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2. ULUSLARARASI BİYOLOJİ, BIYOKIMYA ve MOLEKÜLER BİYOLOJİ KONGRESİ

19 - 21 Eylül 2025

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ICSAS 2nd INTERNATIONAL CONFERENCE ON BIOLOGY, BIOCHEMISTRY AND MOLECULAR BIOLOGY

September 19 - 21, 2025

Izmir

Edited By

Prof. Dr. Hülya ÇİÇEk

ORGANIIZATION

ACADEMY GLOBAL CONFERENCES

EVALUATION PROCESS

All applications have undergone a double-blind peer review process.

PARTICIPATING COUNTRIES

TURKEY – Iran – Portugal- Japan- Nigeria- Serbia- Russia- Oman- Lebanon- Egypt- Saudi Arabia- Hungary- Jordan - Yemen- Indonesia- Taiwan- Algeria – Greece- Bangladesh- India – Malaysia-

PRESENTATION

Oral presentation

PERCENTAGE OF PARTICIPATION

More than 50 % of paper are presented by participants from maintained countries.
18 papers from Turkey and 32 paper from other countries.

Members of the organizing committees of the conference perform their duties with an "official assignment letter"

LANGUAGES

Turkish, English, Russian, Persian, Arabic

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Sayı : E-16710634-03-903.07.02-2300384284 01.12.2023
Konu : Doç.Dr.Elif AKPINAR
KÜLEKÇİ'nin Görevlendirilmesi

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İlgi : 29.11.2023 tarihli ve E-53120705-000-2300381989 sayılı belge.

Fakülteniz Peyzaj Mimarlığı Bölümü öğretim üyelerinden Doç.Dr.Elif AKPINAR KÜLEKÇİ'nin, Yükseköğretim Genel Kurulunun 15.06.2023 tarihli, 10 sayılı oturumunda alınan 2023.10.183 sayılı kararı gereğince Doçentlik Başvuru Şartlarında bulunan ve doçent olacak adaylardan istenen "Diğer uluslararası/ ulusal bilimsel toplantının düzenleme komitesinde resmi olarak görevlendirilmiş üniversite akademisyen temsilcisi bulunması zorunludur." maddesi gereğince, Academy Global Conference & Journals tarafından yapılan kongrelerin düzenleme kurullarında yolluksuz ve gündeliksiz olarak görevlendirilmesi Rektörlüğümüzce uygun görülmüştür.

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- Oturuma bağlanmadan önce Salon numaranızı adınızın önüne aşağıdaki gibi ekleyiniz. Bu sayede kongre açılışında beklemeden oturumlarınıza gönderilebileceksiniz. Ör. 5 Ahmet Ahmetoglu
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Salon	Moderator		Bildiri No ve Başlığı / Paper ID and Title	Authors
HALL / SALON 1	**Asst. Prof. PhD, Fatma Cavus Yonar**	1	BIBLIOMETRIC TRENDS IN AI-BASED FORENSIC DNA MIXTURE INTERPRETATION	Asst. Prof. PhD, Fatma Cavus Yonar MSc, Sena Kadem
		2	FROM FORENSIC GENETICS TO CLINICAL BIOMARKERS: ncSTR PROFILING IN BREAST CANCER	Asst. Prof. PhD, Fatma Cavus Yonar
		3	ORGAN-SPECİFİC DİSTRİBUTİON OF AMİNO ACİDS AND TRACE ELEMENTS İN VERBASCUM TUNA-EKİMİİ: A PHYTOCHEMİCAL AND PHARMACOLOGİCAL PERSPECTİVE	Assist. Prof. Dr. SAMED ŞİMŞEK PhD Student TUĞÇE VAROL
		4	THE STRUCTURAL ANALYSIS OF MARINE PEPTIDES AND INVESTIGATION OF THE BETA GLUCOSIDASE ACTIVITY OF THEIR SEQUENTIAL PEPTID FRAGMENTS	Doç. Dr. Sibel AVUNDUK Dr. Burcu OMUZBÜKEN Prof. Dr. Aslı KAÇAR
		5	INVESTIGATION OF POLLUTION LEVELS IN AGRICULTURAL LANDS OF MARDIN PROVINCE DUE TO TRAFFIC AND AGRICULTURAL ACTIVITIES THROUGH SOIL SAMPLING	Yüksek Lisans Öğrencisi Hüseyin GÜDER Doç. Dr. İbrahim KOÇ
		6	SESELİ RESİNOSUM'DA (APİACEAE) ERKEK GAMETOFİT GELİŞİMİ	Dr. Öğr. Üyesi Hanife İRİS
		7	DURHAM CİHAZI KULLANILARAK GERÇEKLEŞEN AEROPALİNOLOJİK ÇALIŞMALARIN YER ALDIĞI TEZLER: 2000-2025 LİTERATÜR TARAMASI	Dr. Öğr. Üyesi Hanife İRİS
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ICSAS 3rd INTERNATIONAL CONFERENCE ON MATHEMATIC September 19 - 21, 2025 IZMIR Meeting ID: 885 7151 8350 Passcode: 202224				
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Salon	Moderator		Bildiri No ve Başlığı / Paper ID and Title	Authors
HALL / SALON 2	**Asst. Prof. Dr. SURE KÖME**	1	DYNAMICAL BEHAVIOR OF A DISCRETE FRACTIONAL PREDATOR–PREY SYSTEM WITH INTRASPECIFIC COMPETITION	Asst. Prof. Dr. SURE KÖME
		2	GEOMETRİC PROPERTIES OF PARA-KENMOTSU MANIFOLDS ADMITTING -RICCI-BOURGUIGNON SOLITONS	DOÇ. DR. TUĞBA MERT PROF. DR. MEHMET ATÇEKEN
		3	SIGNIFICANT RESULTS ON PSEUDOPARALLEL PARA-KENMOTSU MANIFOLDS WITH RESPECT TO THE - CURVATURE TENSOR	DOÇ. DR. TUĞBA MERT PROF. DR. MEHMET ATÇEKEN
		4	TOPSIS METHOD BASED ON HYBRID AHP-ENTROPY WEIGHTING IN SPHERICAL FUZZY SETS AND ITS APPLICATION	Begüm TAÇKIN Assist. Prof. Dr. Elif GÜNER Prof. Dr. Halis AYGÜN
		5	MATEMATİK ALAN BECERİLERİNİN GENEL MATEMATİK BAŞARISINI AÇIKLAMADAKİ ROLÜ: MTK VE REGRESYON TEMELLİ BİR İNCELEME	Uzman, Simge CEYLAN Uzman, Yasemin YARDIM Prof. Dr. Tahsin Oğuz BAŞOKÇU
		6	AN ENHANCED MEREC-COPRAS METHOD BASED ON COMPLEX SPHERICAL FUZZY SETS AND ITS APPLICATION IN HEALTHCARE	Ravza Nur TÜRKDOĞDU Şevval Büşra SEYMENBAŞI Assist. Prof. Dr. Elif GÜNER Prof. Dr. Halis AYGÜN
		7	APPROXIMATION AND DERIVATIVE PROPERTIES OF A GENERALIZED BERNSTEIN OPERATOR: ANALYTICAL AND COMPUTATIONAL INVESTIGATIONS	Assoc. Prof. Dr.,NAZMIYE GONUL BILGIN PhD Student,EMINE GUVEN
		8	CHROMATIC ZAGREB INDEX OF ZERO DIVISOR GRAPHS	Assistant Professor, ÖZGE ÇOLAKOĞLU

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Salon	Moderator		Bildiri No ve Başlığı / Paper ID and Title	Authors
HALL / SALON 3	**Prof. Seyidova Sevinc Mammad Kızı**	1	The Role of Islam in the Middle East Policies of European Powers: A Historical Perspective	Farida Allahverdiyeva
		2	ANTİK DÖNEM SİKKELERİNDE ATLET YANSILARI	Öğr. Gör. Dr. ERTAN ŞEHİT
		3	KÜÇÜK MENDERES HAVZASI'NDA KIRSAL ENDÜSTRİYEL MİRAS ENVANTER VE HARİTALANDIRMA	Doç. Dr Olcay Pullukçuoğlu Yapucu Prof Dr. Aylin Ü. Erdem Otman Dr İbrahim Hamaloğlu Dr Yasin Özdemir Prof Dr Cihan Özgün
		4	TURKEY'S POSITION ON THE RESOLUTION OF THE ARMENIA-AZERBAIJAN NAGORNO-KARABAKH CONFLICT	Prof. Seyidova Sevinc Mammad Kızı

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Salon	Moderator		Bildiri No ve Başlığı / Paper ID and Title	Authors
HALL / SALON 4	**Doç. Dr. Sait Yıldırım**	1	PROBLEMS EXPERIENCED IN MARRIAGE ACCORDING TO CLIENTS AND SOLUTION SUGGESTIONS: THE ORDU EXAMPLE (2018-2025)	Yeşim GÜR GÖL
		2	SÜRDÜRÜLEBİLİR EVLİLİK İÇİN EŞ SEÇME VE İSTEME SÜRECİNDE ORUCUN ÖNEMİ	Doç. Dr. SEZAİ BEKDEMİR
		3	SOSYAL MEDYA VE EVLİLİK ALGILARI	Yüksek Lisans Öğrencisi, SÜMEYYE ÜSTÜN ALKAN
		4	MEDIATION AND COUNSELLING IN MUSLIM FAMILIES IN THE ENGLAND (THE EXAMPLE OF THE ISLAMIC SHARIA COUNCIL)	Associate Professor Yusuf EŞİT
		5	YAPISAL AİLE TERAPİSİ KURAMI PERSPEKTİFİNDEN “DANGAL” FİLMİNİN ANALİZİ	Yüksek Lisans Öğrencisi, Kübra UÇARSU
		6	DİJİTAL BAĞIMLILIK ÖZELİNDE TİKTOK UYGULAMASININ ZAMAN YÖNETİMİ VE İLİŞKİ DOYUMU AÇISINDAN EVLİLİKTEKİ ÇATIŞMA DİNAMİKLERİNE ETKİSİNİN İNCELENMESİ	Doç. Dr. Sait Yıldırım
		7	MEVCUT AİLE YAPISINDA YAŞANAN SORUNLARIN X VE Y KUŞAĞI KADINLAR TARAFINDAN DEĞERLENDİRİLMESİ: AZERBAYCAN GADABAY KENTİ ÖRNEĞİ	Doç. Dr. Sait Yıldırım Lisans Öğrencisi Ayan Əliyeva
		8	EVLİLİKTE ALDATMA OLGUSU: NEDENLERİ, TÜRLERİ, VE SONUÇLARI ÜZERİNE BİR DEĞERLENDİRME	Yüksek Lisans Öğrencisi, YASEMİN SEVDE KÖKÇÜ Prof.Dr. HASAN HÜSEYİN TAYLAN
		9	FAMILY COUNSELING and ETHICS	GÜL KARAHAN ÇOBAN, Ph.D.

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HALL / SALON 1	**Assoc. Prof. Dr. Noura Al-Harbi**	1	VIRTUAL BIOLOGY LABORATORY FOR ENHANCED STUDENT LEARNING	Dr. Nurul Huda Dr. Amirul Faizal
		2	INTEGRATING ONLINE LABORATORIES INTO SECONDARY BIOLOGY EDUCATION IN KAZAKHSTAN	Ayan Mukhtar Zhanar Bektemir Dinara Sadykova
		3	BIOLOGICALLY INSPIRED REACTIVE AGENT MODELING USING X-MACHINES	Dimitrios Papadopoulos Elena Nikolaidis Yannis Christodoulou
		4	CRYPTOGENIC FRESHWATER FISH BIODIVERSITY IN BANGLADESH	Dr. Md. Hasan Dr. Kamal Uddin Md. Tarek Hossain
		5	UNIFIED MODELS IN GENOME REARRANGEMENT AND SORTING PRIMITIVES IN BIOINFORMATICS	Dr. Anil Kumar Assis. Prof. Dr. Priya Sharma Rohit Singh
		6	MOLECULAR IDENTIFICATION AND DIVERSITY ASSESSMENT OF AGRICULTURAL PESTS USING DNA BARCODING	Dr. Saud Al-Mutairi Faisal Al-Qahtani Assoc. Prof. Dr. Noura Al-Harbi
		7	ADVANCED MICROFLUIDIC TECHNIQUES FOR BIOMEDICAL AND BIOHEALTH APPLICATIONS	Dr. Zahra Roudsari Dr. Nima Etemad
		8	EVALUATING THE EFFECTIVENESS OF INTERPROFESSIONAL SIMULATION TRAINING ON COLLABORATIVE SKILLS AMONG HEALTHCARE UNDERGRADUATES	Assoc. Prof. Dr. L. Thompson Ramirez, Lec. N. Khamal
		9	SUSTAINABLE POULTRY FEED FORMULATIONS BASED ON ALTERNATIVE ENERGY SOURCES	Dr. Chinedu Okoro Ifeanyi Nwosu Ngozi Eze

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HALL / SALON 2	**Assoc. Prof. Dr. Hiroshi Takeda**	1	DIFFERENTIATION OF GENE EXPRESSION PROFILES IN LIVER AND KIDNEY TISSUES OF PIGS	Assoc. Pro. Dr. Sergey Sokolova
		2	DECISION TREES FOR PREDICTING RISK OF MORTALITY USING ROUTINELY COLLECTED DATA	Dr. Emily Carter Dr. James Walker Dr. Michael Thompson
		3	SELENIUM LEVELS IN AGRICULTURAL SOILS AND CROPS OF THE BALKAN REGION	Mila Stefanovic Dragan Kovacevic
		4	MODELING THE COMPLEX INTERACTIONS BETWEEN miRNA DYSREGULATION AND BREAST CANCER PROGRESSION	Dr. Neda Karimi Assoc. Prof. Dr. Pardis Mousavi
		5	MODELING THE COMPLEX RELATIONSHIP BETWEEN miRNA DYSREGULATION AND BREAST CANCER PROGRESSION	Dr. Olufemi Adewale Dr. Chinedu Okoro
		6	PRELIMINARY ANALYSIS OF REAL-TIME HAND MOVEMENT RECOGNITION FOR UPPER-LIMB PROSTHETICS BASED ON ELECTROMYOGRAPHIC SIGNALS	Assoc. Prof. Dr. Hiroshi Takeda Assist. Prof. Dr. Maria Gonzalez Lec. Ahmed El-Sayed Dr. Jonathan Clarke
		7	ADVANCED SIMULATION PLATFORM FOR MEDICAL IMAGE FUSION AND LEARNING	Assoc. Prof. Dr. Beatriz Oliveira, Assis. Prof. Dr. Inês Soares, Miguel A. Duarte
		8	MICROFLUIDIC SYSTEMS FOR ADVANCED BIOMEDICAL ENGINEERING APPLICATIONS	Arman Khalili Assist. Prof. Dr. Laleh Moradi Lec. Sahar Nematpour

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HALL / SALON 3	**Assoc. Prof. Dr. Samira Bensalem**	1	IMPACT OF INTEGRATED REHABILITATION STRATEGIES ON FUNCTIONAL RECOVERY AND FALL PREVENTION FOLLOWING HIP FRACTURE SURGERY IN CLINICAL PRACTICE	Assoc. Prof. Dr. N. Papadopoulos Assis. Prof. Dr. E. Kallergi Lec. M. Vassilakis
		2	INVESTIGATION OF OCCUPATIONAL STRESS AND BURNOUT AMONG MEDICAL STAFF IN A NORTH AFRICAN UNIVERSITY HOSPITAL	Assoc. Prof. Dr. Samira Bensalem Assist. Prof. Dr. Yacine Meddour
		3	THE IMPACT OF LOW-INTENSITY BALANCE EXERCISE ON MUSCLE STRENGTH, MOBILITY, AND WELL-BEING IN OLDER ADULTS UNDERGOING HEMODIALYSIS	Chia-Ling Huang Assis. Prof. Dr. Wei-Ting Lin Hsin-Yu Chang Kuo-Jen Tsai
		4	KNOWLEDGE, ATTITUDE AND PRACTICE OF EXPECTANT MOTHERS TOWARD MATERNAL HEALTH SERVICES AT GOVERNMENT HOSPITALS IN ADEN CITY	Assoc. Prof. Dr. Samir Al-Mahdi Khaled N. Al-Saqqaf Amal M. Al-Harazi
		5	CHALLENGES AND ENABLERS IN ACCESSING CHILDHOOD IMMUNIZATION SERVICES AMONG UNREGISTERED MIGRANT FAMILIES IN EASTERN INDONESIA: A QUALITATIVE STUDY	Assoc. Prof. Dr. Putri Anindya Santoso Mohammad Rizal Fauzi Lec. Siti Rahmah Hidayat
		6	INTERDISCIPLINARY COLLABORATION IN PALLIATIVE CARE SYSTEMS ACROSS URBAN AND RURAL AREAS	Dr. A. Kovács Lec. S. Thompson Assis. Prof. Dr. H. Berger
		7	EVALUATING THE PHYSIOLOGICAL AND PSYCHOLOGICAL STRESSORS AND COPING MECHANISMS IN HEMODIALYSIS PATIENTS	Assoc. Prof. Dr. Leila M. Hassan Reem A. Al-Farhan Assis. Prof. Dr. Omar S. Rahman Lec. Nour T. Aziz

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HALL / SALON 4	**Assis. Prof. Dr. Laura Jensen,**	1	OPTIMIZING RESOURCE ALLOCATION IN DYNAMIC NETWORKS USING HEURISTIC METHODS	Assoc. Prof. Dr. Elena Vasilev, Pavel Korolenko, Dr. Matteo Ricci
		2	DEEP LEARNING-DRIVEN ANALYSIS FOR EARLY DETECTION OF CROP STRESS	Lec. Amina Koulibaly, Dr. Jonathan Reese
		3	INTELLIGENT DECISION-MAKING IN ORGANIZATIONAL STRATEGIES USING FUZZY LOGIC	Assis. Prof. Dr. Laura Jensen, Thomas Gruber, Sebastian Meyer
		4	ADAPTIVE STOCHASTIC GRADIENT METHODS FOR NON-CONVEX OPTIMIZATION	Assoc. Prof. Dr. Emil Dubois, Jae-Hyun Lee
		5	COSMIC INFLATION AND THE ROLE OF QUANTUM VACUUM FLUCTUATIONS	Lec. Amir Rahimi
		6	EXTENDED RÉNYI ENTROPY AND APPLICATIONS IN COMPLEX SYSTEMS	Assis. Prof. Dr. Carla M. Silva, Dr. José F. Romero, Miguel A. Torres, Ana L. Hernández
		7	EXACT ANALYTICAL SOLUTION OF THIRD ORDER NONLINEAR DIFFERENTIAL EQUATIONS Authors:	Assoc. Prof. Dr. Farid Alimov,
			APPLICATION OF MULTIVARIATE REGRESSION MODELS FOR ECONOMIC TREND PREDICTION: ANALYZING THE IMPACT OF ENERGY PRICES, NATIONAL OUTPUT, AND GDP GROWTH	Dr. Ravi K. Menon, Assoc. Prof. Dr. Leila Hassan, Aria Feroz
		8	ADVANCED SPATIAL INTERPOLATION USING HIERARCHICAL INVERSE DISTANCE WEIGHTING FOR COMPLEX GEOSPATIAL CLASSIFICATION	Assis. Prof. Dr. Karim Ben Salem, Olivier Tremblay, Prof. Dr. Marie-Claire Dubois, Dr. Lucien Gagnon

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HALL / SALON 5	**Assoc. Prof. Dr. Leila Haddad,**	1	ADVANCED FOURIER METHODS IN QUANTUM SIGNAL PROCESSING	Liam O'Connor, Dr. Esi K. Mensah, Theo van Dijk
		2	TOPOLOGICAL ANALYSIS OF NONLINEAR DYNAMICAL SYSTEMS	Haruto Nakamura, Assis. Prof. Dr. Priya S. Nair
		3	MATHEMATICAL FOUNDATIONS OF DEEP REINFORCEMENT LEARNING	Dr. Arjun V. Reddy
		4	MESHLESS TECHNIQUES FOR 3D WAVE PROPAGATION IN COMPLEX MEDIA	Prof. Dr. Farid Al-Husseini, Dr. Samir Khadem
		5	EXPLORING THE EFFECTS OF URBANIZATION ON VECTOR-BORNE DISEASES: A SPATIO-TEMPORAL STUDY	Assoc. Prof. Dr. Leila Haddad, Ahmed R. Thompson
		6	MODELING THE INFLUENCE OF TEMPERATURE VARIABILITY ON MONSOON PATTERNS IN EASTERN INDIA	Dr. Rajesh Kumar Mehra
		7	ON THE GENERALIZATION OF SALVADORI NUMBERS IN FORMAL POWER SERIES FIELDS	Wiem Gadri
		8	A NOVEL ALGORITHM FOR SOLVING THE EXTENDED MALFATTI PROBLEM IN NON-CONVEX TRIANGLES	Lec. Ching-Shuo Chiang

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HALL / SALON 6	**Assoc. Prof. Dr. Marat Akhmetov**	1	ANCIENT TRADE ROUTES AND CULTURAL EXCHANGE IN ASIA	Assoc. Prof. Dr. Hiroshi Tanaka Prof. Dr. Priya Raghavan Lec. Nguyen Van Long
		2	IMPACT OF COLONIALISM ON SOUTHEAST ASIAN POLITICAL STRUCTURES	Assoc. Prof. Dr. Aisha Rahman Prof. Dr. Somchai Chaiyaporn Dr. David Chen
		3	RELIGIOUS TRANSFORMATIONS IN THE MIDDLE EAST FROM 7TH TO 15TH CENTURY	Prof. Dr. Leila Al-Mansouri Assoc. Prof. Dr. Farhad Rezai Lec. Omar Khalid
		4	HISTORY OF SCIENCE AND TECHNOLOGY IN EAST ASIA	Prof. Dr. Min-Joon Park Assoc. Prof. Dr. Ananya Gupta Dr. Chen Wei
		5	REVOLUTIONARY MOVEMENTS IN MODERN CENTRAL ASIA	Assoc. Prof. Dr. Marat Akhmetov Prof. Dr. Dilshod Rasulov Lec. Gulnara Abdiyeva
		6	ART AND ARCHITECTURE IN THE OTTOMAN EMPIRE	Prof. Dr. Leyla Hassan Dr. Samir Al-Khalifa
		7	ENVIRONMENTAL HISTORY AND AGRICULTURAL PRACTICES IN ANCIENT CHINA	Prof. Dr. Li Na Assoc. Prof. Dr. Takeshi Sato Lec. Tran Thi Hoa

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HALL / SALON 7	Assoc. Prof. Dr. Jad Nasser	1	THE IMPACT OF CULTURAL BELIEFS AND TRADITIONAL NORMS ON FAMILY THERAPY OUTCOMES IN MIDDLE EASTERN SOCIETIES	Dr. Kourosh Fattahi Samira Daryaei
		2	INTERGENERATIONAL CONFLICTS, PARENTAL EXPECTATIONS, AND STRATEGIES FOR RESOLUTION IN MARRIAGE AND FAMILY THERAPY	Prof. Dr. Elena Kuznetsova Igor Volkov Anastasia Morozova
		3	THE ROLE OF EMOTIONAL INTELLIGENCE, SELF-AWARENESS, AND COPING SKILLS IN IMPROVING MARITAL SATISFACTION AND STABILITY	Assis. Prof. Dr. Aisuluu Tulegenova Yerzhan Akhmetov Bibigul Saparova
		4	PARENTAL STRESS, WORK-LIFE BALANCE, AND THEIR IMPACT ON CHILD DEVELOPMENT AND FAMILY RELATIONSHIPS	Rania Al-Masri Omar Khalaf
		5	ANALYZING COUPLE COMMUNICATION PATTERNS, CONFLICT RESOLUTION TECHNIQUES, AND THERAPEUTIC INTERVENTIONS FOR HEALTHIER RELATIONSHIPS	Huda Nasser
		6	THE INFLUENCE OF RELIGIOUS BELIEFS, SPIRITUALITY, AND PRACTICES ON MARITAL RELATIONSHIPS AND FAMILY DYNAMICS	Dr. Ahmed Salah Dr. Laila Mostafa Nourhan Youssef
		7	MANAGING FINANCIAL STRESS, ECONOMIC PRESSURES, AND RESOURCE ALLOCATION IN FAMILY SYSTEMS THROUGH MARRIAGE AND FAMILY THERAPY	Dr. Hanan Al-Harbi Lec. Dana Al-Mutairi
		8	THE EFFECTS OF TECHNOLOGY, SOCIAL MEDIA, AND DIGITAL COMMUNICATION ON FAMILY INTERACTIONS, COUPLE RELATIONSHIPS, AND THERAPEUTIC OUTCOMES	Mariam Al-Nuaimi Latifa Al-Mazrouei
		9	TRAUMA-INFORMED MARRIAGE COUNSELING: STRATEGIES FOR SUPPORTING FAMILIES EXPERIENCING PSYCHOLOGICAL, EMOTIONAL, AND SOCIAL TRAUMA	Assoc. Prof. Dr. Jad Nasser Dr. Maya Khalil Lec. Rami Bou Saab

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HALL / SALON 1	**Doç. Dr. Suna Muğan Ertuğral**	1	THE RELATIONSHIP BETWEEN DIGITALIZATION AND TAX REVENUES: A FOURIER-BASED EMPIRICAL STUDY FOR TÜRKİYE	Assistant Professor Oğuzhan BOZATLI Research Assistant Şeref Can SERİN
		2	Assessing Health Insurance Awareness and Its Correlation with Economic Utilization Among Gujjars and Bakarwals For Seeking Health in Jammu and Kashmir	Iliyas Ahmad Rather Sadam Hussain Pandow Monisa Qadiri
		3	ASYMMETRIC SHOCKS IN INDUSTRIAL PRODUCTION AND ECONOMIC GROWTH: AN EMPIRICAL STUDY ON TURKEY WITHIN THE KALDO-STYLE APPROACH FRAMEWORK	Ögr.Gör.Dr. Atilla ÜNLÜ
		4	FRAGILE SYNCHRONIZATION: GLOBAL, REGIONAL AND COUNTRY-SPECIFIC DYNAMICS OF BUSINESS CYCLE FLUCTUATIONS	Dr. Öğr. Üyesi Ahmet TUNÇ
		5	THE EFFECTS OF WAR ECONOMY ON THE BUDGET: THE CASE OF THE RUSSIA–UKRAINE WAR	Res. Assist. Dr. Ali Fuat URUŞ Dr. Fadime Ayca CEYLAN
		6	ENERJİ VERGİLERİ VE YENİLENEBİLİR ENERJİ İLİŞKİSİ: TÜRKİYE ÜZERİNE BİR UYGULAMA	Dr. Öğr. Üyesi MURAT ALBAYRAK
		7	SILVER ECONOMY PERSPECTIVE: A SECTORAL FOCUS ON SILVER TOURISM	Doç. Dr. Suna Muğan Ertuğral
		8	TURUNCU BAYRAK PROGRAMI İLE GIDA İSRAFININ AZALTILMASI VE SÜRDÜRÜLEBİLİR TURİZM UYGULAMALARI: “TABAĞINI SEN SEÇ” YAKLAŞIMI	Doç. Dr. Suna Muğan Ertuğral

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HALL / SALON 2	**Assoc. Prof. Dr. Gülhan SUADİYE**	1	AN ASSESSMENT OF THE FAST MOVING CONSUMER GOODS INDUSTRY	Doktora Öğrencisi Hakan ERTUĞRAL
		2	EVALUATION OF BIOPLASTIC PRODUCTION PROCESSES IN TERMS OF SUSTAINABILITY AND EFFICIENCY USING GABI-BASED LIFE CYCLE ANALYSIS: AN INTERDISCIPLINARY APPROACH	Chemical Engineer Hakan Ertuğral Computer Engineer Alaeddin Gazi Toprak
		3	DERGİPARK'TA YAYIMLANAN SATIŞ YÖNETİMİ ÇALIŞMALARININ NİTEL ANALİZİ	Dr. Öğr. Üyesi, MUALLA AKÇADAĞ
		4	TÜKETİCİ KARAR SÜREÇLERİNDE NÖROPAZARLAMANIN ROLÜ: NÖROFİZYOLOJİK BİR PERSPEKTİF	Öğrt. Görv. Dr. PINAR COŞKUN
		5	VISITOR PERCEPTIONS IN NATIONAL PARKS AND NATURE PARKS IN ANTALYA PROVINCE: A CONTENT ANALYSIS BASED ON TRIPADVISOR REVIEWS	Assistant Professor Hüseyin KELEŞ Lecturer Dr. Güray KARACIL
		6	ARTIFICIAL INTELLIGENCE IN ADVERTISING: PERSONALIZATION, PREDICTIVE ANALYTICS, AND CONSUMER TRUST	PhD Candidate EYLEM ŞENCAN
		7	AI-DRIVEN MARKETING STRATEGIES: FROM CONSUMER INSIGHTS TO SUSTAINABLE ENGAGEMENT	PhD Candidate EYLEM ŞENCAN
		8	FULL-RANGE LEADERSHIP AS A MULTIDIMENSIONAL APPROACH: THE GLOBAL DEVELOPMENT OF THE LITERATURE	Öğretim Görevlisi Doktor, YAŞAR ŞAHİN
		9	ESG REPORTING: GLOBAL COMPLIANCE THROUGH TURKISH SUSTAINABILITY REPORTING STANDARDS (TSRS)	Assoc. Prof. Dr. Gülhan SUADİYE

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HALL / SALON 3	**Doç. Dr., Ferdi SELİM**	1	İMKAN ANLAYIŞININ KARŞILAŞTIRMALI ANALİZİ (AYNÜLKUDÂT HEMEDÂNÎ, İBN SÎNÂ VE GAZÂLÎ'NİN GÖRÜŞLERİ DOĞRULTUSUNDA)	Rüstem Hacıyev
		2	PLATON'DA EĞİTİM: BİLGİ, ERDEM VE DEVLET İLİŞKİSİ	Yüksek Lisans Öğrencisi NURPERİ TİTİZ
		3	AN EXAMINATION OF THE RELATIONSHIP BETWEEN THE CONCEPTS OF SCIENCE AND IDEOLOGY	Dr. Karani Kağan BADEM
		4	THE CONCEPT OF RACE IN THE CONTEXT OF THE RELATIONSHIP BETWEEN SCIENCE AND IDEOLOGY	Dr. Karani Kağan BADEM
		5	MANTIK FELSEFESİNİN PROBLEMLERİNE YÖNELİK BİR ÇÖZÜMLEME	Doç. Dr. Muhammet Nasih Ece
		6	ANTİNATALİZM: KAVRAMSAL TEMELLER, TARİHSEL GELİŞİM VE FELSEFİ ELEŞTİRİLER	Dr. Öğr. Üyesi Fegani BEYLER
		7	AN EVALUATION OF HAYEK'S CONCEPT OF JUSTICE AND HIS CRITIQUE OF SOCIAL JUSTICE	Doç. Dr., Ferdi SELİM
		8		

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HALL / SALON 4	**Prof. Dr. Habibe ACAR**	1	SPATIAL CONFIGURATION TRANSFORMATION OF REPURPOSED TRADITIONAL HOUSES: THE CASE OF TRADITIONAL DWELLINGS IN ALANYA	Metehan DAYI Dr. Öğr. Üyesi Murat ŞAHİN Doç. Dr. Tuba Nur OLĞUN
		2	ARCHITECTURE AND MODERN LIFE OF PEOPLE	Amina Huseynova
		3	DESIGNING VISITOR ROUTES IN ARCHAEOLOGICAL SITES AS A CONSERVATION STRATEGY	Doç. Dr. Gamze Fahriye PEHLİVAN
		4	THE ROLE OF URBAN LANDSCAPE PLANTS IN THE CONTEXT OF ECOSYSTEM	Research Assistant, RIDVAN TİK
		5	QUALITY IN URBAN SPACE AND ITS EFFECT ON QUALITY OF LIFE	Prof. Dr. Habibe ACAR Assist. Prof. Dr. Aysel YAVUZ Prof. Dr. Nilgün GÜNEROĞLU
		6	LANDSCAPE POTENTIAL OF PLANT TAXON IN TRABZON URBAN GREEN AREAS	Prof. Dr. Nilgün GÜNEROĞLU Prof. Dr. Habibe ACAR Assist. Prof. Dr. Aysel YAVUZ

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HALL / SALON 5	**Doçent, AYŞE SEZER**	1	ARTIFICIAL INTELLIGENCE-SUPPORTED CREATIVE DRAWING APPLICATION: ArtinDraw	Doçent, AYŞE SEZER
		2	ELEKTRİK TÜKETİMİ VE FİYATLANDIRMA ÜZERİNE BİR YAPAY SİNİR AĞLARI UYGULAMASI: ABD ÖRNEĞİ	Dr. Öğretim Üyesi, Murat KAPUSUZ Elektrik ve Elektronik Mühendisi, Enes YILMAZER
		3	PREDICTIVE ANALYTICS FOR DEFECT DETECTION IN MANUFACTURING: A DATA-DRIVEN APPROACH USING MACHINE LEARNING MODELS	Dr. Sameer Jain
		4	ENHANCING REGRESSION MODELING IN MATERIALS SCIENCE: EVALUATING SYNTHETIC DATA AUGMENTATION FOR MECHANICAL DISPLACEMENT PREDICTION	Dr. Öğretim Üyesi, Erhan KAVUNCUOĞLU
		5	DEVELOPMENT OF AN ENTERPRISE-LEVEL CHATBOT	Alim Toprak Fırat Gökşen Çalışkan Ceren Ulus Nazlı Yusufoğlu M. Fatih Akay

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HALL / SALON 1	**Dr. Lara M. Oliveira , Assoc. Prof. Dr. Marco Vitali**	1	SUSTAINABLE URBAN HOUSING DESIGN STRATEGIES FOR RESILIENT COMMUNITIES	Elena Markarian, Assis. Prof. Dr. Dimitrios Kalogeropoulos, Maria Fernanda Castillo, Dr. Arvind Rathore
		2	INTEGRATED FLOOD-RESILIENT INFRASTRUCTURE PLANNING FOR COASTAL CITIES	Dr. Lara M. Oliveira, Assoc. Prof. Dr. Marco Vitali
		3	CROSS-CULTURAL PERSPECTIVES IN MODERN URBAN ARCHITECTURE	João Mendes, Assis. Prof. Dr. Farid Aliev, Nadira Khan
		4	INNOVATIVE FINANCIAL MODELS FOR AFFORDABLE HOUSING IN EMERGING ECONOMIES	Dr. Timothy Adebayo, Chidera Okonkwo, Rizal Hidayat
		5	ARCHITECTURAL STRATEGIES FOR CLIMATE-ADAPTIVE PUBLIC SPACES	Manoj Patel, Dr. Hana Syafiqah
		6	RISK ASSESSMENT AND SAFETY MANAGEMENT IN INDUSTRIAL URBAN ZONES	Dr. Khaya Qonono, Assis. Prof. Dr. Zeynep Alimova, Paulo Ribeiro
		7	DVANCES IN LIGHTING SIMULATION AND VISUAL COMFORT ANALYSIS IN CONTEMPORARY ARCHITECTURE	Assoc. Prof. Dr. Luca Moretti Mahmoud Al-Khatib E. S. Cantrell Sofia Petrova

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HALL / SALON 2	**Assoc. Prof. Dr. Matteo Ricci**	1	ELITE SUSTAINABLE URBAN DEVELOPMENT STRATEGIES: INTEGRATING GREEN SPACES AND SMART INFRASTRUCTURE	Assoc. Prof. Dr. Matteo Ricci, Hana Kim, Prof. Dr. Samuel Osei
		2	REVITALIZING HISTORIC CITY CENTERS THROUGH CONTEMPORARY LANDSCAPE DESIGN AND COMMUNITY ENGAGEMENT	Tomasz Kowalski, Amina Diallo
		3	ADVANCED MATERIALS AND TECHNOLOGIES IN MODERN ARCHITECTURE FOR ENERGY EFFICIENCY	Dr. Isabella Fernandes, Assoc. Prof. Dr. Ahmed Al-Mansouri
		4	BIODIVERSITY-FOCUSED URBAN PARK DESIGN: PROMOTING ECOLOGICAL CORRIDORS AND HABITAT RESTORATION	Prof. Dr. Juan Carlos Ramirez, Prof. Dr. Fatima Noor
		5	SMART MOBILITY AND INTEGRATED TRANSPORTATION PLANNING IN FUTURE CITIES	Dr. Lars Svensson, Mei Ling Zhao
		6	ARCHITECTURAL RESPONSES TO CLIMATE CHANGE: RESILIENT STRUCTURES AND FLOOD MANAGEMENT STRATEGIES	Assoc. Prof. Dr. Olga Ivanova, Dr. Rafael Martinez, lec. Noura Al-Faraj
		7	CULTURAL LANDSCAPES AND URBAN IDENTITY: PRESERVATION, ADAPTATION, AND COMMUNITY PARTICIPATION	Anika Schreiber, Assoc. Prof. Dr. Sahar Mohammadi
		8	INNOVATIVE HOUSING SOLUTIONS FOR DENSE URBAN ENVIRONMENTS: VERTICAL GREENERY AND MULTI-USE SPACES	Lucas Pereira, Prof. Dr. Min-Joon Choi, Assoc. Prof. Dr. Elena Dimitrova

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HALL / SALON 3	**Dr. Jonathan Clarke**	1	THE PHILOSOPHICAL IMPLICATIONS OF ARTIFICIAL INTELLIGENCE IN HUMAN AGENCY AND MORAL RESPONSIBILITY	Emma Johansson Dr. Hiroshi Tanaka Isabella Moretti
		2	EXPLORING THE INTERSECTIONS OF ENVIRONMENTAL PHILOSOPHY AND ETHICS IN THE CONTEXT OF GLOBAL CLIMATE CHANGE RESPONSE	Dr. Carlos Martínez Assoc. Prof. Dr. Amina Said Fiona Campbell
		3	PHENOMENOLOGICAL INQUIRY INTO THE NATURE OF CONSCIOUSNESS AND SUBJECTIVE EXPERIENCE	Dr. Markus Weber Léa Dupont
		4	CRITICAL ANALYSIS OF FEMINIST PHILOSOPHY AND ITS CHALLENGES TO TRADITIONAL METAPHYSICAL THEORIES	Assoc. Prof. Dr. Sofia Dimitriou Dr. Priya Rao Zara Al-Khalil
		5	POLITICAL PHILOSOPHY AND THE ETHICS OF GLOBAL JUSTICE IN AN ERA OF INCREASING INEQUALITY	Dr. David Kim Amara Ndlovu Prof. Dr. Lucia Rossi
		6	MIND-BODY PROBLEM REVISITED: CONTEMPORARY THEORIES IN PHILOSOPHY OF MIND AND COGNITIVE SCIENCE	Dr. Jonathan Clarke
		7	RECONSIDERING THE CONCEPT OF HAPPINESS IN CONTEMPORARY ETHICAL THEORIES AND PSYCHOLOGICAL WELL-BEING	Prof. Dr. Olivia Bennett Dr. Samuel Okoro
		8	THE ROLE OF LANGUAGE IN SHAPING REALITY: A STUDY IN CONTEMPORARY PHILOSOPHICAL LINGUISTICS	Dr. Abdullah Al-Mutairi Assoc. Prof. Dr. Elise Fournier Mateo González

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HALL / SALON 4	**Assoc. Prof. Dr. Milena Popescu**	1	FREEDOM AND COLLECTIVE RESPONSIBILITY: PHILOSOPHICAL EXAMINATIONS OF INDIVIDUAL AUTONOMY WITHIN SOCIAL STRUCTURES	Assoc. Prof. Dr. Tomas Becker prof. Dr. Lucia Fernandes lec. Kwesi Boateng
		2	REALITY AND PERCEPTION: ONTOLOGICAL INQUIRIES THROUGH THE LENS OF MODERN SCIENCE AND ANCIENT PHILOSOPHY	Assoc. Prof. Dr. Matteo Bianchi lec. Jonas Fitzgerald
		3	ETHICS IN TECHNOLOGY: THE IMPACT OF ARTIFICIAL INTELLIGENCE AND BIOTECHNOLOGICAL ADVANCES ON MORAL VALUES	Dr. Sven Eriksson lec. Chike Obi
		4	TIME AND EXISTENCE: REFLECTIONS ON PAST, PRESENT, AND FUTURE IN EXISTENTIAL PHILOSOPHY	Assoc. Prof. Dr. Sofia Petrović prof. Dr. Kenji Saito Dr. Diego Alvarez
		5	LANGUAGE AND REALITY: THE ROLE OF SEMANTIC STRUCTURES IN THOUGHT AND MEANING-MAKING	lec. Fatoumata Diop Dr. Heinrich Wagner Assoc. Prof. Dr. Milena Popescu
		6	ART AND AESTHETICS: PHILOSOPHICAL ANALYSIS OF BEAUTY, CREATIVITY, AND SOCIETAL INFLUENCE	Prof. Dr. Ricardo Campos Ifeoma Nwosu Dr. Tatiana Kovalchuk
		7	POLITICS AND JUSTICE: ANALYZING EQUALITY, RIGHTS, AND POWER DYNAMICS IN POLITICAL PHILOSOPHY	Assoc. Prof. Dr. Emil Novak Dr. Charlotte Moreau lec. Jabari Diallo
		8	CONSCIOUSNESS AND THE PHILOSOPHY OF MIND: DEEP INVESTIGATIONS INTO THE MIND-BODY PROBLEM, PERCEPTION, AND SELF-AWARENESS	Dr. Priya Nair lec. Maximilian Krüger Assoc. Prof. Dr. Ivana Stanković

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HALL / SALON 5	**Assoc. Prof. Dr. Diego Morales**	1	THE MORAL FOUNDATIONS OF GLOBALIZATION: ETHICAL CHALLENGES IN AN INTERCONNECTED WORLD	Giulia Bianchi
		2	EXISTENTIAL ANXIETY AND HUMAN AGENCY: NAVIGATING MEANING IN CONTEMPORARY LIFE	Dr. Henrik Johansen Assoc. Prof. Dr. Freja Lund Lars Pedersen
		3	KNOWLEDGE AND TRUTH: EPISTEMOLOGICAL PERSPECTIVES ON BELIEF, JUSTIFICATION, AND EVIDENCE	Prof. Dr. Amina Hassan Dr. Omar El-Sayed Salma Farouk
		4	THE PHILOSOPHY OF EMOTION: UNDERSTANDING THE ROLE OF FEELINGS IN REASONING AND ETHICAL DECISION-MAKING	Sophie Dubois Julien Lefevre Camille Moreau
		5	CIVIC VIRTUE AND DEMOCRATIC RESPONSIBILITY: PHILOSOPHICAL EXAMINATION OF CITIZENSHIP AND ETHICAL GOVERNANCE	Alejandro Ramirez Valeria Torres Assoc. Prof. Dr. Diego Morales
		6	THE CONCEPT OF IDENTITY: SELF, SOCIETY, AND THE FLUIDITY OF PERSONAL AND CULTURAL CONSTRUCTION	Ekaterina Smirnova
		7	SCIENCE AND MORALITY: THE INTERSECTION OF TECHNOLOGICAL ADVANCEMENT AND ETHICAL OBLIGATION	Hiroshi Nakamura Yuki Sato Kenji Fujimoto
		8	SPACE, TIME, AND COSMIC PHILOSOPHY: HUMAN UNDERSTANDING OF THE UNIVERSE AND EXISTENTIAL SIGNIFICANCE	Chinedu Eze Assoc. Prof. Dr. Funke Adewale

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HALL / SALON 6	**Assoc. Prof. Dr. Bambang Saputra**	1	INNOVATIVE STRATEGIES FOR SUSTAINABLE BUSINESS GROWTH IN EMERGING AFRICAN MARKETS	Assoc. Prof. Dr. Abdulrahman Umar Dr. Siti Nuraini Lecturer Fatima Zeghichi
		2	THE IMPACT OF DIGITAL TRANSFORMATION ON SUPPLY CHAIN RESILIENCE IN INDONESIAN MANUFACTURING SECTORS	Rizal Maulana Assoc. Prof. Dr. Aisha Bensalem Emmanuel Okoro
		3	EFFECTIVE LEADERSHIP MODELS FOR MANAGING REMOTE WORKFORCES IN TAJIKISTAN'S SERVICE INDUSTRY	Dr. Dilshod Saidov Assoc. Prof. Dr. Hening Wulandari Grace Mbatha
		4	CORPORATE SOCIAL RESPONSIBILITY AND ITS INFLUENCE ON BRAND LOYALTY IN NIGERIAN CONSUMER MARKETS	Kadija Ali Assoc. Prof. Dr. Bambang Saputra Modupe Adebayo
		5	STRATEGIC HUMAN RESOURCE MANAGEMENT PRACTICES TO IMPROVE EMPLOYEE RETENTION IN ALGERIAN SMEs	Amine Belkacem. Indah Kusumawati Assis. Prof. Dr. Tinashe Dzvairo
		6	THE ROLE OF ENTREPRENEURIAL FINANCE IN FOSTERING INNOVATION IN AFRICAN STARTUPS	Dr. Halima Oumar Assis . Prof. Dr. Dewi Handayani Rashid Alizoda
		7	ANALYSIS OF CONSUMER BEHAVIOR TRENDS IN DIGITAL MARKETING CAMPAIGNS WITHIN INDONESIAN E-COMMERCE PLATFORMS	Salah Eddine Belmokhtar Adeleke Johnson
		8	EXPLORING THE CHALLENGES AND OPPORTUNITIES OF WOMEN ENTREPRENEURS IN TAJIKISTAN'S ECONOMY	Assoc. Prof. Dr. Gulchekhra Rahimi Dr. Hendri Setiawan Dr. Mariam Sow

