together with pBluescript II KS between the Bam H1 and EcoRI in the sites of PGA643 plant transformation vector and expressed in the plasmid (PCAMBIA). Here the study is to investigate the possibilities of cholera toxin B subunit to be used as a carrier of peptide vaccine by genetic approach. *Agrobacterium tumefaciens* is capable of infecting intact cells and introduces one of several copies of the transformed DNA in to the plant genome. *Agrobacterium tumefaciens* strain (LBA4404) is carrying the plasmid (pCAMBIA 1301) and will be used for the transformation studies. Constructed plasmid which contains the gene was transferred from its host *E.coli* strain (DH5α) in to *Agrobacterium tumefaciens* (LBA4404) by triparental matting method. In triparental matting *E.coli* harbouring plasmid (PRK2013) will be used as a helper. The result revealed the presence of 11.6 kDa CT-B antigen in constructed plasmid and experimentally confirmed. The transformed gene expression was used for the edible vaccine preparation in Banana Callus.

Keywords: Cholera, Vaccine, P CAMBIA, Gene Transfer,

BIODIVERSITY AND SEASONAL DISTRIBUTION OF CULICOIDES SPP.IN NORTH PART OF SERBIA (VOJVODINA)

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ABSTRACT

Continuous entomological monitoring of Cullicoides spp., was performed in Serbia from 2015 to 2019 on the basis of the Guidelines on how to conduct entomological examinations for the monitoring and control of blue tongue diseases in the territory of the Republic of Serbia, have so far yielded significant results related to biodiversity and seasonal dynamics of these insects Serbia. The research we have done so far has contributed to mapping the geographical distribution of the species we encounter as well as the variations in the number of populations in different years. As monitoring continues, we receive new valuable data every year that will help predict the movement of these insects on the basis of climate condition and enable preventative action to be taken to counteract them. Insects were collected using CDC light traps without dry ice and determination of Culicodes was performed by morphometric method recommended by the Italian National Reference Centre for Exotic Diseases CESME, Reference Laboratory for Bluetongue OIE, IZSAM from Teramo, Italy. In the Vojvodina Province, the presence of Cullicoides spp was found in 38.46% samples in Novi Sad, in Pančevo in 44.18%, Subotica 59.25% and Sombor 40.90%. We did not detect the presence of Cullicoides spp. n the epizootiological area of Zrenjanin. During examination we detected next species: C. circumscriptus, C. deltus, C. fasciipennis, C. furcillatus, C. griseidorsum, C. lupicaris, C. nubeculosus, C. obsoletus, C. pallidicornis, C. parotti, C.picturatus, C. pulicaris, C. punctatus, C. scoticus i C. subfasciipenni. Similar species were also found in border countries Hungaria, Croatia and Romania. Culicoides spp from to Obsoletus complexes, established at 60.05%. Males were found in 22.84% samples; nonpigmented (young) females in 67.97%, females taking the blood at 7.39%, and 1.35% were pregnant females. Culicoides spp. from Pulicaris complexes were found in 38.85% samples. Among tested samples, males were found in 18.91% samples, non-pigmented (young) females in 71.72%, females taking 9.09% and 1.11% pregnant females. Other types of Culicoides are set up in less than 10% of the examined samples. Usually, we have an average season distribution for these insects from April to October.

Keywords: Culicoides sp., biodiversity, season distribution, north part of Serbia (Vojvodina)

MICROBIOTA MODULATION AS THERAPEUTIC APPROACH IN THE NEUROPATHIC PAIN IN DOG WITH SPINAL CORD INJURY: IMPACT OF POLENOPLASMIN

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ABSTRACT

Background Studies have demonstrated the presence of gut dysbiosis (alterations in gut bacterial homeostasis) secondary to spinal cord injury in dogs. The dysbiosis is thought to impair recovery by decreasing the production of short-chain fatty acids which play a role in suppressing inflammation within the central nervous system.