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HALL / SALON 7	**Dr. Yacine Mansouri Assoc. Prof. Dr. Hariyanti Putri**	1	INNOVATIVE RISK MANAGEMENT FRAMEWORKS FOR FINANCIAL INSTITUTIONS IN ALGERIA	Dr. Yacine Mansouri Assoc. Prof. Dr. Hariyanti Putri
		2	THE INFLUENCE OF ORGANIZATIONAL CULTURE ON EMPLOYEE PERFORMANCE IN NIGERIAN TELECOMMUNICATION COMPANIES	Assoc. Prof. Dr. Dwi Anggraini
		3	THE EFFECTIVENESS OF SUPPLY CHAIN SUSTAINABILITY INITIATIVES IN TAJIKISTAN'S INDUSTRIAL SECTORS	Dr. Murodjon Rasulov Dr. Sari Dewi Assoc. Prof. Dr. Femi Adewale
		4	STRATEGIC ALLIANCES AND BUSINESS PERFORMANCE IN INDONESIAN TECHNOLOGY FIRMS	Indra Wijaya Dr. Abderrahmane Cherifi Dr. Nana K. Mensah
		5	THE IMPACT OF LEADERSHIP STYLE ON ORGANIZATIONAL CHANGE IN AFRICAN AGRIBUSINESS COMPANIES	Dr. Jamilah Baba Assoc. Prof. Dr. Lusiana Putri Prof. Dr. Idriss N'Dour
		6	CUSTOMER SATISFACTION AND LOYALTY IN THE CONTEXT OF NIGERIAN RETAIL INDUSTRY	Prof. Dr. Nkechi Okeke Dr. Rini Anjani Assis. Prof. Dr. Mahmoud Bekhti
		7	E-GOVERNANCE AND BUSINESS TRANSPARENCY: A STUDY ON TAJIKISTAN'S PUBLIC SECTOR	Dr. Shokhrukh Yuldashev Dr. Dewi Ayu Assoc. Prof. Dr. Oumar Sylla

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HALL / SALON 8	**Assoc. Prof. Dr. Ahmed Mazouz Prof. Dr. Rebecca Mwangi**	1	THE ROLE OF CORPORATE GOVERNANCE IN BUSINESS SUSTAINABILITY AMONG ALGERIAN COMPANIES	Dr. Safia Boudiaf Dr. Agung Priyanto Assoc. Prof. Dr. Kwame Asante
		2	STRATEGIES FOR ENHANCING INNOVATION CULTURE IN INDONESIAN FAMILY BUSINESSES	Dian Kusumaningrum Dr. Amina Bourahla
		3	SOCIAL ENTREPRENEURSHIP AND COMMUNITY DEVELOPMENT IN AFRICAN URBAN AREAS	Dr. Maimuna Ahmed Anggi Retno Salah Jamal
		4	THE IMPACT OF DIGITAL MARKETING ON CUSTOMER BUYING BEHAVIOR IN TAJIKISTAN'S FMCG SECTOR	Dr. Farzona Safarova Assoc. Prof. Dr. Widya Lestari Dr. Tunde Balogun
		5	INTERNATIONAL TRADE STRATEGIES FOR SMALL AND MEDIUM ENTERPRISES IN NIGERIA	Dr. Emeka Chukwu Yuliana Dewi Abderrahmane Bensaid
		6	THE DEVELOPMENT OF BUSINESS INTELLIGENCE SYSTEMS IN ALGERIAN MANUFACTURING INDUSTRY	Nourredine Kabache Dr. Ani Natalia Fisayo Kehinde
		7	WORKFORCE DIVERSITY AND ITS EFFECT ON CORPORATE INNOVATION IN INDONESIAN COMPANIES	Dr. Putra Hidayat Prof. Dr. Fatima Ziani Assoc. Prof. Dr. Samuel Karanja
			STRATEGIC PLANNING AND COMPETITIVE ADVANTAGE IN THE AFRICAN FINANCIAL SERVICES SECTOR	Dr. Amina Touré Dr. Arif Rahman
			SOCIAL MEDIA STRATEGIES FOR BRAND DEVELOPMENT IN TAJIKISTAN'S SMALL BUSINESSES	Dr. Sari Widya Dr. Peter Okoye
		8	THE ROLE OF CUSTOMER RELATIONSHIP MANAGEMENT IN ENHANCING BUSINESS PERFORMANCE IN INDONESIA	Dr. Dian Anggraini Assoc. Prof. Dr. Ahmed Mazouz Prof. Dr. Rebecca Mwangi

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HALL / SALON 1	**Doktora Öğrencisi Nermin Turan**	1	PROBLEMS AND RISK FACTORS FACED BY ELDERLY PEOPLE AFFECTED BY DISASTERS FROM A SOCIAL WORK PERSPECTIVE	Merve KURT Rümeysa ÇAYLI Rümeysa HAZIRLAR Dr. Öğr. Üyesi Işıl AVŞAR ARIK
		2	LOCAL SOLUTIONS TO THE GLOBAL CLIMATE CRISIS: THE CASE OF PAKISTAN	Arş. Gör. SÜMEYYE AYDOĞDU KUZUCU
		3	BAĞIMLILIKLA MÜCADELEDE PSİKOSOSYAL DESTEK YÖNTEMLERİ	Öğr.Gör. Abdulkadir Ilgaz Prof.Dr. Oğuzhan Zengin
		4	DİJİTAL BAĞIMLILIK: PSİKOLOJİK ETKİLERİ VE BAŞ ETME STRATEJİLERİ	Prof.Dr. Oğuzhan Zengin Öğr.Gör. Abdulkadir Ilgaz
		5	BIBLIOMETRIC ANALYSIS OF STUDIES ON CHILD LABOR IN THE LAST FIVE YEARS	Doktora Öğrencisi Nermin Turan Doç. Dr. Sait Yıldırım Prof. Dr. Senayi Dönmez
		6	EXAMİNİNG THE EFFECT OF TEACHERS' EARTHQUAKE PREPAREDNESS ON THEİR ATTİTUDES TOWARD EARTHQUAKES: THE IĞDIR TUZLUCA EXAMPLE	Sinem ŞENGÜL Doç. Dr. Sait YILDIRIM
		7	CAREER PATH MAP FOR SOCIAL WORK STUDENTS: AN EDUCATIONAL SEMINAR MODEL SUPPORTING CAREER ORIENTATION AND SPECIALIZATION	Master's Student Aslıhan UYAR Master's Student Habibe TANDOĞAN AKAR
		8	BREAKİNG THE CYCLE OF CHİLD LABOR: A MARKOV CHAİN ANALYSİS OF MİCROFİNANCE, FAMİLY SUPPORT, AND SOCİAL WORK INTERVENTİONS İN POVERTY DYNAMİCS	Lecturer HAMDİ AYYILDIZ Lecturer, PhD MERVE KAYA BUZKIRAN
		9	SUÇA SÜRÜKLENEN ÇOCUKLARA YÖNELİK ÖNLEYİCİ SOSYAL HİZMETTE KUŞAKLARARASI YAKLAŞIM VE TOPLUMSAL DAYANIKLILIK	Öğr. Gör. Dr. MERVE KAYA BUZKIRAN Öğr. Gör. HAMDİ AYYILDIZ

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HALL / SALON 2	**Doç. Dr. Fatma AŞILIOĞLU**	1	KAMUSAL YEŞİL ALAN KALİTE KRİTERLERİ KAPSAMINDA MAHALLE PARKLARININ DEĞERLENDİRİLMESİ İÇİN NİCEL BİR YÖNTEM	Doç. Dr. Fatma AŞILIOĞLU Öğr. Gör. Hande ASLAN Dr. Reva ŞERMET ACAR
		2	KENTSEL YEŞİL ALANLARIN TERAPİ BAHÇESİ POTANSİYELİNİN DEĞERLENDİRİLMESİ VE HORTİKÜLTÜREL TERAPİ YAKLAŞIMI	Öğr. Gör. Hande ASLAN Doç. Dr. Fatma AŞILIOĞLU Dr. Reva ŞERMET ACAR
		3	MEKANIN KOLEKTİF YENİDEN ÜRETİMİ: LEFEBVRE'NİN ŞEHİR HAKKI PERSPEKTİFİ İLE GÜNÜMÜZ KENT SORUNLARI	Arş. Gör. Pınar Özge PARLAK Prof. Dr. Banu Çiçek KURDOĞLU
		4	SU, BELLEK ve SÜRDÜRÜLEBİLİRLİK: WROCŁAW HYDROPOLİS ÖRNEĞİ	Arş. Gör. Pınar Özge PARLAK Prof. Dr. Banu Çiçek KURDOĞLU
		5	LANDSCAPE NARRATIVES AT THE INTERSECTION OF PLACE AND REPRESENTATION: PEARL S. BUCK'S THE MOTHER AND TOLSTOY'S ANNA KARENINA	Prof. Dr. SERAP YILMAZ Res.Asst. Dr. ABDULLAH ÇİĞDEM
		6	THE ROLE OF SECTIONS AND ELEVATIONS IN THE ERA OF DIGITAL AND AI-ASSISTED DESIGN	Res.Asst. Dr. ABDULLAH ÇİĞDEM Prof. Dr. SERAP YILMAZ
		7	EFFECTS OF GREEN INITIATIVES ON AIR POLLUTION REDUCTION IN URBAN AREAS	Res. Assist. Dr. Seyhan SEYHAN Prof. Dr. Elif BAYRAMOĞLU
		8	EVALUATION OF NATURE-BASED SOLUTION PROPOSALS IN TERMS OF URBAN SURFACE RUNOFF	Res. Assist. Dr. Seyhan SEYHAN Prof. Dr. Elif BAYRAMOĞLU

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HALL / SALON 3	**Arş. Gör. Büşra KÜTÜK KURT**	1	THE RELATIONSHIP BETWEEN JOB SATISFACTION AND INTENTION TO LEAVE AMONG NURSES: A META-ANALYSIS STUDY	Master's-Prepared Nurse Esma ASLAN SEKİ
		2	YAPAY ZEKA ÇAĞINDA HEMŞİRELİK METAPARADİGMALARINA YENİDEN BAKIŞ	Öğr. Görevlisi, ÖZNUR TUĞBA ÇELEBİ DURSUN Dr. Öğr. Üyesi, NURDAN YALÇIN ATAR
		3	YAPAY ZEKA TEKNOLOJİLERİNİN HEMŞİRELİK BAKIMINA ENTEGRASYONU	Dr. Öğr. Üyesi, NURDAN YALÇIN ATAR Öğr. Görevlisi, ÖZNUR TUĞBA ÇELEBİ DURSUN
		4	REVIEW OF NURSING STUDIES RELATED TO HEALTH LITERACY	Züleyha AYKUT Meryem YAVUZ Van GIERSBERGEN
		5	SCIENTIFIC MAPPING OF ARTIFICIAL INTELLIGENCE IN NURSING: BIBLIOMETRIC ANALYSIS	Züleyha AYKUT Meryem YAVUZ Van GIERSBERGEN
		6	THE EFFECT OF HEMSBALL ACTIVITY ON BALANCE, KINESOPHOBIC ATTITUDE, AND FRAILTY IN OLDER PEOPLE: A RANDOMIZED CONTROLLED TRIAL PROTOCOL	Assoc. Prof. Dr. Fatma Zehra GENÇ Assoc. Prof. Dr. Şükran İRİBALCI
		7	YENİDOĞAN BESLENMESİ VE BEYİN GELİŞİMİ İLİŞKİSİ	Arş. Gör. Büşra KÜTÜK KURT Prof. Dr. Aynur AYTEKİN ÖZDEMİR
		8	ÇOCUKLARDA NONFARMAKOLOJİK AĞRI YÖNETİMİ: AİLE MERKEZLİ BAKIM	Arş. Gör. Büşra KÜTÜK KURT Prof. Dr. Aynur AYTEKİN ÖZDEMİR

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HALL / SALON 4	**Dr. Öğretim Üyesi,Buket AKCAN ALTINKAYNAK**	1	EVALUATION OF THE EXPRESSION LEVELS OF GENES ASSOCIATED WITH SALT STRESS IN COTTON	PhD student, SHADER ALIZADE
		2	DEVELOPMENT OF TECHNOLOGY FOR OBTAINING DRUG NANOPARTICLES FROM MEDICINAL PLANTS USING GREEN SYNTHESIS METHOD	Kamala Gahramanova Ismat Ahmadov
		3	STUDYING THE INTERACTION OF GLYCYRRHIZIN AND P53 PROTEIN FAMILY USING MOLECULAR DOCKING	Leyla Elman GALANDARLI Dr. Gulnara Ahmad AKVERDIEVA
		4	MANAGEMENT OF OBESITY FROM A NUTRIGENOMIC PERSPECTIVE: GENETIC REGULATION WITH FUNCTIONAL COMPOUNDS	Dr. Öğretim Üyesi,Buket AKCAN ALTINKAYNAK Dr. Öğretim Üyesi, Yahya ALTINKAYNAK
		5	EFFECTS OF ZİNC SULFATE NANOPARTİCLES ON EPS STRUCTURE AND GENE EXPRESSİON İN STAPHYLOCOCCUS AUREUS BİOFİLMS	Research Assistant Ayşe ÜSTÜN BAŞKUT

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HALL / SALON 1	**Assis. Prof. Rustambek Sharipov Prof. Dr. Andini Kusuma**	1	REGULATION OF EPIGENETIC MODIFICATIONS IN METABOLIC SYNDROME AND DIABETES: MECHANISTIC INSIGHTS AND THERAPEUTIC POTENTIAL	Dewi Kartika Dr. Sofia Benali Dr. Olalekan Adeyemi
		2	ADVANCES IN ENZYME KINETICS AND ALLOSTERIC REGULATION FOR DRUG DEVELOPMENT IN INFECTIOUS DISEASES	Dr. Sari Widjaja Abdelhak Imene Aisha Nnamdi
		3	MOLECULAR MECHANISMS OF PROTEIN AGGREGATION AND ITS ROLE IN NEURODEGENERATIVE DISORDERS	Prof. Dr. Ratna Sari Assoc. Prof. Karim Bensalem Dr. Chinedu Umeh
		4	INTERACTION OF NON-CODING RNAS IN GENE EXPRESSION REGULATION AND CANCER BIOLOGY	Prof. Dr. Zukhra Yuldasheva Dr. Irfan Pratama
		5	STRUCTURAL BIOLOGY OF MEMBRANE TRANSPORTERS: IMPLICATIONS FOR DRUG RESISTANCE IN BACTERIA	Assis. Prof. Rustambek Sharipov Prof. Dr. Andini Kusuma
		6	METABOLOMIC PROFILING AND BIOMARKERS DISCOVERY IN CARDIOVASCULAR DISEASES USING MASS SPECTROMETRY	Dr. Javokhir Khodjaev Dian Anggraini Lila Haddad Dr. Folashade Adeyinka
		7	CRISPR-CAS9 APPLICATIONS IN GENOME EDITING: CURRENT CHALLENGES AND FUTURE DIRECTIONS IN THERAPEUTICS	Azizbek Tursunov Assoc. Prof. Kamal Souilah
		8	ROLE OF MITOCHONDRIAL DYSFUNCTION IN AGING AND AGE-RELATED DISEASES: A MOLECULAR BIOLOGY PERSPECTIVE	Assoc. Prof. Daler Hasanov Prof. Dr. Sinta Rahmawati

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HALL / SALON 2	**Prof. Dr. Laila Abdallah**	1	IMPACT OF TELEHEALTH IMPLEMENTATION ON MATERNAL AND NEWBORN HEALTH OUTCOMES IN RURAL MIDDLE EASTERN COMMUNITIES	Assoc. Prof. Dr. Layla Hassan Omar Al-Najjar Sara Al-Mutairi
		2	STRATEGIES TO ENHANCE MENTAL HEALTH SUPPORT FOR PREGNANT AND POSTPARTUM WOMEN IN MIDDLE EASTERN HEALTHCARE SETTINGS	Dr. Fatima Suleiman Khaled Al-Farsi
		3	IMPLEMENTING TELEHEALTH IN RURAL AND REMOTE COMMUNITIES FOR PRIMARY CARE	Prof. Dr. Alejandro Ruiz, Dr. Fatima Khan, Assis. Prof. Dr. Morten Larsen
		4	ASSESSMENT OF PAIN MANAGEMENT PRACTICES IN PEDIATRIC CARE UNITS ACROSS MIDDLE EASTERN COUNTRIES	Dr. Rania Khalil Youssef Mahmoud Dr. Leila Mansour
		5	THE ROLE OF NURSES IN CHRONIC DISEASE MANAGEMENT: A CROSS-COUNTRY STUDY IN THE MIDDLE EAST	Prof. Dr. Ahmed Farouk Dr. Salma Nabil Prof. Dr. Dalia Karam
		6	EVALUATION OF NURSING EDUCATION CURRICULA IN THE MIDDLE EAST: ALIGNMENT WITH GLOBAL HEALTHCARE NEEDS AND CULTURAL CONTEXTS	Prof. Dr. Samir Abbas
		7	PEDIATRIC NURSING AND FAMILY-CENTERED CARE: IMPROVING CHILDHOOD HEALTH OUTCOMES	Assoc. Prof. Dr. Helena Schmidt, Dr. Rafael Costa, lec. Priya Sharma
		8	EFFECTIVENESS OF COMMUNITY-BASED HEALTH PROMOTION PROGRAMS LED BY NURSES IN MIDDLE EASTERN URBAN AREAS	Dr. Sara Nasser Assoc. Prof. Dr. Fadi Hassan Prof. Dr. Laila Abdallah
		9	PUBLIC HEALTH NURSING AND EPIDEMIOLOGICAL STRATEGIES FOR INFECTIOUS DISEASE PREVENTION	Prof. Dr. Nnedi Okeke, Dr. Hye-Jin Park, Assis. Prof. Dr. Marco Rossi

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HALL / SALON 3	**Assoc. Prof. Dr. Maria Fernandez**	1	ELDERLY CARE STRATEGIES AND CHRONIC DISEASE MANAGEMENT IN NURSING PRACTICE	Assoc. Prof. Dr. Maria Fernandez, John O'Connor, lec. Aisha Al-Mansouri
		2	ADVANCES IN MIDWIFERY INTERVENTIONS TO REDUCE MATERNAL AND NEONATAL MORTALITY	Prof. Dr. Lillian Mbatha, Assis. Prof. Dr. Kenji Yamamoto, Sofia Petrescu
		3	MENTAL HEALTH NURSING: INTEGRATED APPROACHES FOR ANXIETY AND DEPRESSION TREATMENT	Dr. Samuel Thompson, Assoc. Prof. Dr. Amina Hassan, lec. Clara Nielsen
		4	CULTURAL COMPETENCY AND ITS EFFECT ON PATIENT SATISFACTION IN MIDWIFERY SERVICES IN THE MIDDLE EAST	Mona Al-Shammari Assoc. Prof. Dr. Jamal Ibrahim
		5	IMPACT OF WORKPLACE STRESS AND BURNOUT ON NURSING STAFF PERFORMANCE IN MIDDLE EASTERN HOSPITALS	Assoc. Prof. Dr. Nour El-Din Basma Saleh Dr. Saeed Al-Harith
		6	NUTRITIONAL INTERVENTIONS AND PATIENT EDUCATION IN HOSPITAL SETTINGS	Dr. Abdul Rahman, Prof. Dr. Camille Dubois, Assis. Prof. Dr. Tomasz Kowalski
		7	ADVANCED PRACTICES IN PAIN MANAGEMENT AND PALLIATIVE CARE	Assoc. Prof. Dr. Ingrid Johansen, Dr. Michael Brown, lec. Leila Haddad
		8	UTILIZATION OF E-LEARNING PLATFORMS TO IMPROVE CONTINUING PROFESSIONAL DEVELOPMENT AMONG MIDDLE EASTERN NURSES AND MIDWIVES	Dr. Hanan Al-Muhanna Dr. Wafa Saeed

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		2	INTEGRATING GREEN INFRASTRUCTURE INTO HIGH-DENSITY URBAN ENVIRONMENTS FOR ENHANCED ECOLOGICAL AND SOCIAL BENEFITS	Dr. Marco Rossi Assoc. Prof. Dr. Aisha Al-Khalid
		3	THE ROLE OF HISTORICAL PRESERVATION IN MODERN URBAN PLANNING: BALANCING CULTURAL HERITAGE WITH CONTEMPORARY DEVELOPMENT	Assis. Prof. Dr. Isabelle Dubois
		4	DESIGNING SMART CITIES: THE IMPACT OF TECHNOLOGY AND DATA-DRIVEN DECISION MAKING ON URBAN LIVING SPACES	Olivia Bennett Dr. Wei Zhang Assoc. Prof. Dr. Jamal Hassan Ricardo Silva
		5	LANDSCAPE ARCHITECTURE FOR URBAN WELL-BEING: PROMOTING PSYCHOLOGICAL AND PHYSICAL HEALTH THROUGH PUBLIC SPACES	Prof. Dr. Hanna Karlsson lec. Fatima Noor Assoc. Prof. Dr. Samuel Adeyemi Dr. Miguel Herrera
		6	ADAPTIVE REUSE OF INDUSTRIAL SPACES: TRANSFORMING FORMER FACTORIES INTO VIBRANT URBAN HUBS	Dr. Katarzyna Nowak Assoc. Prof. Dr. Mohammed Al-Farouq
		7	URBAN MOBILITY AND PUBLIC SPACE DESIGN: CREATING PEDESTRIAN-FRIENDLY CITIES AND ENHANCING TRANSPORT CONNECTIVITY	lec. Laura Gonzalez Assoc. Prof. Dr. Tarek Mahmoud Dr. Michael Thompson
		8	CLIMATE-RESPONSIVE ARCHITECTURE: INTEGRATING PASSIVE DESIGN STRATEGIES IN URBAN BUILDINGS TO REDUCE ENERGY CONSUMPTION	Assoc. Prof. Dr. Nadia Rahman Prof. Dr. Johannes Bauer

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HALL / SALON 5	**Dr. Layla Hassan Prof. Dr. Carlos Rivera**	1	THE IMPACT OF COMMUNITY-BASED INTERVENTIONS ON MENTAL HEALTH OUTCOMES IN URBAN POPULATIONS	. Helena Bergström Dr. Samuel Adeyemi Maria Gonzales
		2	EXPLORING THE ROLE OF SOCIAL WORKERS IN ADDRESSING DOMESTIC VIOLENCE IN MULTICULTURAL SETTINGS	Ahmed Al-Mutairi Dr. Fiona MacLeod Ricardo Fernandez
		3	SOCIAL WORK APPROACHES TO SUPPORTING REFUGEE CHILDREN IN EDUCATIONAL ENVIRONMENTS	Noor El-Sayed Tomislav Novak Dr. Lian Zhang
		4	THE EFFECTIVENESS OF ELDERLY CARE PROGRAMS IN PROMOTING SOCIAL INCLUSION AND WELL-BEING	Dr. Aisha Khan Prof. Dr. Jean-Pierre Leblanc
		5	ADDRESSING SUBSTANCE ABUSE THROUGH HOLISTIC SOCIAL WORK INTERVENTIONS	Dr. Layla Hassan Prof. Dr. Carlos Rivera
		6	THE ROLE OF SOCIAL WORK IN COMBATING YOUTH HOMELESSNESS IN MAJOR CITIES	Dr. Keiko Tanaka Daniel Mwangi
		7	INTEGRATING TECHNOLOGY IN SOCIAL WORK PRACTICES FOR REMOTE COMMUNITIES	Anika Johansson Dr. Mariana Costa
		8	SOCIAL WORK STRATEGIES FOR PROMOTING MENTAL HEALTH IN POST-CONFLICT SOCIETIES	Assoc. Prof. Dr. Abdul Rahman Dr. Sofia Marques Tom Havers
		9	THE INFLUENCE OF CULTURAL COMPETENCY TRAINING ON SOCIAL WORK EFFECTIVENESS	Dr. Chandra Iyer Prof. Dr. Michael O'Connor

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HALL / SALON 6	**Dr. Nabilah Rahman**	1	SUPPORTING SURVIVORS OF HUMAN TRAFFICKING THROUGH INTERDISCIPLINARY SOCIAL WORK	Fatima El-Tayeb Dr. Tobias Klein Ana Pereira
		2	ADDRESSING FOOD INSECURITY THROUGH SOCIAL WORK INTERVENTIONS IN URBAN AND RURAL AREAS	Johan Svensson Lucia Ricci
		3	THE IMPACT OF POLICY ADVOCACY ON IMPROVING CHILD WELFARE SERVICES	Emily Thompson Assoc. Prof. Dr. Jovan Milosevic
		4	PROMOTING GENDER EQUALITY THROUGH SOCIAL WORK INITIATIVES IN DEVELOPING COUNTRIES	Dr. Amira Khalid Assoc. Prof. Dr. Viktor Horvath
		5	EXPLORING TRAUMA-INFORMED CARE PRACTICES IN SOCIAL WORK SETTINGS	Rachel Adams Helga Lund
		6	THE ROLE OF SOCIAL WORK IN DISASTER RESPONSE AND EMERGENCY MANAGEMENT	Anna Kowalski Dr. Mateo Jimenez
		7	SUPPORTING MENTAL HEALTH OF IMMIGRANT FAMILIES THROUGH COMMUNITY SOCIAL WORK PROGRAMS	Dr. Nabilah Rahman
		8	EVALUATING THE EFFECTIVENESS OF SOCIAL WORK INTERVENTIONS IN ADDRESSING CHRONIC POVERTY	Assoc. Prof. Dr. Peter Johansson Sofia Ibrahim Miguel Santos
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HALL / SALON 7	**Assoc. Prof. Dr. Mehrbon Tursunov**	1	ECONOMIC IMPACTS OF DIGITAL TRANSFORMATION ON SMALL AND MEDIUM ENTERPRISES IN DEVELOPING ECONOMIES	Nazarbek Sharipov Dr. Yasmine Boukhalfa
		2	ANALYSIS OF AGRICULTURAL SUBSIDY EFFECTS ON RURAL POVERTY AND FOOD SECURITY IN AFRICAN COUNTRIES	Assoc. Prof. Dr. Idrissa Koulibaly Dr. Rustam Ashurov
		3	MODELING THE EFFECTS OF REMITTANCES ON ECONOMIC GROWTH AND INCOME DISTRIBUTION IN EMERGING MARKETS	Prof. Dr. Hasan Rakhmonov Assoc. Prof. Dr. Jamila Cheriet
		4	THE ROLE OF MICROFINANCE IN EMPOWERING WOMEN ENTREPRENEURS IN RURAL AFRICA: A CASE STUDY APPROACH	Fatima Hassan Prof. Dr. Dodik Santoso
		5	IMPACT OF INFRASTRUCTURE DEVELOPMENT ON FOREIGN DIRECT INVESTMENT INFLOWS IN CENTRAL ASIAN ECONOMIES	Dilshod Rahmonov Dr. Rahayu Handayani
		6	EXPLORING THE RELATIONSHIP BETWEEN EDUCATION INVESTMENT AND ECONOMIC PRODUCTIVITY IN AFRICAN URBAN CENTERS	Assoc. Prof. Dr. Mehrbon Tursunov
		7	EVALUATION OF MONETARY POLICY EFFECTIVENESS IN CONTROLLING INFLATION IN DEVELOPING ASIAN AND AFRICAN COUNTRIES	Rustamov Akbar Aminata Diop
		8	AN EMPIRICAL STUDY ON THE CAUSALITY BETWEEN ENERGY CONSUMPTION AND ECONOMIC GROWTH IN SUB-SAHARAN AFRICA	Dr. Tsegaye Kebede Hendra Surya Aicha Chafai
		9	ASSESSING THE IMPACT OF GLOBAL TRADE POLICIES ON LOCAL MANUFACTURING INDUSTRIES IN EMERGING ECONOMIES	Prof. Dr. Jamaliddin Sobirov Assoc. Prof. Dr. Dini Nurhasanah
		10	SOCIAL PROTECTION PROGRAMS AND THEIR EFFECTS ON INCOME INEQUALITY IN AFRICAN AND ASIAN DEVELOPING COUNTRIES	Dr. Halima Adeyemi Prof. Dr. Bambang Pranoto Dr. Fouad Benali

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HALL / SALON 8	**Prof. Dr. Nizom Umedov Assoc. Prof. Dr. Yayan Zuhri**	1	EXPLORING THE ROLE OF DIGITAL FINANCE IN PROMOTING INCLUSIVE GROWTH IN LOW-INCOME AFRICAN COUNTRIES	Assoc. Prof. Dr. Mukhlis Juraev Dr. Dian Puspitasari Boubaker Djerah Ahmed Boussouf
		2	INFLUENCE OF FOREIGN AID ON ECONOMIC DEVELOPMENT AND GOVERNANCE: COMPARATIVE STUDY OF SELECT AFRICAN AND CENTRAL ASIAN COUNTRIES	Assoc. Prof. Dr. Riana Kartika
		3	TRADE LIBERALIZATION AND ITS IMPACT ON POVERTY REDUCTION IN AFRICAN AGRICULTURAL SECTORS	Prof. Dr. Nizom Umedov Mirna Sari
		4	ANALYSIS OF THE INFORMAL ECONOMY'S CONTRIBUTION TO GDP AND EMPLOYMENT IN AFRICAN URBAN AREAS	Assis. Prof. Dr. Salem Benhamadi
		5	FISCAL DECENTRALIZATION AND ITS EFFECTS ON REGIONAL ECONOMIC DEVELOPMENT IN TAJIKISTAN AND INDONESIA	Dr. Tonia Abubakar Rustam Nizomov Dr. Ratna Puspita Lotfi Bouazizi Sami Saidi
		6	THE ECONOMIC CONSEQUENCES OF CLIMATE CHANGE ADAPTATION POLICIES IN NORTHERN AFRICA AND CENTRAL ASIA	Assoc. Prof. Dr. Yayan Zuhri
		7	THE ROLE OF ENTREPRENEURSHIP AND INNOVATION IN DRIVING ECONOMIC GROWTH IN AFRICAN AND INDONESIAN EMERGING MARKETS	Prof. Dr. Azizbek Rahmatov Dr. Dewi Anggraini Abdelkader Zerari
		8	MODELING THE IMPACT OF CORRUPTION ON ECONOMIC PERFORMANCE IN AFRICAN COUNTRIES AND TAJIKISTAN	Komiljon Usmonov Siti Aisyah Dr. Lamine Oumar

ICSAS 2nd INTERNATIONAL CONFERENCE ON GASTRONOMY and FOOD ENGINEERING September 19 - 21, 2025 İZMİR Meeting ID: 885 7151 8350 Passcode: 202224				
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HALL / SALON 1	**Prof.Dr.Özlem Tokuşoğlu**	1	MAD HONEY: BIOACTIVE COMPONENTS AND EFFECTS ON HUMAN HEALTH	Dr. Ekin VAROL Prof. Dr. Banu YÜCEL
		2	IMPORTANCE OF HONEY AND FRESH BEE POLLEN IN HEALTHY DIETS	Prof. Dr. Banu YÜCEL Dr. Ekin VAROL
		3	TÜRKİYE İLE İSPANYA'YA AİT GASTRONOMİK UNSURLARIN KARŞILAŞTIRILMASI	Doç. Dr. EMRE HASTAOĞLU
		4	TÜRKİYE'DEKİ SİMİTLER VE ÖZELLİKLERİ	Doç. Dr. EMRE HASTAOĞLU
		5	PORTAKAL VE LİMON YAPRAKLARININ BİYOAKTİF ÖZELLİKLERİ VE FENOLİK BİLEŞİKLERİNDEKİ DEĞİŞİMLER ÜZERİNE KURUTMANIN ETKİSİ	Yüksek Lisans Öğrenci, MELİHA ÇETİN Doç. Dr., NURHAN USLU Doktora Öğrenci, HAVVANUR YILMAZ Prof. Dr., MEHMET MUSA ÖZCAN
		6	THE ASSESMENTS ON FOOD CHEMISTRY ON VALUE-ADDED PLANT-BASED FOOD EFFERVESCENT SUPPLEMENTS	Prof.Dr.Özlem Tokuşoğlu
		7	MICROENCAPSULATED RASPBERRY LAMBERTIANIN C (LC) POWDER AND RASPBERRY LC BASED CHEWING GEL CANDY	Prof.Dr.Özlem Tokuşoğlu
		8	GASTRONOMİ TURİZMİ VE SÜRDÜRÜLEBİLİR DESTİNASYON PAZARLAMASI	DAMLA KARADAYI PROF. DR. NESRİN M. BAHÇELERLİ

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HALL / SALON 2	**Assist. Prof. Hilal OK ERGÜN**	1	METAL EŞYA, MAKİNE, ELEKTRİKLİ CİHAZLAR ve ULAŞIM ARAÇLARI SEKTÖRÜNDE FİNANSAL PERFORMANSININ ENTROPİ AĞIRLIKLANDIRMALI TOPSIS YÖNTEMİ İLE DEĞERLENDİRİLMESİ	Dr. Osman Nuri AKARSU
		2	THE RELATIONSHIP BETWEEN AUDIT COMMITTEE STRUCTURE AND FINANCIAL PERFORMANCE: EVIDENCE FROM THE BIST-100 INDEX	Dr. Öğr. Üyesi Yavuz KILINÇ
		3	ACCOUNTİNG OF MURABAHA FİNANCİNG: A COMPARATİVE STUDY OF TURKİSH ACCOUNTİNG STANDARDS AND INTEREST-FREE FİNANCE ACCOUNTİNG STANDARDS	Dr. Öğr. Üyesi Mehmet Murat GUTNU Yüksek Lisans Öğrencisi Abdullah ADANIR
		4	COUNTERFEITING'S RIPPLE EFFECT ON SUSTAINABILITY: INSIGHTS AND STRATEGIES FOR CHANGE	Dr. Ali Galip Ayvat Talat Yörük Levent Köseoğlu Assoc. Prof. Dr. Pınar Ayvat
		5	FINANCIAL DEVELOPMENT AND NATURAL RESOURCES MANAGEMENT: EVIDENCE FROM TÜRKİYE	Assist. Prof. Hilal OK ERGÜN
		6	THE IMPACT OF STRATEGIC MANAGEMENT PRACTICES ON EMPLOYEE PERFORMANCE IN CUSTOMS CONSULTANCY FIRMS	Master Student, FERİZA DEMİR GİTMİŞOĞLU Assist. Prof. Dr., FATİH MEHMET BULUT

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HALL / SALON 3	**Prof. Dr. Faruk ÖZDEMİR**	1	ISMĀ'IL RUSŪHĪ ANKARĀWĪ'S MAQĀṢID AL-ʿĀLIYYA FĪ SHARH AL-TĀIYYA AND ITS IMPACT ON OTTOMAN THOUGHT	Doç. Dr. Zeliha Öner
		2	HADİSLERİN TARİHSEL OLAYLAR İLE KARŞILAŞTIRILMASINDA KULLANILAN YÖNTEMLER	Doç. Dr. FUAT İSTEMİ
		3	KONJOKTÜRÜN HADİS TASNİFİNE YANSIMASI	Doç. Dr. FUAT İSTEMİ
		4	THE ROLE OF CIVIL INITIATIVES IN PREVENTING GLOBAL INJUSTICES: THE EXAMPLE OF THE HILF AL-FUDUL	Prof. Dr. Faruk ÖZDEMİR
		5	KIND WORD AS A UNIVERSAL HUMAN AND MORAL VALUE: A STUDY FROM THE PERSPECTIVE OF ITS POWER TO TRANSFORM HOSTILITY INTO FRIENDSHIP AND ESTABLISH PEACE	Prof. Dr. Faruk ÖZDEMİR
		6	MANTIK VE İLAHİYAT	Doç. Dr. Muhammet Nasih Ece

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HALL / SALON 4	**Dr. Öğr. Üyesi HAKAN AVAN**	1	TECHNOLOGY-SUPPORTED FAMİLY-CENTERED NURSİNG INTERVENTİONS İN CHİLDREN WİTH CHRONİC ILLNESSES: A COMPREHENSİVE NARRATİVE REVİEW FOCUSED ON TYPE 1 DİABETES	Dr. Öğr. Üyesi HAKAN AVAN
		2	SCREEN ADDİCTİON AND SLEEP QUALİTY İN CHİLDHOOD: A REVİEW OF NURSİNG INTERVENTİONS	Dr. Öğr. Üyesi HAKAN AVAN
		3	STIGMATISING ATTITUDES OF HEALTHCARE PROFESSIONALS TOWARDS INDIVIDUALS WITH AIDS AND INFLUENCING FACTORS: A DESCRIPTIVE-CROSS-SECTIONAL STUDY	Doç. Dr. Meryem Türkan IŞIK Doç. Dr. Rana CAN ÖZDEMİR Öğretim Görevlisi İbrahim Duman
		4	TAZELENME ÜNİVERSİTESİNE KATILAN YAŞLI BİREYLERİN BAŞARALI YAŞLANMA DÜZEYİNİN BELİRLENMESİ	Öğr. Gör. İbrahim DUMAN
		5	DIABETES CARE IN A CHANGING CLIMATE: FROM RISK TO ADAPTATION, FROM ADAPTATION TO RESILIENCE	Öğr. Gör., Merve MURAT MEHMED ALİ Prof. Dr., Selda ÇELİK
		6	THE DUAL FACE OF INSULIN: DIABULIMIA AND ITS MANAGEMENT IN ADOLESCENT DIABETES CARE	Öğr. Gör., Merve MURAT MEHMED ALİ Prof. Dr., Selda ÇELİK
		7	NURSES' INFORMATİCS COMPETENCİES: A COMPREHENSİVE LİTERATURE REVİEW	Prof. Dr. Meryem YAVUZ Van GİERSBERGEN Nurse Nebihat TEKİN
		8	INFORMATICS NURSING IN GRADUATE NURSING PROGRAMS IN TÜRKIYE	Prof. Dr. Meryem YAVUZ Van GİERSBERGEN Nurse Nebihat TEKİN

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HALL / SALON 1	**Prof. Dr. Aigerim Tursynova**	1	IMPROVING PATIENT OUTCOMES THROUGH EVIDENCE-BASED NURSING PRACTICES IN CRITICAL CARE SETTINGS	Assoc. Prof. Dr. Ayan Mukhtar, Assis. Prof. Dr. Serik Tulegenov,
		2	MATERNAL MENTAL HEALTH: ASSESSING THE IMPACT OF POSTPARTUM SUPPORT PROGRAMS	Prof. Dr. Zharaskan Amanov Ayesha Khan, Prof. Dr. Rizwan Iqbal, lec. Sana Farooq
		3	THE ROLE OF MIDWIVES IN REDUCING INFANT MORTALITY IN RURAL COMMUNITIES	Assoc. Prof. Dr. Aliya Bek, Assis. Prof. Dr. Nurlan Sadykov,
		4	ENHANCING NURSING EDUCATION THROUGH SIMULATION-BASED LEARNING AND VIRTUAL REALITY	Hamza Malik, Sadaf Javed, Dr. Mahnoor Iqbal
		5	INTEGRATING CULTURAL COMPETENCY TRAINING INTO HEALTHCARE PROFESSIONAL DEVELOPMENT	Prof. Dr. Shazia Abbas, Assis. Prof. Dr. Faizan Tariq, lec. Hina Rauf
		6	STRATEGIES FOR PREVENTING HOSPITAL-ACQUIRED INFECTIONS IN INTENSIVE CARE UNITS	Leila Hariri, Prof. Dr. Marwan Haddad, Nadine Karam
		7	ADVANCEMENTS IN NEONATAL CARE: EARLY INTERVENTIONS FOR HIGH-RISK INFANTS	Assoc. Prof. Dr. Samina Iqbal Prof. Dr. Imran Aslam, Noor Baloch
		8	ASSESSING THE EFFECTIVENESS OF TELEHEALTH SERVICES IN CHRONIC DISEASE MANAGEMENT	Assoc. Prof. Dr. Zarina Sadykova, Assis. Prof. Dr. Bauyrzhan Kairat, Prof. Dr. Aigerim Tursynova

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HALL / SALON 2	**Prof. Dr. Rahmatullah Hashemi,**	1	THE IMPACT OF NURSING LEADERSHIP ON EMPLOYEE SATISFACTION AND RETENTION	Assoc. Prof. Dr. Layla Hamidi, Prof. Dr. Farid Wardak,
		2	PROMOTING BREASTFEEDING PRACTICES THROUGH COMMUNITY-BASED INTERVENTIONS	Assoc. Prof. Dr. Amal Hassan, Zeinab Khatib, Rania Touma
		3	EXPLORING THE ROLE OF NURSES IN MANAGING EMERGING INFECTIOUS DISEASE OUTBREAKS	Dr. Nabil Zayani, Assis. Prof. Dr. Samir Belkacem,
		4	PAIN MANAGEMENT IN PALLIATIVE CARE: EVALUATING MULTIDISCIPLINARY APPROACHES	Assoc. Prof. Dr. Jasmin Kabuli, Prof. Dr. Haroon Rahman,
		5	IMPLEMENTING MENTAL HEALTH SCREENING IN PRIMARY HEALTHCARE SETTINGS	Assoc. Prof. Dr. Leila Bennis, Assis. Prof. Dr. Anis Cherif, Prof. Dr. Amira Boudjelal
		6	THE USE OF MOBILE HEALTH APPLICATIONS FOR PATIENT EDUCATION AND SELF-MANAGEMENT	Assoc. Prof. Dr. Maryam Farooqi, Prof. Dr. Tariq Azhar Sana Qureshi
		7	NURSE-LED INTERVENTIONS IN REDUCING HOSPITAL READMISSION RATES AMONG ELDERLY PATIENTS	Assoc. Prof. Dr. Fawzia Rahimi, Prof. Dr. Rahmatullah Hashemi, lec. Sahar Mohammadi
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HALL / SALON 3	**Assis. Prof. Dr. Bilal Benyamina, Prof. Dr. Karima Ouchene**	1	ADDRESSING NUTRITIONAL CHALLENGES IN NEONATAL INTENSIVE CARE UNITS	Assis. Prof. Dr. Bilal Benyamina, Prof. Dr. Karima Ouchene
		2	EVALUATING THE EFFECTIVENESS OF STRESS REDUCTION PROGRAMS FOR NURSES IN HIGH-INTENSITY ENVIRONMENTS	Prof. Dr. Rana Al-Khatib, Prof. Dr. Jad Saade, Nour El Hage
		3	IMPROVING PATIENT SAFETY THROUGH ELECTRONIC HEALTH RECORDS AND DIGITAL MONITORING	Assoc. Prof. Dr. Amirullah Safi, Dr. Hakim Wazir,
		4	DEVELOPING TRAINING MODULES FOR MIDWIVES ON COMPLICATIONS DURING CHILDBIRTH	Dr. Anisa Rahimi, Dr. Abdul Qadir Khan, Samina Mir
		5	IMPROVING PATIENT SAFETY AND QUALITY OF CARE THROUGH ADVANCED NURSING INTERVENTIONS IN ACUTE CARE SETTINGS	Assoc. Prof. Dr. Ayan Bektemir lec. Zhanar Tulegenova Prof. Dr. Yerlan Sadykov Assoc. Prof. Dr. Asma Riaz Hamza Qureshi
		6	MENTAL HEALTH PROMOTION AMONG ADOLESCENTS IN RURAL AREAS: CHALLENGES AND STRATEGIES FOR NURSES AND HEALTH PROFESSIONALS	Prof. Dr. Rustam Kairat Dilshad Akhmed
		7	MATERNAL AND NEWBORN HEALTH OUTCOMES: INTEGRATING EVIDENCE-BASED MIDWIFERY PRACTICES WITH COMMUNITY HEALTH INITIATIVES	Dr. Nadia Al-Khatib Dr. Faridah Mansoor
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ICSAS 1ST INTERNATIONAL CONFERENCE ON MARRIAGE AND FAMILY THERAPY SEPTEMBER 19 - 21, 2025 IZMIR Meeting ID: 885 7151 8350 Passcode: 202224				
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HALL / SALON 4	**Prof. Dr. Yacine Bensalem**	1	MARITAL COMMUNICATION AND CONFLICT RESOLUTION STRATEGIES IN LONG-TERM RELATIONSHIPS	Amina Belkacem Prof. Dr. Adewale Okoye Rizky Pratama
		2	IMPACT OF DIFFERENT PARENTING STYLES ON CHILD EMOTIONAL AND SOCIAL DEVELOPMENT	Dr. Fatimah Zainal Prof. Dr. Hassan Alimov Maria Santos
		3	COUPLE THERAPY APPROACHES FOR BLENDED FAMILIES AND STEP-PARENTING CHALLENGES	Nurul Hidayah Dr. Leila Karimova Juan dela Cruz
		4	THE ROLE OF CULTURAL VALUES AND BELIEFS IN FAMILY THERAPY INTERVENTIONS	Assoc. Prof. Dr. Anisa Rahman Timur Beketov Sofia Mammadova
		5	PREMARITAL COUNSELING AND STRATEGIES TO ENHANCE RELATIONSHIP SATISFACTION	Assis. Prof. Dr. Ahmed Benyamina Rizal Fahri Kristine Reyes
		6	FAMILY THERAPY TECHNIQUES FOR SUPPORTING SUBSTANCE ABUSE RECOVERY AND RELAPSE PREVENTION	Halima Olanrewaju Alif Prasetyo Elina Nazarova
		7	THE EFFECTS OF DIGITAL TECHNOLOGY AND SOCIAL MEDIA ON FAMILY DYNAMICS AND INTERACTIONS	Prof. Dr. Yacine Bensalem Farida Iskandarova Miguel Santos
		8	TRAUMA-INFORMED FAMILY THERAPY APPROACHES FOR HEALING EMOTIONAL AND PSYCHOLOGICAL WOUNDS	Dr. Aisha Mohammed Dwi Lestari Rashid Akhmedov
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ICSAS 1st INTERNATIONAL CONFERENCE ON HISTORY September 19 - 21, 2025 IZMIR Meeting ID: 885 7151 8350 Passcode: 202224				
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HALL / SALON 5	**Prof. Dr. Yasmin Al-Hussein**	1	ANCIENT CIVILIZATIONS AND THEIR ECONOMIC, SOCIAL, AND POLITICAL STRUCTURES	Assoc. Prof. Dr. Khalid Al-Mansouri Lec. Ahmed Rezaei
		2	OTTOMAN EMPIRE: SOCIAL HIERARCHIES, GOVERNANCE, AND CULTURAL TRANSFORMATIONS	Dr. Nour Al-Farouq Lec. Fatima Al-Hadid
		3	HISTORY OF ISLAMIC SCIENCE, TECHNOLOGY, AND KNOWLEDGE TRANSMISSION ACROSS REGIONS	Prof. Dr. Omar Al-Khalifa Assoc. Prof. Dr. Rania Saeed
		4	MODERN MIDDLE EAST POLITICAL HISTORY: NATION BUILDING, CONFLICTS, AND INTERNATIONAL RELATIONS	Dr. Layla Abou-Taleb Assoc. Prof. Dr. Tariq Al-Zahra Lec. Samira Al-Basri
		5	TRADE ROUTES, CULTURAL EXCHANGES, AND THE SPREAD OF IDEAS IN HISTORICAL CONTEXTS	Prof. Dr. Salma Shalabi Lec. Mohammad Al-Saadi
		6	HISTORY OF WOMEN IN THE ARAB WORLD: SOCIAL ROLES, RIGHTS, AND HISTORICAL NARRATIVES	Assoc. Prof. Dr. Dina Al-Mahdi Dr. Leila Kanaan Lebanon
		7	COLONIALISM AND POST-COLONIAL TRANSFORMATIONS IN MIDDLE EASTERN SOCIETIES	Prof. Dr. Hana Al-Mutairi Lec. Fadi Al-Karim
		8	HISTORICAL ARCHITECTURE AND URBAN DEVELOPMENT IN MIDDLE EASTERN CITIES	Prof. Dr. Yasmin Al-Hussein
		9	MILITARY STRATEGIES, CONFLICTS, AND WARFARE IN MIDDLE EASTERN HISTORY	Prof. Dr. Samah Al-Saleh Lec. Nabil Al-Ahmad