Objective Therefore, targeting gut dysbiosis could have significant therapeutic value in the management of spinal cord injury. The purpose of this study is to determine if gut dysbiosis occurs in dogs with spinal cord injury. Another area of potential intervention interest is in situations of spinal injury where there is an urgent need to generate new neurons. To arrive at these observations, the authors examined how Polenoplasmin and diet solve paralysis in dogs.

Materials and methods The most common cause of spinal problems in dogs is trauma. We are currently assessing whether indoles can also stimulate formation of neurons in dogs with paralysis.

Results We found that gut microbes that metabolize tryptophan-an essential amino acidsecrete small molecules called indoles, which stimulate the development of new brain cells in dogs, also demonstrated that the indole-mediated signals elicit key regulatory factors known to be important for the formation of new neurons.

Conclusion This study is another intriguing piece of the puzzle highlighting the importance of lifestyle factors and diet. The link between the health of the microbiome and the health of the brain shows how microorganisms in the gut solve paralysis, gut microbe secreted molecule linked to formation of new nerve cells in paralyzed dogs.

Keywords: gut dysbiosis, indole, paralyzed dog, Polenoplasmin.

BASIC MORPHOMETRIC PARAMETERS OF THE ANTLERS OF THE GOLDEN TROPHY RED DEERS (Cervus elaphus L.)

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ABSTRACT

Research was conducted on a sample consisting of 42 red deer antlers from hunting grounds in Hungary. The parameters that were analyzed (length of antlers, circumference of the antlers, length of brow tines, length of tray tines, circumference of coronets, circumference of below the coronets, number of tine ends and the weight of the antlers) were measured according to the propositions adopted by the The International Council for Game and Wildlife. The aim of the paper was to determine the absolute and mean values of the length of antlers, the circumference of the antlers, length of brow tines, length of tray tines, circumference of coronets, circumference of below the coronets, number of tine ends and the weight of the antlers, as well as the existence of mutual dependence between certain parameters of reed deer trophies. Using the method of descriptive statistics, the mean values were obtained. Using the method of descriptive statistics, the mean values of the length of the left and right antlers were obtained, and it was determined that the left antler was slightly more developed in the observed population. Namely, the mean value of the length of the left antler is larger, while the mean values of the length of tines are almost the same. The results of Pearson's correlation showed a statistically significant positive correlation between certain morphometric parameters of the antlers, such as the length of the antlers and brow tines. However, the results of Pearson's correlation showed, also, a statistically significant negative correlation between certain morphometric parameters of the antlers, such as the length of the antlers circumference of the antlers.

Keywords: red deer, antlers, morphometry, trophy, morphometric characteristics

PREPARATION AND EVALUATION OF NANOPARTICLES OF ZINC OXIDE COATED INTRAMAMMARY INFUSION FOR THE TREATMENT OF SUBCLINICAL BOVINE MASTITIS

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ABSTRACT

Mastitis in dairy animals is highly prevalent infectious disease causing considerable economic losses estimated to be \$35 billion annually at world level. Various traditional medications have been used for treatment of mastitis such as herbal, homeopathic and antibiotics. The increasing microbial resistance and antibiotic failure in the treatment needs to find other effective ways. The use of nanoparticles-based therapy is cheap with excellent efficacy. Inorganic metal nanoparticles proved to be helpful in improving the health of udder and teat. The present study was conducted to check efficiency of Zinc Oxide nanoparticles in the treatment of subclinical mastitis in cattle. The study was consist of 50 animals divided into five groups, each having 10 animals. The diagnosis of subclinical mastitic animals was confirmed on basis of Surf Field Mastitis Test. Evaluation was done by SFMT score, somatic cell count and milk composition(Fat, Protein and SNF contents) and Draminiski mastitis detector reading on day 0,day 07 and day 14 post imitation of treatment. Bacteriological examination was also performed to isolate the bacteria casuing subclinical mastitis. The results shows there was significant decrease in SFMT score in animals of group treatment III in which animals were given amoxicillin 15% along with intramammary infusion of ZnO nanoparticles. The Draminiski value increases significantly, Somatic cell count decreased and

milk composition improved after giving combination of non anti antibiotic and antibiotic. As for as could be ascertained from the available literature, The present study is the first one on Preparation and evaluation of ZnO nanoparticles cated intramammary infusion for the treatment of subclinical mastitis in bovines.

Key words: Bovine, sub clinical mastitis, zinc oxide, nano particles, intramammary infusion

A META-ANALYSIS OF THE ASSOCIATION BETWEEN PROLACTIN (PRL) GENE POLYMORPHISM WITH LACTATION MILK YIELD AND PROTEIN PRODUCTION TRAITS IN CATTLE

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ABSTRACT

In certain areas of animal research summarizations of literature data are needed, statistical methods dealing for the analysis of summary data from the literature are known as meta-analysis. The method of meta-analysis is used to combine the result from several independent studies which have been done in different regions or areas on a specific subject as qualitative and quantitative and assist to achieve a consensus. The current meta-analysis was performed to provide the association between prolactin PRL polymorphism with some productive milk traits in Holstein crossbreed dairy cattle. The data was collected from the years 2002 to 2021 and a total of 26 published studies were included in milk yield study, 14 studies for protein yield, and 18 studies included for protein content. For the performance of statistical evaluation four genetic models, dominant; AA + AB versus BB, recessive; AA versus AB + BB, co-dominant; AA versus BB versus AB were employed to obtain standardized mean difference (SMD) between genotypes. In this analysis cattle with AB

versus BB genotype (SMD= 0.289, 95% CI 0.005, 0.573) and a statistically significant (p<0.05) higher protein yield were found compared to AA versus AB and AA versus BB genotype. In the remaining cases, the association between prolactin polymorphism and milk yield and protein content was not statistically significant (p>0.05).

Keywords: Meta-analysis, crossbreed, Polymorphism, co-dominant, PRL, SMD.

1. Introduction

Milk production traits are very important in dairy cattle. Breeding programs are the main factor in dairy farming to achieve and improve these traits. Genomic selection increases the efficiency of selection more than traditional methods. Selection methods at the DNA and quantitative trait locus (QTL) level can assist in speeding up quantitative selection by diagnosing major genes that control important economic traits [1],[21].

The research on genetics mainly focuses to identify genes with important economicaly traits. Most studies on dairy cattle have identified genes determining variations in milk production traits[16]. Meta-analysis represents a statistical test or technique employed to combine the results of multiple studies into a single estimate. The results of a meta-analysis increase the precision of estimates of effect, and new hypotheses are established [15]. The process of milk production is complicated and prolactin is one of the most essential hormones in this process [12]. PRL genes, which are necessary for the development of mammary glands and milk production[5] [11]. It produced by the anterior pituitary gland and plays a key role in lactogenesis, synthesis, regulating the growth of the udder, and secretion of milk proteins in dairy cows [6]. The prolactin (PRL) gene is found on chromosome 23, is approximately 10 kb in size, includes 5 exons and 4 introns, and encodes a 199 amino-acid polypeptide [6],[16]. This site plays as a genetic marker for the genetic characterization of cattle populations [16].

The polymorphisms in prolactin (PRL) gene has significant associations with milk traits cattle [6],[14]. A change of adenine to guanine (A103G) in prolactin gene make a point mutation, the outcome is two alleles (A and B). Three genotypic patterns AA, BB and AB were revealed from the digestion of a 156 bp fragment of exon 3 region in the prolactin gene by RsaI. [18][2]. The present analysis was carry out to combine results from different studies related to prolactin gene polymorphism and its relationship with protein and milk yield.

2. Material and Methods

The studies related to this research were searched in Scientific journals. For the obtaining of a standardized mean difference two effect models (the random effect model and the fixed effect model) are used. Q statistic was employed for estimation of heterogeneity between studies.