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HALL / SALON 6	**Prof. Dr. Adeel Khan,**	1	THE IMPACT OF NATURAL FERMENTATION TECHNIQUES ON THE NUTRITIONAL QUALITY OF TRADITIONAL DAIRY PRODUCTS	Yerlan Akhmetov, Assoc. Prof. Dr. Aigul Sadykova, Bauyrzhan Tleugabyl
		2	INNOVATIVE METHODS FOR PRESERVING SHELF-LIFE IN READY-TO-EAT MEALS USING BIOACTIVE PACKAGING	Sana Ullah, Prof. Dr. Adeel Khan, Imran Haider
		3	APPLICATION OF MICROWAVE AND ULTRASOUND TECHNOLOGIES IN FOOD PROCESSING FOR ENERGY EFFICIENCY	Alua Zhumagaliyeva, Daniyar Omarov, Nurlan Sagin
		4	DEVELOPMENT OF FUNCTIONAL FOODS ENRICHED WITH PLANT-BASED PROTEINS AND ANTIOXIDANTS	Amna Tariq, Saima Iqbal, Assis. Prof. Dr. Fahad Rashid
		5	UTILIZATION OF AGRICULTURAL WASTE IN BIOACTIVE FOOD INGREDIENT PRODUCTION	Hina Malik, Prof. Dr. Imran Abbas, Farah Zaman
		6	APPLICATION OF 3D FOOD PRINTING IN CULINARY INNOVATIONS AND PERSONALIZED NUTRITION	Aisha Rahimi, Lec. Dr. Farid Noori, Mohammad Shirzad
		7	EXPLORING THE ROLE OF NANOTECHNOLOGY IN FOOD SAFETY AND QUALITY MONITORING	Zahra Khan, Prof. Dr. Ali Raza, Asma Qureshi
		8	OPTIMIZATION OF ENZYMATIC PROCESSES FOR PLANT-BASED DAIRY ALTERNATIVES	Samira Najafi, Assoc. Prof. Dr. Nadia Karimi, Ramin Farhad

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HALL / SALON 1	**Asst. Prof. Dr. HALIL FEDAI**	1	THE RELATIONSHIP BETWEEN VENTRICULAR EXTRASYSTOLE FREQUENCY AND C-REACTİVE PROTEIN ALBUMIN RATIO	Asst. Prof. Dr. HALIL FEDAI
		2	THE EFFECT OF BODY IMAGE ON SEXUAL QUALİTY OF LİFE İN WOMEN WİTH BREAST CANCER WHO HAVE RECEİVED NEOADJUVANT CHEMOTHERAPY	Dr. Öğretim Üyesi, Mehmet Emin ŞANLI Öğr.Gör.Dr. Mahmut DİNÇ Öğr. Gör. Dr. Uğur ÖNER Dr. Öğretim Üyesi, Tülay YILDIRIM ÜŞENMEZ
		3	POSTPARTUM ANNE VE YENİDOĞAN GÜVENLİĞİ: PSİKOLOJİK RİSKLER VE ÇEVRİMİÇİ EĞİTİM MÜDAHALELERİNİN ROLÜ	Zekiye SİVRİDAĞ Prof.Dr. Şengül YAMAN SÖZBİR
		4	MENOPAUSE AND SEXUAL LIFE	Ebe Remziye KARADOĞAN KOSANOĞLU Doç. Dr. Ayça ŞOLT KIRCA Doç. Dr. Elif DAĞLI
		5	HEART DISEASES DURING PREGNANCY	Ebe Remziye KARADOĞAN KOSANOĞLU Doç. Dr. Ayça ŞOLT KIRCA Doç. Dr. Elif DAĞLI
		6	SEZARYENİN KLİNİK ETKİLERİ VE POSTOPERATİF YÖNETİM	Arş. Gör., SONGÜL KEKİL
		7	GEBELİKTE KÜLTÜREL İNANIŞLAR VE GELENEKSEL UYGULAMALAR	Arş. Gör., SONGÜL KEKİL
		8	THREE-MONTH FOLLOW-UP OF GREATER OCCIPITAL NERVE BLOCK EFFICACY IN CHRONIC MIGRAINE	Assis. Prof. Dr. Derya Yavuz Demiray

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HALL / SALON 2	**Assist. Prof. Dr. KEZBAN YILDIZ-DALGINLI**	1	MONOAMİN OKSİDAZ A'NIN GENETİK MANİPÜLASYONU: NÖROTRANSMİTTER METABOLİZMASINDAN DAVRANIŞA	Uzman Biyoteknolog/Projeler Koordinatörü, SELİN URAL Araştırmacı Öğrenci, SEDEN TOLUNAY
		2	KEDİLERDE HERPES VİRÜS ENFEKSİYONLARININ OKSİDATİF STRES PARAMETRELERİ ÜZERİNE GÜNCEL RAŞTIRMALARI	ESRA KÖSE Prof. Dr. SENA ÇENESİZ
		3	KÖPEKLERDE PARVOVİRÜS ENFEKSİYONLARININ GÜNCEL TEDAVİ YÖNTEMLERİ	ESRA KÖSE Prof. Dr. SENA ÇENESİZ
		4	CONTRIBUTION OF ARTVİN (TÜRKİYE) BROWN BEAR POPULATIONS TO THE MOLECULAR PHYLOGENY OF Ursus arctos	MSc Student Serap ÖZDEMİR Dr. Gökçe Ali KELEŞ Asst. Prof. Dr. Ahmet Yesari SELÇUK Asst. Prof. Dr. Perinçek Seçkinozan ŞEKER
		5	SHILAJIT ATTENUATES 5-FLUOROURACIL-INDUCED HEPATOTOXICITY THROUGH ANTIOXIDANT AND SIRTUIN PATHWAYS IN RATS	Assist. Prof. Dr. KEZBAN YILDIZ-DALGINLI Lecturer, MELEK OZTURKLER-DUNDAR Prof. Dr. ONUR ATAKISI
		6	INVESTIGATION OF THE CAUSES OF EUCALYPTUS CAMALDULENSIS SEEDLINGS MORTALITY IN TARSUS FOREST NURSERY	Öğr. Gör. Dr. Deniz ÇAKAR Doç. Dr. Ebru DERELLİ TÜFEKÇİ Fatih AYTAR Prof. Dr. Seçil AKILLI ŞİMŞEK

Hanife burada sunum yapdı

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HALL / SALON 3	**Assoc. Prof. Ceyda GÜRMAN**	1	A PSYCHOLOGICAL EXAMINATION OF THE RELATIONSHIP BETWEEN POSTMODERNISM AND RELIGIOUS FATIGUE	Dr. Öğr. Üyesi, Mehmet Emrullah DURAN
		2	WHAT IS JERUSALEM?	Assistant Professor KENAN KARAGÖZ
		3	İBÂZİYYE'DE HALKU'L-KUR'AN TARTIŞMALARI	Doç. Dr. Metin YILDIZ
		4	İBÂZİYYE'DE EF'ÂL-İ İBÂD	Doç. Dr. Metin YILDIZ
		5	THE GOVERNANCE PRINCIPLES AND EXEMPLARITY OF THE PROPHET	Dr. Öğr. Üyesi, Sadettin GÜRMAN
		6	The Ottoman Ulema's Defence of Ahl al-Sunnah Against the Muʿtazila: Treatises on al-Anʿām 6:158	Assoc. Prof. Ceyda GÜRMAN

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HALL / SALON 4	**Assoc. Prof. Dr., Şengül Başarı**	1	STUDENTS' VIEWS ON PLACE-BASED EDUCATION PRACTICES IN SCIENCE COURSE	Uzman Öğretmen, Cahide SERDAROĞLU Prof. Dr. Munise Handan GÜNEŞ
		2	TÜRKİYE YÜZYILI MAARİF MODELİNE PROGRAM GELİŞTİRME VE FELSEFİ YAKLAŞIM AÇISINDAN ELEŞTİREL BİR BAKIŞ	Dr. Okan DEDE
		3	SINIF ÖĞRETMENLERİNİN AKRAN ZORBALIĞINA YÖNELİK GÖRÜŞLERİNİN YAPAY ZEKA DESTEKLİ EĞİTİM YAKLAŞIMLARIYLA İNCELENMESİ	Assoc. Prof. Dr., Fatma Köprülü Assoc. Prof. Dr., Şengül Başarı
		4	EVALUATİNG THE PRİMARY SCHOOL CLASSROOM GUİDANCE PROGRAM THROUGH THE CIPP MODEL	Esma TAŞKIRAN ÇAPRAK Dr. Öğr. Üyesi Uğur EPÇAÇAN
		5	EVALUATING SOCIAL PARTICIPATION IN THE CONTEXT OF WOMEN THROUGH THEIR PARTICIPATION IN LIFELONG LEARNING	Dr. Deniz Yalçınkaya Hediye Acar
		6	ORTAOKUL ÖĞRENCİLERİNİN ETKİLİ İLETİŞİM BECERİLERİ İLE DİNLEME MOTİVASYONLARI ARASINDAKİ İLİŞKİNİN İNCELENMESİ	Yüksek Lisans Öğrencisi, Yener Emre SEVGİLİ Doç. Dr. Ata PESEN Dr. Öğr. Üyesi Burhan ÜZÜM
		7	BEDEN EĞİTİMİ VE SPOR ÖĞRETMENLİĞİ ÖĞRENCİLERİNDE ÖĞRETİM PROGRAMI OKURYAZARLIĞI	Dr. RUKİYE AYDOĞAN DENİZ ÖRSAN ÖRS
		8	ORTAOKUL, LİSE VE ÜNİVERSİTE ÖĞRENCİLERİNDE NOMOFOBİ DÜZEYLERİNİN İNCELENMESİ: CİNSİYETİN VE EĞİTİM DÜZEYİNİN ROLÜ	Dr. Öğr. Üyesi Halil ASLAN

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HALL / SALON 1	**Assoc. Prof. Dr. Maria Teresa Santos Prof. Dr. Angelo Villanueva**	1	THE ROLE OF INTERFAITH DIALOGUE IN PROMOTING RELIGIOUS TOLERANCE AND SOCIAL COHESION	Assoc. Prof. Dr. Yerzhan Bektas Prof. Dr. Aisulu Muratova Amanzhol Kairat
		2	RECONCILING TRADITIONAL BELIEFS WITH MODERN CHRISTIAN THEOLOGY IN CONTEMPORARY SOCIETIES	Prof. Dr. Haroon Qureshi Lec. Nadia Khattak
		3	ETHICS AND MORALITY IN ISLAMIC PHILOSOPHY: CHALLENGES AND MODERN INTERPRETATIONS	Dr. Kiran Jameel
		4	THEOLOGICAL PERSPECTIVES ON THE CONCEPT OF DIVINE JUSTICE IN ISLAM	Assoc. Prof. Dr. Faridullah Ahmadi Dr. Hameed Safi Zarina Wardak
		5	MYSTICISM AND SPIRITUAL EXPERIENCE IN SUFI TRADITIONS: HISTORICAL AND CONTEMPORARY VIEWS	Prof. Dr. Layth Al-Khatib Prof. Dr. Rana Daher Fadi Tahan Katrina Delos Reyes
		6	INTERPRETATIONS OF SACRED TEXTS IN MODERN PHILIPPINE CATHOLIC THEOLOGY	Assoc. Prof. Dr. Maria Teresa Santos Prof. Dr. Angelo Villanueva
		7	THE IMPACT OF RELIGIOUS EDUCATION ON ETHICAL DEVELOPMENT IN MUSLIM COMMUNITIES	Iqbal Khan Sana Riaz Bilal Ahmed Youssef Benali
		8	CHRISTIAN THEOLOGY AND ENVIRONMENTAL ETHICS: TOWARDS A SUSTAINABLE WORLDVIEW	Assoc. Prof. Dr. Ahmad Hariri Prof. Dr. Leila Mounir

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HALL / SALON 2	**Dr. Askar Zhaksylyk**	1	THEOLOGICAL REFLECTIONS ON SUFFERING AND THEODICY IN ISLAMIC AND CHRISTIAN TRADITIONS	Assoc. Prof. Dr. Abdul Rahman Azimi Prof. Dr. Laila Hamidi Farid Noorzai Timur Akhmetov
			THE INFLUENCE OF ISLAMIC PHILOSOPHY ON CONTEMPORARY ETHICAL THEORY	Dr. Askar Zhaksylyk Prof. Dr. Gulmira Nurgaliyeva
			THE ROLE OF WOMEN IN RELIGIOUS LEADERSHIP: PERSPECTIVES FROM ISLAMIC AND CHRISTIAN TRADITIONS	Dr. Shazia Malik Hina Tariq
			MODERN CHALLENGES IN THEOLOGICAL EDUCATION AND RELIGIOUS STUDIES	Dr. Ahmad Sultani Lec. Lailuma Rahimi
		2	THE CONCEPT OF MERCY AND FORGIVENESS IN DIFFERENT RELIGIOUS TRADITIONS	Prof. Dr. Sami Najjar
		3	HISTORICAL DEVELOPMENT OF CHRISTIAN MONASTICISM AND ITS SOCIO-CULTURAL IMPACT	Felicity Ramos Assoc. Prof. Dr. Maria Angela Flores Dr. Jonathan Cruz
		4	THE INTERSECTION OF POLITICS AND RELIGION: THEOLOGICAL PERSPECTIVES	Samina Rauf Assoc. Prof. Dr. Iqbal Hussain Dr. Anwar Siddiqui
		5	ISLAMIC ESCHATOLOGY AND THE CONCEPT OF THE AFTERLIFE: A COMPARATIVE STUDY	Assoc. Prof. Dr. Nurlan Seitov Prof. Dr. Aiman Tuleyev Dinara Zhumagaliyeva Rami Mansour Lina Saab
			RELIGION, SCIENCE, AND FAITH: NAVIGATING CONTEMPORARY THEOLOGICAL DEBATES	Assoc. Prof. Dr. Ahmad Al-Khalil
			THE ROLE OF RELIGION IN CONFLICT RESOLUTION AND PEACEBUILDING	Assoc. Prof. Dr. Khalid Benamara Samira Bouaziz Yasmine Cherif
		6	THE IMPACT OF GLOBALIZATION ON TRADITIONAL RELIGIOUS PRACTICES AND BELIEFS	Assoc. Prof. Dr. Maria Lourdes Reyes

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HALL / SALON 3	**Prof. Dr. Asif Javed**	1	THE IMPACT OF DIGITAL LEARNING PLATFORMS ON STUDENT ENGAGEMENT IN HIGHER EDUCATION	Yerlan Tulegenov Assoc. Dr. Danaer Beketova Prof. Dr. Aibek Zhumatayev
		2	EXPLORING INCLUSIVE EDUCATION POLICIES FOR CHILDREN WITH SPECIAL NEEDS	Assoc. Prof. Dr. Saadullah Kabirov lAisulu Altynbekova
		3	THE ROLE OF INTERCULTURAL COMPETENCE IN INTERNATIONAL STUDENT SUCCESS	Gulnara Tulegen Assoc. Prof. Dr. Almas Zharkynov Daniyar Serikbay Madina Sarsenova
		4	EFFECTIVE TEACHING STRATEGIES FOR MULTILINGUAL CLASSROOMS	Dr. Sanaullah Qureshi Dr. Rabia Tariq Hamid Raza
		5	THE USE OF AI-DRIVEN ASSESSMENTS TO IMPROVE LEARNING OUTCOMES	Prof. Dr. Asif Javed Samina Khalid
		6	CHALLENGES AND OPPORTUNITIES IN ONLINE STEM EDUCATION	Dr. Mirza Rahman Prof. Dr. Ayesha Khan
		7	THE INFLUENCE OF EDUCATIONAL GAMIFICATION ON STUDENT MOTIVATION	Fahad Riaz Dr. Lubna Ahmed
		8	IMPLEMENTING SUSTAINABLE EDUCATION PRACTICES IN PRIMARY SCHOOLS	Dr. Farid Gulzhan Dana Yerzhan

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HALL / SALON 4	**Assoc. Prof. Dr. Samir Nasser**	1	THE EFFECTIVENESS OF PROJECT-BASED LEARNING IN ENGINEERING PROGRAMS	Dr. Shahrukh Malik Dr. Saba Javed Imran Hussain
		2	LEADERSHIP DEVELOPMENT PROGRAMS FOR SCHOOL ADMINISTRATORS	Khalid Mehmood Sana Tariq
		3	INTEGRATING CULTURAL HERITAGE INTO MODERN CURRICULA	Dr. Farzana Rahimi Omar Karimi Waliullah Faiz
		4	THE ROLE OF PARENTAL INVOLVEMENT IN EARLY CHILDHOOD EDUCATION	Assoc. Prof. Dr. Jamal Alawi Nadia Khoury Rania Saab Tarek Husseini
		5	ADAPTIVE LEARNING SYSTEMS AND PERSONALIZED EDUCATION	Prof. Dr. Imad Zayed Assoc. Prof. Dr. Layla Maroun
		6	THE INFLUENCE OF SCHOOL ENVIRONMENT ON STUDENT WELL-BEING	Faridah Alawi Assoc. Prof. Dr. Hadi Hassan
		7	MOBILE LEARNING APPLICATIONS AND STUDENT PERFORMANCE	Prof. Dr. Khaled Mansour Yasmin Farah Assoc. Prof. Dr. Samir Nasser

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HALL / SALON 5	**Assis. Prof. Dr. Ahmed Belkacem**	1	THE IMPACT OF EDUCATIONAL POLICY REFORMS ON TEACHER MOTIVATION	Prof. Dr. Wali Khan Assoc. Prof. Dr. Nadia Rahim lec. Farzana Hamidi
		2	INNOVATIVE APPROACHES TO LANGUAGE ACQUISITION IN SECONDARY SCHOOLS	Assoc. Prof. Dr. Yasin Qureshi
		3	THE ROLE OF ART EDUCATION IN CHILDREN'S COGNITIVE DEVELOPMENT	Rania Khalil Dr. Sami Youssef Dr. Lina Hariri
		4	E-LEARNING AND DIGITAL DIVIDE IN RURAL COMMUNITIES	Assis. Prof. Dr. Ahmed Belkacem
		5	TEACHER TRAINING PROGRAMS FOR EMERGING EDUCATIONAL TECHNOLOGIES	Prof. Dr. Reynaldo Santos Lorna Cruz Assoc. Prof. Dr. Marco dela Rosa
		6	ASSESSING THE IMPACT OF SOCIAL EMOTIONAL LEARNING ON ACADEMIC PERFORMANCE	Fatima Zohra Assis. Prof. Dr. Ali Amrani
		7	PROMOTING ENVIRONMENTAL EDUCATION THROUGH SCHOOL CURRICULA	Kareem Haddad Maya Khoury Rachid Bensaid
		8	THE EFFECTS OF COOPERATIVE LEARNING ON STUDENT INTERACTION	Assis. Prof. Dr. Farid Noorzai Aisha Habibi
		9	EDUCATIONAL INNOVATIONS IN TEACHING MATHEMATICS THROUGH TECHNOLOGY	Dr. Alvaro Santiago Maria Lopez

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HALL / SALON 6	**Prof. Dr. Rania Kassem,**	1	THE EFFECT OF PROBIOTIC ENRICHMENT ON FERMENTED BEVERAGE MICROBIOLOGY	Layla Haddad, Dr. Karim Saab, Nour El-Hayek
		2	ADVANCEMENTS IN NON-THERMAL FOOD PRESERVATION TECHNOLOGIES	Assoc. Prof. Dr. Yasmine Bensalem, Omar Aloui, Hocine Charef
		3	SUSTAINABLE SOURCING AND PROCESSING OF SEAFOOD PRODUCTS FOR GLOBAL MARKETS	Mary Grace Santos, Bianca Cruz Assoc. Prof. Dr. Miguel Reyes,
		4	INFLUENCE OF PLANT EXTRACTS ON THE PHYSICOCHEMICAL PROPERTIES OF BAKERY PRODUCTS	Prof. Dr. Rania Kassem,
		5	APPLICATION OF BIOINFORMATICS IN FOOD ENGINEERING FOR FLAVOR PREDICTION	Dr. Kamran Shafiei,
		6	DEVELOPMENT OF LOW-CALORIE SWEETENERS WITH ENHANCED FUNCTIONALITY	Abdelkader Benyahia,
		7	EFFECTS OF HIGH-PRESSURE PROCESSING ON VITAMIN AND MINERAL RETENTION IN FRUITS	Prof. Dr. Naveed Shah, Asif Iqbal
		8	INNOVATIVE FERMENTATION STRATEGIES FOR THE PRODUCTION OF VEGAN CHEESE	Sohail Ahmed, Fatima Noor, Assoc. Prof. Dr. Danish Malik Elias Fares
		9	INTEGRATION OF SENSORY SCIENCE AND FOOD ENGINEERING IN CULINARY PRODUCT DESIGN	Jamal Al-Khalil, Dr. Layla Karam,
		10	APPLICATION OF BIOPOLYMERS IN EDIBLE COATING TO IMPROVE FRESH PRODUCE SHELF-LIFE	Ayesha Khan, Assoc. Prof. Dr. Iqra Malik,

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HALL / SALON 7	**Assis. Prof. Dr. Usman Ali**	1	ADVANCED NANOTECHNOLOGY APPLICATIONS IN FOOD PRESERVATION AND SAFETY	Zhandos Akhmetov
		2	SUSTAINABLE FOOD PROCESSING METHODS FOR REDUCING ENVIRONMENTAL IMPACT IN GASTRONOMY	Assoc. Prof. Dr. Rakhim Zhumabayev Dinara Kassenova Prof. Dr. Yerlan Abilkhan
		3	INNOVATIVE FERMENTATION TECHNIQUES FOR DEVELOPING FUNCTIONAL FOODS AND BEVERAGES	Aigerim Bektemir Dr. Saltanat Orazbayeva
		4	DEVELOPMENT OF PLANT-BASED PROTEINS AND THEIR INDUSTRIAL APPLICATIONS IN FOOD ENGINEERING	Sana Riaz Assoc. Prof. Dr. Muhammad Ahsan
		5	APPLICATION OF MICROENCAPSULATION TECHNOLOGY TO ENHANCE FLAVOR AND NUTRITIONAL VALUE	Bilal Khan Assis. Prof. Dr. Hira Javed Assoc. Prof. Dr. Fatima Zahra
		6	ADVANCES IN SMART KITCHEN TECHNOLOGIES FOR GASTRONOMIC INNOVATION AND FOOD SAFETY	Assis. Prof. Dr. Usman Ali
		7	EVALUATION OF TRADITIONAL AND MODERN FOOD PRESERVATION METHODS IN EXTREME CLIMATES	Dr. Rahimullah Wardak Fariba Nazari Ahmad Shah
		8	APPLICATION OF NATURAL FOOD COLORANTS AND FLAVOR ENHANCERS IN MODERN CUISINE	Layla Karam Prof. Dr. Omar Benyamina Assoc. Prof. Dr. Nabil Salim lYoussef Bensalem

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HALL / SALON 1	**Assoc. Prof. Dr. Cagla YIGITBAS**	1	EVALUATING WEBINAR-BASED NURSING EDUCATION DURING THE COVID- 19 PANDEMIC: A RETROSPECTIVE ANALYSIS	MSc, SALİHA KOÇ ASLAN
		2	IMPLEMENTING THE BALANCED SCORECARD IN NURSING SERVICES: DEVELOPMENT OF A NURSE PERFORMANCE SCORECARD FOR STRATEGIC PERFORMANCE MANAGEMENT	MSc, SALİHA KOÇ ASLAN
		3	THE MEDIATING ROLE OF PATIENT TRUST IN THE EFFECT OF PERCEIVED HEALTHCARE SERVICE QUALITY ON OUTPATIENTS' BEHAVIORAL INTENTIONS	Doç. Dr. Fuat YALMAN Prof. Dr., Yalçın KARAGÖZ
		4	THE EFFECT OF SOCIAL SUPPORT ON ORGANIZATIONAL SUPPORT AND ORGANIZATIONAL TRUST: AN APPLICATION ON HEALTHCARE WORKERS	Prof. Dr., Yalçın KARAGÖZ Doç. Dr. Fuat YALMAN
		5	THE GLOBAL OUTLOOK OF TECHNOLOGY-FACILITATED VIOLENCE AGAINST GIRLS: A BIBLIOMETRIC ANALYSIS	Assoc. Prof. Dr. Çağla YİĞİTBAŞ
		6	NUCHAL TRANSLUCENCY MEASUREMENT AND MATERNAL STRESS: A BIBLIOMETRIC ANALYSIS OF GLOBAL RESEARCH TRENDS	Assoc. Prof. Dr. Cagla YIGITBAS

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		2	HPV VE BAĞIŞIKLAMA	Ebe Meltem YAVUZ Doç. Dr. Ayça ŞOLT KIRCA Doç. Dr. Elif DAĞLI
		3	UYKU BOZUKLUKLARINDA TAMAMLAYICI VE ALTERNATİF TIP: PALYATİF BAKIM HASTALARINA YÖNELİK YAKLAŞIMLAR	Dr. Öğr. Üyesi, NURDAN YALÇIN ATAR PhD, AKBAŞ
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		3	YEREL VE ULUSAL DÜZEYDE SİYASAL LİDERLİK TEMSİLLERİ: KATILIMCI SÖYLEMLER ÜZERİNDEN BİR LİDERLİK TİPOLOJİSİ ANALİZİ	Dr. Öğr. Üyesi, MUSTAFA DEMİRCİ
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		9	FROM ELECTRONIC STATE TO SMART STATE: ANALYSIS OF DIGITAL TRANSFORMATION IN PUBLIC ADMINISTRATION	Dr. Öğr. Üyesi Ömer ÇAMUR

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BIBLIOMETRIC TRENDS IN AI-BASED FORENSIC DNA MIXTURE INTERPRETATION

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Abstract

This study aims to systematically analyze the scientific literature on artificial intelligence (AI)-based forensic DNA mixture interpretation using bibliometric methods. A total of 193 academic publications indexed in the Web of Science database between 1991 and 2025 were examined. The analysis covered publication trends, author and institutional collaborations, country-based research networks, keyword clusters, and citation linkages. The findings revealed a marked increase in publication output after 2015, peaking in 2022. Co-authorship and co-citation analyses indicated that the field is shaped around core research groups primarily based in the United States, New Zealand, Australia, and Europe. Keyword mapping demonstrated that the literature converges on three major axes: (i) statistical and theoretical modeling (likelihood ratio, Bayesian inference), (ii) software development and validation processes (STRmix™, EuroForMix, TrueAllele), and (iii) applications and legal dimensions (evidence admissibility, inter-laboratory comparisons). Furthermore, the integration of next-generation sequencing (NGS) and microhaplotype technologies has emerged as a prominent theme for future research directions. In conclusion, AI-assisted probabilistic genotyping systems are playing an increasingly critical role in forensic DNA mixture analysis. However, parameter uncertainties, transparency, and the necessity of compliance with international standards remain key priorities on the research agenda.

Keywords: Artificial intelligence, forensic DNA, mixture samples, probabilistic genotyping, likelihood ratio, bibliometric analysis

1. Introduction

Forensic DNA analysis holds a central position within forensic sciences as it enables the identification of individuals' biological identity and provides scientifically grounded evidence to judicial proceedings (Bukyya et al., 2021). Contributing directly to the functioning of the criminal justice system, this method plays a crucial role not only in determining the responsibility of individuals linked to criminal acts but also in exonerating those wrongfully

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accused, thereby reinforcing the reliability of the judicial system (Laporte, 2018). Moreover, in cases of mass disasters and missing persons, the comparison of genetic findings with reference samples allows for the identification of remains, thereby supporting the delivery of justice at both individual and societal levels (Kumar, 2022). Within this context, DNA analysis technology, pioneered by Jeffreys and colleagues, has progressively become an indispensable tool for biological identification in various legal contexts, including criminal investigations, paternity testing, and immigration cases (Butler, 2015). Today, the analysis of high-quality samples under controlled laboratory conditions enables the generation of reliable genetic profiles, which, when compared with material collected from crime scenes, substantially reduce uncertainties in identity determination (Alketbi, 2024; Arjamand et al., 2024).

In forensic genetic applications, biological samples collected from the field often contain limited amounts of DNA, include material originating from multiple individuals, and may be subject to molecular degradation, all of which render the analytical process technically challenging (Bieber et al., 2016). The most prominent example of this complexity is mixture samples, in which genetic material from different contributors is intermingled in varying proportions. Such samples, frequently encountered in biological traces collected from crime scenes, represent some of the most difficult data types to resolve in forensic DNA analysis and pose significant methodological challenges during interpretation (Tao et al., 2018). Within the forensic sciences literature, these complex samples are widely reported in contexts such as sexual assault cases and mass disaster scenarios. The presence of multiple material types, the difficulty in determining the exact number of contributors, and the variability in each component's proportion within the sample render the analysis substantially more complex compared to single-source samples (Butler et al., 2024; Costa et al., 2025; Tao et al., 2018).Particularly in cases where biological traces from both the victim and the suspect are present within the same sample, a critical interpretative process is required for investigative purposes (Butler et al., 2024). In such scenarios, technical issues such as low-template DNA, allele drop-out, allele drop-in, and stutter artifacts further complicate interpretation, exposing the limitations of conventional approaches in both analytical and statistical evaluation processes (Bieber et al., 2016; Butler et al., 2024). This necessitates not only more advanced and highly sensitive analytical protocols but also the refinement of interpretative algorithms. Consequently, forensic genetic experts are increasingly required to rely on statistical modeling and probabilistic frameworks in their decision-making processes.

The reliable interpretation of complex DNA mixtures has therefore mandated the development of software-based probabilistic modeling systems that go beyond traditional methodologies. In this regard, the use of software for the evaluation of DNA profile data has been systematically adopted in forensic biology since the late 1990s, with subsequent applications being classified under the heading of "probabilistic genotyping" (PG) systems (Gill et al., 2021). PG systems analyze DNA profile data within a probabilistic framework and employ likelihood ratio (LR) calculations to express the weight of the evidence. The LR represents the relative probability of the observed DNA profile under two competing propositions and is defined as the ratio of the weighted sums of genotype sets. Within this conceptual framework, PG systems have become indispensable tools in contemporary forensic genetics, particularly for the interpretation of

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complex DNA mixtures. Widely used software such as STRmix™, EuroForMix, and DNAStatistX enable the evaluation of genetic data through algorithms grounded in distinct statistical foundations (Buckleton et al., 2024). The statistical differences among these software packages were comprehensively discussed in the review by Gill and colleagues (2021), which highlighted that STRmix™ adopts a Bayesian approach, whereas EuroForMix and DNAStatistX rely on a maximum likelihood estimation (MLE)-based γ (gamma) model (Gill et al., 2021).

Although these systems are widely employed in forensic genetic analysis, the definition and implementation of model parameters (such as mixture proportions, allele peak height variances, and drop-in/drop-out probabilities) differ across software platforms, potentially leading to substantial discrepancies in LR values. This issue was examined in detail by Buckleton and colleagues (2024), who compared LR outputs between EuroForMix and STRmix™. Their study demonstrated that these deviations primarily stem from differences in how MLE-based parameter estimates are applied under competing hypotheses (Buckleton et al., 2024). These findings highlight the need to carefully evaluate not only the algorithmic structures but also the parameter definitions and statistical assumptions when conducting comparative analyses of probabilistic genotyping systems.

In this context, AI and machine learning (ML) techniques have been increasingly integrated into forensic DNA analysis technologies, aiming to overcome the parametric limitations of conventional PG systems and reduce uncertainties in interpretation processes (Sessa et al., 2024). Deep learning models offer innovative solutions for tasks such as automated allele calling and distinguishing artifacts like stutter and drop-out, while explainable AI approaches address the demand for transparency in the context of forensic validity and courtroom admissibility (de Wit et al., 2025). These advancements not only enhance technical accuracy but also introduce new possibilities for interpretation. However, this transformation also raises structural and methodological debates. Central to these discussions is the high-resolution analytical capacity that AI-based approaches bring to the evaluation of complex mixtures. Although the growing number of applied studies in recent years has demonstrated the potential of AI-assisted systems, critical research gaps remain. These include the comparative assessment of software, elucidation of the sources of parameter discrepancies, standardization of validation protocols, and clarification of legal and ethical frameworks.

The aim of this study is to systematically examine the use of AI and probabilistic genotyping systems in forensic DNA mixture interpretation through bibliometric methods, thereby mapping changes in publication output, identifying leading authors and institutions, exploring international collaboration networks, delineating key conceptual clusters, and highlighting future research gaps. In doing so, the study seeks to provide a comprehensive analysis of both the technical and applied dimensions, offering an integrated perspective on the scientific trajectory of the field and its potential research directions.

2. Materials and Methods

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In this study, a bibliometric analysis method was employed to reveal the scientific production trends related to AI-based forensic DNA mixture interpretation. Bibliometrics is a methodology that enables the systematic identification of the developmental trajectory of the literature, areas of influence, collaboration networks, and research gaps through the quantitative examination of scientific publications (Aria & Cuccurullo, 2017). Since the present study relied solely on publication data for mapping and did not involve research with human or animal subjects, no ethical approval was required.

2.1. Data Sources and Search Strategy

The data used in this study were retrieved from the Web of Science Core Collection (WoS) database in September 2025. The search strategy was structured to comprehensively capture the scope of the topic. The primary keyword combination employed was as follows:

TS=("DNA mixture" OR "forensic mixture interpretation" OR "mixed DNA sample*") AND TS=("probabilistic genotyping" OR "artificial intelligence" OR "machine learning" OR "deep learning")*

The scope of the study was limited to articles, conference papers, and review publications published between 1991 and 2025, yielding a total of 193 records. This time frame represents the period during which the transition from the initial applications of probabilistic genotyping software (e.g., STRmix™, EuroForMix) to AI-based algorithms can be observed (Buckleton et al., 2024; Gill et al., 2021).

2.2. Data Processing and Analytical Tools

The retrieved data were exported in a “tab-limited” format and subsequently analyzed using VOSviewer (v.1.6.20) and Bibliometrix (R package). Through these tools, various dimensions of the literature were visualized and systematically assessed, including annual publication trends, the most productive authors, institutions, and countries, keyword co-occurrence networks, international collaboration networks, and the most frequently cited publications.

3. Results

3.1 Distribution of Publications by Year

An examination of the 193 publications identified through the bibliometric search reveals that the literature on AI-based forensic DNA mixture interpretation first emerged in the early 1990s (initial record: 1991) but gained significant momentum only after 2010. A particularly notable increase in publication output was observed from 2018 onwards (Figure 1). During the 1991–2010 period, the annual number of publications remained very low (1–5 per year), representing a preparatory phase in which probabilistic genotyping approaches and the earliest software applications (e.g., early STR modeling) were being developed. Between 2011 and 2017, a gradual rise in publication output was observed, with a minor peak in 2015 (10 publications),

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corresponding to the growing visibility of methodological frameworks underpinning software such as STRmix™ and EuroForMix in the international literature. The period from 2018 to 2021 marks a distinct phase of acceleration, with 20 publications recorded in 2019 and 23 in 2021, reflecting the integration of PG systems into routine laboratory practice. Although a relative decline was noted in 2020, likely attributable to the pandemic, the overall production trend continued to rise. The year 2022 stands out as the peak, with 30 publications, corresponding to the increased adoption of AI-based algorithms (e.g., deep learning, variational inference) in DNA mixture interpretation. While a slight decrease was recorded between 2023 and 2025, the sustained annual output of 11–17 publications indicates that the field remains an active area of research. The decline observed in 2025 is most likely due to incomplete database updates and the fact that the publication cycle for the year had not yet closed.

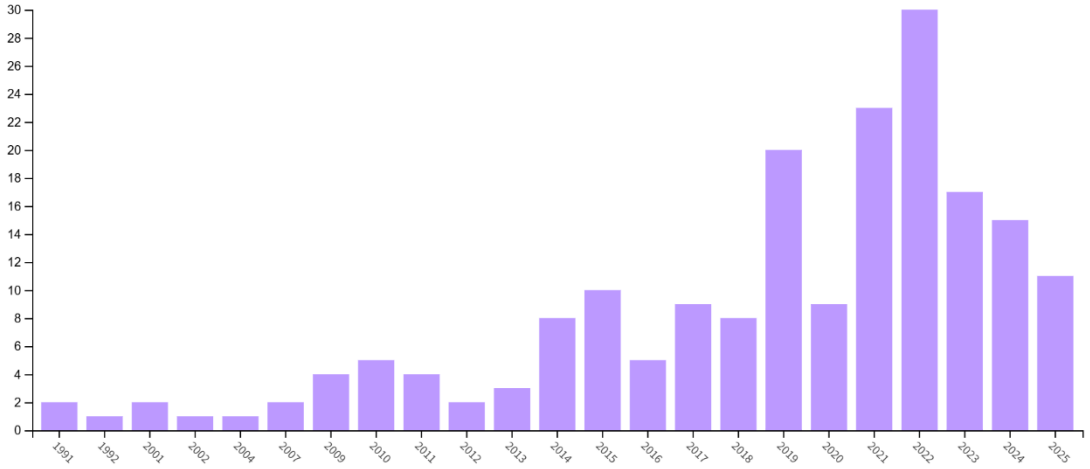

Figure 1. Annual Distribution of Publications

The publication trends observed in Figure 1 clearly demonstrate that technological evolution has been directly reflected in scientific output. The transition from probabilistic genotyping systems (e.g., STRmix™, EuroForMix, TrueAllele) to AI-assisted methodologies (e.g., artificial neural networks, variational inference, explainable AI approaches) closely parallels the sharp increases in publication numbers within the literature. The production peak observed in 2022 highlights the growing global academic interest driven by methodological innovations and indicates that the field has secured a central position within the contemporary research agenda.

3.2. Co-authorship of Authors Analysis

To examine collaboration patterns among researchers, a network map was constructed under the criteria of at least one publication and one citation (Figure 2). The analysis revealed that the cluster represented by Michael D. Coble and his collaborators (John M. Butler, Bruce Budowle, Frederick Bieber) stands out for their foundational contributions to forensic DNA profiling, STR validation, and early studies on mixture interpretation. Another cluster, composed of John Buckleton, James Curran, Tim Kalafut, Safia Boodoosingh, and Todd Billie, is primarily focused on STRmix™ software and statistical modeling approaches. The group including Jo-Anne Bright, Hannah Kelly, and Maarten Kruijver, based in New Zealand and Australia, has

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made significant contributions to the development of PG software. Meanwhile, the cluster represented by Duncan Taylor, Denise Ward, Lianne Henry, and Damien Abarno is characterized by its focus on Australia-based laboratory applications, validation studies, and PG software evaluations. When cross-cluster connections are examined, the Buckleton–Bright–Kelly axis emerges as a central hub, interacting intensively with both the red and green clusters. This highlights the role of Buckleton and colleagues as "bridge authors" in the methodological advancement of the field. Overall, the network structure indicates strong collaborative ties between U.S.-based researchers (Coble, Butler, Budowle) and Australia–New Zealand-based researchers (Buckleton, Bright, Taylor). This pattern underscores the fact that software development and methodology validation processes have been advanced within a framework of international scientific collaboration.

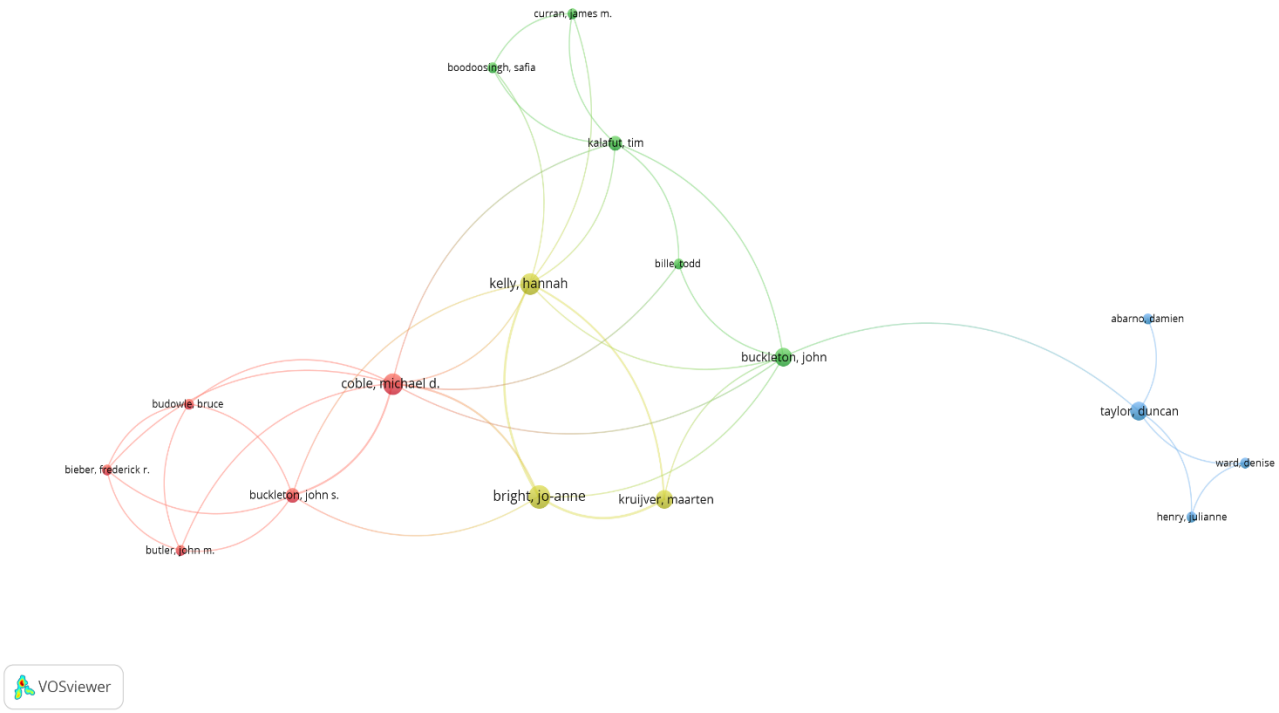

Figure 2. Co-authorship Network of Authors

The co-authorship network depicted in Figure 2 illustrates that the field of AI- and probabilistic genotyping-based DNA mixture interpretation is organized around a few core research groups. The U.S.-based cluster (Coble, Butler, Budowle) has been leading in establishing methodological foundations and defining standards. The New Zealand–Australia-based group (Buckleton, Bright, Taylor) focuses primarily on the development of STRmix™ software, statistical modeling, and validation processes. Bridging authors such as Kelly, Kruijver, and Curran facilitate knowledge transfer between clusters, contributing to the integrated structure of the network. This configuration indicates a highly collaborative field that is guided by several global hubs.