The selection of models defined from the study effect were homogeneous or heterogeneous and Cohen's method was used for the standardized mean difference [16].

In this study, the I^2 test was conducted with the objective of estimating heterogeneity between the studies. The random effect model was applied due to the high heterogeneity.

2.1, Data Extraction and search strategy.

The data were extracted and removed errors by authors and a total of 26 published studies were included in milk yield, 14 studies for protein yield, and 18 studies for protein content. The important information, involves the author's name, sample size, the year of publication, breed, lactation milk yield (LMY), protein yield, genotypes, and country.

Essential criteria were used for data collection and study selection. A comprehensive search was done among studies published in different languages, journals, and databases on the association between prolactin (PRL) gene polymorphism with lactation milk and protein production traits in cattle. A comprehensive search was done with Springer, ResearchGate, Google Scholar, Wiley, PubMed, and Elsevier for studies.

2.2, Statistical Analysis

The Stata 11.2 software (StataCorp 2001; Stata Statistical Software) was used in this analysis and P<0.05 was accepted as a significance level. For the gene locus, the database was arranged individually, and the four methods below were followed;

- The following four genetic models were selected in this investigation: dominant; AA + AB versus BB, recessive; AA versus AB + BB, co-dominant; AA versus BB versus AB.
- Two effect models (random and fixed) were used to define the difference between means.
- The standardized mean differences (SMDs) and standard deviation were computed at a 95% CI (Confidence Interval) to estimate the capabilities between the three genetic models for every trait.
- Cohen's method is used for standardized mean differences(SMD) to assess the effect size.

3. Results and Discussion

In the present meta-analysis, two productive traits (lactation milk yield and protein yield) were investigated. Each character was analyzed separately, random and fixed effect models are used and.

Meta-analysis offers a more powerful analysis. When more similar studies have been performed on a particular subject there is a need for meta-analysis and there will be differences of opinion in some of these studies. Table 1 contains the statuses of the heritage

pattern of alleles with the results for heterogeneity, standardized mean difference (SMD) with a 95% CI, and significances.

Table1. Results of meta-analysis of the association between PRL polymorphism and milk traits

Traits	n	AA Versus AB						AA Versus BB					AB Versus BB						
		I ²	model	SMD	90%	CI	P	I^2	model	SMD	90%	CI	Р	I ²	model	SMD	90%	CI	P
Lactaion milk yield	26	47.1**	R	0.011	0.074	0.096	0.796	32.7*	R	0.1	0.010	0.022	0.470	39.9*	R	0.087	-0.063	0.237	0.252
Protein yield	14	4.3	F	0.057	0.125	0.011	0.101	15.8	F	-0.03	0.213	0.146	0.717	62.2**	R	0.289	0.0.005	0.573	0.046
Protein content	18	0.0	F	0.006	0.054	0.066	0.851	0.0	F	-0.01	0.145	0.118	0.846	0.0	F	0.030	-0.096	0.156	0.642

^{*} P<0.10; ** P<0.01; n: number of publication; I²: variation in SMD attributable to

heterogeneity; F: Fixed; R: Random

In the analysis of 26 studies for lactation milk yield (LMY), all genotypes showed no significant (P>0.05) effect on milk yield. A similar result is obtained by many researchers [18]. However, the obtained results contradict with obtained by some other researchers [4],[8], [7],[9], indicating that the polymorphisms of the prolactin gene had an impact on milk yield.