3.3. Citation of Authors

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To examine citation relationships among authors, a network map was generated using the criterion of at least one publication and one citation (Figure 3). Among the 135 authors included, the Bright–Taylor–Kruijver axis represents the core group that has received the highest number of citations in recent years and has shaped contemporary scientific discourse. The Buckleton–Barash axis, which made substantial early methodological contributions, has become secondary in the evolutionary structure of the network, now primarily connected to newer studies led by Bright and Taylor. Contributions from Europe-based researchers (Benschop, Prieto) highlight the field's global interaction capacity and regional diversity. Overall, the post-2016 period is characterized by the citation dominance of New Zealand–Australia-based researchers, reflecting the strong methodological impact of STRmix™ and probabilistic genotyping systems in the international literature and their influential role in guiding the direction of the field.

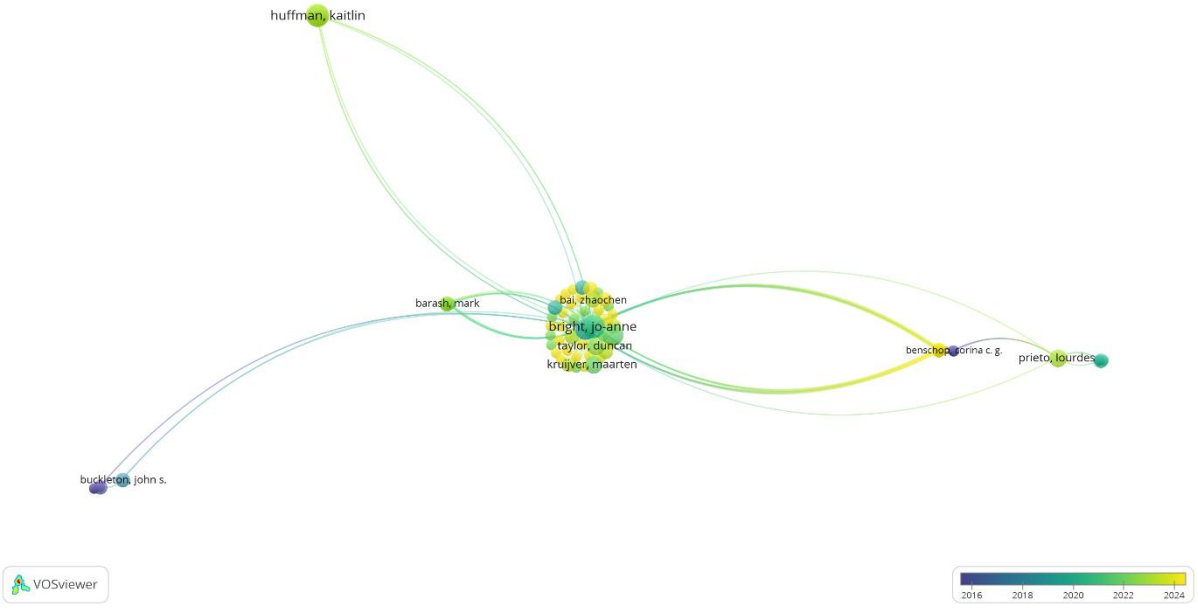

Figure 3. Citation Network of Authors

3.4. Citation of Countries Analysis

The analysis of citations by country, conducted using the criterion of at least one publication and one citation, reveals that among the 18 countries represented, the United States, New Zealand, and Australia serve as central hubs with the most extensive connections, occupying the core of the network. These countries play a decisive role in shaping the literature through their contributions to both software development (e.g., STRmix™, TrueAllele) and validation and application studies. Germany, Switzerland, and the Netherlands constitute a strong European core group, characterized by dense collaborative ties. The People's Republic of China has emerged prominently, particularly after 2021, contributing an increasing number of publications and citations, as visually highlighted in the yellow-toned clusters. Countries such as Japan, the United Arab Emirates, Finland, Ireland, and Canada, although producing fewer publications, provide strategically significant contributions. Within Europe, strong collaboration patterns are observed among Italy, Norway, the Netherlands, Denmark, and Switzerland, with most of these collaborations facilitated through European consortia. Overall,

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the trend indicates that while the U.S.–Australia–New Zealand axis was dominant in 2019–2020, European countries and China have become increasingly visible in the literature post-2021.

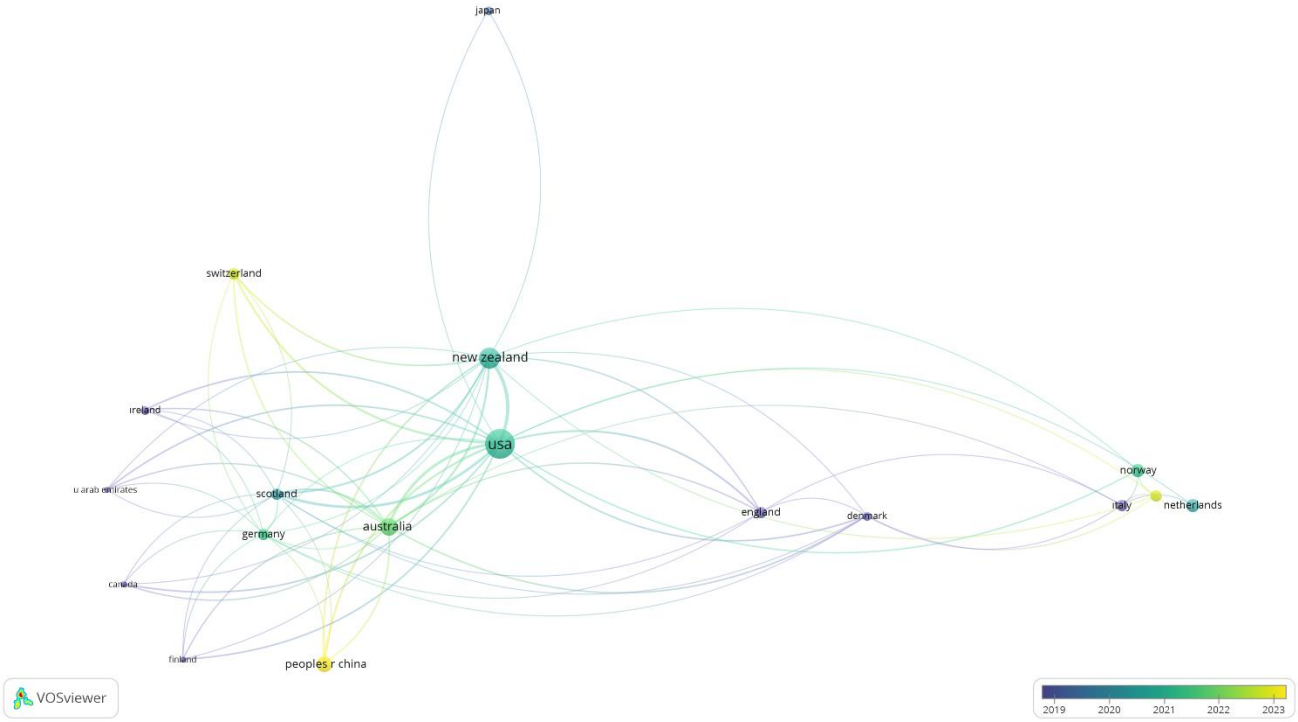

Figure 4. Citation Network of Countries

This network map illustrates that the field of AI- and probabilistic genotyping-based forensic DNA mixture interpretation has developed through globally collaborative processes. The United States–Australia–New Zealand triad occupies a central position in methodological innovations and software development. European countries contribute primarily in validation, standardization, and legal aspects. China has emerged as a rising actor in the field, reflecting its increasing contributions in recent years. Overall, this collaboration map highlights both the geographic distribution of scientific influence and the field's multi-centric structure.

3.5. Citation of Organizations Analysis

Scientific interactions among organizations were analyzed based on the criterion of at least one publication and one citation (Figure 5). The analysis, which included 69 institutions, identified leading organizations in terms of methodological innovations, software development, and validation studies. In this context, the University of Auckland (New Zealand), under the leadership of John Buckleton, Jo-Anne Bright, and their team, has become a global reference point in probabilistic genotyping-based interpretation with the development of STRmix™ software. The University of North Texas (USA), led by Michael D. Coble, provided significant methodological contributions, particularly during the 2016–2018 period, and occupies a central position in the network. The University of Oslo (Norway) has made important contributions to the validation of European probabilistic genotyping software and the enhancement of methodological diversity. The Netherlands Forensic Institute (NFI) has become a central node

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in the network post-2020, through European-based validation studies and STR applications. The University of Roma Tre (Italy) stands out for its work on the legal dimensions and methodological diversity of forensic DNA interpretation. The National Center for Forensic Science (USA) emerges as a key node due to its international collaborations focused on validation and training.

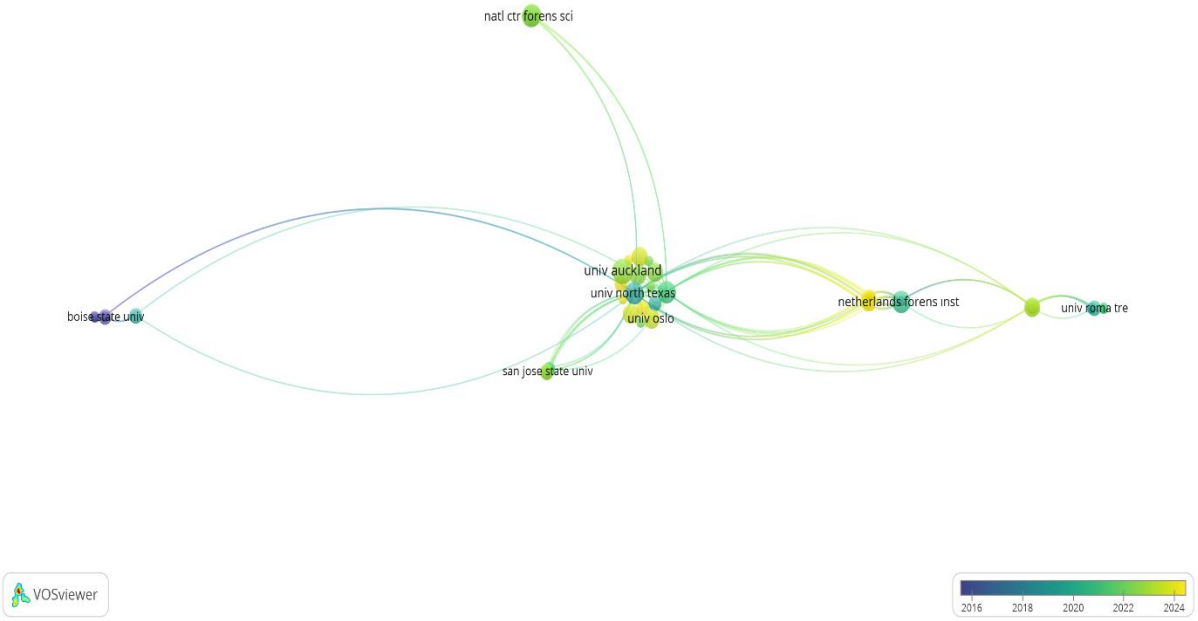

Figure 5. Citation Network of Organizations

In summary, a few key institutions are central to AI- and probabilistic genotyping-based DNA mixture interpretation. The University of Auckland (New Zealand) and the University of North Texas (USA) occupy leading positions in software development and statistical modeling. The University of Oslo (Norway) and the Netherlands Forensic Institute (NFI, Netherlands) guide European validation protocols, standardization efforts, and methodological discussions. Smaller U.S.-based universities, such as Boise State University and San Jose State University, provide supportive contributions to the development of the field. Overall, the institutional leadership in forensic DNA mixture interpretation is concentrated around hubs in New Zealand, the USA, Norway, the Netherlands, and Italy, with international collaborations largely channeled through these centers, giving the field a multi-centric and coordinated structure.

3.6. Co-occurrence of All Keywords Analysis

The prominent keywords in publications on AI-assisted DNA profiling of mixture samples were analyzed (Figure 6). In this bibliometric network, the term *probabilistic genotyping* occupies the largest node, indicating its centrality in the field and its connection to related subthemes. The red cluster, including terms such as “drop-in, validation, admissibility of evidence, population stratification, and high order mixtures”, emphasizes methodological reliability, courtroom acceptance, and complex mixture analysis. The green cluster, featuring “likelihood ratio, DNA mixture, inter-laboratory comparison, massively parallel sequencing, and EuroForMix”, reflects statistical modeling approaches, inter-laboratory comparison studies,

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and the integration of NGS technologies. The blue cluster, with "STRmix, forensic DNA interpretation, continuous DNA interpretation, and mixture deconvolution", encompasses software-based probabilistic genotyping applications and algorithmic analysis processes. The yellow cluster, including "criminal casework, CPI, and allele drop-out", highlights practical applications, forensic case analyses, and challenges associated with low-template DNA samples. The green sub-cluster, represented by "microhaplotypes and complex DNA mixtures", emphasizes the potential of next-generation genetic markers and microhaplotypes in analyzing complex mixtures. The purple cluster, containing "Bayesian inference, continuous models, and forensic decision making", focuses on theoretical modeling approaches and decision-making mechanisms. Overall, the literature reveals two main axes: the first is a methodological and statistical axis defined by concepts such as PG, LR, and Bayesian models; the second revolves around tools such as STRmix, EuroForMix, and NGS, emphasizing inter-laboratory comparisons, courtroom admissibility, and application-driven validation processes. This dual-axis structure comprehensively reflects both the theoretical foundations and practical applications of forensic DNA mixture interpretation.

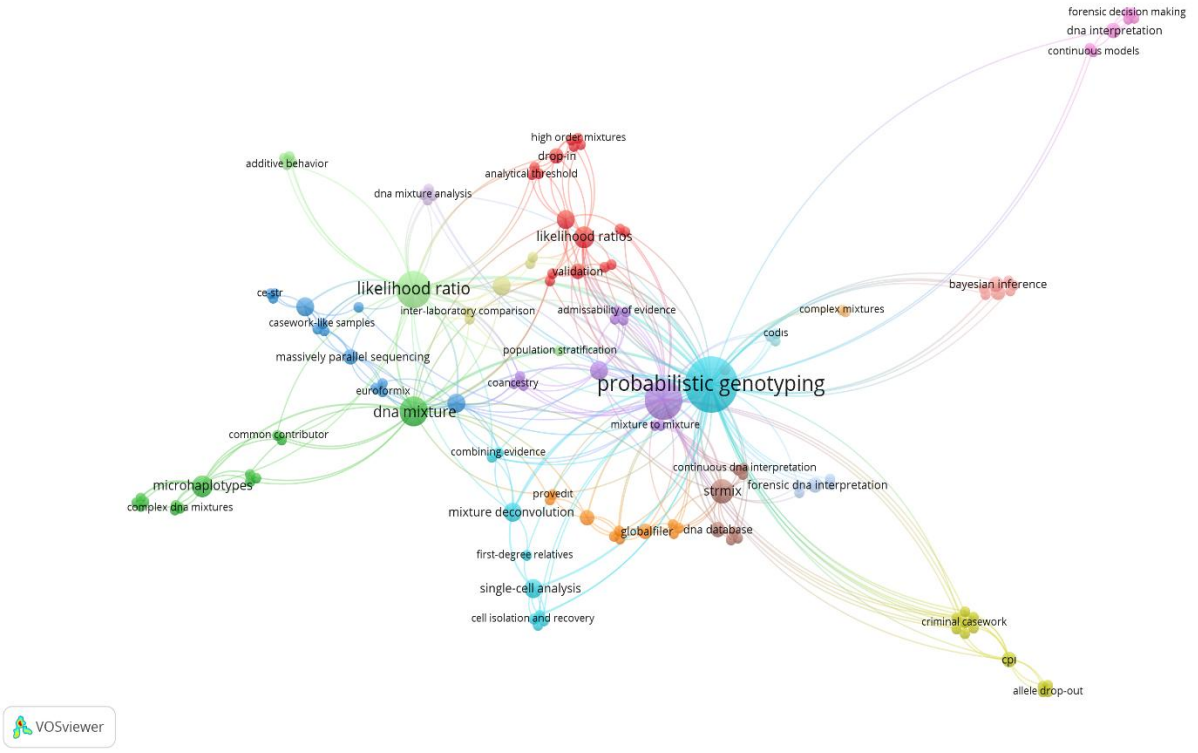

Figure 6. Co-occurrence Network of Most Frequently Used Keywords

This visualization illustrates that AI and PG based DNA mixture interpretation constitutes a multidimensional research field. In this context, PG, as a central concept, is directly linked to both statistical modeling approaches (e.g., likelihood ratios, Bayesian inference) and application-oriented components (e.g., STRmix, casework). Next-generation technologies, including NGS and microhaplotypes, hold the potential to enhance resolution in DNA mixture analysis, indicating future methodological directions in the field. Meanwhile, legal concepts such as *admissibility* and *validation* provide a critical framework for integrating technological

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innovations into judicial systems. Overall, the literature can be seen to rest on three pillars: statistical/theoretical models, software and algorithmic solutions, and practical application with legal validity.

3.7. Bibliographic Coupling of Documents Analysis

Bibliographic coupling among publications was conducted based on documents with at least one citation, and the resulting network analysis of 43 interconnected publications (Figure 7) revealed the methodological and application-oriented development dynamics in the field. *Dror (2011)*, *Coble (2019)*, and *Haned (2015)* emerged as highly connected nodes; Dror's work is foundational regarding cognitive biases and decision-making processes (Dror & Hampikian, 2011), while Coble and Haned's studies represent key methodological cornerstones in PG approaches (Coble & Bright, 2019; Haned et al., 2015). In the subsequent period, *Manabe (2017)* and *Swaminathan (2018)* established strong connections, contributing significantly to the development of the algorithmic foundations of PG software (Manabe et al., 2017; Swaminathan et al., 2018).

Examining the literature clusters, the red cluster includes Asia-based researchers such as *Bai (2022)*, *Manabe (2022)*, *Ling (2024)*, and *Slooten (2022)*, who introduced innovative applications in PG algorithms (Bai et al., 2022; Ling et al., 2024; Manabe et al., 2022; Slooten, 2022). The green cluster, featuring *Hampikian (2019)*, *Green (2021)*, and *Wang (2024)*, focuses on genetic marker diversity and case-based analyses (Green et al., 2021; Hampikian, 2019; Wang et al., 2024). The blue cluster, composed of *Coble (2019)*, *Susik (2022)*, *Adamowicz (2022)*, and *Boodoosingh (2024)*, represents methodological advancements and statistical modeling approaches (Adamowicz et al., 2022; Boodoosingh et al., 2024; Coble & Bright, 2019; Susik et al., 2022). The purple cluster highlights *Huffman's* highly productive contributions to next-generation PG applications (Huffman et al., 2022; Huffman & Ballantyne, 2023), while the yellow cluster encompasses New Zealand–Australia–based collaborations, including *Bright (2019)*, *Kelly (2020)*, and *Haddrill (2021)*, particularly related to STRmix studies (Bright et al., 2019; Haddrill, 2021; Kelly et al., 2020).

In terms of temporal trends, publications such as *Dror (2011)* and *Manabe (2017)* laid the methodological foundations during 2011–2017 (Dror & Hampikian, 2011; Manabe et al., 2017). Between 2018–2021, researchers including *Swaminathan (2018)*, *Bright (2019)*, and *Haddrill (2021)* became prominent in application and algorithm development (Bright et al., 2019; Haddrill, 2021; Swaminathan et al., 2018). After 2022, contributions from *Bai (2022)*, *Slooten (2022)*, *Huffman (2022–2023)*, and *Ling (2024)* have represented emerging directions and novel research trajectories within the field (Bai et al., 2022; Huffman et al., 2022; Huffman & Ballantyne, 2023; Ling et al., 2024; Slooten, 2022).

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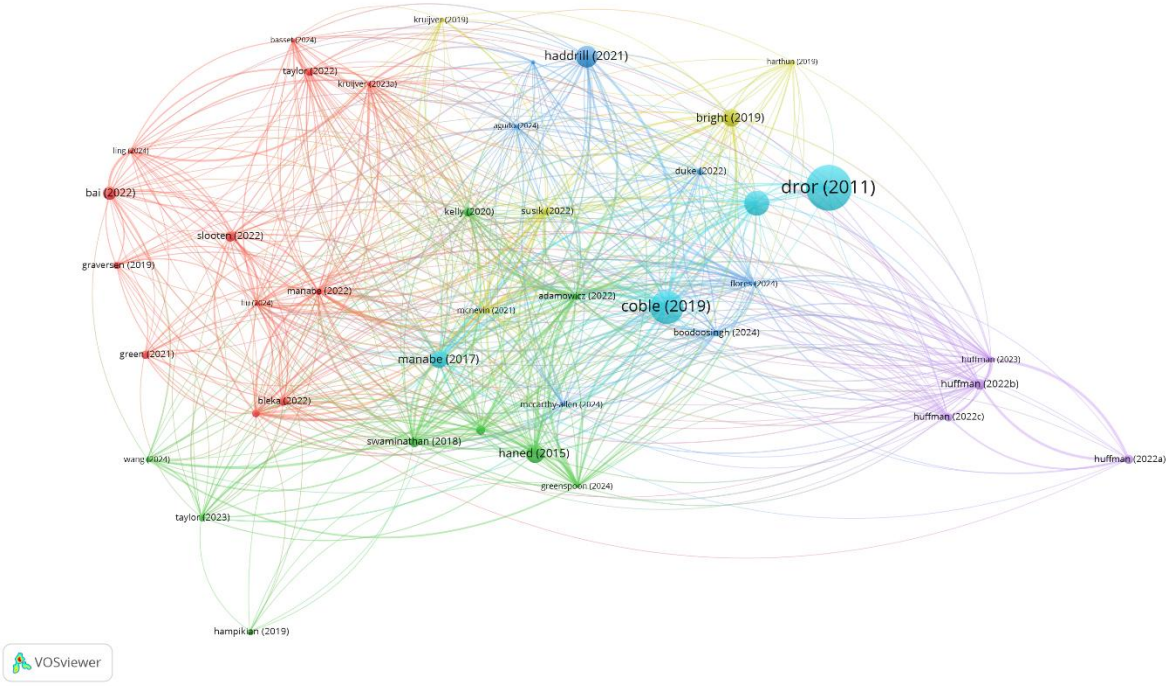

Figure 7. Bibliographic Coupling of Authors

This network map illustrates that the literature on AI and PG based DNA mixture interpretation initially relied on a few foundational reference works but has notably expanded in recent years, particularly with contributions from Asia- and Europe-based researchers. *Dror (2011)* marked a pivotal point in shaping methodological approaches by emphasizing the influence of cognitive biases on decision-making processes within forensic science (Dror & Hampikian, 2011). *Coble (2019)* and *Haned (2015)* have emerged as key references in the development of the statistical underpinnings of PG systems (Coble & Bright, 2019; Haned et al., 2015). More recent contributors, such as *Huffman (2022–2023)* and *Ling (2024)*, have gained prominence through high levels of productivity and citation connectivity, reflecting their influence on the current development of the field (Huffman et al., 2022; Huffman & Ballantyne, 2023; Ling et al., 2024). Overall, the bibliographic coupling network demonstrates that the field, which began with the establishment of methodological foundations in the 2010s, evolved after 2020 through software development, algorithmic innovations, and application-driven expansion.

3.8. Co-citation of Co-authors Analysis

The co-citation analysis examined authors who were cited multiple times within the same publication. Using a threshold of at least three co-citations, the resulting network of 115 authors revealed interaction patterns within the literature (Figure 8). Jo-Anne Bright (JA Bright) and Duncan Taylor (D Taylor) occupy central positions in the network, emerging as the most frequently co-cited authors, which highlights their pivotal role in the literature, particularly regarding the development and validation of STRmix™. Michael Coble (MD Coble), Øyvind Bleka (O Bleka), Corina Benschop (CCG Benschop), and Maarten Kruijver (M Kruijver) are prominent in Europe-centered statistical modeling and PG research. Mark Perlin (MW Perlin), as the developer of the TrueAllele system, forms a strong and relatively independent node in

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the network. Cluster analysis also reflects thematic and geographic distinctions in the literature. The green cluster consists of New Zealand–Australia-based researchers, including Bright, Taylor, Curran, and Haned, representing the core STRmix™ and PG software development team. The red cluster, including Coble, Kruijver, Green, Cowell, and Benschop, reflects Europe-based methodological research and validation studies. The blue cluster, featuring Bleka, Kelly, Steele, and Torres, focuses on statistical model development and software applications. The purple cluster centers on Perlin and associates, representing TrueAllele and US-based contributions. The yellow cluster, including Garrett, Morrison, and Thompson, emphasizes legal, decision science, and statistical methodology studies. The dense connections observed between the Bright–Taylor cluster and the Coble–Kruijver cluster reflect collaboration and knowledge flow between New Zealand–Australia–based groups and Europe-based research teams. In contrast, the relatively isolated position of Perlin's node indicates that the TrueAllele system represents an independent, US-centered line of research.

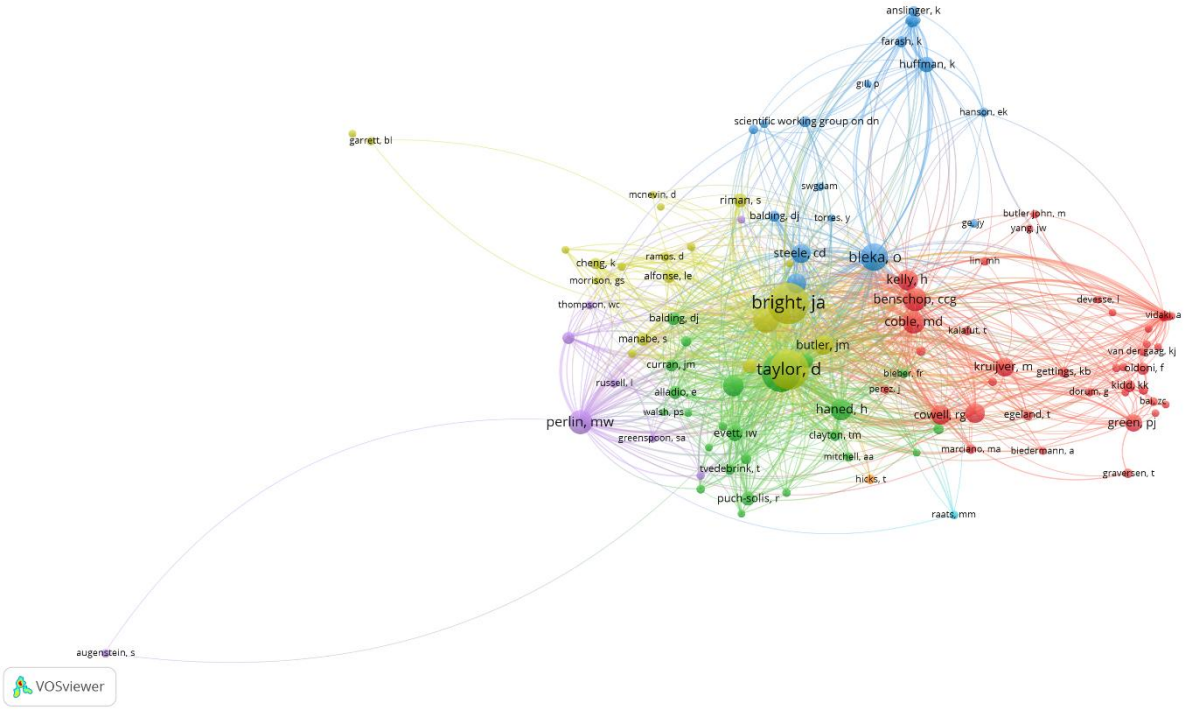

Figure 8. Co-citation Links Among Authors

The co-citation analysis presented in Figure 8 reveals that the field is structured around three primary axes. The New Zealand–Australia axis, represented by researchers such as Bright, Taylor, Curran, and Haned, embodies STRmix™ software development and statistical modeling efforts. The European axis, with contributors including Coble, Kruijver, Green, and Cowell, focuses on probabilistic model diversity, validation protocols, and inter-laboratory comparative analyses. The US axis, led by Mark Perlin, is characterized by the TrueAllele system and independent applications. This configuration highlights that AI and probabilistic genotyping-based DNA mixture interpretation constitutes a globally guided, interdisciplinary field, coordinated across multiple centers yet unified by common methodological foundations.

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4. Discussion

This study presents findings based on a bibliometric analysis of the literature on AI assisted forensic DNA mixture interpretation. The rapid increase in publication numbers, the pronounced centralization within author, institution, and country networks, the thematic clustering revealed through keyword co-occurrence, and the structural groupings emerging from co-citation and bibliographic coupling analyses collectively reflect the developmental dynamics of the field. One quantitative indicator of this progression, the "Annual Distribution of Publications" graph (Figure 1), demonstrates a marked acceleration in the literature from 2010 onward, with publication output peaking notably in 2022. This increase can be attributed to the broader adoption of PG software (e.g., STRmix™, EuroForMix) in forensic laboratories and the accelerated integration of AI/ML techniques with these systems. This trend is similarly corroborated by the study of Gill, Benschop, and colleagues (2021), which provides a comprehensive overview of the historical development of EuroForMix, DNAStatistX, and STRmix™ systems, alongside the increasing volume of research conducted using these platforms (Gill et al., 2021).

The co-authorship and author citation analyses clearly position researchers such as Bright, Taylor, Coble, Buckleton, Bleka, and Benschop as "core actors" in both the methodological and applied dimensions of the field. These findings indicate that the literature is organized around specific central institutions, with research output largely shaped by these hubs. For instance, the study *Internal Validation of STRmix™ – A Multi-Laboratory Validation* evaluates the reliability of the STRmix™ software using data from 31 different laboratories, providing a concrete example of inter-institutional standardization efforts (Bright et al., 2018). Additionally, studies such as *Developmental Validation of STRmix™ NGS* focus on integrating new technologies with existing systems, offering significant methodological contributions, particularly in assessing the performance of STRmix™ across different data types (Cheng et al., 2023).

Keyword analysis revealed that terms such as "probabilistic genotyping," "likelihood ratio," "drop-in/drop-out," "validation," "STRmix," "EuroForMix," "continuous DNA interpretation," and "massively parallel sequencing (MPS)" are among the most frequently used concepts. This finding suggests that the literature on forensic DNA mixture interpretation has evolved around three main axes:

(i) In the methodological/statistical modeling axis, approaches aimed at characterizing uncertainties—such as LR, Bayesian models, and the number of contributors—have emerged as central methods.
(ii) Within the software applications and validation axis, frequent research topics include the development of probabilistic genotyping software such as STRmix™ and EuroForMix, inter-laboratory comparisons, adaptation to NGS/MPS data types, and the management of artifacts such as drop-out and stutter.
(iii) In the legal/forensic application dimension, ethical and procedural considerations—including the admissibility of evidence in court, evidential strength, accessibility, transparency, and decision-making processes—are increasingly emphasized.

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These categories are further reflected in bibliographic coupling and co-citation analyses, where the clustering of publications and authors aligns closely with these three axes.

As clearly demonstrated in the visualizations, the differences between STRmix™, EuroForMix, and other probabilistic genotyping systems are not limited to algorithmic structures; they also stem from parameter selections such as the number of contributors, drop-in/drop-out rates, stutter modeling, and allele height variance. The study *A Diagnosis of the Primary Difference Between EuroForMix and STRmix*, conducted by Buckleton, Curran, Susik, Cheng, Taylor, Bright, and colleagues, provides a detailed examination of how these parameter differences influence LR outputs and, consequently, decision-making power (Buckleton et al., 2024). Additionally, the study *Validation of Probabilistic Genotyping Software for Single Cell STR Analysis* evaluates the sensitivity and accuracy of probabilistic genotyping software when analyzing samples with low DNA quantities or limited cell numbers. In such cases, the occurrence of artifacts such as drop-in and drop-out is increased, making the impact of these parameters on software performance more pronounced (Huffman & Ballantyne, 2023). The study assessed the validity of STRmix™ and EuroForMix for interpreting single-cell or low-cell-count STR profiles, demonstrating the analytical capacity these systems provide for low-template DNA analysis.

Country and institution level analyses indicate that the United States, Australia, and New Zealand play pivotal roles in forensic DNA interpretation, particularly in the development of licensed software, validation processes, and practical applications. European countries, including Germany, the Netherlands, Norway, and Switzerland, contribute significantly to methodological innovations and the establishment of forensic standards. This underscores the necessity of testing PG software across genetically diverse populations (e.g., allele frequency distributions) and laboratory protocols to ensure their global validity, as variables such as allele frequencies and population structure can directly influence the sensitivity of LR and other statistical outputs.

Visualizations and literature reviews reveal that certain limitations of PG software for forensic DNA mixture interpretation remain pronounced. Although recent studies have increasingly addressed low-template DNA samples and highly complex, multi-contributor mixtures, the numerical representation of such cases in the literature remains limited. These scenarios are critical for evaluating software performance under boundary conditions. Observed uncertainties in parameter selection are thought to stem from a lack of standardization in model components, including the predetermined number of contributors, drop-in/drop-out rates, and allele height variance. In alignment with principles of transparency and explainability, information regarding the internal model structures and algorithmic decision-making mechanisms of AI-based PG software must be accepted and understood within forensic systems. However, the literature in this area is still relatively recent and limited, and methodological clarity regarding algorithm interpretability remains largely insufficient. A similar limitation exists regarding data diversity: most validation studies using allele frequencies from different populations, laboratory protocols, and STR kit brands are concentrated within the same centers and follow similar

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procedures, thereby restricting methodological diversity and limiting the global generalizability of findings.

When findings derived from visual analyses are considered alongside those supported by the literature, it is evident that PG software for forensic DNA mixture interpretation has undergone a marked maturation process over the past five to seven years, both theoretically and in terms of practical application. During this period, particular attention has been given to software validation, management of parameter uncertainties, and admissibility in court. Nevertheless, despite these advances, methodological gaps persist in areas such as the influence of subjectivity in parameter selection, the limited representation of low-template and complex mixture samples, and the insufficient consideration of population- and country-specific differences. To address these gaps in the future, the creation of large-scale datasets supported by field-derived data, comparative analyses across different PG software platforms, the development of open-source modeling approaches, and the transparent articulation of algorithmic decision-making within explainable AI frameworks are recommended. Such efforts are expected to substantially enhance both the scientific validity of the field and the reliability of its forensic applications.

5. Conclusions and Recommendations

This bibliometric analysis demonstrates that the field of AI driven forensic DNA mixture interpretation has undergone substantial evolution over the past three decades, with a particularly pronounced growth trajectory since 2015. The increase in publication output indicates that the field has progressed beyond a purely methodological research topic, becoming increasingly integrated into routine forensic practice. Notably, 2022 marks a pivotal point in the literature, reflecting the integration of advanced algorithms such as deep learning, variational inference, and explainable AI (XAI) into probabilistic genotyping software.

Based on the bibliometric findings discussed in detail, research production in forensic DNA analysis is concentrated geographically and institutionally within specific centers, while thematically it revolves around statistical modeling, software validation, and legal application. This existing structure of the literature informs the focus of the following conclusions and recommendations, particularly emphasizing the resolution of methodological uncertainties and the standardization of software systems within forensic workflows. In this context, parameter variability across different software platforms has emerged as a significant source of uncertainty in LR calculations, especially for low-template or multi-contributor samples. Addressing these uncertainties necessitates the establishment of standardized validation protocols through international consortia and comprehensive performance testing for these challenging sample types. This underscores the urgency of creating globally harmonized validation frameworks. Furthermore, to enhance the admissibility of explainable AI systems in forensic contexts, decision-making processes should be rendered transparent, and these approaches should be aligned with international forensic standards such as ISO/IEC 17025 and 21043. Another critical limitation in the current literature is the narrow diversity of datasets, with most studies focused on specific populations and a limited set of STR kits. Future research should therefore emphasize population-based datasets from diverse geographic regions and integrate

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technologies such as microhaplotypes and NGS. From an interdisciplinary collaboration perspective, multidisciplinary projects involving statistics, computer science, forensic genetics, and law hold substantial potential to advance both scientific progress and courtroom acceptance. To overcome regional contribution limitations, developing countries in particular should integrate population genetic data into international databases and actively participate in software validation studies, thereby providing more visible and high-quality contributions to the literature.

In conclusion, AI driven forensic DNA mixture interpretation systems have demonstrated significant methodological advancements, both in statistical modeling approaches and software-based applications. The dynamic development of the field necessitates research strategies that focus not only on technical diversity but also on the reliability of applications, transparency in decision-making processes, and alignment with international standards. Structuring future studies in accordance with these principles will further enhance the scientific validity of forensic genetic analyses and their admissibility in legal proceedings.

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FROM FORENSIC GENETICS TO CLINICAL BIOMARKERS: ncSTR PROFILING IN BREAST CANCER

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ABSTRACT

Breast cancer is one of the most frequently diagnosed malignancies in women and represents a major global health concern in terms of both incidence and mortality. Genomic instability plays a central role in the pathogenesis of cancer, and alterations observed particularly in non-coding Short Tandem Repeat (ncSTR) regions are considered important indicators of this process. Although ncSTR markers are widely used in forensic genetics for individual identification, they are also increasingly recognized as valuable tools for tumor biology and biomarker research. In this study, blood, normal tissue, and tumor tissue samples obtained from 74 breast cancer cases were analyzed using ncSTR profiling, and the occurrence of loss of heterozygosity (LOH) and microsatellite instability (MSI) was systematically assessed. The findings revealed complete and stable STR profiles in blood and normal tissues, whereas tumor tissues displayed significant levels of genetic instability. Specifically, 34 cases of cLOH, 33 cases of pLOH, and 46 cases of MSI were detected. In terms of allele distribution, alleles 16 and 17 at D3S1358, allele 13 at D19S433, alleles 19 and 23 at D2S1338, and allele 11 at D16S539 were found to be predominant. These results suggest that certain ncSTR loci may be more susceptible to genetic instability in breast cancer. Overall, the data emphasize the dual significance of ncSTR profiling: (i) from a forensic genetics perspective, DNA profiles derived from tumor tissues may lead to misleading matches or erroneous exclusions; and (ii) from a clinical biology perspective, ncSTR variations may reflect genomic instability in breast cancer and serve as potential biomarkers. Therefore, ncSTR-based analyses should be considered not only as a critical factor in forensic reporting but also as a complementary approach in cancer biology, particularly for early diagnosis, prognostic assessment, and prediction of therapeutic response.

Keywords: Breast cancer, ncSTR, LOH, MSI, forensic genetics, biomarker

1. Introduction

Breast cancer is the most common malignancy among women worldwide and ranks second in terms of mortality (Giaquinto et al., 2024). The early diagnosis of the disease and the identification of therapeutic biomarkers are of critical importance for clinical biology and public health. At the molecular level, genomic instability is considered one of the fundamental

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mechanisms in the development of breast cancer, and this instability is particularly observed in microsatellite repeat regions (STR – Short Tandem Repeats).

STRs are generally located in non-coding regions and, due to their high levels of polymorphism, have become the gold standard in forensic genetic analyses (Pelotti et al., 2007). It has been demonstrated that non-coding STR regions (ncSTRs) can be utilized not only for identification and population genetics studies but also for cancer biomarker discovery and the understanding of tumor biology (Omar et al., 2024). In particular, events such as loss of heterozygosity (LOH) and microsatellite instability (MSI) are considered both molecular signatures reflecting cancer development and sources of variability that may lead to misinterpretations in forensic DNA profiling.

LOH and MSI events observed in tumor tissues manifest as allele loss, the emergence of novel alleles, or imbalances in allelic ratios within DNA profiles (Pelotti et al., 2007). Such alterations may lead to misleading matches, incomplete profiles, and erroneous exclusions in forensic identification processes. Therefore, careful evaluation of STR profiles derived from tumor tissues is of critical importance in forensic reporting. From a clinical perspective, ncSTR variations are suggested to be associated with the loss of function of tumor suppressor genes, impairment of DNA repair mechanisms, and cancer progression (Omar et al., 2024). Genomic alterations frequently observed in breast cancer have been reported to cluster in specific ncSTR loci, which may serve as early molecular indicators in cancer diagnosis and therapeutic monitoring (Mesquita et al., 2024). In conclusion, ncSTR profiling studies hold strong potential not only for enhancing the reliability of DNA analyses in forensic genetics but also for the identification of novel biomarkers in clinical biology.

The primary aim of this study is the systematic comparison of ncSTR profiles obtained from three different biological materials (blood, healthy tissue, and tumor tissue) in breast cancer cases, and the evaluation of LOH and MSI variations observed in these profiles from both forensic genetics and clinical biology perspectives. In the literature, the majority of studies have either focused exclusively on tumor tissues or investigated only specific STR loci. In contrast, this study offers a dual perspective by simultaneously comparing different biological materials obtained from the same individual. The originality of our work lies in its ability to highlight both the reliability issues of ncSTR profiling in forensic identification processes and its contribution to the identification of potential biomarkers in breast cancer. In this regard, the study serves as an interdisciplinary bridge connecting the fields of forensic genetics and cancer biology.

2. Materials and Methods

2.1 Sample Collection

This study was conducted with the approval of the Medipol University Non-Interventional Clinical Research Ethics Committee (No: E-10840098-202.3.02-5292; 02.09.2024) and in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all participants, and their confidentiality was preserved. A total of 74 volunteers over the

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age of 18, without kinship relations, with histologically confirmed invasive cancer diagnoses, untreated, and without chimeric characteristics, were included. A history of blood transfusion/organ transplantation, the presence of another cancer diagnosis, or chronic illness constituted exclusion criteria.

The study was carried out at the Anagen Analysis Research Laboratory. Blood, healthy, and tumoral tissue samples of cancer-diagnosed volunteers who had applied to the Forensic Molecular Genetics Laboratory of Istanbul University-Cerrahpaşa, Institute of Forensic Sciences and Legal Medicine, for DNA identification were collected. Seventy-four cases with an active disease course at the time of sampling were included. Venous blood samples were collected into 5 ml EDTA tubes and stored at +4 °C until analysis. The storage duration of the obtained FFPE tissue blocks ranged between 1 and 12 months (mean = 6.74 ± 2.68), while the participants' ages ranged between 20 and 39 years (mean = 29.81 ± 5.49).

2.2 DNA Isolation and Quantification

To prevent bacterial growth and contamination, all surfaces were cleaned with 10% benzalkonium chloride (Zefiran IM) and 10% bleach, and consumables were sterilized by autoclaving. From FFPE blocks coded by a pathologist, sections of approximately 3 µm thickness were obtained using a scalpel, followed by deparaffinization with xylene and ethanol. Genomic DNA was isolated from FFPE tissues and venous blood using the QIAamp DNA Mini Kit (Qiagen, Germany) in accordance with the manufacturer's protocol (QIAGEN Sample and Assay Technologies, 2016). During the isolation procedure, proteinase K digestion, lysis, and column-based purification steps were performed. The obtained DNA samples were quantified fluorometrically using a Qubit® Fluorometer and the Quant-iT™ dsDNA HS Kit (Thermo Fisher Scientific). Measurements were carried out in triplicate; when necessary, high concentrations were diluted to 0.2 ng/µl, and DNA isolates were stored at –20 °C until further analysis.

2.3 STR Analysis

The obtained DNA samples were amplified using the AmpFlSTR® GlobalFiler™ STR Kit (Applied Biosystems, USA) with the GeneAmp® 9700 PCR System, in accordance with the manufacturer's protocol (Thermo Fisher Scientific Inc., 2019). The GlobalFiler™ kit covers 24 STR loci (D3S1358, vWA, D16S539, CSF1PO, TPOX, D8S1179, D21S11, D18S51, D2S441, D19S433, TH01, FGA, D22S1045, D5S818, D13S317, D7S820, SE33, D10S1248, D1S1656, D12S391, D2S1338, DYS391, Y-indel, AMEL). Analyses were performed using the different fluorescent dyes included in the PCR kit and the GeneScan™ 600 LIZ™ standard. Thanks to MiniSTRs, reliable results could also be obtained from samples containing low amounts of DNA or inhibitors.

Amplification reactions were carried out in a total volume of 12.5 µL, and the amplified products under standard PCR conditions were stored at +4 °C. In most samples, complete profiles were obtained in a single attempt; in a small number of tumor samples with missing alleles, PCR was repeated.

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Amplification products were genotyped using the Applied Biosystems ABI 3500 capillary electrophoresis (CE) system. For this purpose, a mixture containing 9.6 µL Hi-Di™ formamide and 0.4 µL GeneScan™ 600 LIZ™ Size Standard was prepared per sample, and 1 µL of PCR product was added to this mixture. Along with control wells containing the allelic ladder, samples were electrophoresed using POP-4 polymer.

2.4 Data Evaluation Criteria

CE results were analyzed using GeneMapper™ ID-X v1.6 software. A threshold of 150 RFU and a kit-specific reading range of 74–444 nt were applied for allele calling. The allelic ladder and LIZ 600 internal standard were used as references. Negative and positive controls were included in each run to verify contamination status and kit performance. Analyses were conducted in accordance with SWGDAM guidelines, and non-allelic peaks were excluded from reporting.
LOH and MSI assessments were performed using RFU values based on the mean of three replicates. The Allelic Imbalance Ratio (AIR) was used to evaluate LOH. Homozygous loci were considered non-informative for LOH and included only in MSI assessment. PCR artifacts (e.g., drop-out, stutter) were excluded before interpretation; in doubtful cases, isolation and PCR were repeated.

LOH: cLOH (complete allele loss), pLOH (allelic ratio <0.30 or >1.67)
MSI: A novel allele ≥150 RFU not present in healthy tissue.

2.5 Statistical Analysis

One-way ANOVA was applied for numerical data, and the Pearson Chi-square test was used for categorical data; Tukey HSD post-hoc analysis was performed in cases of significant differences ($p < 0.05$). Excel 2019 was used for visualization and basic calculations, while GraphPad Prism v8.4.3 and SPSS v27.0 were employed for advanced statistical analyses. STRAF 2 software was used for allele frequency analyses (Gouy & Zieger, 2025).

3. Results

3.1 DNA Quality

The DNA concentrations obtained from breast cancer cases ranged from 2.58–9.05 ng/µl in blood, 0.59–2.42 ng/µl in healthy breast tissue, and 0.49–1.75 ng/µl in tumoral breast tissue (Figure 1). The DNA yield in blood was found to be significantly higher than that of both healthy and tumoral breast tissues. Furthermore, DNA concentration in healthy breast tissue was significantly higher than in tumoral tissue ($p < 0.001$ for all comparisons).

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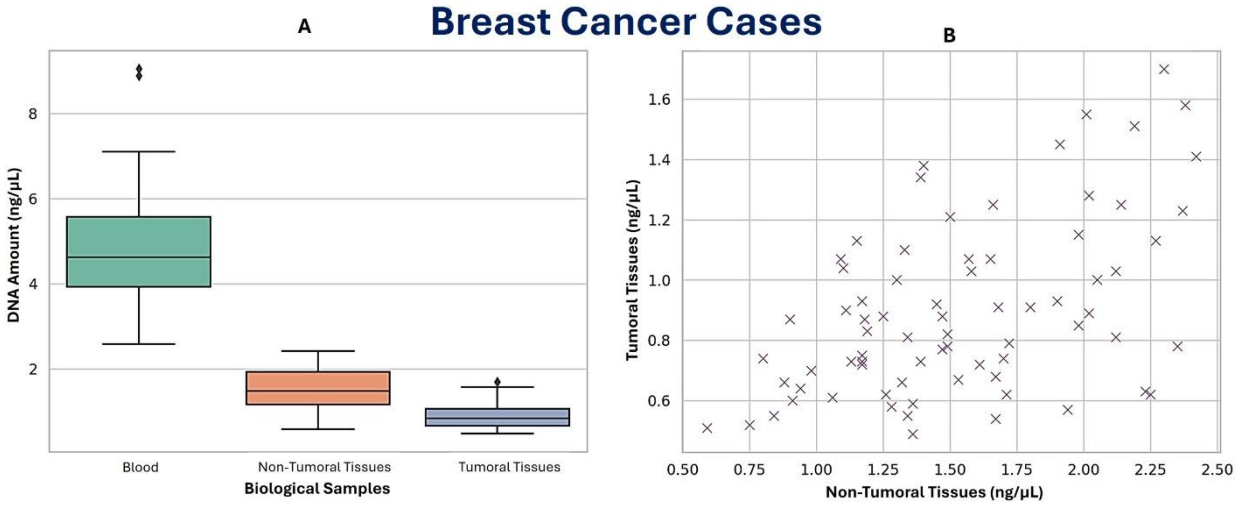

Figure 1. Distribution of DNA quantities among groups in breast cancer cases. (A) Boxplot of DNA quantities, (B) Scatterplot illustrating the relationship between DNA quantities in healthy and tumoral tissues.

3.2 Allelic Distribution

While ncSTR profiles in blood samples showed complete and heterozygous distributions, marked allele losses were detected in tumor tissues. Since the PCR analysis kit used covers 24 loci, a total of 1,776 loci from 74 breast cancer cases were evaluated. The genotyping success rate in blood and healthy tissue samples was found to be 100%. The success rate was calculated using the formula: (Number of observed loci / Number of expected loci) × 100. According to Hardy–Weinberg Equilibrium (HWE) analysis, the genotype distribution of STR markers was $p = 1.0$ across all loci, indicating that the data were fully consistent with Hardy–Weinberg equilibrium. Although deviations may be expected in small sample sizes, no observed–expected genotype differences were found in our study, and the calculated distributions were in complete agreement with theoretical expectations. Figure 2 presents the allele frequencies observed at each locus in the study cohort.

3.3 LOH and MSI

When the locus-based distributions of genomic instability presented in Table 1 were evaluated, MSI and LOH analyses revealed that certain STR loci exhibited higher instability compared to others. pLOH was most frequently observed at loci D13S317 (5 cases), D16S539 (4 cases), and vWA (3 cases). cLOH was particularly prominent at D21S11 and D16S539 (5 cases each), D19S433 (4 cases), and vWA and SE33 (3 cases each). In terms of MSI events, the highest instability was recorded at D21S11 (8 cases), D16S539 (6 cases), SE33 and D19S433 (5 cases each), and vWA (4 cases). According to the widely accepted 33% rule in forensic genetic studies (Tozzo et al., 2021), when locus-based MSI distribution was evaluated, among the cases analyzed, MSI was detected in 10 out of 21 loci (47.6%). These ratios indicate that the cases fall into the MSI-H category, as more than 33% of the analyzed loci exhibited instability.

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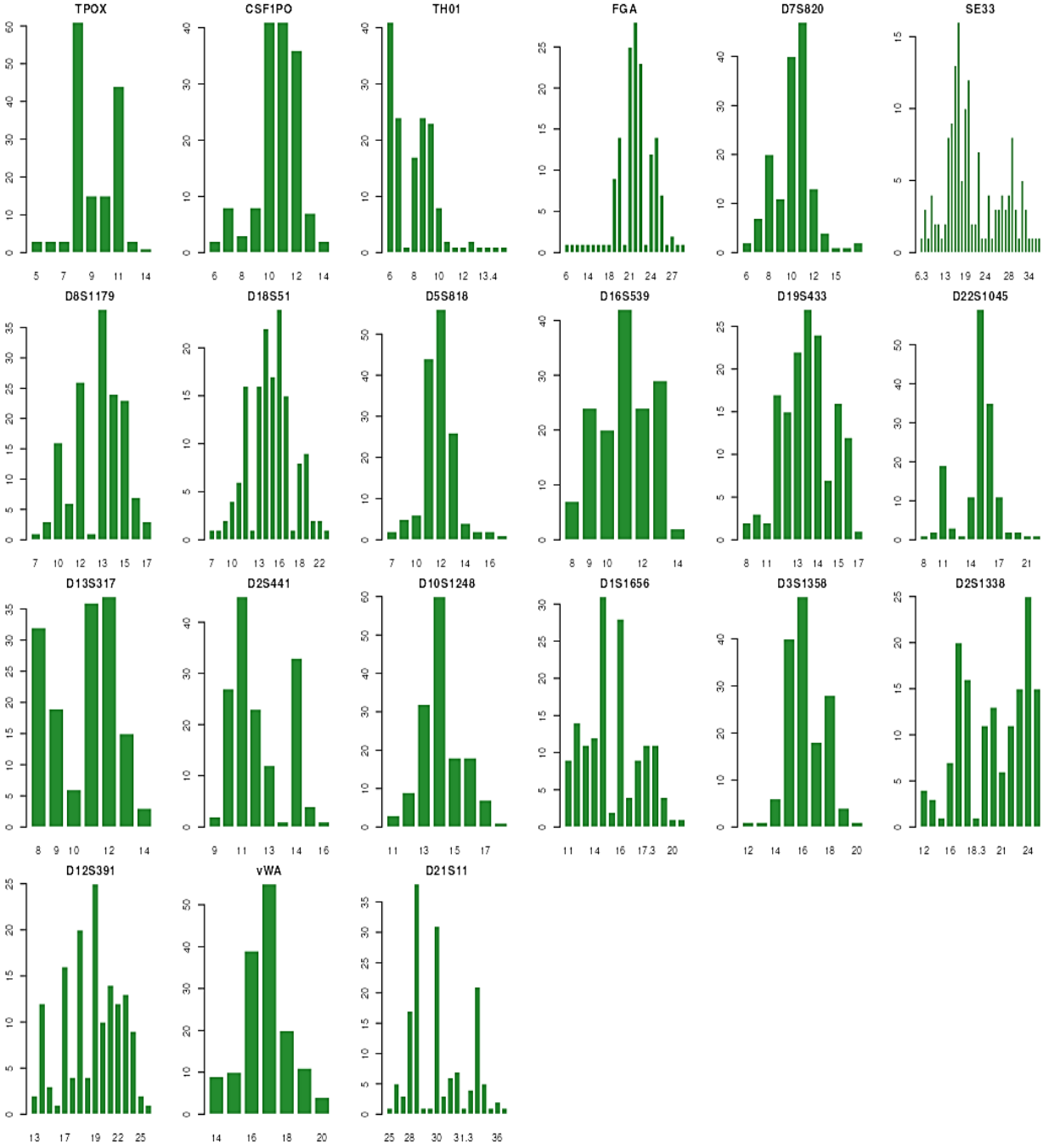

Figure 2. Distribution of allele frequencies per locus in subjects

In Figure 3, examination of the case × locus matrices through the MSI heatmap revealed the most pronounced instability at D21S11, with weaker levels also observed at D16S539 and SE33. In Figure 4, analysis of the LOH heatmap based on case × locus matrices indicated notable LOH at D16S539 and D13S317, while D21S11 exhibited moderate-to-high levels of LOH.

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Table 1. Distribution of STR locus-specific mutational events across tumor tissue.

Locus	*cLOH*	*pLOH*	*MSI*
Amelogenin	0	0	0
CSF1PO	0	0	0
D10S1248	0	0	0
D12S391	2	2	3
D13S317	1	5	1
D16S539	5	4	6
D18S51	2	0	3
D19S433	4	2	5
D1S1656	1	2	2
D21S11	5	2	8
D22S1045	0	1	1
D2S1338	1	1	1
D2S441	0	0	0
D3S1358	0	0	0
D5S818	2	2	2
D7S820	1	1	1
D8S1179	-	-	-
DYS391	-	-	-
FGA	2	2	2
SE33	3	2	5
TH01	2	3	2
TPOX	0	1	0
Y-Indel	-	-	-
vWA	3	3	4
Total	34 cLOH, 33 pLOH, 46 MSI		

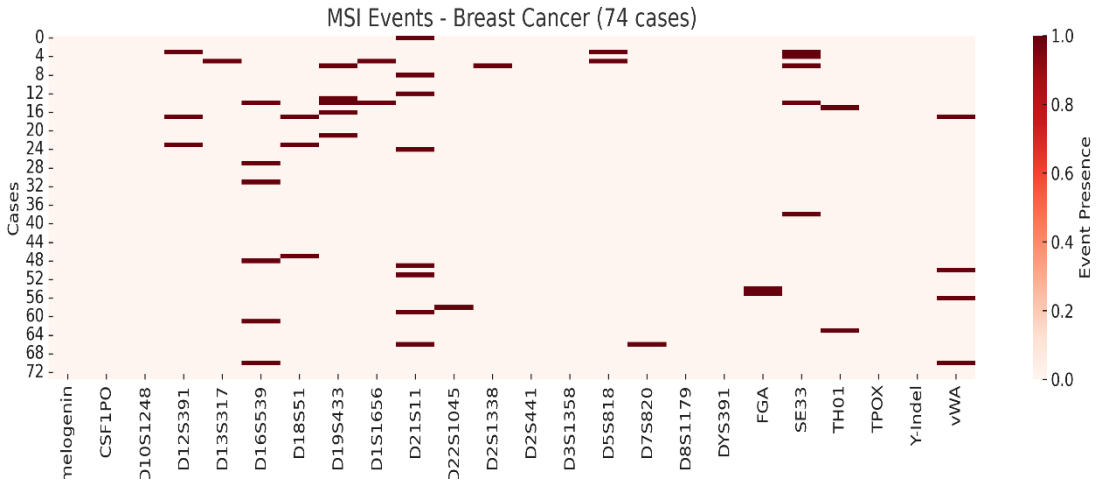

Figure 3. MSI heatmap: Microsatellite instability distribution on a case × locus basis in breast cancer samples (Red tones indicate which locus exhibits MSI in which case)

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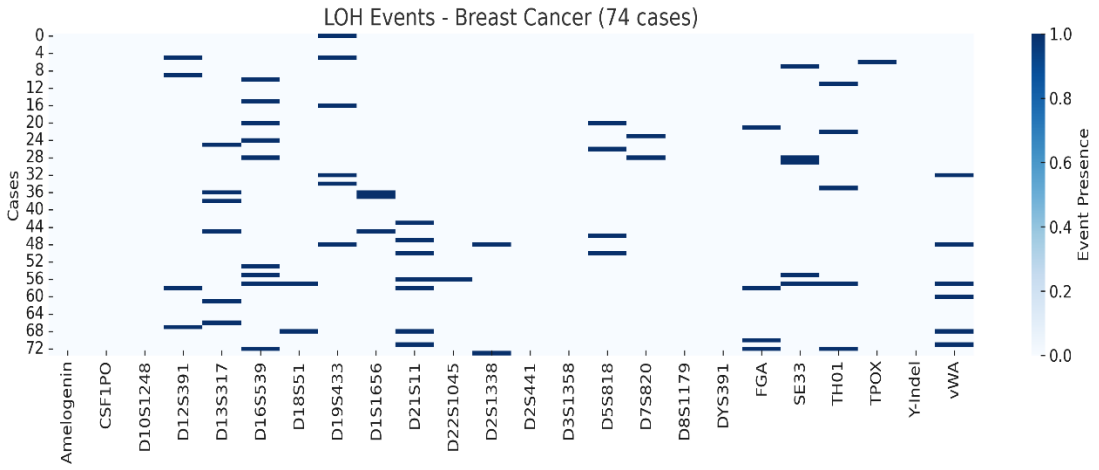

Figure 4. LOH heatmap: Loss of Heterozygosity distribution on a case × locus basis in breast cancer samples (Blue tones indicate which locus exhibits LOH in which case).

4. Discussion

In this study, STR profiles obtained from tumor tissues in breast cancer cases showed significant differences when compared with profiles derived from blood and healthy tissues. In particular, the high frequency of LOH (pLOH and cLOH) and MSI events indicates that tumor-derived DNA may substantially limit the reliability of forensic genetic analyses. This finding highlights the potential risks of using tumor tissues as a DNA source in forensic identification studies. Similarly, Pelotti et al. (2007) and Omar et al. (2024) emphasized that STR instability in cancer tissues may increase the likelihood of false matches or erroneous exclusions in forensic applications such as identification and kinship testing.

One of the loci where MSI was most frequently observed in our study was D21S11. This result is consistent with the MSI distribution reported by Mesquita et al. (2024) in breast cancer cohorts. This finding suggests that certain STR loci may be more susceptible to genomic instability specific to breast cancer. In particular, STR loci exhibiting high variability may increase the margin of error in forensic interpretation. In this context, the obtained results strongly support the need to include ‘cancer tissue–derived variations’ as routine evaluation parameters in forensic reporting processes.

From the perspective of clinical biology, the observation of ncSTR variations can be regarded not only as a forensic reliability issue but also as a molecular signature of the carcinogenesis process. LOH events are generally associated with the loss of tumor suppressor genes, while MSI arises as a consequence of impaired DNA repair mechanisms (Boland & Goel, 2010). Therefore, the high LOH and MSI rates observed in our study may be considered a reflection of the fundamental molecular mechanisms contributing to tumor progression in breast cancer. Moreover, MSI has been reported as a strong biomarker for predicting responses to immunotherapies in different cancer types (Hause et al., 2016). In this regard, ncSTR-based analyses may provide not only diagnostic but also clinically informative indicators for guiding treatment.

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On the other hand, the findings of our study are also important in the context of population genetics. The distribution of major and private alleles demonstrated that certain loci possess discriminative potential to reveal genetic differentiation among groups. Supporting these differences with FST analyses would highlight that ncSTRs can be used not only for individual identification but also for population-based genetic studies. In particular, variants defined as 'private alleles' appear to provide unique signatures both for cancer biology and for forensic genetic interpretation.

The limited sample size, the inability to fully control tumor heterogeneity, and the evaluation of only certain ncSTR loci restrict the generalizability of the results. Nevertheless, these limitations do not diminish the originality of our study; rather, they underscore the need for larger-sample, multicenter studies encompassing different cancer types.

In conclusion, the findings deliver a dual message: (i) From a forensic genetics perspective, ncSTR variations observed in tumor tissues should be carefully considered in identification and kinship analyses; (ii) From a clinical biology perspective, these variations may serve as potential biomarkers for early diagnosis, prognostic evaluation, and prediction of treatment response in breast cancer. Approaching ncSTR-based studies with an interdisciplinary perspective will not only enhance the reliability of forensic reporting but also provide new clinical insights into cancer biology.

5. Conclusion and Recommendations

In this study, ncSTR profiles obtained from blood, healthy tissue, and tumor tissues in breast cancer cases were compared, and it was revealed that LOH and MSI were particularly frequent in tumor tissues. The findings indicate that tumor-derived DNA samples may lead to misleading results in STR-based identification processes from a forensic genetics perspective. Therefore, it is recommended that tumor tissues be evaluated with caution in forensic applications, and that blood or healthy tissues be used as references whenever possible.

From a clinical perspective, ncSTR profiling has the potential to serve as a valuable biomarker reflecting genomic instability in breast cancer cases. In particular, loci with high MSI frequencies are predicted to be useful for early diagnosis, prognostic monitoring, and the assessment of treatment response. In this context, ncSTR-based analyses are considered to play a complementary role alongside conventional molecular biology tests.
For the future, it is recommended that similar analyses be conducted on larger cohorts and in different populations, that ncSTR variations be systematically compared across various cancer types, and that ncSTR profiling be incorporated into the standard analysis panels of clinical biobanks.

In conclusion, ncSTR profiling holds dual significance in breast cancer for both forensic genetics and clinical biology. Supporting this approach through interdisciplinary research is expected to enhance the reliability of forensic reporting and contribute to the discovery of novel biomarkers in cancer biology.

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ORGAN-SPECİFİC DİSTRİBUTİON OF AMİNO ACİDS AND TRACE ELEMENTS İN *VERBASCUM TUNA-EKİMİİ*: A PHYTOCHEMİCAL AND PHARMACOLOGİCAL PERSPECTİVE

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ABSTRACT

The genus *Verbascum* L. comprises more than 2,500 species worldwide and is recognized as the largest genus of the Scrophulariaceae family. In the flora of Turkey and the East Aegean Islands, 228 species of this genus have been identified, 185 of which are endemic. *Verbascum* species are known to possess various biologically active compounds, including flavonoids, phenylethanoid and neolignan glycosides, saponins, iridoid and monoterpene glycosides, and have been widely used in traditional medicine worldwide. In this study, the amino acid profile and trace element content of methanolic extracts derived from the root and stem organs of *Verbascum tuna-ekimii* Karavel., a locally endemic species from Erzincan (Turkey), were investigated.

A total of 43 amino acids were analyzed. The highest concentration was observed in the stem as L-glutamine (150.18 nmol mL^{-1}), while the root exhibited the highest level of L-proline (32.45 nmol mL^{-1}). Valine, norvaline, threonine, serine, and L-histidine were found only in stem samples; in contrast, no amino acid was specific to the root. The generally higher levels of amino acids observed in the stem suggest that this organ may function as a major site of amino acid biosynthesis and accumulation, while the root appears to be more actively involved in transport and metabolic processing. Amino acids such as L-proline, L-glutamine, aspartic acid, alanine, serine, glutamate, and γ-aminobutyric acid (GABA), found at high levels in the

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stem, are known to be associated with various biological activities. In particular, proline and glutamine are involved in osmotic stress tolerance and antioxidant defense mechanisms, while tryptophan, tyrosine, and phenylalanine serve as essential precursors in the biosynthesis of secondary metabolites.

Trace element analysis identified 13 elements. Aluminum (Al) was highly accumulated in the root (2998.9 μg g^{-1} dry weight), which may indicate an adaptive response to tolerate Al-induced toxicity. In contrast, a significant accumulation of sodium (Na) was observed in the stem (10,564.5 μg g^{-1} dry weight). Given the roles of zinc (Zn) in protein synthesis and sodium in osmotic regulation, these elements may be related to the high amino acid levels observed in the stem.

The findings indicate that *Verbascum tuna-ekimii* is characterized by a diverse amino acid composition and a valuable content of biologically active compounds and trace elements, highlighting its potential applications in pharmaceutical, nutraceutical, and phytotherapeutic fields.

Keywords: Amino acid, Trace element and *Verbascum tuna-ekimii.*

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DENİZEL PEPTİDLERİN YAPI TAYİNİ VE ARDIŞIK PEPTİD FRAGMANLARININ BETA GLUKOZİDAZ İNHİBİTÖR AKTİVİTELERİNİN ARAŞTIRILMASI

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Özet

Biyoaktif peptidler takviye besin olarak kullanıldığında insan sağlığına faydası olan protein parçalarıdır ve insan vücudu üzerinde değişik fizyolojik fonksiyonlara sahiptirler. Bunun yanısıra bazı aktif peptidler dışarıdan alınan daha büyük peptid ya da proteinlerin sindirim sisteminde bulunan proteaz enzimleriyle parçalanması ile oluşurlar. Dünya'da morbititesi yüksek olan kardiyovasküler, kan basıncı yüksekliği, diyabet, kanser gibi hastalıkların tedavisinde verilen ilaçların sürekli kullanımı ve dozaj ayarlanamaması sonucu oluşan zehirlenme vakaları hastalıkların tedavisinde her zaman problem yaratmaktadır. Zehirlenme vakası ile karşılaşılmasa bile uzun süreli ilaç kullanımı en azından ciddi yan etkileri ve ilaç bağımlılığı gibi negatif durumları da beraberinde getirir. Bu yüzden biyoaktif doğal besin kaynakları söz konusu riskleri en aza indirgemede başvurulacak alternatif ilaç kaynaklarıdır. Denizel kaynaklı peptidler antidiabetik, antihipertansif, antiHIV, antikoagülan, antimikrobiyal, antiobezite, antioksidan, antiproliferatif, kalsiyum bağlayıcı gibi birçok biyoaktiviteye sahiptirler. Literatürde denizel kaynaklı peptidler daha çok makroorganizmalardan ve bunların üzerlerine yerleşmiş funguslardan izole edilmiştir. Özellikle Türkiye kaynaklı Denizel bakterilerden yapılmış peptid izolasyon çalışmasının olmaması bizi bu bakterilerden sekonder metabolit izole etmeye ve yapılarını tanımlayıp antidiyabetik aktivitelerini araştırmaya itmiştir. Bu nedenle antidiyabetik aktivite gösteren β glukozidaz enzim inhibitörleri analiz edilmiştir. TÜBİTAK-1002 projesi kapsamında bakterilerden ekstrakte edilen peptidlerden üçünün Edman parçalanması yöntemiyle amino asit dizilimleri saptanmış ve parçalanmalar sonrası ardışık peptid fragmanlarının β glukozidaz enzim inhibitörü aktivitesi ölçülmüştür. Çalışmamızın sonucunda *Alkalihalobacillus macyae* MW559742'den izole ettiğimiz G7 kodlu bileşiğimizin amino asit dizilimini "CMMC" yani Cys-Met-Met-Cys olan bir tetrapeptid; *Kocuria rosea* MW559735'ten izole ettiğimiz B78 kodlu bileşiğimizin amino asit dizilimini "LCHMCHMLH" yani Leu-Cys-His-Met-Cys-His-Met-Leu-His olan bir nonapeptid; *Bacillus simplex* KJ161411'den izole ettiğimiz K3848 kodlu bileşiğimizin amino asit dizilimini "RLSLRRRGREDF" yani Arg-Leu-Ser-Leu-Arg-Arg-Arg-Gly-Arg-Glu-Asp-Phe olan bir siklik dodekapeptid olarak saptanmıştır. Ayrıca her bir Edman parçalanmasından elde edilen su fazlarında bulunan peptid parçalarının β glukozidaz enzim inhibitörü aktiviteleri de test edilmiştir. B78'den elde edilen His-Met-Cys-His-Met-Leu-His dizilimli heptapeptid ve Met-Cys-His-Met-Leu-His dizilimli hekzapeptid parçaları ve G7'den elde edilen Met-Met-Cys

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dizilimli tripeptid parçası ile Cys amino asidi enzim inhibitörü aktivitesi göstermiştir. Elde edilen enzim inhibitörlerinin ileri analizleri yapılarak, medikal kullanımları yönünde çalışmalar sürdürülmelidir.
Anahtar kelimeler: Peptid, Edman Parçalaması, Antidiyabetik Etki, β Glukozidaz İnhibisyon Aktivitesi.

1. GİRİŞ

Biyoaktif peptitlerin birçok önemli biyoaktiviteye sahip oldukları bilinmektedir. Fonksiyonel gıdalar, kozmetikler, evcil hayvan maması üretimi ve sağlık sektörü de dahil olmak üzere çeşitli uygulamalarda kullanılmaktadırlar [1-2]. Bu peptitlerin moleküler ağırlıkları 2500 Da'dan azdır ve boyutları 2-20 amino asittir. Peptitlerin biyoaktivitesi, bileşime ve amino asit dizisine bağlıdır. Peptitlerin, yapısal özelliklerine, amino asit bileşimlerine ve dizilime göre antihipertansif, antioksidatif, hipokolesterolemik, antibakteriyel, immünomodülatör, opiat benzeri, mineral bağlayıcı ve antitrombotik aktivitelere sahip olabildikleri [3-4], Denizel kaynaklı peptidlerin alkolik olmayan karaciğer yağlanmasının önlenmesi ve tedavisinde [5], yara iyileştirmede [6], bağışıklık sistemi güçlendirmede [7], HIV enfeksiyonlarını tedavi etmede kullanılabilecekleri araştırmalarla kanıtlanmıştır [8]. Ayrıca denizel kaynaklı peptidlerin DPP-IV (Dipeptidil peptidaz-IV) inhibitör özellikleri yani antidiyabetik özelliklerinin olduğu da yapılan çalışmalarla keşfedilmiştir [9-11].
Edman metodunda [12-14] amino asit zincirinden N-terminal amino asit ayrılır, geride kalan reaksiyona girmemiş peptid ya da proteini orijinal halinden bir amino asit eksik bir şekilde ortama bırakır. Edman reaktifinin ana bileşiği fenilizotiyosiyanat (PITC) bazik ortamda peptidin N-ucundaki amino asit ile bir feniltiyokarbamoil türevi oluşturur. Daha sonra peptid asidik koşullarda ortama bir amino asit feniltiyohidantoin türevi vererek bir amino asidinden ayrılır. Bu metod sayesinde peptidlerin yapılarının aydınlatılmasında yani amino asit dizilimlerinin bulunmasında manuel olarak Edman reaksiyonu ya da otomatize şekli olan Edman dizileyicisi kullanılır. Daha sonra elde edilen amino asit-PTH bileşiklerinin yapıları ve dolayısıyla amino asit dizilimleri LC-MS/MS veya HPLC-MS kullanılarak belirlenir.
β-Glukozidaz enzimi glikozidik bağı hidrolizleyen ve organizmada sekonder metabolizma, biyotransformasyon, bitkilerde patojenlere karşı savunma, insan dokularında ve hücre duvarlarında seramid glikozidinin yıkılması gibi normal biyolojik işlemlerin sürdürülmesinden rol alır [15]. Klinik teşhislerde β-Glukozidaz aktivitesinin seviyesi nekrotizan enterokolit ve gaucher hastalığı için kullanılır. Farmasötik çalışmalarda ise β-Glukozidaz diyabet, HIV enfeksiyonu, metastatik kanser, lizozomal depo hastalığı gibi çok çeşitli hastalıkla ilişkilendirilir.
Çalışmamızda amacımız 3 farklı denizel bakteriden izole ettiğimiz üç peptidin amino asit dizilimini saptayarak yapılarını aydınlatmak ve bu peptidlerden Edman parçalanması ile elde edilen 1 amino asit eksik ardışık peptidlerin antidiyabetik özelliklerini beta-glukozidaz inhibisyon aktivitelerini saptayarak araştırmaktı.

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2. DENEYSEL ÇALIŞMALAR

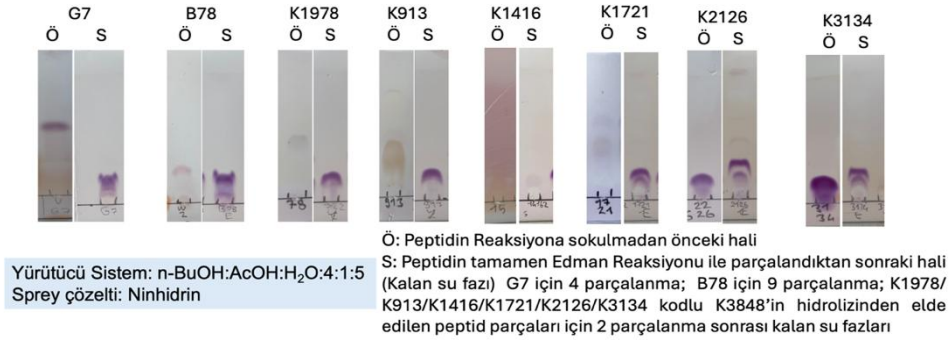
Araştımamızda;

- Elimizde olan standart amino asitlerin feniltiyohidantoin türevleri sentezlenmiştir.
- 3 farklı denizel mikroorganizmadan elde edilen saf peptidin Edman yöntemi ile parçalanması gerçekleştirilmiş amino asit feniltiyohidantoin türevleri sentezlenmiştir.
- Amino asit-feniltiyohidantoin türevlerinin LC-MS/MS yöntemi ile yapıları tanımlanmıştır.
- Amino asit-feniltiyohidantoin türevlerinin yapılarının doğrulanması ince tabaka kromatografisinde standart amino asitlerin feniltiyohidantoin türevlerinin Rf değerleri ile kıyaslama ve
- 3 peptidin asidik hidrolizatların LC-MS/MS'lerinden elde edilen verilerle gerçekleştirilmiştir.
- Her bir Edman çevrimi sonrası elde edilen bir amino asit eksik peptid parçaları üzerinde Beta-glukozidaz enzim inhibisyon testleri gerçekleştirilmiştir.

3. SONUÇLAR VE DEĞERLENDİRME

3.1 Standart amino asitlerin ve peptidlerin Edman Yöntemi ile Parçalanması ve Kontrolü

Sentezlenen türevler için TLC yürütücü solvent sistemi olarak $CHCl_3$: Aseton: 29: 3 [16-18] kullanıldı ve plak ninhidrin ile renklendirildi ve Rf değerleri hesaplanarak çizelge haline getirildi. Parçalanmaların bitimi su fazlarının (CW) TLC kontrolü ile belirlendi (Görsel 1). G_7 için 4 kez parçalanma, B_{78} için ise 9 parçalanma gerçekleştirildi. Elde edilen ürünlerin TLC fotoğrafları Görsel 2'de verilmiştir. K_{3848} kodlu peptidimizde ise Edman reaksiyonu gerçekleşmedi yani parçalanma olmadı (Görsel 3). Bu durum, bu peptidin N-ucunun bloke olduğunu veya halkalı yani bir siklopeptid olduğunu ortaya çıkardı [19].



Görsel 1. Edman parçalanması bitimi su fazları ve peptidlerin yanyana TLC Profilleri

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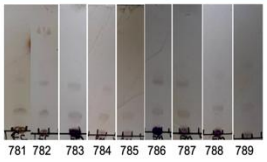
Yürütücü Sistem: $CHCl_3$:Aseton:29:3
Sprey çözelti: Ninhidrin

Amino asit-PTH	Rf x100	Karşılık gelen amino asit
G71	44	Cys
G72	22	Met
G73	22	Met
G74	45	Cys

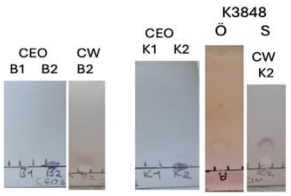
Yürütücü Sistem: $CHCl_3$:Aseton:29:3
Sprey çözelti: Ninhidrin



Amino asit-PTH	Rf x100	Karşılık gelen amino asit
B781	50	Leu/Ileu/NLE
B782	44	Cys
B783	43	His
B784	42	Met
B785	45	Cys
B786	43	His
B787	42	Met
B788	52	Leu/Ileu/NLE
B789	43	His

Görsel 2. G_7 ve B_{78}'den elde edilen amino asit-PTH türevlerinin TLC profilleri-Rf değerleri-Karşılık gelen amino asit

B1: Bir çevrim kör Edman Reaksiyonu sonucunda elde edilen su fazı
B2: İki çevrim kör Edman Reaksiyonu sonucunda elde edilen su fazı
K1: Bir çevrim K3848'in Edman Reaksiyonu sonucunda elde edilen su fazı
K2:İki çevrim K3848'in Edman Reaksiyonu sonucunda elde edilen su fazı
Ö: Peptidin Reaksiyona sokulmadan önceki hali
S: Peptidin tamamen Edman Reaksiyonu ile parçalandıktan sonraki hali (Kalan su fazı) K3848 için 2 parçalanma sonrası kalan su fazı
CEO: Edman Reaksiyonunda PTH türevinin olduğu organik faz
CW: Edman Reaksiyonu sonucunda elde edilen su fazı

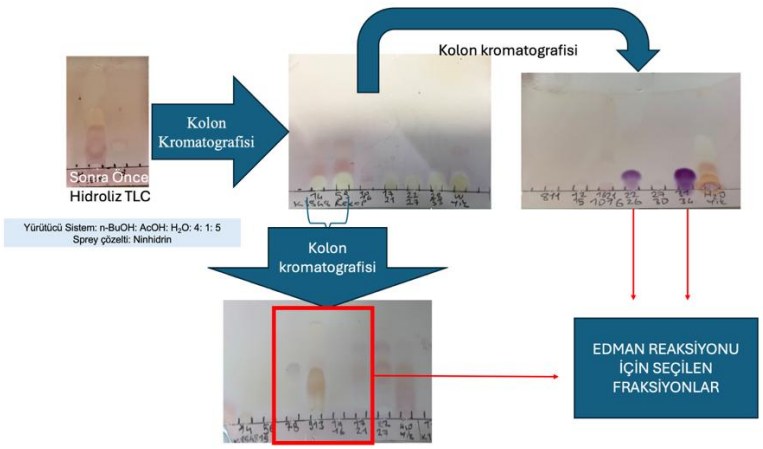


Yürütücü Sistem: n-BuOH:AcOH:H_2O:4:1:5 (CW TLC'leri için)
$CHCl_3$:Aseton:29:3 (CEO TLC'leri için)
Sprey çözelti: Ninhidrin

Görsel 3. Kör ve K_{3848}'in CEO ve CW TLC Profilleri

3.2 K_{3848} Siklopeptidinin Hidrolizlenmesi ve Elde Edilen Peptid Parçalarının İzole Edilmesi

K_{3848} peptidi asit ile hidrolizlenerek elde edilen parçalar kromatografik yöntemlerle ayrıldı (Görsel 4).



Görsel 4. K_{3848} Hidrolizatının kromatografik yöntemlerle izolasyonu

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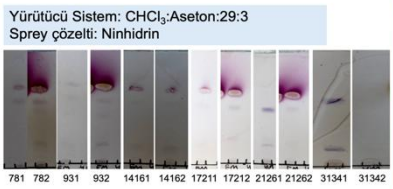
3.3 Elde Edilen Hidrolizat Parçalarının Edman Yöntemi ile Parçalanması

Edman reaksiyonunun bitimi su fazlarının (CW) TLC kontrolü ile belirlendi (Görsel 1). 1978, 913, 1416, 1721, 2226, 3134 kodlu peptid parçaları 2'şer kez parçalandı. Elde edilen ürünlerin Edman ürünlerinin TLC fotoğrafı Görsel 5'te verilmektedir.



Amino asit-PTH	Rf x100	Karşılık gelen amino asit
K19781	64	Asp
K19782	90	Phe
K9311	63	Arg
K9312	53	Leu/Ileu/Nle
K14161	73	Ser
K14162	53	Leu/Ileu/Nle
K17211	63	Arg
K17212	60	Arg
K21261	60	Arg
K21262	52	Gly
K31341	63	Arg
K31342	0	Glu

Görsel 5. K_{3848} hidrolizat fraksiyonlarından den elde edilen amino asit-PTH türevlerinin TLC profilleri-Rf değerleri-Karşılık gelen amino asit

3.4 Elde Edilen Fenil Tiyohidantoin Türevlerinin LC-MS/MS ile Kütlelerinin Belirlenmesi

LC-MS/MS cihazı ile her bir ürün için karakteristik fenil tiyohidantoin piki literatürdeki [20] standart amino asit-PTH kütle verileri ve online kütle tanılama web siteleri (https://massbank.eu/MassBank/Search, https://www.sisweb.com/software/ms/nistsearch.htm?name=cysteine&ei=on&search=Search+NIST) ile kıyaslanarak belirlenmiştir (Çizelge 1).

Çizelge 1. Amino asit-PTH türevlerinin kütleleri ve karşılık gelen amino asit-PTH türevleri

PTH-Ürünü	Kaynağı	m/z	Karşılık gelen amino asit-PTH		
			Adı	Kısaltmalar	
				3 Harfli	Tek Harfli
G71	G7	238,58	Sistein	L-Cys	C
G72		266,60	Metiyonin	D/L-Met	M
G73		266,60	Metiyonin	D/L-Met	M
G74		238,58	Sistein	L-Cys	C
B781	B78	248,55	Lösin/İzolösin/ Norlösin	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
B782		238,56	Sistein	L-Cys	C
B783		274,55[M+2]	Histidin	L-His	H
B784		266,61	Metiyonin	D/L-Met	M
B785		238,56	Sistein	L-Cys	C
B786		274,52[M+2]	Histidin	L-His	H
B787		266,61	Metiyonin	D/L-Met	M
B788		248,57	Lösin/İzolösin/ Norlösin	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
B789		274,53[M+2]	Histidin	L-His	H
K19781	K3848	257 [M+7]	Aspartik asit	L-Asp	D
K19782		286 [M+4]	Fenil alanin	L-Phe	F
K9131		295 [M+4]	Arginin	L-Arg	R
K9132		247 [M-1]	Lösin/İzolösin/ Norlösin	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
K14161		223 [M+1]	Serin	D/L-Ser	S
K14162		247 [M-1]	Lösin/İzolösin/ Norlösin	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
K17211		293 [M+2]	Arginin	L-Arg	R
K17212		295 [M+4]	Arginin	L-Arg	R
K21261		295 [M+4]	Arginin	L-Arg	R
K21262		197 [M+5]	Glisin	Gly	G
K31341		295 [M+4]	Arginin	L-Arg	R
K31342		265 [M+1]	Glutamik asit	L-Glu	E

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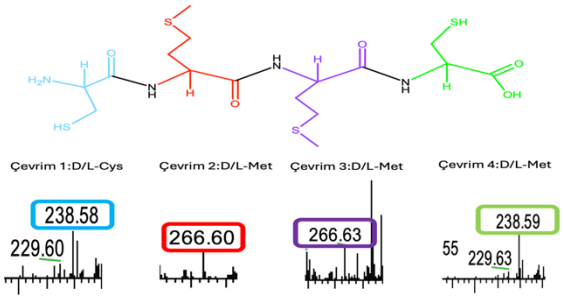
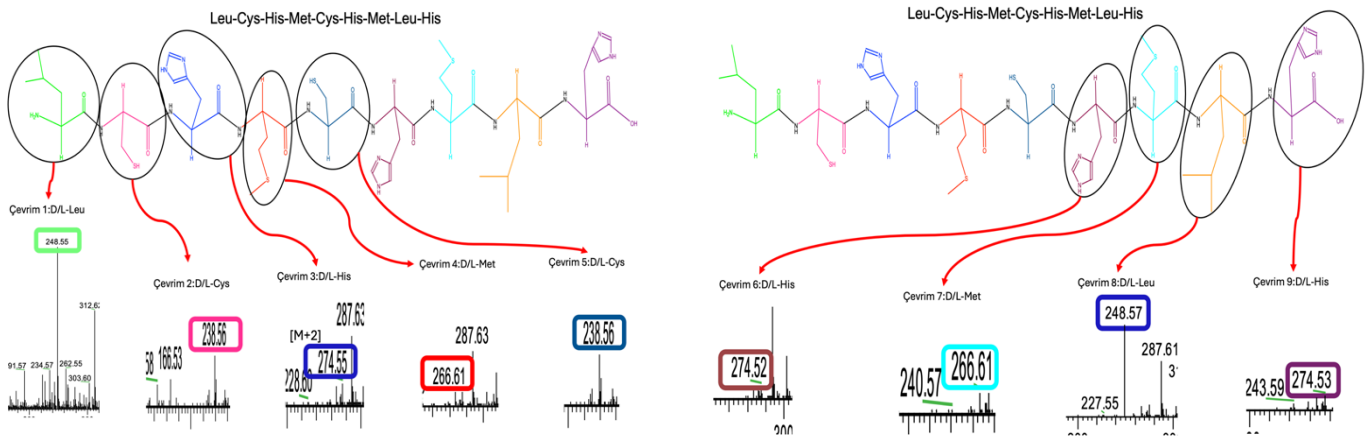
Elde edilen bulgulara göre G_7 ve B_{78}'in molekül yapıları çizilmiştir (Görsel 6-7).

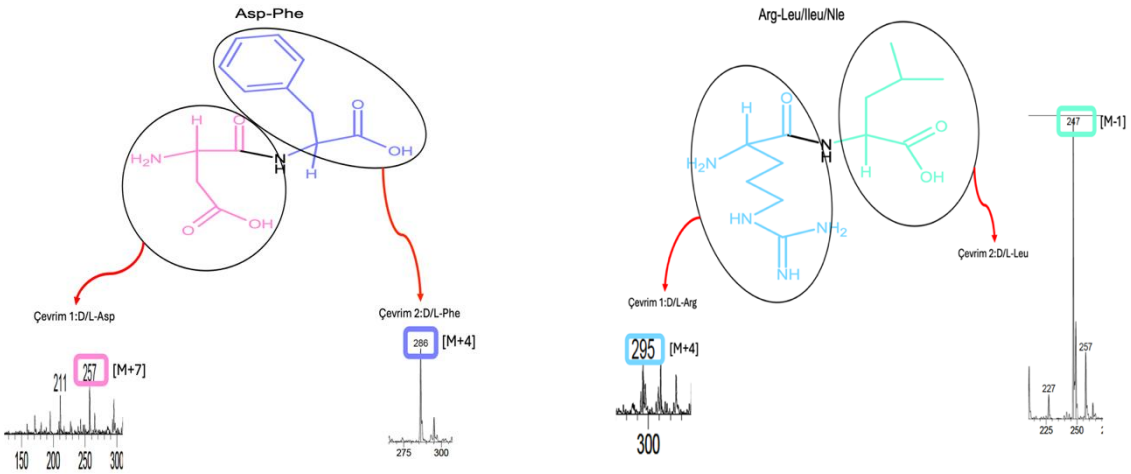


Görsel 6. G_7'nin molekül yapısı



Görsel 7. B_{78}'in molekül yapısı

K_{3848}'in hidrolizinden elde edilen peptid parçalarının Edman ürünlerinin LC-MS/MS sonuçlarına göre yapıları çizilmiştir (Görsel 8-10). Ayrıca Görsel 11'de K_{3848}'in yapısı ortaya çıkarılan dipeptid parçaları eklenerek olası bir siklik yapı çizilmiştir.