In protein yield, the association between polymorphisms in prolactin gene and the AB and BB genotype was found a significant (P<0.05) and it is same as the results were reported by some authors [4],[8],[20], [10],[21]. However, this result is different from the results reported by [7]. Considering protein content, no significant association was revealed between prolactin gene polymorphisms and all genetic models (P>0.05). Similar results were reported by a number of authors [4],[8], [10],[13],[19]. It is thought that the results obtained in this study will make a contribution to developing new strategies necessary for breeding dairy cattle. In accordance with the results obtained from the current meta-analysis, a single significant association was found between prolactin gene polymorphism and protein yield in the AB and BB genotypes. No significant associations were observed between milk yield, protein yield, and protein content. Since various conflicting results have been reported by the authors on this subject, more studies should be conducted to determine the PRL gene polymorphism and investigate its impact on milk yield traits. Moreover, to obtain more reliable results, the genotype x environment interaction should be taken into account, group comparisons should

be made to minimize outcome variability with more articles, and the usability of the results obtained by applying the correct statistical model for breeding purposes shouldbe discussed.

4. Conclusions

According to the results obtained from the meta-analysis of this study. The significant result was found among the polymorphism of prolactin gene and protein yield in AB vs BB genotype. The non-significant association of PRL polymorphism observed with the genotype of milk yield and protein content. Several results reported by the authors which were in contrast with this study. Therefore more study should be done for determination of polymorphism of PRL gene and its effect on milk production traits.

References

- 1. A. Anggraeni, C. Sumantri, A.Saputra and L. Praharani, "Association Between GH (g.1456inst), GHRH (g.4474(<A), and Pit-1 (g.244G>A) Polymorphisms and Lactation Traits In Holstein Friesian Cattle," Tropical Anim Sci Journal., vol.43,pp. 291-299. 2020.
- 2. B. Akyüz, K. Arslan, D. Bayram and K. M. işcan, "Allelic frequency of kappacasein, growth hormone and prolactin gene in Holstein, Brown Swiss and Simmental cattle breeds in Turkey," Kafkas Univ Vet Fak Derg, Vol. 3, pp. 439-444. 2013.
- 3. M. Akkaya and B. Akyuz, "Investigation of the Relationship between GHRH and PRL Genes Polymorphsims and Milk Yield in Holstein Cattle Breed Reared in Turkey," KSU J Agric Nat, Vol. 5, pp.763-771, 2019.
- 4. M.Alipanah, L. Kalashnikova, G. Rodionov, "Association of prolactin gene variants with milk production traits in Russian Red Pied cattle," Iran J Biotechnol, Vol.5, pp. 158-161, 2007.
- 5. K. Arslan, S. Taheri, E.F. Şener, B. Akyüz, A. Akçay, Y. Özkul and K.M. Işcan, "Investigation of the promoter polymorphisms of the growth hormone(GH1), growth hormone receptor (GHR), insulin-like growth factor (IGF-I), and prolactin (PRL) genes and the correlation between gene expression and milk yields in Holstein cattle raised in Central Anatolia," Turk J Vet Anim Sci, Vol. 40, pp. 609-615, 2016.
- 6. Y.C. Bangar, C.S Patil, A. Magotra and A.S. Yadav, "Meta-analysis of gene polymorphism of beta-lactoglobulin gene in indian dairy cows," Biochem Genet, vol.3, pp. 1039-1048, 2022.