Görsel 8. K_{3848}'in 1978 ve 913 nolu fraksiyonlarının molekül yapısı

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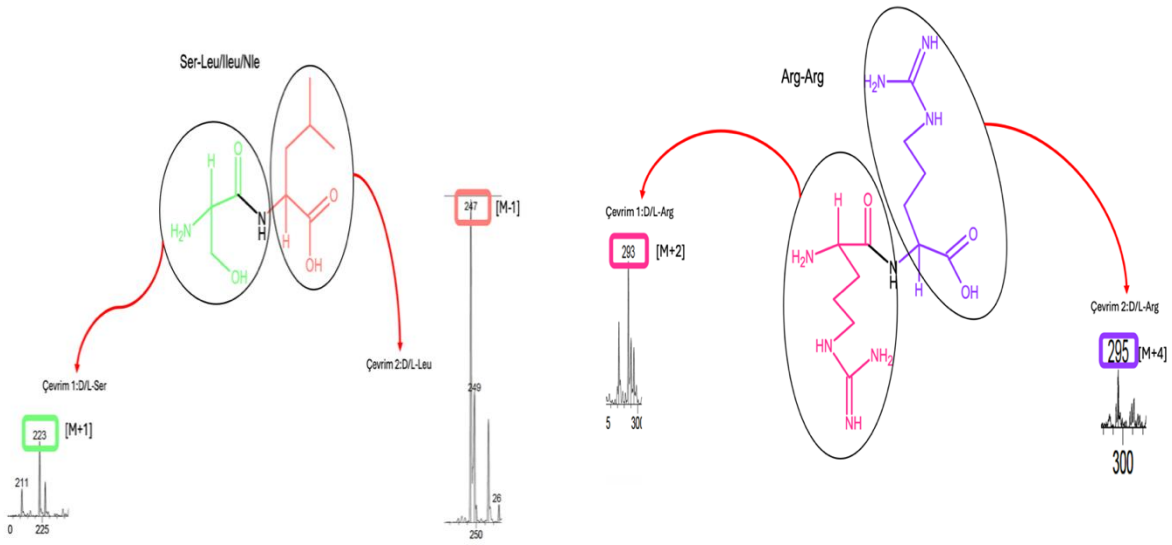
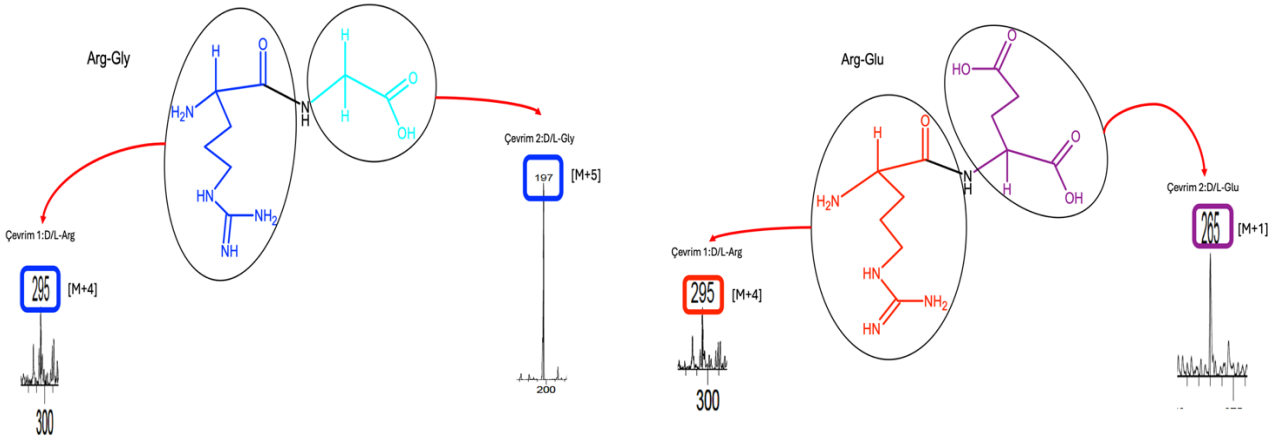
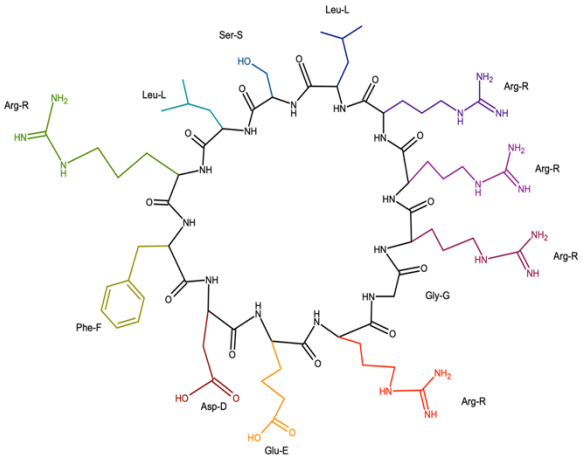


Görsel 9. K_{3848}'in 1416 ve 1721 nolu fraksiyonlarının molekül yapısı



Görsel 10. K3848'in 2126 ve 3134 nolu fraksiyonunun molekül yapısı



Görsel 11. K_{3848}'in dipeptid parçalarının birleştirilmesi sonucu oluşan olası yapılardan biri

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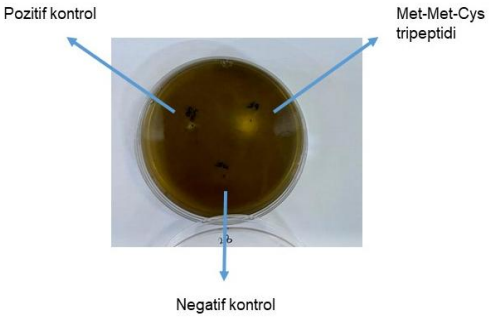
3.5 Elde edilen peptidlerin Beta-Glikozidaz Aktivite İnhibisyon Sonuçları

Alkalihalobacillus macyae MW559742, *Kocuria rosea* MW559735 ve *Bacillus simplex* KJ161411 denizel bakterilerinin MeOH ekstrelerinin, ekstrelerden elde edilen sırasıyla G_7, B_{78} ve K_{3848} kodlu saf metabolitlerinin ve bu metabolitlerin Edman yöntemi ile parçalanmasıyla elde edilen peptid parçalarının beta glikozidaz inhibitörü üretim özellikleri enzim agar plak yöntemiyle incelenmiş ve sonuçlar pozitif ve negatif kontroller ile birlikte değerlendirilmiştir (Çizelge 2). Pozitif kontrol olarak Conduritol β Epoksit (5mg/mL DMSO) kullanılmış, tüm enzim agar plaklarında 0,7 cm çaplı bir renk açımı göstermiştir. Negatif kontrol olarak Dimetilsülfoksit (DMSO) uygulanmış, enzim agar plaklarında renk açılması gözlenmemiştir (Görsel 12).

Çizelge 2. Beta-Glikozidaz Aktivite İnhibisyon Sonuçları

Beta Glikozidaz İnhibisyon Deneyi										
Ekstrakt		Saf Biyomolekül		Edman Parçaları						
Örnek Adı	İnhibisyon Çapı (cm)	Örnek Adı	İnhibisyon Çapı (cm)	Örnek Adı	İnhibisyon Çapı (cm)					
Bacillus simplex KJ161411	1,5 cm	K3848	Negatif	Hidroliz		1.Edman Parçası		2.Edman Parçası		
				K3848 1978	Negatif	19781	Negatif	19782	0,3 cm	
				K3848 19913	Negatif	9131	Negatif	9132	0,5 cm	
				K3848 19 1416	Negatif	14161	0,2 cm	14162	Negatif	
				K3848 191721	0,3 cm	17211	Negatif	17212	0,2 cm	
				K3848 1016 2126	Negatif	21261	Negatif	21262	Negatif	
				K3848 1016 3134	0,2 cm	31341	0,2 cm	31342	0,4 cm	
Kocuria rosea MW559735	1 cm	B78	0,3 cm	B781	Negatif					
				B782	0,2 cm					
				B783	0,7 cm					
				B784	Negatif					
				B785	Negatif					
				B786	Negatif					
				B787	Negatif					
				B788	Negatif					
				B789	0,2 cm					
Alkalihalobacillus macyae MW559742	2 cm	G7	0,5 cm	G71	0,2 cm					
				G72	Negatif					
				G73	0,3 cm					
				G74	0,7 cm					



Görsel 12. Alkalihalobacillus macyae MW559742 bakterisinden elde edilen Met-Met-Cys tripeptidinin enzim-agar plak yöntemi ile görüntülenmesi (İnhibisyon çapı 0,2 cm)

Özetle, *Bacillus simplex* KJ161411 bakterisinin K_{3848} saf metabolitinden elde edilen 6 adet hidroliz parçasının 4'ü negatif sonuç vermiştir. K_{3848} peptidi enzim inhibisyonu yapmamıştır, hidroliz parçalarına uygulanan Edman parçalanması ürünlerinden olan Leu/ILeu/Nle ve Glu

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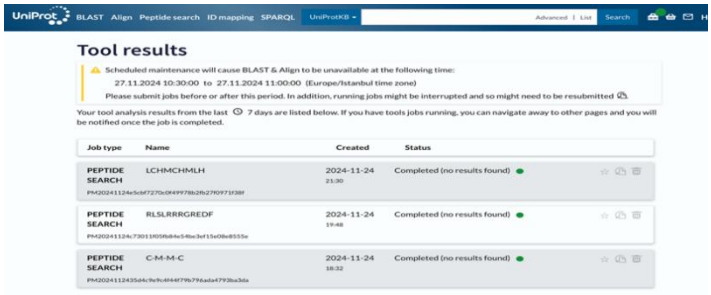
amino asitlerinin ayrı ayrı inhibitör özelliğe sahip oldukları bulunmuştur. *Kocuria rosea* MW559735 bakterisinden izole edilen B_{78} peptidine uygulanan Edman reaksiyon ürünlerinden His-Met-Cys-His-Met-Leu-His heptapeptidi ile Met-Cys-His-Met-Leu-His hekzapeptidi inhibitör özellik göstermiştir. *Alkalihalobacillus macyae* MW559742 bakterisinden elde edilen G_7 peptidinin Met-Met-Cys dizilimli tripeptid parçası ve Cys amino asidi beta glukozidaz inhibitörü olarak aktivite göstermiştir. Bunların yanı sıra, K_{14162} ve K_{21262} Edman reaksiyonu yan ürünü karışımı hariç, tüm Edman reaksiyonu yan ürünü karışımları uygulandığı enzim agar plaklarında inhibisyon zonu oluşturmuştur. Bunun nedeni Edman reaksiyonunda yan ürün olarak ortamda bulunan tiyoüre türevleri olan difeniltiyoüre (DPTU), dimetil feniltiyoüre (DMPTU) ve diğer üre bileşikleri difenilüre (DPU), ditiyotireitol (DTT) bileşiklerinden özellikle tiyoüre türevlerinin diyabetle ilişkili enzimleri inhibe etmesidir, bu özellikleri ve DM tedavisinde ilaç adayı olarak kullanılabilecekleri birçok çalışma ile kanıtlanmıştır [21].

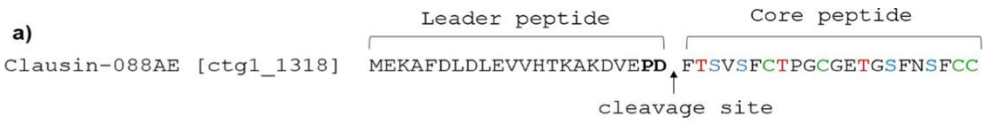
Bakteri peptidlerinin Edman ürünleri olan peptid ve aminoasit parçalarının hiçbiri, beta-glukozidaz inhibisyonu özelliği bakımından bakterinin metanol ekstraktlarından daha aktif bulunmamıştır.

Yapılarını tanımladığımız G_7, B_{78} ve K_{3848}'i daha önceki çalışmalarımızda asidik hidrolize tabi tutmuştuk. Bu hidrolizatların da LC-MS/MS'leri çekildi. https://www.biosyn.com/tew/amino-acid-masses-tables.aspx web sitesindeki tablolar kullanılarak gözlenen kütle pikleri yorumlanmıştır. G_7 hidrolizatında karboksimetil sisteine ait bir pik olan m/z 161 gözlendi. Bu yapımızdaki 2 adet sistein varlığını kanıtlar. B_{78} hidrolizatında ise m/z 139 histidin piki, 149 metiyonin piki, 161 karboksimetil sistein piki, 245 Metiyonin + Leu/Ileu/Nle piki gözlenerek yapıdaki bu amino asitlerin varlığını doğrulamıştır. K_{3848} hidrolizatında varlığı doğrulanan amino asit pikleri ise m/z 156 arginin piki, 165 fenil alanin piki, 263 Aspartik asit + Phe piki, 200 Ser + Leu/Ileu/Nle piki, 312 Arg + Arg (M +5 şeklinde), 269 Arg + Leu/Ileu/Nle piki (M+ 4 şeklinde) dir. Doğrulanan yapıların dizilim taramaları G_7 için "CMMC", B_{78} için "LCHMCHMLH", K_{3848} için "RLSLRRRGREDF" şeklinde https://www.uniprot.org/tool-dashboard peptid veritabanında taratılmış ve eşleşme bulunamamıştır (Görsel 13).



Görsel 13. Üç yapımıza ait amino asit dizilimlerinin Uniport Peptid Arama motorundaki sonuçları

Literatürde *Alkalihalobacillus macyae*'den izole edilmiş bir peptid çalışması bulunmamaktadır. Dixit vd. (2023) tarafından *Alkalihalobacillus clausii* 088AE'dan elde edilen Clausin-088AE isimli bir peptid izole edilmiştir (Görsel 14) [22]. Peptidin sistein (Cys-C) içeriği fazladır. G_7 yapımızın amino asit diziliminde de (CMMC) 2 adet sistein bulunmaktadır.



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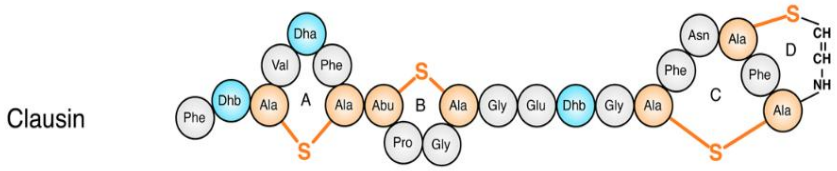
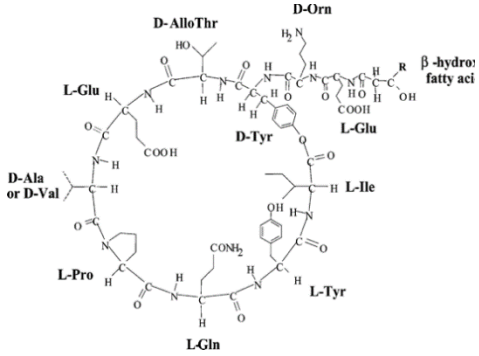
Görsel 14. Clausin-088AE'nin amino asit dizilimi

Ahire vd. (2020) *Bacillus clausii* UBBC07'den Görsel 15' deki clausin türevinin izole etmiştirlerdir [23].



Görsel 15. *Bacillus clausii* UBBC07'den elde edilen clausin türevi [23]

Bu da bize clausin yapısındaki peptidlerin Bacillus cinsi bakterilerde de var olduğunu göstermiştir. Bu yüzden bu yapıyı K_{3848} maddesinin amino asit içeriği ile de karşılaştırabiliriz. K_{3848}'in dipeptidlerini birleştirerek elde ettiğimiz olası dizilim "RLSLRRRGREDF" şeklindedir. Yapımızdaki fenil alanin (Phe-F), Glisin (Gly-G) ve aspartik asit (Asp-D) amino asitleri Bacillus cinsi bakteriden izole edilen clausindeki amino asitler ile ortaktır.
Bacillus cinsi bakterilerden çok geniş sayıda aktif peptid elde edilmiştir ve bu çalışmalar yeni inhibitör madde arayışı için umut verici bir başlangıç noktası olmuştur [24-26]. Literatürde *Bacillus simplex*'in birçok suşundan peptid izolasyonu yapılmıştır. Bunlardan biri Brezilya Amazon Havzasından yakalanmış bir balığın bağırsak içeriğinde bulunan bir Bacillus sp. bakterisinden elde edilen bir Fengycin peptididir (Görsel 16) [27-28]. P34 olarak kodlandırılan bu peptidin amino asit içeriğini K_{3848} molekülümüzün amino asitleri ile karşılaştırdığımızda Glutamik asit (Glu-E), lösinin bir türevi olan izolösin (Ileu-I) amino asitlerinin ortaklık gösterdiğini görmekteyiz.



Görsel 16. Fengycin Yapısı [28]

B_{78}'in kaynağı olan bakterimiz *Kocuria rosea* ile yapılan bir çalışmada Linares-Otoya vd. (2017) tarafından yeni koçurin isimli tiyopeptid izole edilmiştir ve antimikrobiyal aktivitesi çalışılmıştır [29]. Görsel 17'de Kocuria rosea'dan elde edilen Kocuria rosea S17 isimli tiyopeptidi ve diğer Kocuria türlerinden elde edilen (Kocuria flava HO-9041, Kocuira sp. UCD-OTCP) tiyopeptidlerin amino asit dizilimleri verilmiştir. Bu dizilimleri B_{78}'e ait

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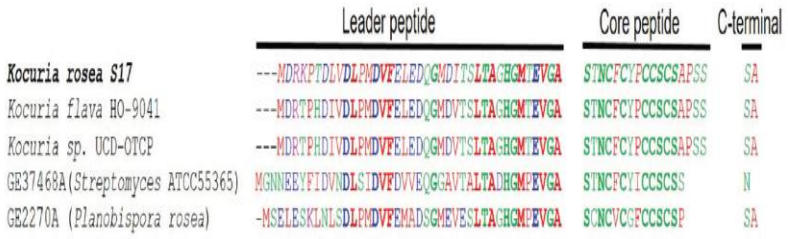
LCHMCHMLH ile karşılaştırdığımızda yapıdaki tüm amino asitleri yani lösin (Leu-L), metiyonin (Met-M), sistein (Cys-C), histidin (His-H)'i içerdiğini görmekteyiz.



Görsel 17. Kocuria sp.'den elde edilen peptidlerin amino asit dizilimleri [29]

4. GENEL DEĞERLENDİRME VE SONUÇLAR

Projemizde yapılarının aydınlanmasını amaçladığımız *Alkalihalobacillus macyae* MW559742'den elde edilen G_7, *Kocuria rosea* MW559735' dan elde edilmiş B_{78} ve *Bacillus simplex* KJ161411'den elde edilmiş K_{3848}'in amino asit dizilimleri LC-MS/MS ve TLC analizleri ile aydınlatılmıştır. Yapılardaki amino asitlerin kütle verileri bilinen amino asitler ile örtüştüğü ve bilinen amino asitlerden oluştuğu için IR- ve NMR-spektroskopik analizlerine ihtiyaç duyulmamıştır. Ancak yapıların doğrulanması için kanıtları arttırabilmek adına söz konusu analizler daha sonra gerçekleştirilecektir. Amino asit konfigürasyonlarının belirlenmesi için CD-spektrumları da çekilecektir.

Mikroorganizmaların birçoğunun potansiyel terapötik özelliğe sahip sınırsız bir doğal ürün kaynağı olduğu iyi bilinmektedir. Bu nedenle, biyoinformatik ve moleküler biyoloji temelli teknolojileri birleştirerek antidiyabetik aktiviteyle bağlantılı peptitlerin yapısal özelliklerinin araştırılması, bol miktarda bulunan bu denizel kaynaklardan keşfedilecek yeni ve aktif peptitleri kullanmak için güçlü bir araç olacaktır. Gelecekte bu çalışmaların sonuçlarından elde edilen veriler insan modelleri veya klinik denemeler kullanan araştırma çalışmalara da yön verecektir.

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THE STRUCTURAL ANALYSIS OF MARINE PEPTIDES AND INVESTIGATION OF THE BETA GLUCOSIDASE ACTIVITY OF THEIR SEQUENTIAL PEPTID FRAGMENTS

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ABSTRACT

As a nutritional supplement, bioactive peptides are protein fragments that are beneficial to human health and have various physiological functions within the human body. Some active peptides are also produced by the hydrolysis of exogenous larger peptides or proteins using protease enzymes. The continuous use of drugs, which has cured the high morbidity illnesses of the world, like cardiovascular diseases, hypertension, diabetes, cancer, and poisoning cases, is problematic because of the wrong dosage application, which is always causing problems in the treatment of these diseases. Even if it has not been faced with poisoning cases, long-term drug use is accompanied by negative situations such as serious side effects and drug addiction. Therefore, bioactive natural food sources are an alternative to reduce the risks. Marine peptides have many bioactivities, such as antidiabetic, antihypertensive, anti-HIV, anticoagulant, antimicrobial, anti-obesity, antioxidant, antiproliferative, and calcium-binding properties. Marine peptides are more isolated from the macroorganism and their related fungi in the literature. Our research on peptid isolation from marine bacteria, particularly in the unique marine environment of Turkey, has the potential to impact the field significantly. Therefore, β-glucosidase enzyme inhibitors with antidiabetic activity were analyzed. In the present study, the amino acid sequences of three peptides extracted from bacteria within the scope of the TÜBİTAK-1002 project were determined using Edman fragmentation. After fragmentation, the inhibitory activity of the β-glucosidase of consecutive peptide fragments was measured. As a result of our study, the G7 coded compound isolated from Alkalihalobacillus macyae MW559742 was determined to be a tetrapeptide with the amino acid sequence "CMMC" i.e. Cys-Met-Met-Cys; the B78 coded compound isolated from Kocuria rosea MW559735 was detected to be a nonapeptide with the amino acid sequence "LCHMCHMLH" i.e. Leu-Cys-His-Met-Cys-His-Met-Leu-His; the K3848 coded compound isolated from Bacillus simplex KJ161411 was determined to be a cyclic dodecapeptide with the amino acid sequence "RLSLRRRGREDF" i.e. Arg-Leu-Ser-Leu-Arg-Arg-Arg-Gly-Arg-Glu-Asp-Phe. In addition, the inhibitory activities of the β-glucosidase enzyme were tested for the peptide fragments found in the water phases obtained from each Edman degradation. The His-Met-Cys-His-Met-Leu-His heptapeptide and Met-Cys-His-Met-Leu-His hexapeptide fragments obtained from B78, the Met-Met-Cys tripeptide fragment obtained from G7, and the Cys amino acid showed

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enzyme inhibitory activity. Further analyses of the obtained enzyme inhibitors should be conducted, and studies on their medical use should be continued.
Keywords: Peptide, Edman Degradation, Antidiabetic Effect, β Glucosidase Inhibition Activity.

1. INTRODUCTION

Bioactive peptides are known to possess many essential bioactivities. They are used in various applications, including functional foods, cosmetics, pet food production, and healthcare [1-2]. These peptides have a molecular weight of less than 2500 Da and a size of 2-20 amino acids. The bioactivity of peptides depends on their composition and amino acid sequence. Depending on their structural properties, amino acid composition, and sequence, peptides can have antihypertensive, antioxidative, hypocholesterolemic, antibacterial, immunomodulatory, opiate-like, mineral-binding, and antithrombotic activities [3-4]. Studies have shown that marine-derived peptides can be utilized in the prevention and treatment of non-alcoholic fatty liver disease [5], wound healing [6], immune system strengthening [7], and treating HIV infections [8]. In addition, studies have discovered that marine peptides have DPP-IV (Dipeptidyl peptidase-IV) inhibitory properties, i.e., antidiabetic properties [9-11].

In the Edman method [12-14], the N-terminal amino acid is cleaved from the amino acid chain, leaving the remaining unreacted peptide or protein with one amino acid missing from its original state. The main compound of the Edman reagent, phenylisothiocyanate (PITC), forms a phenylthiocarbamoyl derivative with the amino acid at the N-terminus of the peptide in a basic condition. The peptide is then separated from one of its amino acids under acidic conditions, yielding a phenylthiohydantoin derivative. This method provides for the structure elucidation of peptides, that is, the determination of amino acid sequences, using either the manual Edman reaction or its automated version: the Edman sequencer. The resulting amino acid-PTH compounds' structures, and hence the amino acid sequences, are then determined using LC-MS/MS or HPLC-MS.

The enzyme β-glucosidase breaks up the glycosidic bonds and is involved in maintaining normal biological processes in the body, such as secondary metabolism, biotransformation, defense against pathogens in plants, and the degradation of ceramide glycoside in human tissues and cell walls [15]. In clinical diagnostics, β-glucosidase activity levels assess necrotizing enterocolitis and Gaucher disease. In pharmaceutical studies, β-glucosidase has been linked to a wide variety of diseases, including diabetes, HIV infection, metastatic cancer, and lysosomal storage disease.

Our study aimed to elucidate the structures of three peptides isolated from three different marine bacteria by determining their amino acid sequences and to investigate the antidiabetic properties of sequential peptides lacking one amino acid obtained from these peptides by Edman degradation.

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2. EXPERIMENTAL

In our research;
• Phenylthiohydantoin derivatives of available standard amino acids were synthesized.
• Pure peptides obtained from three marine microorganisms were fractionated using the Edman method, and the amino acid phenylthiohydantoin derivatives were synthesized.
• The structures of the amino acid-phenylthiohydantoin derivatives were determined using LC-MS/MS.
• To verify the structures of the amino acid-phenylthiohydantoin derivatives, they are compared with the Rf values of the phenylthiohydantoin derivatives of standard amino acids and
• LC-MS/MS data obtained from acidic hydrolyzates of the three peptides.
• Beta-glucosidase enzyme inhibition tests were performed on peptide fragments lacking one amino acid obtained after each Edman cycle.

3. RESULTS AND DISCUSSION

3.1 The standard amino acid, peptides degradations with Edman Reaction and TLC controls

For the synthesized derivatives, $CHCl_3$: Acetone: 29: 3 [16-18] was used as the TLC running solvent system, and the plate was stained with ninhydrin, and the Rf values were calculated and tabulated. The completion of the fragmentations was determined by TLC control of the water phases (CW) (Figure 1). 4 fragmentations were performed for G_7, and nine fragmentations were performed for B_{78}. TLC photographs of the obtained products are given in Figure 2. The Edman reaction of K_{3848} did not occur, i.e., no fragmentation occurred (Figure 3). This situation showed us that the N-terminus of this peptide was blocked or cyclic, i.e., it was a cyclopeptide [19].

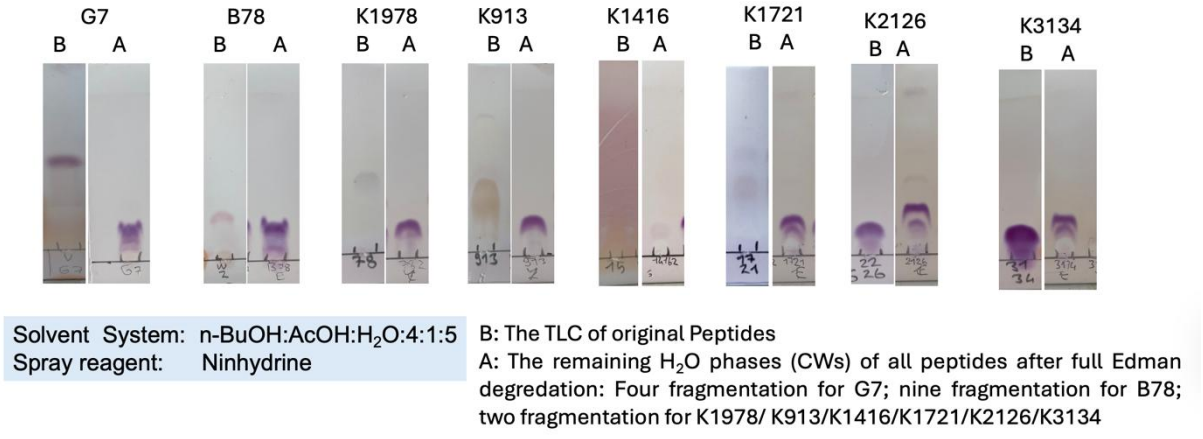
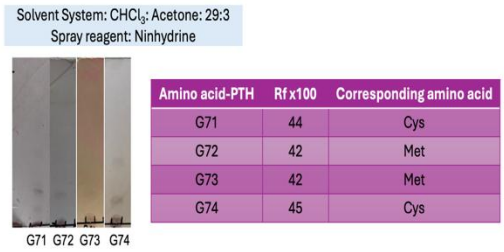
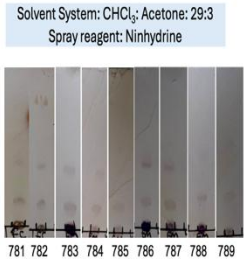


Figure 1. The TLC profile of the completion of the fragmentations H_2O phases and original peptides



Amino acid-PTH	Rf x100	Corresponding amino acid
G71	44	Cys
G72	42	Met
G73	42	Met
G74	45	Cys



Amino acid-PTH	Rf x100	Corresponding amino acid
B781	50	Leu/Ileu/NLE
B782	44	Cys
B783	43	His
B784	42	Met
B785	45	Cys
B786	43	His
B787	42	Met
B788	52	Leu/Ileu/NLE
B789	43	His

Figure 2. TLC profile and Rf values of amino acid-PTH derivatives obtained from G_7 ve B_{78}-Corresponding amino acid

CEO B1: The organic phase of 1. Blank Edman cycle
CEO B2: The organic phase of 2. Blank Edman cycle
CW B2: After two cycles of blank Edman Reaction, the remaining H_2O phase

CEO K1: The organic phase of 1. K3848 Edman cycle
CEO K2: The organic phase of 2. K3848 Edman cycle
B: K3848 before the Edman Reaction
A CW K2: K3848 after two cycles of Edman Reaction, the remaining H_2O phase

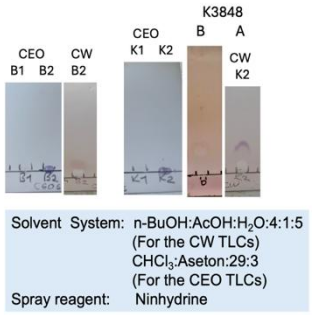


Figure 3. The CEOs ve CWs TLC Profile of Blank and K_{3848}

3.2 The Hyrolysis of Cyclopeptide: K_{3848} and the isolation of its' peptide fragments

K_{3848} hydrolysate,obtained by hydrolyzing the peptide with acid, was separated by chromatographic methods into the peptide fragments (Figure 4).

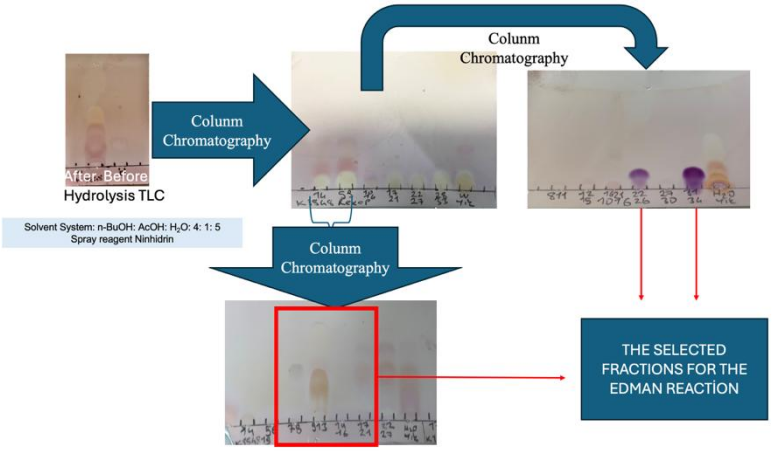


Figure 4. The separation of K_{3848} Hydrolysate with chromatographic methods

3.3 The Edman degradation of peptide fragments of K_{3848} Hydrolysate

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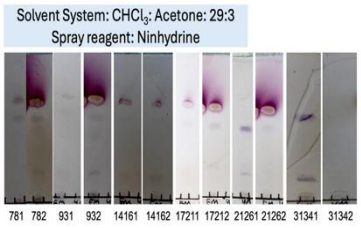
The completion of the Edman reaction was determined by TLC control of the water phases (CWs) (Figure 1). Peptide fragments coded 1978, 913, 1416, 1721, 2226, and 3134 were fragmented twice. Figure 5 shows TLC photographs of the Edman products.



Amino acid-PTH	Rf x100	Corresponding amino acid
K19781	64	Asp
K19782	90	Phe
K9311	63	Arg
K9312	53	Leu/Ileu/Nle
K14161	73	Ser
K14162	53	Leu/Ileu/Nle
K17211	63	Arg
K17212	60	Arg
K21261	60	Arg
K21262	52	Gly
K31341	63	Arg
K31342	0	Glu

Figure 5. TLC profile and Rf values of amino acid-PTH derivatives obtained from the peptide fragments of K_{3848} Hydrolysate-Corresponding amino acid

3.4 The Mass Determination of Phenylthihydantoin derivatives with LC-MS/MS

The characteristic phenylthiohydantoin peak for each product was determined by an LC-MS/MS instrument by comparison with standard amino acid-PTH mass data from literature [20] and online mass identification websites (https://massbank.eu/MassBank/Search, https://www.sisweb.com/software/ms/nistsearch.htm?name=cysteine&ei=on&search=Search+NIST) (Table 1).

Table 1. The Mass of Amino acid-PTH derivatives and ve corresponding Amino acid-PTH derivatives

PTH-Product	Source	m/z	Corresponding amino acid-PTH		
			Name	Abbreviation	
				Three-Letter	One-Letter
G71	G7	238,58	Cysteine	L-Cys	C
G72		266,60	Methionine	D/L-Met	M
G73		266,60	Methionine	D/L-Met	M
G74		238,58	Cysteine	L-Cys	C
B781	B78	248,55	Leucine/Isoleucine/ Norleucine	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
B782		238,56	Cysteine	L-Cys	C
B783		274,55 [M+2]	Histidine	L-His	H
B784		266,61	Methionine	D/L-Met	M
B785		238,56	Cysteine	L-Cys	C
B786		274,52 [M+2]	Histidine	L-His	H
B787		266,61	Methionine	D/L-Met	M
B788		248,57	Leucine/Isoleucine/ Norleucine	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
B789		274,53 [M+2]	Histidine	L-His	H
K19781	K3848	257 [M+7]	Aspartic acid	L-Asp	D
K19782		286 [M+4]	Phenylalanine	L-Phe	F
K9131		295 [M+4]	Arginine	L-Arg	R
K9132		247 [M-1]	Leucine/Isoleucine/ Norleucine	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
K14161		223 [M+1]	Serin	D/L-Ser	S
K14162		247 [M-1]	Leucine/Isoleucine/ Norleucine	D/L-Nle/ D/L-Ileu/ L-Leu	Nle/I/L
K17211		293 [M+2]	Arginine	L-Arg	R
K17212		295 [M+4]	Arginine	L-Arg	R
K21261		295 [M+4]	Arginine	L-Arg	R
K21262		197 [M+5]	Glycine	Gly	G

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According to findings, the structure of G_7 and B_{78} were drawn. (Figure 6-7).

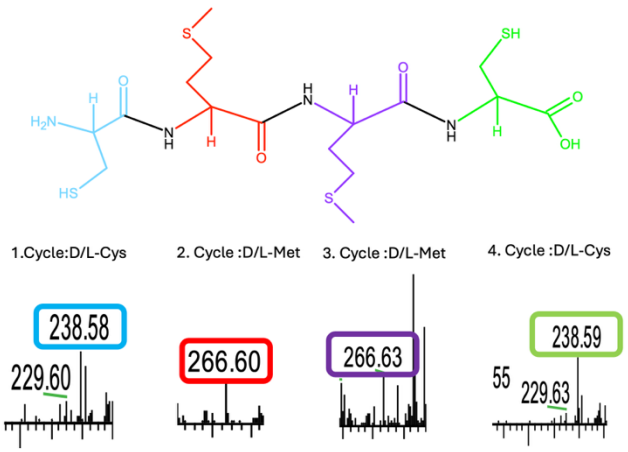

Figure 6. The molecular structure of G_7

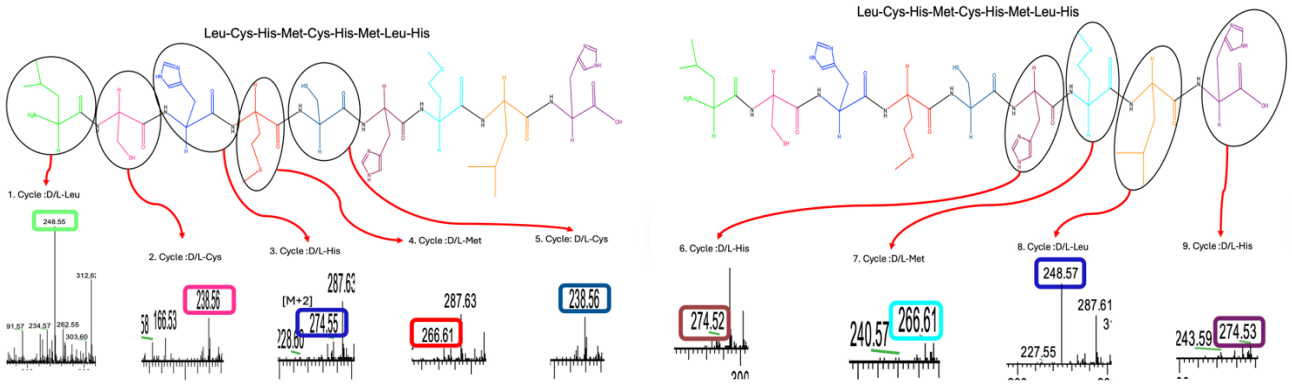

Figure 7. The molecular structure of B_{78}

The structures of the peptide fragments obtained from the hydrolysis of K_{3848} were drawn based on the LC-MS/MS results of the Edman products (Figures 8-10). Additionally, a possible cyclic structure was drawn by adding the dipeptide fragments from which the structure of K_{3848} was revealed in Figure 11.

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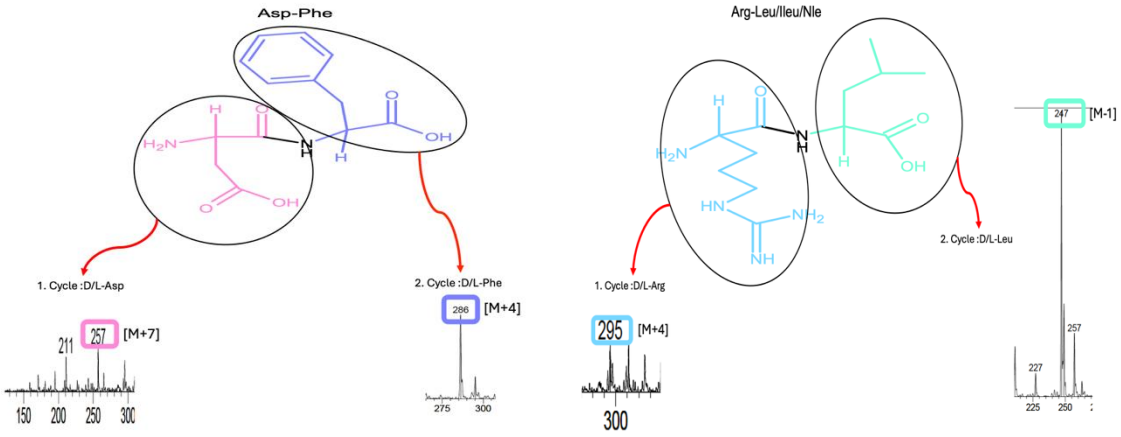

Figure 8. The molecular structure of 1978 and 913 codded peptide fragments of K_{3848} hydrolysate

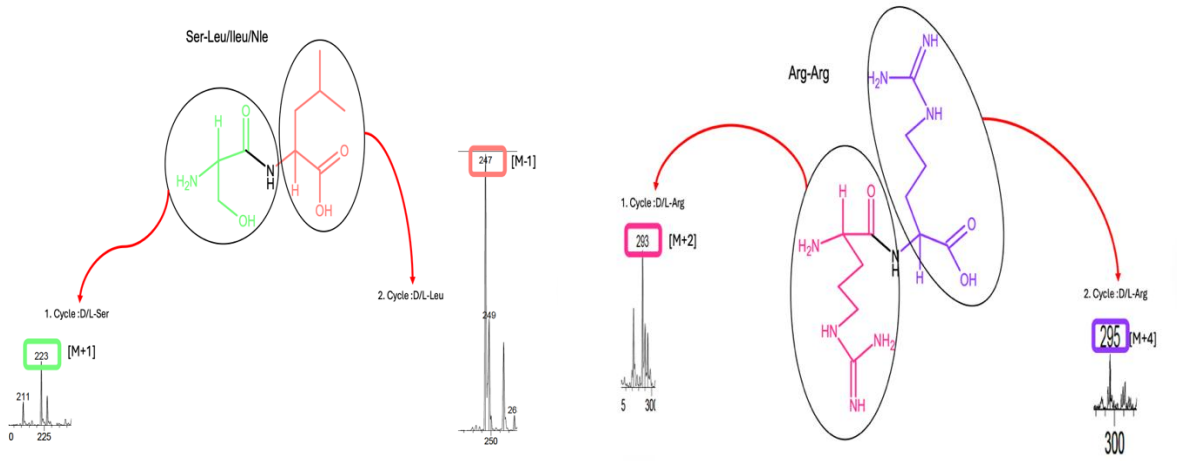

Figure 9. The molecular structure of 1416 and 1721 codded peptide fragments of K_{3848} hydrolysate

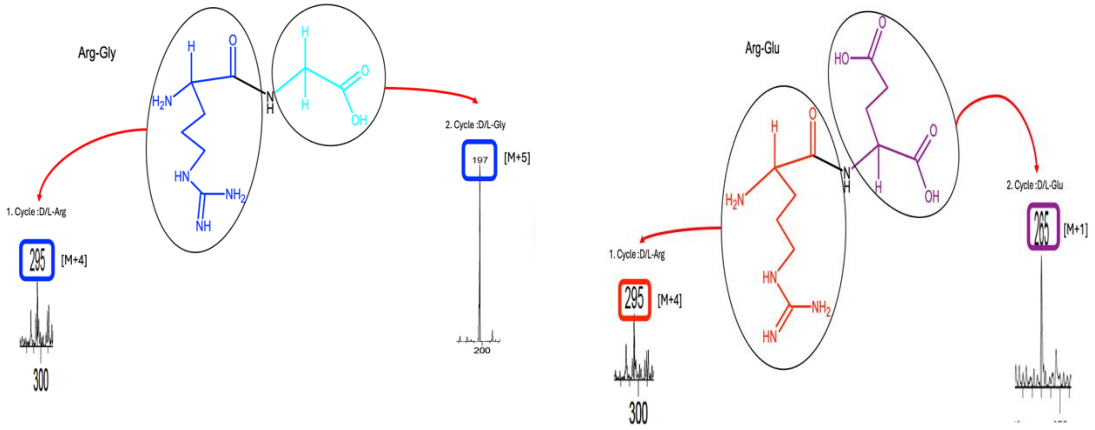

Figure 10. The molecular structure of 2126 and 3134 codded peptide fragments of K_{3848} hydrolysate

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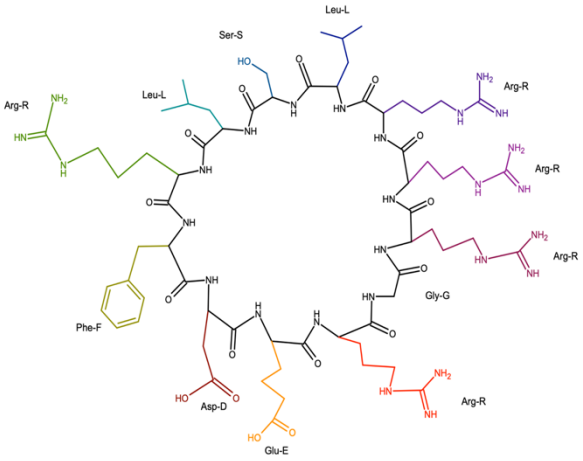

Figure 11. A possible cyclic structure was drawn by adding the dipeptide fragments from which the structure of K_{3848}

3.5 The results of Beta-Glucosidase inhibitory activity of the obtained peptides

Beta-glucosidase inhibitory properties of MeOH extracts of marine bacteria *Alkalihalobacillus macyae* MW559742, *Kocuria rosea* MW559735, and *Bacillus simplex* KJ161411, their pure metabolites, coded G_7, B_{78}, and K_{3848}, obtained from the extracts, respectively, and peptide fragments obtained by Edman method were investigated by the enzyme-agar plate method. The results were evaluated with positive and negative controls (Table 2-4). Conduritol β-Epoxide (5 mg/mL DMSO) was used as the positive control, and a color lightening of 0.7 cm in diameter was observed on all enzyme agar plates. Dimethylsulfoxide (DMSO) was used as the negative control, and no color lightening was observed on the enzyme agar plates (Figure 12).

Table 2. The Results of Beta-Glucosidase Inhibitory Activity for G_7

Beta Glucosidase Inhibition Assay					
Extract		Pure Biomolecule		Edman Products	
Sample	The Diameter of Inhibition (cm)	Sample	The Diameter of Inhibition (cm)	Sample	The Diameter of Inhibition (cm)
Alkalihalobacillus macyae MW559742	2	G_7	0.5	G_{71}	0.2
				G_{72}	Negatif
				G_{73}	0.3
				G_{74}	0.7

Table 3. The Results of Beta-Glucosidase Inhibitory Activity for B_{78}

Beta Glucosidase Inhibition Assay					
Extract		Pure Biomolecule		Edman Products	
Sample	The Diameter of Inhibition (cm)	Sample	The Diameter of Inhibition (cm)	Sample	The Diameter of Inhibition (cm)
Kocuria rosea MW559735	1	B_{78}	0.3	B_{781}	Negatif
				B_{782}	0.2
				B_{783}	0.7
				B_{784}	Negatif
				B_{785}	Negatif
				B_{786}	Negatif
				B_{787}	Negatif
				B_{788}	Negatif
				B_{789}	0.2

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Table 4. The Results of Beta-Glucosidase Inhibitory Activity for K_{3848}

Beta Glucosidase Inhibition Assay									
Extract		Pure Biomolecule		Edman Products					
Sample	The Diameter of Inhibition (cm)	Sample	The Diameter of Inhibition (cm)	Sample	The Diameter of Inhibition (cm)				
				Hydrolysis		1.Edman product		2.Edman Product	
Bacillus simplex KJ161411	1.5	K_{3848}	Negatif	1978	Negatif	K19781	Negatif	K19782	0.3
				913	Negatif	K9131	Negatif	K9132	0.5
				1416	Negatif	K14161	0.2	K14162	Negatif
				1721	0.3	K17211	Negatif	K17212	0.2
				2126	Negatif	K21261	Negatif	K21262	Negatif
				3134	0.2	K31341	0.2	K31342	0.4

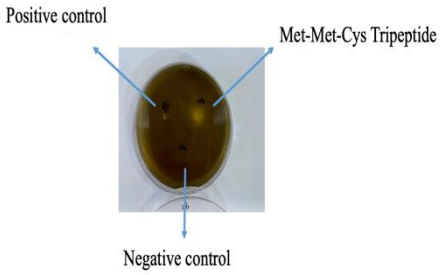

Figure 12. The agar-enzyme plate photo of Met-Met-Cys tripeptite obtained from *Alkalihalobacillus macyae* MW559742 (Inhibition diameter: 0,2 cm)

In summary, 4 of 6 hydrolysis fractions obtained from the pure metabolite K_{3848} of *Bacillus simplex* KJ161411 gave negative results. The K_{3848} peptide did not inhibit the enzyme, whereas its Edman degradation products, Leu/ILeu/Nle and Glu, were found to have individual inhibitory properties. The His-Met-Cys-His-Met-Leu-His heptapeptide and Met-Cys-His-Met-Leu-His hexapeptide, which were Edman reaction products of B_{78} peptide isolated from the bacterium *Kocuria rosea* MW559735, showed inhibitory properties. The tripeptide fragment with the sequence Met-Met-Cys and the amino acid Cys of the G_7 peptide obtained from the *Alkalihalobacillus macyae* MW559742 showed activity as beta-glucosidase inhibitors. In addition, all Edman reaction by-product mixtures, except for the K_{14162} and K_{21262} Edman reaction by-product mixtures, formed an inhibition zone on enzyme agar plates. Since thiourea derivatives such as diphenylthiourea (DPTU), dimethyl phenylthiourea (DMPTU), and other urea compounds, diphenylurea (DPU), and dithiothreitol (DTT), as by-products in the Edman reaction, inhibit diabetes-related enzymes. These properties and their potential as drug candidates in the treatment of DM have been proven by many studies [21].

None of the Edman products was found to be more active than the bacteria's methanol extracts in terms of beta-glucosidase inhibition.

Our previous studies subjected G_7, B_{78}, and K_{3848} to acidic hydrolysis. LC-MS/MS analyses were also performed on these hydrolyzates. The observed mass peaks were interpreted using the tables available at https://www.biosyn.com/tew/amino-acid-masses-tables.aspx. In the G_7 hydrolysate, a peak at m/z 161 belonging to carboxymethyl cysteine was observed. This proves

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the presence of cysteine in our structure. In the B_{78} hydrolysate, histidine peak at m/z 139, methionine peak at 149, carboxymethyl cysteine peak at 161, and methionine + Leu/Ileu/Nle peak at 245 were observed, confirming the presence of these amino acids in the structure. The amino acid peaks confirmed in the K_{3848} hydrolysate are m/z 156 arginine peak, phenylalanine peak at 165, aspartic acid + Phe peak at 263, ser + Leu/Ileu/Nle peak at 200, arg + Arg (as M +5), and arg + Leu/Ileu/Nle peak at 269 (as M +4). The sequence scans of the confirmed structures were searched in the peptide database https://www.uniprot.org/tool-dashboard as "CMMC" for G_7, "LCHMCHMLH" for B_{78}, and "RLSLRRRGREDF" for K_{3848}, and no matches were found (Figure 13).

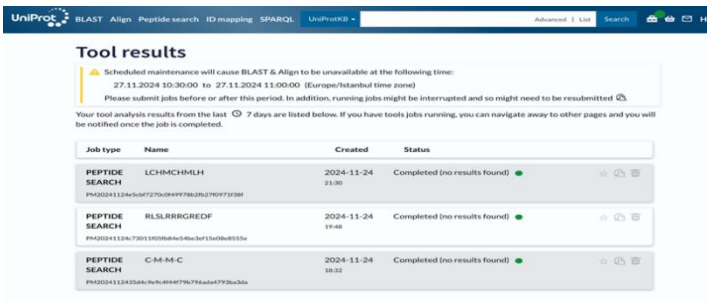

Figure 13. The scanning results of three structure in the Uniport Peptide Research engine

There are no studies on a peptide isolated from Alkalihalobacillus macyae. A peptide named Clausin-088AE was isolated from Alkalihalobacillus clausii 088AE by Dixit et al. (2023) (Figure 14) [22]. The peptide has a high cysteine (Cys-C) content. We also have two cysteines in the amino acid sequence (CMMC) of the G7 structure.

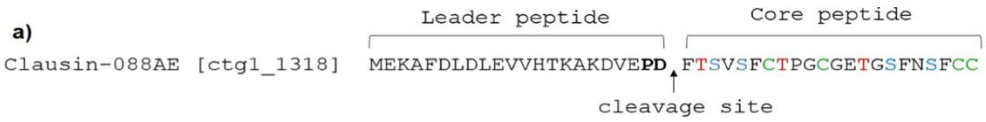

Figure 14. The amino acid sequence of Clausin-088AE

Ahire et al. (2020) isolated the clausin derivative from Bacillus clausii UBBC07 (Figure 15) [23].

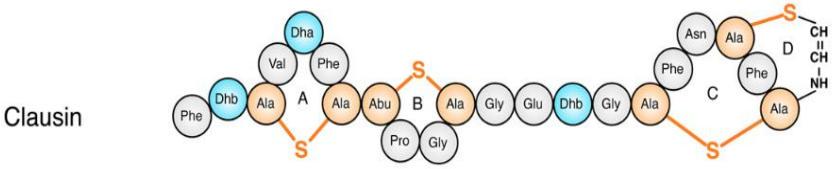

Figure 15. The clausin derivative from *Bacillus clausii* UBBC07 [23]

This showed us that peptides with the clausin structure also exist in the genus Bacillus. Therefore, we can compare this structure with the amino acid content of K_{3848}. The probable sequence we obtained by combining the dipeptides of K3848 is "RLSLRRRGREDF." The

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amino acids phenylalanine (Phe-F), glycine (Gly-G), and aspartic acid (Asp-D) in our structure are similar to the amino acids in clausin isolated from Bacillus bacteria.

Many active peptides have been obtained from the genus Bacillus, and these studies have provided a promising starting point for the search for new inhibitors [24-26]. Peptides have been isolated from many strains of *Bacillus simplex* in the literature. One of these is the Fengycin peptide (Figure 16) [27-28], obtained from a Bacillus sp. bacterium found in the intestinal contents of a fish caught in the Brazilian Amazon Basin. When we compare the amino acid content of this peptic $_8$ molecule, we see that the amino acids glutamic acid (Glu- ve of leucine, are common.

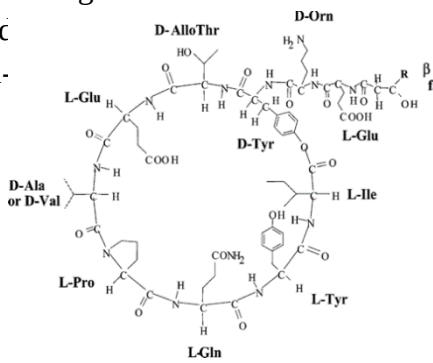

Figure 16. The molecular structure of Fengycin [28]

In another study conducted with our bacterium, Kocuria rosea, the source of B_{78}, a new thiopeptide named kocurine was isolated by Linares-Otoya et al. (2017), and its antimicrobial activity was studied [29]. Figure 17 shows the amino acid sequences of the thiopeptide named Kocuria rosea S17 obtained from Kocuria rosea and other Kocuria species (Kocuria flava HO-9041, Kocuira sp. UCD-OTCP). When we compare these sequences with B_{78} (LCHMCHMLH), we see that it contains all the amino acids in the structure, namely leucine (Leu-L), methionine (Met-M), cysteine (Cys-C), and histidine (His-H).

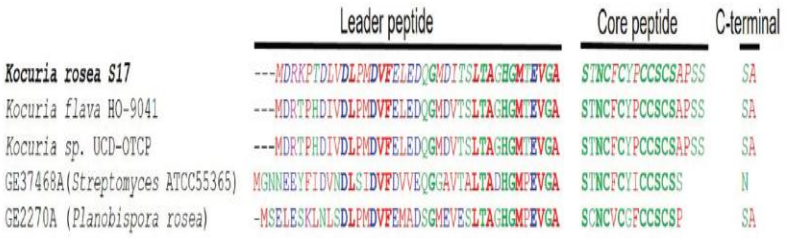

Figure 17. The amino acid sequence of some Kocuria sp. peptides [29]

4. CONCLUSION

In our project, we aimed to elucidate the amino acid sequences of G_7 from *Alkalihalobacillus macyae* MW559742, B_{78} from *Kocuria rosea* MW559735, and K_{3848} from *Bacillus simplex* KJ161411. These sequences were elucidated using LC-MS/MS and TLC analyses. Because the amino acid mass data in the structures matched those of known amino acids and the structures were composed of known amino acids, IR and NMR spectroscopic analyses were not required.

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However, these analyses will be performed later to increase the evidence for structural confirmation. CD-spectra will also be obtained to determine amino acid configurations.

It is well known that microorganisms represent an unlimited source of natural products, many of which possess potential therapeutic properties. Therefore, investigating the structural properties of peptides associated with antidiabetic activity by combining bioinformatics and molecular biology-based technologies will be a powerful tool for exploiting the discovery of new and active peptides from these abundant marine resources. Future data from these studies will also guide research using human models or clinical trials.

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MARDİN İLİ TARIM ARAZİLERİNİN TRAFİK VE TARIMSAL FAALİYET KAYNAKLI KİRLİLİK DÜZEYİNİN TOPRAK ÖRNEKLERİYLE İNCELENMESİ

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ÖZET

Kara yolu kenarındaki tarım arazileri hem trafikten kaynaklanan hem de tarımsal faaliyetlerden kaynaklanan kirliliğe maruz kalmaktadır. Bu durum, toprağın verimliliğinin azalması, su kaynaklarının kirlenmesi ve insan ile diğer canlıların olumsuz yönde etkilenmesi gibi birçok istenmeyen duruma yol açmaktadır. İpek yolu, Mardin ilinin Kızıltepe ve Nusaybin ilçelerinden geçen ve yoğun bir trafiğin olduğu tarihi bir yol özelliğindedir. Aynı zamanda, yolun her iki tarafında bulunan verimli arazilerde yıllardır tarımsal faaliyetler yürütülmektedir. Konu olan arazi topraklarının etkilenme durumu ve derecesinin bilinmesi hayati bir önem taşımaktadır. Bu bağlamda, mevcut çalışmanın amacı, Kızıltepe-Nusaybin ilçeleri arasındaki İpek Yolu güzergâhındaki tarım topraklarında trafik ve tarımsal faaliyetlerden kaynaklanan değişimleri belirlemektir. Çalışma 2025 yılında yapılmış olup, yüzey toprak (N=20) örnekleri yolun sağ ile solundan 10 km'lik ara ile yola 5 m ve 50 m mesafeden ve 0–30 cm derinlikten alınmıştır. Örneklerde, toprak tekstürü, saturasyon, pH, kireç, organik madde, azot ve ICP-OES ile birlikte çeşitli elementlerin (Pb, Cd, Ni, Zn, Cu ve Cr) konsantrasyonları belirlenmiştir. Analizler sonucunda, toprak tekstürünün killi tınlı bir yapıya sahip olduğu, pH değerlerinin 6.30-7.60, kireç değerlerinin %15.61-30.04, organik madde miktarının %0.05-1.14, azot değerinin %0.09-0.18 ve saturasyon değerinin %58.96-68.42 arasında değiştiği tespit edilmiştir. Ayrıca, Pb, Cd, Ni, Zn, Cu ve Cr bakımından en yüksek değerin sırasıyla 0.489, 0.394, 0.883, 3.569, 5.014 ve 1.989 mg/kg olduğu bulunmuştur. Topraklardaki yol mesafesinin artmasıyla birlikte Pb, Ni, Fe, Mn, Zn, Cr ve Cu içeriklerinin azaldığı; karayolu ile trafiğin ve tarımsal faaliyetlerin toprağı etkileyebileceği görülmüştür. Sonuç olarak, elde edilen verilerin Türkiye ve Avrupa'da toprakta müsaade edilen ağır metal sınır değerlerinin altında olduğu belirlenmiştir.

Anahtar Kelimeler: Ağır metal, Sürdürülebilirlik, Toprak kirliliği, İpek Yolu, ICP-OES

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INVESTIGATION OF POLLUTION LEVELS IN AGRICULTURAL LANDS OF MARDIN PROVINCE DUE TO TRAFFIC AND AGRICULTURAL ACTIVITIES THROUGH SOIL SAMPLING

ABSTRACT

Agricultural lands along the roadside are exposed to pollution from both traffic and agricultural activities. This situation leads to many undesirable outcomes, such as decreased soil fertility, contamination of water resources, and adverse effects on humans and other living organisms. The Silk Road is a historical route that passes through the districts of Kızıltepe and Nusaybin in Mardin Province, characterized by heavy traffic. Additionally, agricultural activities have been carried out for years in the fertile lands on both sides of the road. Understanding the extent and degree of the impact on these soils is of vital importance. In this context, the aim of the present study is to identify the changes in agricultural soils along the Silk Road route between the districts of Kızıltepe and Nusaybin due to traffic and agricultural activities. The study was conducted in 2025, and surface soil samples (N=20) were collected at 10 km intervals from both the right and left sides of the road, at distances of 5 m and 50 m from the road and at a depth of 0–30 cm. The samples were analyzed for soil texture, saturation, pH, lime content, organic matter, nitrogen, and the concentrations of various elements (Pb, Cd, Ni, Zn, Cu, and Cr) using ICP-OES. The analyses revealed that the soil texture was clayey loam, with pH values ranging from 6.30 to 7.60, lime content between 15.61% and 30.04%, organic matter content from 0.05% to 1.14%, nitrogen content from 0.09% to 0.18%, and saturation values between 58.96% and 68.42%. Furthermore, the highest concentrations for Pb, Cd, Ni, Zn, Cu, and Cr were found to be 0.489, 0.394, 0.883, 3.569, 5.014, and 1.989 mg/kg, respectively. It was observed that as the distance from the road increased, the contents of Pb, Ni, Fe, Mn, Zn, Cr, and Cu decreased, indicating that highways, traffic, and agricultural activities can affect the soil. As a result, it was determined that the obtained data are below the permissible heavy metal threshold values for soil in Turkey and Europe.

Keywords: Heavy metal, Sustainability, Soil pollution, Silk Road, ICP-OES

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DURHAM CİHAZI KULLANILARAK GERÇEKLEŞEN AEROPALİNOLOJİK ÇALIŞMALARIN YER ALDIĞI TEZLER: 2000-2025 LİTERATÜR TARAMASI

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ÖZET

Bu çalışma ile Türkiye' deki bölgelerde çalışılan ve yayınlanan Durham Cihazı kullanılarak yapılan aeropalinolojik çalışmalardan tez olarak kabul edilen çalışmaların değerlendirmesi amaçlanmıştır. Bu amaçla, Yükseköğretim Kurulu Başkanlığı Tez Merkezi'nde kayıtlı 2000-2025 yılları arasında Durham Cihazı kullanılarak yapılan aeropalinolojik çalışmaladan oluşan tezler araştırmanın kapsamını oluşturmaktadır. Sonuç olarak Tez Merkezinde yer alan 45 tezde Durham cihazı kullanılmış olup tezler içerik analizi ile incelenmiştir.

Anahtar Kelimeler: Durham, Aeropalinoloji, Gravimetrik yöntem

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SESELİ RESİNOSUM'DA (APİACEAE) ERKEK GAMETOFİT GELİŞİMİ

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ÖZET

Zonguldak-Bartın yörelerinde yayılış gösteren ve endemik bir bitki olan Seseli resinosum 'un Freyn & Synth embriyolojisini çalışmak amacıyla erkek gametofit gelişimi incelenmiştir. Seseli resinosum'un çiçek tomurcuklarından alınan enine kesitlerde mikrospor ana hücresinden itibaren bir redüksiyon bölünme olan mayoz bölünmenin safhaları ile mikrospor oluşumu, genç polen ve olgun polen evreleri gözlenmiştir. Birbirinden farklı 5 evrede (leptoten, zigoten, pakiten, diploten, diakinez) izlenebilen Profaz I'in 4 evresi (leptoten, zigoten, pakiten, diploten) ve tüm mayoz bölünme safhaları ayırt edilebilmiştir.

Çiçekli bitkilerde II. mayozda iğ ipliklerinin birbirine olan konumlarına göre oluşan 5 tip mikrospor tetradından (tetrahedral, izobilateral, dekusat, T-şeklinde, Linear) Seseli resinosum' da Đzobilateral tatrad ve Tetrahedral tetrad'a rastlanılmıştır.

Anahtar Kelimeler: Seseli resinosum, Embriyoloji, Mikrospor

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EVALUATION OF THE EXPRESSION LEVELS OF GENES ASSOCIATED WITH SALT STRESS IN COTTON

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Abstract:

Soil salinity affects growth and development of all agricultural plants. Depending on how well they can withstand the impacts of salt stress, some plants are more impacted than others. Cotton is a plant that plays an important role in the industry, and our daily lives, and is of exceptional importance in the socio-economic development of Azerbaijan. Among agricultural crops, cotton has a moderate tolerance to salt stress. The production of salt-tolerant cotton germplasm, which is then followed by indirect selection or hybridization procedures, requires variation for salinity tolerance increasing factors (morphological, physiological, and genetic). Because this feature depends on a number of parameters, the production of salt-tolerant genotypes has had limited success. Furthermore, the factors and their interactions are not fully understood. However, the complexity of salt tolerance may now be explored through transcriptome profiling because to developments in molecular-genetic approaches. Since most commercial cotton varieties are sensitive to salt, identification of resistant genotypes, investigation of the molecular-genetic basis of salt resistance, identification of gene sources resistant to salinity stress, and their application in breeding remain important issues. The main objective of the research was to assess the expression level of genes associated with salt stress in cotton varieties and lines that differ in salt (NaCl) resistance stored in the Azerbaijan National Genebank. A total of 48 genotypes were used as the material for the study, including 32 genotypes belonging to the species *G. hirsutum L.*, one genotype belonging to the species *G. barbadense* L., and 15 cotton lines. 13 of the genotypes were local (Azerbaijan) and 35 were introduced genotypes. During a comprehensive comparison of the morphophysiological parameters studied for the selection of salt-resistant genotypes, it was found that AP-317 was resistant among local varieties, and among introduced varieties, Navai-9, Tashkent-2, Tashkent-3, from Uzbekistan, Kyrgyzstan-174 from Kyrgyzstan and Beyaz altun-440 from Turkey were resistant. Among the lines, CSB-05, CSB-16, CSB-11, and CSB-22 genotypes were identified as resistant genotypes, showing a minimum decrease in morphophysiological indicators under the studied high-concentration stress of NaCl salt. According to the results of the least significant difference test for the control and stress-treated variants, it was determined that there was a significant difference (mean difference significant at the 0.05 level) in the expression levels of the *GhSOD, GhCAT1* and *GhMT3a* genes under both stress variants and the control, in the expression levels of the *GhDi19-1* gene under the control and 100 mM NaCl salt, and in the expression levels of the *GhNHX1, GhERF2, GhAPX1, GhDREB, GhFSD1, GhDi19-2* and *GhCIPK6* genes under the control and 200 mM NaCl salt stress conditions. However, during the analysis of the change in expression patterns under stress conditions compared to the control variant, both a decrease and an increase in the expression of the 13 genes studied were observed in resistant and sensitive genotypes selected according to biometric parameters. Thus, based on the obtained data, similar and different levels of transcripts in samples belonging to different geographical groups and

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differing in salt tolerance indicate that salt tolerance has a complex genetic control and such diversity in resistant varieties has an individual potential level of resistance.

Keywords: cotton, salinity, gene expression

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DEVELOPMENT OF TECHNOLOGY FOR OBTAINING DRUG NANOPARTICLES FROM MEDICINAL PLANTS USING GREEN SYNTHESIS METHOD

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Abstract

The main goal of the study is to develop an optimal version of the technology for obtaining medicinal nanoparticles from extracts and homogenates of medicinal plants using the green synthesis method. The objects of the study will be the medicinal plants Melissa officinalis L., Eleaegnus caspica, and Scutellaria baicalensis. Extracts and homogenates will be prepared from various organs of these plants (leaves, flowers, fruits, roots). In these extracts and homogenates, medicinal Ag and Fe0, FeO nanoparticles will be synthesized from silver AgNO3, iron FeCl2, FeCl3, FeSO4, Fe (NO3) salts. The physical and morphological properties of the nanoparticles will be analyzed by SEM, TEM, XRD, UV-vis, FTIR, GC-MS methods. UV-Vis spectroscopy proves the formation of medicinal nanoparticles with different surface plasmon resonance bands between 300 - 450 nm. Medicinal plants contain terpenes, phenolic components, volatile compounds, phenols, etc. These components play an important role in the synthesis of nanoparticles as reducing and stabilizing agents, thus helping them to transform into drug nanoparticles. The dependence of the size, shape, and amount of drug nanoparticles on the dose, extraction time, and stabilization time will be studied. The sizes and shapes of the synthesized nanoparticles will be analyzed by SEM and TEM spectroscopy, the crystallinity properties by XRD analysis, and the functional groups involved in the synthesis process of biologically active molecules in the extracts by FTIR method. The pharmacological properties of the synthesized Ag and Fe nanoparticles will be investigated using cell lines to treat various diseases such as bronchitis, asthma, cough and fever, menstrual problems, migraine, dizziness, skin problems, eczema, gout, insect bites and stings, and various forms of cancer.

Keywords: medicinal plants, nanopartcles, extracts

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STUDYING THE INTERACTION OF GLYCYRRHIZIN AND P53 PROTEIN FAMILY USING MOLECULAR DOCKING

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ABSTRACT

Licorice root (Glycyrrhiza glabra) is a widely used medicinal plant with a long history in both traditional and modern medicine. Its pharmacological activity is largely attributed to glycyrrhizic acid and its aglycone, glycyrrhetinic acid. These include anti-inflammatory, antiviral, hepatoprotective, antioxidant, and anticancer properties. Due to their ability to interact with multiple cellular targets, these compounds have gained significant attention as lead molecules in drug discovery, particularly in the field of oncology. The present study aims to investigate the molecular interaction between glycyrrhizin and the tumor suppressor p53 protein, as well as other members of the p53 protein family, including p63 and p73, using in silico molecular docking approaches. The p53 protein functions as a transcription factor that maintains genomic stability by regulating DNA repair, apoptosis, and cell cycle arrest in response to cellular stress. It is encoded by the TP53 gene, which is found to be mutated in nearly 50% of all human cancers. Such mutations often result in the loss or alteration of p53 function, thereby facilitating tumor progression and resistance to therapy. Molecular docking simulations were carried out to determine the binding affinities of glycyrrhizin with isolated proteins (p53, p63, and p73), their DNA complexes, and standalone DNA structures. As summarized , glycyrrhizin exhibited the highest binding affinity with the p53–DNA complex (−12.9 kcal/mol), followed by the p53 protein alone (−12.6 kcal/mol), and DNA (−11.7 kcal/mol). Comparable interactions were also observed with p63 and p73 and their respective DNA complexes. These results suggest that glycyrrhizin may function as a potential stabilizer

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or allosteric modulator of tumor suppressor proteins, offering new avenues for anticancer drug development.

Keywords: Glycyrrhizin, p53 protein, molecular docking, anticancer activity, licorice root.

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NUTRİGENOMİK PERSPEKTİFTEN OBEZİTENİN YÖNETİMİ: FONKSİYONEL BİLEŞİKLERLE GENETİK REGÜLASYON

MANAGEMENT OF OBESITY FROM A NUTRIGENOMIC PERSPECTIVE: GENETIC REGULATION WITH FUNCTIONAL COMPOUNDS

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ÖZET

Obezite, genetik yatkınlık ile yaşam tarzı ve beslenme alışkanlıklarının etkileşimi sonucu ortaya çıkan kompleks bir metabolik sendromdur. Günümüzde nutrigenomik, besin bileşenlerinin gen ekspresyonu ve epigenetik düzenlemeler üzerindeki etkilerini inceleyerek obezitenin önlenmesi ve tedavisinde kişiselleştirilmiş beslenme stratejilerinin geliştirilmesine olanak sağlamaktadır. Obezite ile ilişkili temel yolaklar arasında adipogenez (PPARγ, SREBP-1c, FAS), termojenez (UCP1, PRDM16, PGC-1α), mitokondriyal biyogenez (TFAM, NRF1/2) ve inflamasyon (TNF-α, IL-6, NF-κB) öne çıkmaktadır. Son yıllarda yapılan in vitro, hayvan ve klinik çalışmalar; resveratrol, pterostilben, ellagik asit, kurkumin, EGCG ve L-theanin gibi fonksiyonel bileşiklerin bu gen ve yolakları hedef alarak obeziteye karşı koruyucu ve terapötik etki gösterebildiğini ortaya koymuştur. Bu bileşikler, PPARγ ve SREBP-1c ekspresyonunu baskılayarak lipogenezi azaltmakta; UCP1 ve PGC-1α'yı aktive ederek enerji harcamasını ve mitokondriyal fonksiyonları artırmakta; NF-κB ve pro-inflamatuar sitokinlerin ekspresyonunu düşürerek sistemik inflamasyonu sınırlamaktadır. Preklinik düzeyde elde edilen güçlü kanıtlara rağmen, insanlarda yapılan klinik araştırmalarda sonuçlar daha mütevazı olup genellikle heterojen bulunmuştur; bu durumun genetik varyasyonlar, bağırsak mikrobiyotası farklılıkları, biyoyararlanım kısıtlılığı ve müdahale süresinin yetersizliğinden kaynaklandığı düşünülmektedir. Gelecekte, uzun süreli ve genotipe dayalı klinik çalışmalar, fonksiyonel

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bileşiklerin farmakokinetik engellerini aşacak yeni formülasyon stratejileri ve çoklu -omics yaklaşımları ile desteklenmiş kişiselleştirilmiş beslenme uygulamaları, obezitenin yönetiminde önemli bir tamamlayıcı araç haline gelebilecektir.

Sonuç olarak, nutrigenomik perspektiften "genlere uygun beslenme" yaklaşımı, obezitenin önlenmesi ve tedavisinde yenilikçi, bireyselleştirilmiş ve umut vadeden bir yol haritası sunmaktadır.

Anahtar Kelimeler: Obezite, Nutrigenomik, PPARγ, L-theanin, Pterostilben

ABSTRACT

Obesity is a complex metabolic disorder that arises from the interaction between genetic predisposition and lifestyle factors, particularly dietary patterns. Nutrigenomics, the study of how dietary components influence gene expression and epigenetic regulation, offers promising avenues for the prevention and management of obesity through personalized nutrition strategies. Key molecular pathways implicated in obesity include adipogenesis (PPARγ, SREBP-1c, FAS), thermogenesis (UCP1, PRDM16, PGC-1α), mitochondrial biogenesis (TFAM, NRF1/2), and inflammation (TNF-α, IL-6, NF-κB). Recent *in vitro*, animal, and clinical studies demonstrate that functional compounds such as resveratrol, pterostilbene, ellagic acid, curcumin, EGCG, and L-theanine can beneficially modulate these pathways. These bioactive molecules suppress lipogenesis by downregulating PPARγ and SREBP-1c, enhance energy expenditure and mitochondrial function through the activation of UCP1 and PGC-1α, and attenuate systemic inflammation by reducing NF-κB and pro-inflammatory cytokine expression. While preclinical evidence is compelling, human clinical studies have yielded more modest and heterogeneous outcomes, likely due to interindividual genetic variation, differences in gut microbiota composition, limited bioavailability of compounds, and insufficient intervention durations. Future directions include long-term, genotype-stratified clinical trials, advanced formulations to overcome pharmacokinetic limitations, and integrative multi-omics approaches to refine personalized nutrition.

In conclusion, a nutrigenomic perspective on "gene-tailored nutrition" represents an innovative and promising strategy for obesity prevention and management, with the potential to shift the paradigm toward precision health.

Key Words: Obesity, Nutrigenomic, PPARγ, L-theanine, Pterostilbene

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GİRİŞ

Nutrigenomik, diyetin ve besinlerin gen ifadesini nasıl etkilediğini ve bireysel genetik çeşitliliğin diyete yanıtı nasıl etki ettiğini inceleyen bilim dalıdır (Duarte et al., 2024). Bu çerçevede, genom beslenme gereksinimlerinin bir düzenleyicisi olarak görülmektedir; örneğin, bir tanımda nutrigenomiğin "genetik kodumuzun besin ihtiyaçlarımızı nasıl etkilediğini ve optimal sağlığımızı nasıl koruduğumuzu açıkladığı" belirtilmektedir (Duarte et al., 2024).

Obezite, genler, yaşam tarzı ve çevrenin etkileşiminden kaynaklanan karmaşık, çok faktörlü bir hastalıktır. Nutrigenomik, belirli besin öğelerinin ve biyoaktif gıda bileşiklerinin obeziteyle ilişkili yolları nasıl olumlu yönde değiştirebileceğini ve tersine metabolik genlerdeki polimorfizmler gibi genetik yatkınlıkların beslenme etkilerini nasıl düzenlediğini ortaya çıkarmayı amaçlamaktadır (Duarte et al., 2024; Kiani et al., 2022). Gen-besin etkileşimlerini belirleyerek nutrigenomik, kronik hastalık riskini azaltmak için beslenme müdahalelerini kişiselleştirmeyi amaçlamaktadır. Örneğin, araştırmalar obezitenin genellikle iştah ve metabolizmayla ilişkili yollarda genetik varyantlar içerdiğini vurgulamaktadır. Bunların anlaşılması, obeziteyi önlemek veya tedavi etmek için "kişiselleştirilmiş" diyetlere rehberlik edebilir (Peña-Romero et al., 2018). Nitekim, yakın tarihli bir anlatı incelemesinde, "beslenme genomiği ve nutrigenetik testlerin, hastaların obeziteyi önlemesine veya tedavi etmesine yardımcı olma vaadiyle öne çıktığı" belirtilmektedir (Duarte et al., 2024)

OBEZİTE İLE İLİŞKİLİ GENLER

Obezite, adipogenez, lipogenez, enerji harcaması ve inflamasyonun birçok genetik düzenleyicisini içerir. Önemli örnekler arasında Peroksisom Proliferatör-aktif Reseptör gama (PPARγ), Sterol Düzenleyici Element Bağlayıcı Protein 1c (SREBP-1c), Ayrışma proteini 1 (UCP1), Peroksisom Proliferatör-aktif Reseptör γ Koaktivatör-1α (PGC-1α) ve Mitokondriyal Transkripsiyon Faktörü A (TFAM) bulunur (Benbaibeche et al., 2025; Hammad & Jones, 2017). Bu faktörler, beslenme sinyallerini metabolik yanıtlara entegre eder (Benbaibeche et al., 2025).

PPARγ

PPARγ yağ hücresi farklılaşmasını ve lipit depolamasını kontrol eden bir ana transkripsiyon faktörüdür. Aktive edildiğinde PPARγ, yağ hücresi oluşumunu desteklemek için C/EBPα ve SREBP-1c gibi genlerin upregülasyonunu sağlar. PPARγ'yi aktive eden bazı yağ asitleri gibi besinler yağ hücresi oluşumunu artırırken, polifenolik bileşikler bunu inhibe edebilir. Örneğin, resveratrol ve EGCG'nin PPARγ ve kofaktörlerini down regüle ederek yağ hücresi farklılaşmasını engellediği gösterilmiştir (Benbaibeche et al., 2025). İn vitro ve hayvan çalışmaları, resveratrol ve ilgili stilbenlerin PPARγ/C/EBPα sinyallemesini baskıladığını ve bunun lipojenik genlerin (SREBP-1c, FAS, aP2) ekspresyonunun azalmasına ve yağ birikiminin azalmasına yol açtığını bildirmektedir (Benbaibeche et al., 2025). Dolayısıyla, diyet kaynaklı bileşikler PPARγ aktivitesini düzenleyerek yağ hücresi oluşumunu ve yağ depolamasını sınırlayabilir.

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SREBP-1c

SREBP-1c, karaciğer ve yağ dokusunda yağ asidi ve trigliserit sentezini yönlendiren bir transkripsiyon faktörüdür (Hammad & Jones, 2017). Normalde insülin ve beslenme ile aktive olur, ancak AMP ile aktive olan protein kinaz (AMPK) sinyallemesi ile inhibe edilebilir. Polifenoller gibi besinler dolaylı olarak SREBP-1c'yi baskılar: örneğin, yağ hücrelerinde resveratrol tedavisi SREBP-1c mRNA'sını azaltır ve yeşil çay kateşinleri (EGCG), adipogenez sırasında SREBP-1c aktivasyonunu önler(Benbaibeche et al., 2025). SREBP-1c'nin inhibisyonu, yağ asidi sentazını (FAS) ve diğer lipojenik enzimleri azaltarak lipit birikimini sınırlar.

UCP1

UCP1, kahverengi ve bej yağ hücrelerinin ayırt edici termojenik proteinidir. UCP1, ATP yerine ısı üretmek için mitokondriyal solunumu ayırır ve enerji harcamasını artırır. UCP1'in aktivasyonu ve beyaz yağ dokusunun kahverengiye dönüşmesi, soğuk ve bazı bileşikler tarafından β-adrenerjik ve AMPK/PGC-1α yolları aracılığıyla uyarılır. Örneğin, all-trans-retinoik asit ve pterostilbenin UCP1 ekspresyonunu artırarak beyazdan kahverengiye yağ dönüşümünü tetiklediği ve lipit depolanmasını önlediği gösterilmiştir (Benbaibeche et al., 2025; Zheng et al., 2023). Kemirgen modellerinde, polifenollerle (örneğin resveratrol, EGCG, epikateşin, pterostilben) tedavi, UCP1 ve diğer termojenik belirteçleri (PRDM16, TMEM26) artırarak mitokondriyal biyogenezisi ve yağ oksidasyonunu hızlandırır (Benbaibeche et al., 2025)

PGC-1α

PGC-1α, kas ve yağ dokusunda mitokondriyal biyogenezi ve oksidatif metabolizmayı yönlendiren bir koaktivatördür. Enerji harcaması için genleri transkribe etmek üzere nükleer reseptörlerle, PPAR'lar dahil, etkileşime girer. AMPK ve sirtuinler aracılığıyla gelen besin sinyalleri PGC-1α'yı upregüle eder. Örneğin, resveratrol ve pterostilben, AMPK/SIRT1'i aktive ederek PGC-1α protein seviyelerinin artmasına neden olur (Benbaibeche et al., 2025). Yükselen PGC-1α ise mitokondriyal transkripsiyon faktörü olan TFAM ekspresyonunu artırır. TFAM, mitokondriyal DNA'nın replikasyonunu ve transkripsiyonunu yönetir (Benbaibeche et al., 2025). Çalışmalar, "PGC-1α'nın mitokondriyal biyogenezin önemli bir düzenleyicisi olduğunu; [TFAM] ekspresyonunu düzenlediğini" belirtmektedir (Dos Santos et al., 2018). Besinler, PGC-1α ve TFAM'ı artırarak mitokondri sayısını ve işlevini genişletebilir, oksidatif kapasiteyi iyileştirebilir ve böylece enerji harcamasını artırabilir.

TFAM

TFAM mitokondriyal DNA kopya sayısını ve mitokondriyal genlerin transkripsiyonunu kontrol eder. TFAM, PGC-1α tarafından indüklenir ve yeni mitokondrilerin inşasında merkezi bir rol oynar (J. Liu et al., 2019). Dolayısıyla, PGC-1α'yı artıran besinler, TFAM'ı da yükseltir. Örneğin, bir inceleme, PGC-1α'yı (SIRT1/AMPK aracılığıyla) aktive eden polifenollerin nihayetinde TFAM ve diğer mitokondriyal genleri yükselttiğini belirtmektedir (Benbaibeche et al., 2025; J. Liu et al., 2019). TFAM'ın işlev bozukluğu veya eksikliği, obezite ve insülin

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direnciyle bağlantılı olan zayıf mitokondriyal fonksiyona yol açar (Fernandez-Marcos & Auwerx, 2011). Özetle, obezojenik diyetler genellikle AMPK/SIRT1→PGC-1α sinyallemesini körelterek TFAM ve UCP1'i azaltır; bunun tersine, biyoaktif bileşikler bu ekseni yeniden aktive ederek yağ asidi oksidasyonunu ve termojenezi teşvik edebilir.

Bu genler ve yollar birlikte, besinlerin yağ depolaması ile enerji yakımı arasındaki dengeyi nasıl değiştirebileceğini göstermektedir. Örneğin, AMPK'yi diyet veya bileşikler yoluyla aktive etmek, lipojenik faktörleri (PPARγ, SREBP-1c) baskılar ve mitokondriyal programları (PGC-1α, TFAM, UCP1) güçlendirir(Benbaibeche et al., 2025). Dolayısıyla, temel obezite genlerinin nutrigenomik düzenlenmesi, fonksiyonel besinlerin metabolik sağlığı iyileştirmesi için birden fazla hedef sağlar.

FONKSİYONEL GIDA BİLEŞENLERİ VE MOLEKÜLER MEKANİZMALAR

Resveratrol

Resveratrol; üzüm ve meyvelerde bulunan bir stilben polifenoldür (Barber et al., 2022; Springer & Moco, 2019). Resveratrol, SIRT1 ve AMPK'yi aktive eder ve anti-inflamatuar ve anti-adipojenik etkilere sahiptir (Benbaibeche et al., 2025) İn vitro'da, preadipositlerin resveratrol ile tedavisi, PPARγ ve C/EBPα protein ekspresyonunu inhibe ederek ve aşağı akış lipojenik genleri (SREBP-1c, FAS, aP2, SCD-1) aşağı düzenleyerek adipogenezi azaltır (Benbaibeche et al., 2025). Obez farelerde ve insanlarda, resveratrol takviyesi serum lipitlerini ve glikozunu düşürür, daha küçük (daha az hipertrofik) adipositlerin sayısını artırır ve mitokondriyal aktivite belirteçlerini yükseltir(Timmers et al., 2011). Özellikle klinik çalışmalar, 30 gün boyunca günde 150 mg resveratrolün iskelet kası SIRT1 ve PGC-1α düzeylerini artırdığını, AMPK'yi aktive ettiğini ve insülin direncini ve inflamatuar sitokinleri (IL-6, IL-8, TNF-α) azalttığını göstermektedir (Timmers et al., 2011). Bu etkiler, resveratrolün yağ ve kas metabolizmasını artan enerji harcamasına doğru kaydırdığını göstermektedir.

Kurkumin

Kurkumin zerdeçaldan (*Curcuma longa*) elde edilen bir polifenoldür. Kurkumin, anti-inflamatuar ve anti-adipojenik etkiler gösterir. Hücre modellerinde kurkumin, NF-κB aktivasyonunu baskılar ve makrofajlarda pro-inflamatuar sitokin salınımını (örn. IL-1β) azaltır (Kong et al., 2016). Hayvan çalışmalarında, diyet kurkumini yağ dokusunda makrofaj infiltrasyonunu azaltır ve JNK ve NF-κB yollarını inhibe eder (Shao et al., 2012). Ayrıca metabolik hormonları da etkileyen kurkumin, adiponektini artırır ve leptini azaltır, böylece obeziteyle bağlantılı inflamasyonu tersine çevirir(Benbaibeche et al., 2025). Klinik olarak, kurkumin takviyesi mütevazı kilo kaybı ve metabolik faydalar sağlamıştır: Aşırı kilolu deneklerde yapılan 30 günlük bir deneme, vücut ağırlığında, yağ kütlesinde, BMI'de ve inflamasyon belirteçlerinde (CRP, TNF-α, IL-6) azalmalar göstermiştir (F.Di Pierro etal., 2015). Mekanik olarak, kurkumin, insülin duyarlılığını iyileştirmek için PPARγ sinyallemesini aktive eder (anti-adipojenik bağlamına rağmen) ve NF-κB/STAT3 kaynaklı inflamasyonu azaltır(Shao et al., 2012)

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Ellagik asit

Ellagik asit meyvelerde ve kuruyemişlerde bol miktarda bulunan tanen türevi bir polifenoldür. Ellagik asit (EA) ve bağırsaktan türetilen metabolitleri (ürolitinler), yağ hücresi lipit metabolizmasını ve inflamasyonu etkiler. 3T3-L1 yağ hücresi çalışmalarında, EA ve ürolitin A, yağ hücresi oluşumunu engellemeden lipit birikimini orta düzeyde azaltmıştır (Cisneros-Zevallos et al., 2020). GLUT4 ve adiponektin gen ekspresyonunu artırarak glukoz alım yollarını güçlendirmiş ve böylece daha iyi lipit yönetimi sağlamıştır (Cisneros-Zevallos et al., 2020). Daha da önemlisi, EA ve ürolitinler, LPS ile zorlanan yağ hücrelerinde inflamatuvar gen ekspresyonunu (TNF-α, iNOS, IL-6, MCP-1) baskılamıştır (Cisneros-Zevallos et al., 2020). Protein düzeyinde, ellagik asit (ve ürolitin B), PPARγ ve C/EBPα ekspresyonunu ve yağ asidi oksidasyon kapasitesini artırmıştır (Wong-a-nan et al., 2018). Bu nedenle, ellagik asidin, lipid metabolizması kapasitesini orta düzeyde artırırken, inflamasyon sinyallerini azaltarak yağ hücresi fonksiyonunu hassas bir şekilde ayarladığı görülmektedir.

L-Theanin

L theanin yeşil çayda bulunan protein olmayan bir amino asittir. L-theaninin, öncelikle AMPK aktivasyonu yoluyla obeziteyle ilişkili komplikasyonları iyileştirdiği gösterilmiştir. Yüksek yağlı diyet (HFD) fare modellerinde, L-theaninin takviyesi, insülin ve AMPK sinyal yollarını aktive ederek glukoz ve lipit metabolizmasını iyileştirmiştir(Du et al., 2024). Beyaz yağ dokusunun kahverengileşmesini indüklemiş ve insülin duyarlılığını iyileştirmiştir(Du et al., 2024). Transkriptomik analizler, L-theaninin obez farelerde hepatik inflamatuar genleri (TNF-α, IL-1β, IL-6, MCP-1) down regüle ettiğini ortaya koymuştur (Du et al., 2024) Bu da anti-inflamatuar bir etkiye işaret etmektedir. Bir çalışmada belirtildiği gibi, yüksek doz L-theaninin karaciğerdeki temel sitokin genlerinin "ekspresyonunu önemli ölçüde azalttığı" belirtilmiştir (Liang et al., 2022). Genel olarak L-theanine, diyet kaynaklı inflamasyonu baskılarken AMPK kaynaklı enerji harcamasını (esmerleşme ve yağ asidi oksidasyonu) aktive eder.