- 7. J. Boleckova, J.Matejickova, M.Stipkova, J. Kyselova and L. Barton, "The association of five polymorphisms with milk production traits in Czech Fleckvieh cattle,". Czech J Anim Sci, Vol. 57,pp. 45-53, 2012.
- 8. P.Brym,S. Kaminski and E. Wojcik, "Nucleotide sequence polymorphism within exon 4 of the bovine prolactin gene and its associations with milkperformance traits," J Appl Genet, Vol. 4, pp.179-185, 2005.
- 9. C.H. Dong, X.M. Song, L. Zhang, J. F. Jiang, J.P.Zhou and Y.Q. Jiang, "New insights into the prolactin-RsaI (PRL-RsaI) locus in Chinese Holstein cows and its effect on milk performance traits," Genet Mol Res, 12, 5766-5773,2013. DOI: 10.4238/2013.November.22.3
- 10. A. Dybus, W. Grzesiak, H. Kamieniecki, I. Szatkowsk, Z. Sobek, P. Blaszczyk, P.E. Czerniawska, S. Zych and M. Muszynska, "Association of genetic variants of bovine prolactin with milk production traits of Black-and-White and Jersey cattle," Arch Tierzucht, vol. 48, pp. 149-156, 2005.
- 11. M.A. Edriss, V. Edriss, H.R. Rahmani, "Association Of PIT-1 Gene Polymorphism With Birth Weight, Milk And Reproduction Traits In Isfahan Holstein Cows" Archiv Tierzucht. Vol. 52, pp. 445-447, 2009.
- N. Ghasemi, M.Z. Rahmani, G. Rahimi and S.H. Hafezian Associations between prolactin gene polymorphism and milk production in montebeliard cows. Int J Gen Mol Biol, vol. 1, pp. 48-51, 2009.
- 13. L. A. Kalashnikova, Y.A., Khabibrakhmanova, A. Tinaev, "Effect of polymorphism of milk protein and hormone genes on milk productivity of Black Pied cows," Russ Agri Sci, Vol. 35, pp. 192-195, 2009.
- 14. A. Lu , X. Hu , H. Chen , J. Jiang, C. Zhang , H. Xu , H. Gao , "Single nucleotide polymorphisms in bovine PRL gene and their associations with milk production traits in Chinese Holsteins," Mol Biol Rep, Vol. 37, pp. 547-551, 2010.
- 15. I. J. Lean , A. R. Rabiee , T. Duffield, I. Fand and R. Dohoo, "Invited Review: Use Of Meta-Analysis In Animal Health And Reproduction Methods And Applications," J Dairy Sci. Vol. 92, pp. 3545–3565. 2009.
- 16. Z. Motmain, M. Ozdemir, K. Ekinci and E. Saygılı and E. Bilgin, "A Meta-Analysis of the Associations Between Prolactin (PRL) Gene Polymorphism and Milk Production Traits in Cattle," Kafkas Univ Vet Fak Derg, vol. 28, pp.627-631, 2022.
- 17. M. Ozdemir, S. Kapuzlu, M. Topal and O.C. Bilgin, "Relationships between milkprotein polymorphisms and production traits in cattle: A systematic review and meta-analysis,". Arch Anim Breed, Vol. 61, pp.197-206, 2018.
- 18. M.Ozdemir, Z. Sonmez, V. Aksakal," Associations between PRL/RsaI polymorphism and some performance traits in Holstein cattle reared underorganic condition. J Anim Plant Sci, Vol. 31, pp. 900-905, 2021.

- J.C. Rincon, L. Herrera and J.J. Echeverri JJ, "Effect of two single nucleotide polymorphisms on milk yield and composition,". Genet Mol Res, Vol. 12. pp. 995-1004, 2013.
- 20. G. Sacravarty, V.P.Vadodaria, C.G. Joshi, B.P. Brahmkshtri, R.R.Shah and J.V Solanki, "Prolactin gene polymorphism and its association with economictraits in Kankrej cattle," Indian J Dairy Sci, Vol. 61, pp. 273-276, 2008.
- 21. N.T.D. Thuy, N.T. Thu, L.V.T. Cuong ,T.T.B. Nguyen and D.V.A. Khoa (2018) Polymorphism Of PIT-1 And Prolactin Genes And Their Effects On Milk Yield In Holstein Frisian Dairy Cows Bred In Vietnam. Russian Journal Of Genetics. 54:346–352, 2018.

ROLE OF RUTIN IN ATTENUATION OF METABOLIC GLUCOSE AND INSULIN IMPAIRMENT

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ABSTRACT

Diabetes mellitus is a condition that affects the body's ability to produce insulin. DM occurs when the pancreas is unable to secrete insulin and the body's insulin isn't used properly. The purpose of the current investigation was to assess how rutin contributes to the reduction of impaired insulin secretion and glucose metabolism. Antioxidant, anti-inflammatory, antidiabetic, cardioprotective, and anti-cancer properties are only a few of the pharmacological actions of rutin. In this study, 24 Wister rats were used for 28 days. Rats were divided into four groups, group 1 was the normal control (reared on a normal diet), group 2 was the negative control (Streptozotocin; 55 mg/kg), group 3 was the reference group (metformin; 250 mg/kg) and group 4 was the treatment group (rutin; 15 mg/kg). The biochemical and histopathological investigations were used to evaluate the antidiabetic efficacy of the flavonoid compound rutin. The statistical analysis of variance (ANOVA) was conducted, and Tukey's test was used to establish the significance between the various groups. The study's findings showed that rutin improved glycemic and antioxidant status, which prevented streptozotocin-induced hyperglycemia. Of comparison to the negative control group, the physical parameters in the Rutin-treated rats were also noticeably improved. Rutin has restored the pancreatic beta cells' normal shape and active beta cell count, according to a histopathology study.

Keywords: Flavonoids, dietary flavonoids, type 2 diabetes, insulin signaling, Antioxidant, Cancer Cardiovascular diseases, Anti-inflammatory

PERI-IMPLANT MARGINAL BONE LOSS PROGRESSION AND A-MMP-8 CAN BE CONSIDERED AS INDICATORS OF THE SUBSEQUENT ONSET OF PERI-IMPLANTITIS. A 5-YEAR STUDY

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What is known:

It has documented that dental implant with a high degree of early marginal bone (MBL) loss are likely to achieve additional increased MBL during function. Moreover, it has been speculated that an early increased MBL might be a predictive factor for the subsequent onset peri-implant inflammatory diseases.

What this study adds:

The present study showed that, after 5 years of function, implants with increased MBL rates at 6 months after loading are likely to achieve additional high values of MBL. No statistically significant relationship between MBL progression and the onset of peri-implantitis was found, whereas high MMP-8 levels, 6 months after loading, could have the distinct ability to predict the onset peri-implantitis.

ABSTRACT

The aim of this retrospective study was to investigate the relationship between the amount of early bone remodeling, the marginal bone loss (MBL) progression, and the peri-implant sulcular fluid concentration of active metalloproteinase-8 (a-MMP-8) and incidence of peri-implantitis during 5 years of implant function.

Materials and Methods: Clinical and radiographic documentation at implant placement (T0), at restoration delivery (TR) at 6 months (T1), at 2- (T2) and at 5-years (T5) post-loading were retrospectively collected. MBL levels/rates (MBLr) and peri-implant sulcular fluid levels/rates of a-MMP-8 were assessed at TR, T1, T2, and T5. Implants were divided into two groups: group 1 with peri-implantitis (P+) and group 2 without peri-implantitis (P-). A multilevel simple binary logistic regression, using generalized estimation equations (GEE), was used to assess the association between each independent variable and P+. Receiver Operating Characteristics (ROC) curve was used to evaluate an optimal cut-off point of T1 MBL degree and a-MMP-8 level to discriminate between P+ and P- implants.

Results: A total of 80 patients receiving 80 implants [39 implants with a laser-microtextured collar surface (LMS) and 41 implants with a machined collar surface (MS)] were included. Periapical radiographs and a software package were used to measure MBL rates. Peri-implant sulcular Implant fluid samples were analyzed by a chairside mouth rinse test, (ImplantSafe®), in combination with a digital reader, (ORALyzer®). Twenty-four implants (6 with LMS, and 18 with MS) were classified with P+. No statistically significant association was found between the amount of early bone remodeling, MBL progression, MBLr, and incidence of peri-implantitis. Implants with a-MMP-8 levels >15.3 ng/mL at T1 presented significant influence on the probability of P+.

Conclusion: The amount of early, marginal bone remodeling cannot be considered as indicators of the subsequent onset of P+, whereas high a-MMP-8 levels, 6 months after loading, could have the distinct ability to predict P+.

KEYWORDS: Implants; MMP-8; Peri-Implantitis; Prognosis; Marginal Bone Loss; MBL; Periodontal Indices.