Pterostilben

Pterostilben Resveratrolün dimetillenmiş bir analoğu olup Resveratrolden daha yüksek biyoyararlanıma sahiptir. Yaban mersini ve Pterocarpus'ta bulunur. Pterostilben, resveratrolün birçok etkisini daha düşük dozlarda taklit eder (Y. Liu et al., 2020; Nagarajan et al., 2022). Yakın zamanda yapılan bir hayvan çalışmasında, pterostilben uygulaması AMPK/PGC-1α ekseni aracılığıyla yağ dokusunun kahverengileşmesini önemli ölçüde desteklemiştir (Zheng et al., 2023). Yüksek yağlı diyette vücut ağırlığı kazanımını azaltmış ve beyaz yağ dokusunda kahverengi yağ belirteçlerinin (UCP1, PRDM16, TMEM26) mitokondriyal içeriğini ve ekspresyonunu artırmıştır(Zheng et al., 2023). Hem in vivo hem de yağ hücre kültürü çalışmalarında, pterostilben AMPK'yi aktive etmiş ve PGC-1α'yı yukarı regüle etmiştir ve bu etkiler farmakolojik AMPK inhibisyonu veya PGC-1α baskılanmasıyla ortadan kaldırılmıştır(Zheng et al., 2023). Yapılan bu hayvan deneyi çalışması ile yazarlar, "pterostilbenin, AMPK/PGC-1α yoluyla beyaz yağ hücrelerinin kahverengileşmesini sağlayarak kilo alımını azaltıcı bir etki gösterdiği" sonucuna varmıştır(Zheng et al., 2023). Bu

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nedenle, pterostilben, termojenik metabolizmayı ve enerji harcamasını artırarak diyet kaynaklı obeziteyle mücadeleye yardımcı olur.

Epigallokateşin-3-gallat

EGCG başlıca yeşil çay kateşinidir. EGCG, çok yönlü anti-obezite etkilerine sahiptir. ghrelini inhibe ederek ve CCK/leptini uyararak iştahı bastırır ve adiponektin salgılanmasını artırır(Wang et al., 2014). EGCG, yağ oluşumunu güçlü bir şekilde engeller: 3T3-L1 hücrelerinde PI3K/Akt sinyallemesini bloke eder ve PPARγ, C/EBPα, FAS ve SREBP-1c'yi aşağı düzenler(Wu et al., 2017). Ayrıca, EGCG termojenezi ve mitokondriyal biyogenezisi destekler. Obez farelerde EGCG tedavisi, kahverengi yağ UCP1 seviyelerini yükseltmiş, vücut sıcaklığını artırmış ve BAT'taki mitokondriyal DNA içeriğini genişleterek daha düşük kilo alımına ve lipit seviyelerine yol açmıştır(Lee et al., 2017). Mekanik olarak EGCG, AMPK'yi aktive eder ve SIRT1'i güçlendirerek yağ ve kaslarda PGC-1α ile yönlendirilen termojenik programları (özellikle UCP1) daha da uyarır. Ayrıca, yağ oksidasyonunu desteklemek için bağırsak mikrobiyotasını ve safra asidi metabolizmasını değiştirir(Kim et al., 2010; Lee et al., 2017). İnsan çalışmalarında, EGCG (genellikle kafeinle) yağ oksidasyonunu ve kilo kaybını orta düzeyde artırır.

Bu bileşiklerin her biri, "fonksiyonel gıdaların" obeziteyle ilgili gen ifadesini ve sinyal iletim basamaklarını nasıl düzenleyebileceğini göstermektedir. Metabolizmayı artan enerji harcamasına ve azalan inflamasyona yönlendirmek için genellikle AMPK aktivasyonu, NF-κB inhibisyonu, PPARγ down regülasyonu, UCP1 up regülasyonu gibi ortak hedeflerde birleşirler (Benbaibeche et al., 2025). Tablo 1 de bazı fonksiyonel bileşikler ve obezite üzerine etkileri gösterilmiştir (Benbaibeche et al., 2025)

Tablo1. Fonksiyonel Bileşikler ve Obezite Üzerine Etki Mekanizmaları

Molekül / Biyoaktif Bileşik	**Kaynak**	**Etki**	**Potansiyel Mekanizma**
Fenolik asitler	Meyveler, tam tahıllar ve kuruyemişler	3T3-L1 adipositlerinde adipogenezi inhibe etti. TNFα, IL-6, MCP-1 salınımını ve makrofaj infiltrasyonunu azalttı.	SCD1'i baskılar, PPARγ'yı aktive eder. NF-κB'yi baskılar.
EGCG + piperin	Yeşil çay, karabiber	3T3-L1 adipositlerinde	PPARγ, SREBP-1c, FAS, C/EBP-α gibi adipogenik faktörlerin

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(alkaloid) 20 mM		adipogenezi inhibe etti.	ekspresyonunu düşürdü. UCP1 ekspresyonunu artırdı. Leptini azalttı, adiponektini yükseltti.
EGCG 40 mg/kg/gün + kafein: 20 mg/kg/gün (4 hafta)	Yeşil çay	HFD- obez sıçanlarda kilo alımını engelledi, beyaz yağ dokusu kütlesini azalttı.	F/B oranını azalttı. Asetik, propiyonik ve bütirik asit gibi SCFA'ları artırdı. Bifidobacterium, Alloprevotella ve Allobaculum, Faecalibaculum bolluğunu artırdı.
EGCG	Yeşil çay	3T3-L1 preadipositlerinde adipogenezi inhibe etti.	PI3K/AKT yolunu inhibe ederek PPARγ ve FAS ekspresyonunu azalttı.
Maackianin ve ononin (flavonoid türevleri)	Ononis spinosa L. köklerinden ekstre	İnsan SGBS hücrelerinde adipogenik farklılaşmayı inhibe etti.	Maackianin PI3K, PPARγ/C/EBPα sinyalini baskıladı. Ononin SIRT1'i aktive edip PI3K, PPARγ ve adiponektini inhibe etti.
Fenolik bileşikler	Kahve kabuğu ve kahve silverskin	İnflamasyonu azalttı, insülin direncini ve mitokondriyal disfonksiyonu önledi (3T3-L1).	GLUT4 translokasyonunu artırdı, insülin/PI3K/AKT, NF-κB/MAPK ve AMPK yollarını düzenledi.
Resveratrol 200 mg/kg	Üzüm çekirdeği	Obez sıçanlarda leptin duyarlılığını geri kazandırdı, kilo alımını azalttı.	Karaciğerde SIRT1 aktivitesini artırdı, kasta leptin

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			reseptörlerini yükseltti.
Resveratrol 0.1–10 μM	Üzüm çekirdeği	Makrofajlarda IL-6 ve TNF-α düzeylerini azalttı. Adipositlerde insülin duyarlılığını iyileştirdi.	NF-κB aktivasyonunu ve ERK1/2 fosforilasyonunu inhibe etti. AKT'nin Ser/Thr fosforilasyonunu modifiye etti.
Antosiyaninler	Siyah soya fasulyesi	HFD sıçanlarda obeziteyi baskıladı. Kilo alımını, besin tüketimini, yağ dokusu boyutunu azalttı.	Hipotalamusta NPY'yi baskıladı, GABA reseptörlerini artırdı.
Kuersetin	Tohumlar	3T3-L1 hücrelerinde adipogenezi azalttı. Adipoz dokularda apoptozu artırdı.	AMPK yolunu aktive etti. JNK ve ERK1/2 fosforilasyonunu baskıladı.
Rutin	Dut	BAT'ı aktive etti, WAT'ta kahverengileşmeyi artırdı. Kilo alımını azalttı, enerji harcamasını yükseltti.	BAT'ta SIRT1'i aktive ederek PGC-1α proteini, TFAM ve UCP1'i artırdı.
3-Kafeoilkinik asit (klorojenik asit)	Yeşil kahve çekirdeği	HFD farelerinde kilo alımını ve WAT kütlesini azalttı. Adiposit çoğalmasını inhibe etti.	C/EBPα, SREBPs ve PPARγ gibi adipogenez genlerinin ekspresyonunu azalttı. AMPK'yı aktive etti.

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6-gingerol ve 6-shogaol	Zingiber officinale (zencefil)	Adipositlerde enerji harcamasını artırdı. 3T3-L1 adipositlerinde adipogenezi baskıladı.	Karaciğerde PPARα ve CPT1 genlerini aktive etti. PPARγ, C/EBP-α ve lipogenik enzimlerin ekspresyonunu azalttı.
Karnosik asitler	Rosmarinus officinalis	3T3-L1 preadipositlerinde farklılaşmayı inhibe etti.	PPARγ ve FABP4 ekspresyonunu baskıladı.
6-paradol	Aframomum melegueta	HFD farelerinde vücut ağırlığını ve adipogenez farklılaşmasını azalttı.	PGC-1α ve PPARγ ekspresyonunu azalttı.

OBEZİTEDE HASSAS BESLENME VE NUTRİGENOMİK UYGULAMALAR

Hassas beslenme, diyet önerilerini bireyin genetik yapısına, metabolizmasına ve yaşam tarzına göre uyarlamayı amaçlar. Obezite bağlamında bu, makro ve mikro besin hedeflerine rehberlik etmek için anahtar varyantların (örneğin PPARγ, FTO, APOE, ADRB2 vb.) genotiplenmesini içerebilir. Örneğin, belirli PPARγ polimorfizmleri Akdeniz diyetine kıyasla düşük yağlı diyete daha iyi yanıtı öngörebilir. Kişiselleştirilmiş diyetleri geliştirmek için çoklu omik yaklaşımlar (genomik, epigenomik, metabolomik ve mikrobiyom verilerini entegre eden) da araştırılmaktadır. Dijital araçlar ve yapay zekâ modelleri, bu verileri bir bireyin belirli yiyeceklere verdiği glisemik veya kilo yanıtını tahmin etmek için kullanabilir. Nihai amaç, tek tip tavsiyelerden, kilo kaybını ve metabolik sağlığı optimize eden özelleştirilmiş rejimlere geçmektir. Bir incelemede vurgulandığı gibi, "bu kronik durumda kaç varyantın rol oynadığını belirlemek ve hastaların tedavisinde beslenme genomiğinin kullanımını yönlendirmek için obezitenin genetik profilini bilmek çok önemlidir" (Duarte et al., 2024).

Obezite ile ilgili bazı nutrigenomik uygulamalar halihazırda geliştirilme aşamasındadır. Örneğin, şirketler obeziteyle ilişkili SNP'leri test eden ve diyet değişiklikleri öneren paneller sunmaktadır. POUNDS LOST denemesi gibi klinik çalışmalar, genotip rehberliğindeki diyetlerin standart tavsiyelere göre daha iyi kilo sonuçları sağlayıp sağlamadığını araştırmıştır. Şimdiye kadar elde edilen sonuçlar karışıktır. Kişiselleştirilmiş yaklaşımlar bazen lipidlerde veya inflamasyon belirteçlerinde daha mütevazı iyileşmeler sağlasa da fikir birliğine varan

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bilimsel kuruluşlar, örneğin Beslenme ve Diyetetik Akademisi, şu anda obezite yönetimi için nutrigenetik testlerin rutin kullanımını önermemektedir(Duarte et al., 2024). Eleştiri, çoğu gen varyantının yalnızca düşük risk taşıması ve diyet tepkilerinin büyük ölçüde poligenik ve çevre odaklı kalmasıdır.

Bununla birlikte, bu konuya olanilgi artmaktadır. Obezite için hassas beslenme, gelecekte bağırsak mikrobiyom profillemesini ve sürekli glukoz ölçümünü entegre ederek diyetleri gerçek zamanlı olarak ayarlayabilir. Nutrigenomik, hangi diyet değişikliklerinin belirli bir bireye en çok fayda sağlama olasılığı konusunda fikir verir; örneğin, proinflamatuar gen profiline sahip biri polifenol açısından zengin bir diyetten daha fazla fayda görebilir. Ancak, sağlam translasyonel çalışmalara hala ihtiyaç duyulmaktadır. Yakın tarihli bir anlatı, nutrigenomik ile "hastaların obeziteyi önlemesine veya tedavi etmesine yardımcı olma vaadini" vurgularken, aynı zamanda mevcut kanıt eksikliğini de belirtmektedir(Duarte et al., 2024). Uygulamada, hassas beslenme, davranışsal ve sosyal faktörlerin yanı sıra genetik yatkınlıkları da göz önünde bulunduran, kanıta dayalı, veri odaklı bir diyet planını vurgular.

SONUÇ

Nutrigenomik, diyetteki biyoaktif bileşikleri temel genetik ve metabolik yolların düzenlenmesiyle ilişkilendirerek obeziteyi anlamak ve yönetmek için yeni bir çerçeve sunar. İn vitro ve hayvan çalışmalarından elde edilen kanıtlar, resveratrol, kurkumin, ellagik asit, EGCG, L-theanin ve pterostilben gibi fonksiyonel bileşiklerin adipogenezi baskılama, mitokondriyal biyogenezi ve termojenezi artırma ve PPARγ, SREBP-1c, UCP1, PGC-1α ve TFAM modülasyonu yoluyla kronik inflamasyonu hafifletme kapasitesini güçlü bir şekilde desteklemektedir. Bununla birlikte, klinik bulgular mütevazı ve heterojen olmaya devam etmekte olup, bireyler arası değişkenliğin, bağırsak mikrobiyotasının, biyoyararlanımın ve müdahale süresinin etkisini vurgulamaktadır. Bu sınırlamalara rağmen, nutrigenomiğin hassas beslenmeye entegrasyonu, obeziteyi önlemek ve yönetmek için kişiselleştirilmiş diyet stratejileri geliştirme konusunda büyük umut vaat etmektedir. Çoklu omik teknolojilerindeki gelecekteki gelişmeler, biyoaktifler için geliştirilmiş dağıtım sistemleri ve geniş ölçekli, genotip bazlı klinik çalışmalar, nutrigenomik içgörülerin etkili ve kanıta dayalı müdahalelere dönüştürülmesinde hayati önem taşıyacaktır.

Sonuç olarak, genlere özel beslenme, obeziteyle küresel mücadelede güçlü bir tamamlayıcı araç olarak ortaya çıkabilir.

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ÇİNKO SÜLFAT NANOPARTİKÜLLERİNİN *Staphylococcus aureus* BİYOFİLMİ ÜZERİNE HÜCRE DIŞI POLİMERİK MADDE(EPS) YAPISI VE GEN EKSPRESYONU ÜZERİNE ETKİSİ

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ÖZET

Bu çalışmada, *Staphylococcus aureus* (ATCC 25923) suşuna karşı sentezlenen çinko sülfat nanopartiküllerinin ($ZnSO_4$-NP) antimikrobiyal ve antibiyofilm etkinliği değerlendirilmiştir. Ayrıca biyofilm matriksine ait ekstraselüler polimerik madde (EPS) bileşenleri ile biyofilm oluşumunda görev alan icaA, icaD ve sarA genlerinin ekspresyon düzeyleri incelenmiştir. $ZnSO_4$-NP'ler sentezlenmiş ve SEM ile morfolojik yapısı, zeta potansiyel analizi ile yüzey yükü belirlenmiştir. Biyofilm oluşumu kristal viyole (CV) yöntemi ile kantitatif olarak analiz edilmiş; EPS içeriği ise polisakkarit, protein ve eDNA düzeyleri üzerinden değerlendirilmiştir. Antibiyofilm etkinlik CV testleriyle doğrulanmış, gen ekspresyonu RT-qPCR ile analiz edilmiştir. Elde edilen sonuçlara göre $ZnSO_4$-NP'lerin boyutunun 300–400 nm aralığında olduğu ve kolloidal stabilite gösterdiği belirlenmiştir. Nanopartikül uygulaması biyofilm kütlesinde ve EPS bileşenlerinde belirgin bir azalmaya yol açmıştır. CV testleri hücre canlılığında düşüş ve biyofilm yapısında bozulma olduğunu ortaya koymuştur. RT-qPCR analizlerinde ise icaA, icaD ve sarA genlerinin aşağı regülasyona uğradığı gözlenmiştir. Sonuç olarak, çinko sülfat nanopartikülleri *S. aureus* biyofilmlerine karşı güçlü antibiyofilm ve antimikrobiyal potansiyele sahiptir. EPS yapısını bozma ve biyofilm genlerini baskılama etkileri sayesinde, gelecekte biyofilm kaynaklı enfeksiyonların tedavisinde alternatif bir strateji olarak değerlendirilebilir.

Anahtar Kelimeler: *Staphylococcus aureus*, $ZnSO_4$ nanopartikülleri, antibiyofilm, EPS, gen ekspresyonu

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EFFECT OF ZINC SULFATE NANOPARTICLES ON EXTRACELLULAR POLYMERIC SUBSTANCE (EPS) STRUCTURE AND GENE EXPRESSION IN *Staphylococcus aureus* BIOFILM

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Abstract

In this study, the antimicrobial and antibiofilm activity of zinc sulfate nanoparticles ($ZnSO_4$-NPs) synthesized against *Staphylococcus aureus* (ATCC 25923) was evaluated. In addition, extracellular polymeric substance (EPS) components of the biofilm matrix and the expression levels of biofilm-associated genes icaA, icaD, and sarA were investigated. $ZnSO_4$-NPs were synthesized, and their morphological structure was characterized by SEM, while the surface charge was determined using zeta potential analysis. Biofilm formation was quantitatively assessed by the crystal violet (CV) assay, and EPS content was evaluated in terms of polysaccharides, proteins, and eDNA. Antibiofilm activity was confirmed by CV testing, and gene expression was analyzed by RT-qPCR. The results revealed that $ZnSO_4$-NPs had a particle size range of 300–400 nm and exhibited colloidal stability. Nanoparticle treatment led to a significant reduction in biofilm biomass and EPS components. CV assays demonstrated a decrease in cell viability and disruption of the biofilm structure. RT-qPCR analysis showed that icaA, icaD, and sarA genes were downregulated. In conclusion, zinc sulfate nanoparticles exhibited strong antibiofilm and antimicrobial potential against *S. aureus* biofilms. Through their ability to disrupt EPS structure and suppress biofilm-related genes, $ZnSO_4$-NPs may serve as a promising alternative strategy for the treatment of biofilm-associated infections in the future.

Keywords: *Staphylococcus aureus*, $ZnSO_4$ nanoparticles, antibiofilm, EPS, gene expression

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1. INTRODUCTION

Biofilms are multicellular and organized communities formed by microorganisms adhering to biotic or abiotic surfaces. These communities are embedded in a matrix that facilitates cell-to-cell and cell-to-surface adhesion while providing resistance against environmental stresses. The most important components of the biofilm matrix are extracellular polymeric substances (EPS), which mainly consist of polysaccharides, proteins, lipids, and extracellular DNA (eDNA). EPS constituents form the three-dimensional architecture of the biofilm, facilitate communication among microbial cells, and act as a protective barrier against antimicrobial agents (Flemming & Wingender, 2010). Therefore, the biofilm structure plays a key role in enabling bacteria to develop much higher resistance compared to their planktonic forms.

Staphylococcus aureus is one of the most significant pathogens responsible for both community- and hospital-acquired infections. Biofilms that develop on the surfaces of catheters, prostheses, and other medical implants cause persistent infections that are difficult to eradicate. The resistance of these biofilms is primarily attributed to the protective function of the EPS matrix and the regulation of biofilm-associated genes. In particular, the *icaA* and *icaD* genes play a critical role in the synthesis of polysaccharide intercellular adhesin (PIA), which has a key function in intercellular adhesion. Moreover, transcriptional regulators such as *sarA* control cellular communication and adhesion mechanisms during biofilm development (Arciola et al., 2015). Thus, investigating the expression levels of these genes is of great importance for understanding the mechanisms underlying biofilm formation.

To address the clinical challenges posed by antibiotic-resistant biofilm layers, nanotechnological approaches have attracted increasing attention. Metal and metal oxide nanoparticles have emerged as promising agents in antimicrobial and antibiofilm strategies due to their large surface area and high reactivity. Nanoparticles can disrupt the integrity of the bacterial cell membrane, induce the production of reactive oxygen species (ROS), and directly interact with the components of the biofilm matrix, thereby weakening its structure (Pelgrift & Friedman, 2013). Zinc-based compounds have long been recognized for their antimicrobial properties. Zinc sulfate nanoparticles ($ZnSO_4$-NPs), in particular, have recently been the focus of intensive research due to their biocompatibility and potential to directly affect the biofilm matrix. Previous studies have demonstrated that ZnO or $ZnSO_4$ nanoparticles can bind to bacterial cell walls, increase membrane permeability, trigger oxidative stress mechanisms, and thereby exert antibacterial effects (Raghupathi et al., 2011). In addition, nanoparticles have been reported to disrupt the biofilm EPS structure by reducing polysaccharide and protein content and suppressing the expression of biofilm-associated genes. In this context, elucidating the effects of $ZnSO_4$ nanoparticles on the EPS structure of *Staphylococcus aureus* biofilms and their influence on the expression levels of biofilm-related genes will contribute to a better understanding of biofilm biology and the development of novel antibiofilm strategies. The results of this study will provide an important scientific basis for evaluating the potential use of $ZnSO_4$ nanoparticles in biomedical applications, particularly for the prevention and treatment of medical device-associated infections (Seil & Webster, 2012).

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2. MATERYAL -METOD

Synthesis and Characterization of $ZnSO_4$ Nanoparticles

$ZnSO_4$ nanoparticles ($ZnSO_4$-NPs) were synthesized and subjected to structural characterization. For morphological evaluation, the nanoparticles were suspended in ethanol (0.1–0.2 mg/mL) and sonicated for 10 min to obtain a uniform dispersion. A small aliquot was deposited onto aluminum SEM stubs covered with conductive carbon tape and air-dried at room temperature. The samples were then sputter-coated with a thin layer of Au/Pd (~5–10 nm) and visualized under scanning electron microscopy (SEM) at 5–15 kV with a working distance of 8–12 mm. Representative images were captured at multiple magnifications and at least 100 particles were analyzed to determine shape and size distribution (ISO 22412, 2017; Hunter, 1981).

The surface charge and colloidal stability of $ZnSO_4$-NPs were evaluated by zeta potential measurements, and particle size distribution was determined by dynamic light scattering (DLS). Nanoparticles were diluted in 1 mM KCl to a final concentration of approximately 0.1–0.3 mg/mL and measured in disposable cuvettes at 25 °C. Hydrodynamic diameter (Z-average, PdI) was recorded in backscatter mode (173°), and electrophoretic mobility was used to calculate the zeta potential. Each sample was measured in triplicate, and the results were expressed as mean ± SD (ISO 22412, 2017).

Biofilm Quantification

The effect of $ZnSO_4$-NPs on Staphylococcus aureus biofilm biomass was assessed using the crystal violet (CV) assay. An overnight bacterial culture was diluted to approximately 10^6 CFU/mL in tryptic soy broth (TSB), and 200 µL was inoculated into the wells of sterile flat-bottom 96-well polystyrene plates. Plates were incubated at 37 °C for 24 h under static conditions to allow biofilm formation. Following incubation, non-adherent cells were removed, and the wells were gently washed three times with phosphate-buffered saline (PBS). Biofilms were fixed with 99% methanol for 15 min, air-dried, and then stained with 0.1% (w/v) crystal violet for 15 min. Excess stain was removed by rinsing with distilled water, and the bound dye was solubilized with 95% ethanol for 15 min. Biofilm biomass was quantified by measuring absorbance at 570 nm using a microplate reader. Results were normalized to untreated control wells (Merritt et al., 2005; O'Toole, 2011).

EPS Component Analyses

To evaluate the effect of $ZnSO_4$-NPs on EPS production, the contents of polysaccharides, proteins, and extracellular DNA (eDNA) in the biofilm matrix were determined. Total polysaccharides were quantified by the phenol–sulfuric acid method. Briefly, 50 µL of sample was mixed with 50 µL of 5% phenol, followed by the rapid addition of 300 µL of concentrated H_2SO_4. After incubation at room temperature for 10 min and an additional 10 min in a boiling water bath, the absorbance was measured at 490 nm. Glucose was used to construct a calibration curve, and results were expressed as glucose equivalents (Dubois et al., 1956). Total protein content was determined using the bicinchoninic acid (BCA) assay. Samples were mixed with BCA reagent according to the manufacturer's instructions and incubated at 37 °C for 30 min. Absorbance was measured at 562 nm, and protein concentrations were calculated from a bovine serum albumin (BSA) standard curve (Smith et al., 1985). Extracellular DNA (eDNA) was

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quantified spectrophotometrically by measuring absorbance at 260 nm using a NanoDrop spectrophotometer. DNA concentration was calculated based on the conversion factor that 1 absorbance unit at 260 nm corresponds to 50 µg/mL double-stranded DNA (Frølund et al., 1996).

Gene Expression Analysis

The effect of $ZnSO_4$-NPs on biofilm-related gene expression was determined by real-time quantitative PCR (RT-qPCR). Biofilms were grown for 24 h in the presence and absence of $ZnSO_4$-NPs, washed twice with PBS, and harvested for RNA extraction. Total RNA was isolated using TRIzol reagent according to the manufacturer's protocol and treated with DNase I to eliminate contaminating genomic DNA. RNA purity and integrity were confirmed by spectrophotometry (A260/A280 ratio between 1.9 and 2.1). Complementary DNA (cDNA) was synthesized from 500 ng of RNA using a reverse transcription kit with random hexamers.

Quantitative PCR was performed in a 20 µL reaction mixture containing SYBR Green master mix, 0.4 µM of each primer, and 10 ng of cDNA. The cycling conditions consisted of an initial denaturation at 95 °C for 2 min, followed by 40 cycles of 95 °C for 10 s and 60 °C for 30 s, and a melting curve analysis. Target genes included icaA, icaD, and sarA, with 16S rRNA or gyrB serving as housekeeping reference genes. Each reaction was performed in triplicate, and gene expression levels were analyzed using the comparative ΔΔCt method. Data were expressed as fold changes relative to untreated control biofilms (Bustin et al., 2009).

Table 1. Primers used in RT-PCR for biofilm-related genes.(Liang et al.2019).

Target gene	Primer	Primers sequence (5′-3′)
sarA	*sarA*-F	TCTTGTTAATGCACAACAACGTAA
	sarA-R	TGTTTGCTTCAGTGATTCGTTT
icaA	*icaA*-F	GTCAGACACTTGCTGGCGCA
	icaA-R	GAGCCCATCTCACGCGTTGC
icaD	icaD-F	GGGTGGATCCTTAGTGTTACAATTTT
	icaD-R	TGACTTTTTGGTAATTCAAGGTTGTC
16S rRNA	*16S rRNA*-F	GCTGCCCTTTGTATTGTC
	16S rRNA-R	AGATGTTGGGTTAAGTCCC

2. RESULTS AND DISCUSSION

Characterization of $ZnSO_4$ Nanoparticles

SEM Analysis

The morphological characteristics of the synthesized $ZnSO_4$ nanoparticles were examined by scanning electron microscopy (SEM). As shown in **Figure 1**, the nanoparticles exhibited an aggregated structure composed of nearly spherical primary particles. Such clustering behavior is common among metal-based nanoparticles, as their high surface energy and strong intermolecular forces promote agglomeration during drying. The observed nanoscale morphology is consistent with earlier reports describing spherical zinc oxide and zinc sulfate nanoparticles (Raghupathi et al., 2011; Zhang et al., 2016).

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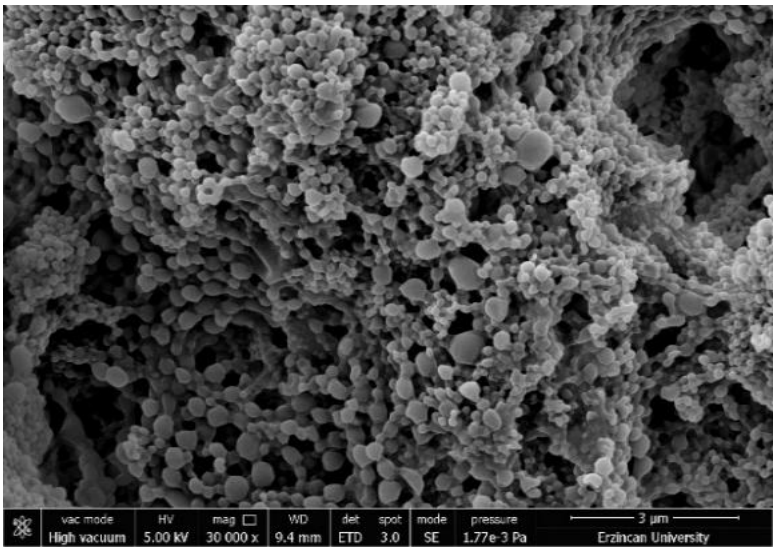

Figure 1. SEM micrograph of $ZnSO_4$ nanoparticles (30,000× magnification, scale bar = 3 µm).

Zeta Potential and Polydispersity Index (PDI)

Dynamic light scattering (DLS) analysis was performed to determine the surface charge and dispersion stability of $ZnSO_4$ nanoparticles. As summarized in **Table 1**, the nanoparticles showed a negative zeta potential value of −14 ± 0.473 mV, suggesting moderate colloidal stability. Zeta potential values between ±10 and ±30 mV are generally indicative of incipient stability, with some tendency toward aggregation (Hunter, 1981). Nevertheless, negatively charged nanoparticles can exhibit enhanced electrostatic interactions with bacterial cell walls, which may contribute to their antimicrobial efficiency (Seil & Webster, 2012).

The polydispersity index (PDI) was measured as 0.407 ± 0.077, reflecting a moderately broad particle size distribution. According to ISO 22412 (2017), PDI values below 0.3 are considered monodisperse, whereas values ranging from 0.3 to 0.7 indicate moderate polydispersity. Thus, the obtained PDI confirms that the $ZnSO_4$ nanoparticles were heterogeneous but suitable for biological applications.

Table 1. Zeta potential (ZP) and polydispersity index (PDI) values of $ZnSO_4$ nanoparticles.

Kod	ZP ± SD	PDI ± SD
NP0	-14 ± 0,473	0,407 ± 0,077

Effect of $ZnSO_4$ Nanoparticles on Biofilm Viability and EPS Composition Results

The antibiofilm activity of $ZnSO_4$ nanoparticles was assessed by crystal violet (CV) assay. As shown in Figure 2, treatment with $ZnSO_4$-NPs resulted in a significant reduction in biofilm biomass compared to the untreated control. The control group exhibited 100% cell viability, whereas exposure to $ZnSO_4$-NPs reduced the viability to approximately 40%, indicating a 60%

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inhibition of biofilm-associated cells. This result demonstrates the strong disruptive effect of $ZnSO_4$ nanoparticles on the integrity of *Staphylococcus aureus* biofilms.

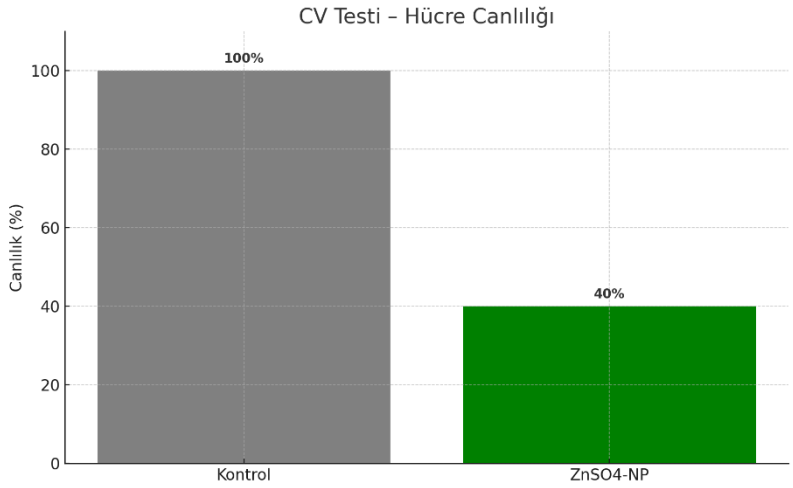

Figure 2. Effect of $ZnSO_4$ nanoparticles on S. aureus biofilm cell viability measured by CV assay.

The observed decrease in biofilm biomass suggests that $ZnSO_4$ nanoparticles interfere with biofilm formation and maintenance. One plausible mechanism is the disruption of the extracellular polymeric substances (EPS) matrix, which provides structural stability and protection to bacterial communities. EPS is composed of polysaccharides, proteins, and extracellular DNA (eDNA), which collectively shield biofilm-embedded bacteria from antibiotics and host defenses (Flemming & Wingender, 2010).

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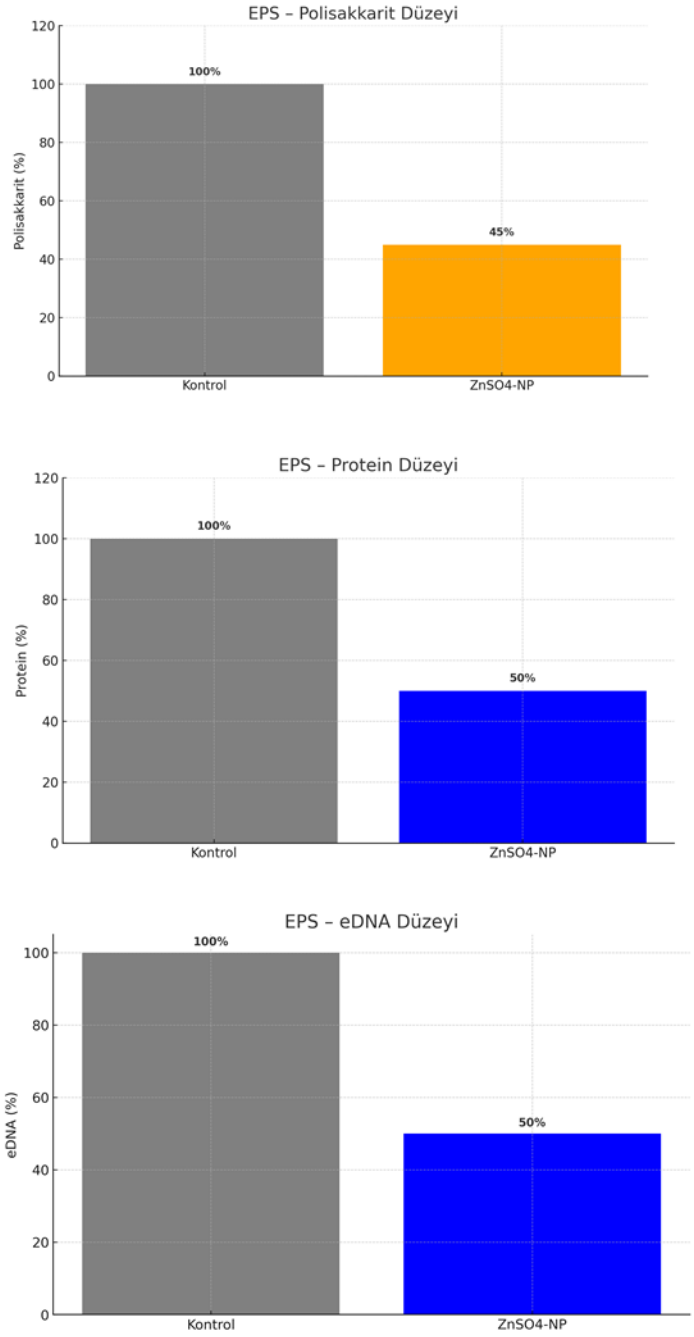

Figure 3. Polysaccharide, protein and EPS analysis of biofilm cells

Nanoparticles are known to impair EPS production through multiple pathways, including direct interactions with the negatively charged components of the matrix and the generation of reactive oxygen species (ROS). These processes compromise the structural integrity of the EPS and reduce its protective capacity (Seil & Webster, 2012). Furthermore, zinc-based nanoparticles have been reported to downregulate biofilm-associated genes such as icaA, icaD, and sarA, which are responsible for polysaccharide intercellular adhesin (PIA) synthesis and regulatory pathways essential for biofilm formation (Arciola et al., 2015; Liang et al., 2019). The reduction of biomass to 40% viability in the $ZnSO_4$-NP treated group is in agreement with earlier studies that demonstrated the ability of metal nanoparticles to significantly inhibit S. aureus biofilms by targeting both microbial cells and the EPS matrix (Pelgrift & Friedman, 2013). These findings strongly support the potential application of $ZnSO_4$ nanoparticles as

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antibiofilm agents, particularly in medical and food-related environments where S. aureus biofilms pose serious risks. The obtained results demonstrated a significant reduction in the extracellular polymeric substance (EPS) components of Staphylococcus aureus biofilms upon treatment with $ZnSO_4$ nanoparticles ($ZnSO_4$-NP). Compared to the control group (100%), $ZnSO_4$-NP exposure reduced the polysaccharide level to 45%, protein level to 50%, and eDNA content to 50%. These findings suggest that $ZnSO_4$-NP exerts a disruptive effect on the structural integrity of biofilm matrices by simultaneously targeting multiple EPS constituents. Polysaccharides are the major scaffolding components of the biofilm matrix, contributing to bacterial adhesion and biofilm stability. Their substantial reduction following $ZnSO_4$-NP treatment indicates that the nanoparticles interfere with matrix cohesion and adherence capacity, consistent with previous reports that metal-based nanoparticles can inhibit polysaccharide synthesis and weaken biofilm mechanical resistance (Gupta et al., 2016; Liang et al., 2019). Similarly, proteins in EPS act as enzymes, adhesins, and structural stabilizers, facilitating nutrient retention and intercellular communication. The observed 50% decrease in EPS protein content supports the hypothesis that $ZnSO_4$-NPs disrupt bacterial metabolism and matrix-associated protein secretion, thereby compromising biofilm development. Comparable findings were reported by Kalishwaralal et al. (2010), where metal nanoparticles reduced biofilm-associated protein fractions and promoted structural disintegration. Moreover, extracellular DNA (eDNA) is a critical component that enhances biofilm cohesion and horizontal gene transfer within microbial communities (Whitchurch et al., 2002; Okshevsky & Meyer, 2015). The observed 50% reduction in eDNA levels suggests that $ZnSO_4$-NPs may either degrade extracellular DNA or inhibit its release from bacterial cells. Since eDNA is often stabilized by cationic interactions with polysaccharides and proteins, its concurrent reduction further highlights the broad-spectrum antibiofilm potential of $ZnSO_4$-NPs. Overall, the simultaneous suppression of polysaccharide, protein, and eDNA levels underscores the multifaceted antibiofilm mechanism of $ZnSO_4$-NPs. By impairing multiple EPS components, $ZnSO_4$-NPs hinder biofilm maturation and may sensitize bacterial communities to antimicrobial agents. These findings align with recent studies suggesting that nanoparticle-mediated EPS disruption is a promising strategy to overcome biofilm-associated infections (Liang et al., 2019; Singh et al., 2017).

Effect of $ZnSO_4$ Nanoparticles on Biofilm-Associated Gene Expression

Gene expression analysis was performed by RT-qPCR to determine the effect of $ZnSO_4$ nanoparticles on the transcription of biofilm-associated genes in *Staphylococcus aureus*. As shown in Figure 3, the relative expression levels of icaA, icaD, and sarA were significantly downregulated in the presence of $ZnSO_4$-NPs compared to the untreated control. For the control group, all three genes were expressed at baseline levels (set as 1.0), whereas treatment with $ZnSO_4$-NPs reduced the expression of icaA to ~0.3-fold, icaD to ~0.4-fold, and sarA to ~0.2-fold. These results indicate that $ZnSO_4$ nanoparticles strongly suppress the transcriptional activity of genes critical for biofilm formation.

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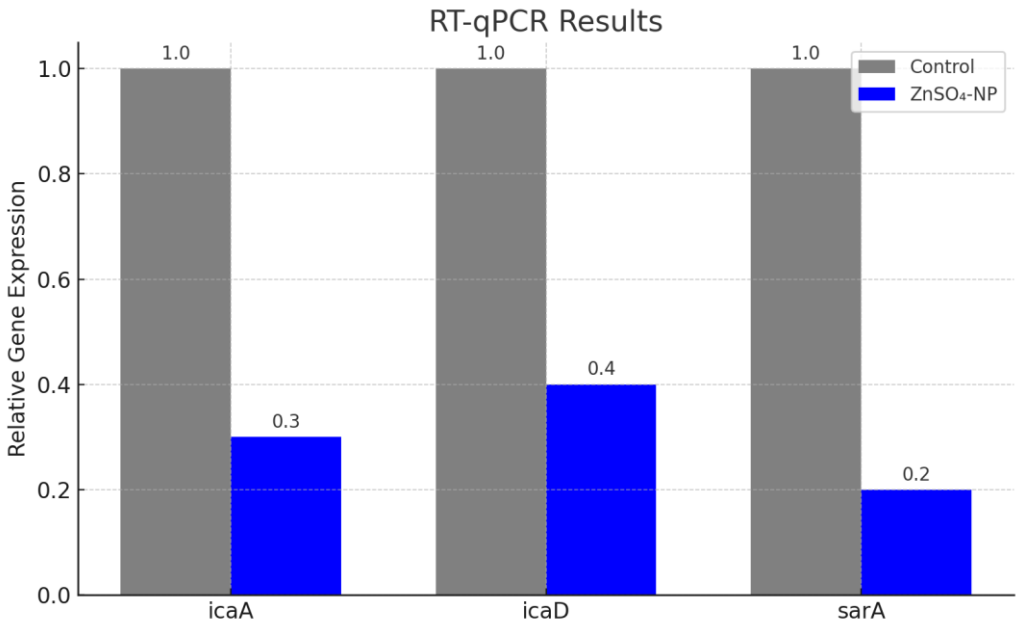

Figure 4. Relative gene expression levels of icaA, icaD, and sarA in *S. aureus* biofilms treated with $ZnSO_4$ nanoparticles compared with untreated control.

The significant downregulation of icaA and icaD observed in $ZnSO_4$-NP treated biofilms suggests an inhibition of polysaccharide intercellular adhesin (PIA) biosynthesis, which is essential for intercellular adhesion and biofilm accumulation (Arciola et al., 2015). Since the icaADBC operon plays a key role in the synthesis of poly-β-1,6-N-acetylglucosamine (PNAG), its suppression by $ZnSO_4$ nanoparticles directly affects the structural stability of the biofilm matrix. Furthermore, the decreased expression of sarA, a global transcriptional regulator, indicates that $ZnSO_4$ nanoparticles not only target structural genes but also interfere with regulatory networks controlling biofilm development. sarA is known to upregulate adhesion and matrix production genes, thereby promoting robust biofilm formation (Beenken et al., 2003). Its downregulation in the present study highlights the ability of $ZnSO_4$-NPs to weaken biofilm development at both structural and regulatory levels. These findings are consistent with previous reports that metal-based nanoparticles, including zinc oxide, exert antibiofilm effects by disrupting gene expression in addition to damaging the extracellular matrix (Liang et al., 2019; Seil & Webster, 2012). Together with the CV assay results, the RT-qPCR data confirm that $ZnSO_4$ nanoparticles exert a dual antibiofilm effect: impairing EPS production and downregulating biofilm-related gene expression, which collectively leads to substantial inhibition of *S.aureus* biofilms.

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MONOAMİN OKSİDAZ A'NIN GENETİK MANİPÜLASYONU: NÖROTRANSMİTTER METABOLİZMASINDAN DAVRANIŞA

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ÖZET

Monoamin Oksidaz A (MAOA) geni, serotonin, dopamin ve norepinefrin gibi nörotransmitterlerin yıkımında görev alan kritik bir enzim kodlamaktadır. Beyindeki kimyasal dengenin düzenlenmesinde rol oynayan bu gen, özellikle düşük aktiviteye sahip varyantları nedeniyle bilimsel araştırmalarda öne çıkmaktadır. Yapılan çalışmalar, düşük MAOA ekspresyonunun saldırganlık, dürtüsellik ve antisosyal davranışlarla ilişkili olduğunu göstermiştir. Bununla birlikte, genetik yatkınlığın tek başına belirleyici olmadığı, çevresel faktörlerle (örneğin çocuklukta travmatik deneyimler) etkileşime girdiğinde bu davranışsal sonuçların daha güçlü şekilde ortaya çıkmaktadır. Bu çalışmada, MAOA geninin düzenlenmesine yönelik biyoteknolojik yaklaşımların incelenmesi ele alınmaktadır. CRISPR-Cas9 temelli gen düzenleme ile doğrudan DNA dizisinde değişiklik yapılabilirken, RNA girişim teknikleri (siRNA, shRNA) geçici olarak gen ekspresyonunu baskılayabilmektedir. Ayrıca, epigenetik modifikasyon yöntemleri gen dizisini değiştirmeden ekspresyon seviyesini kontrol etmeye olanak tanımaktadır. Viral vektörler aracılığıyla gen transferi ise genin işlevini artırma veya susturma yönünde farklı araştırma fırsatları sunmaktadır. Ancak bu yöntemlerin her biri, hedef dışı mutasyonlar, bağışıklık sistemi tepkileri ve uzun vadeli yan etkiler gibi riskler taşımaktadır. MAOA genine müdahale etmeyi gündeme getiren bu yaklaşımlar yalnızca biyolojik değil, aynı zamanda etik, psikolojik ve toplumsal boyutlar açısından da dikkatle tartışılmalıdır. İnsan davranışlarını genetik düzeyde değiştirme fikri, kişilik bütünlüğü, özgür irade ve toplumsal normlar bağlamında önemli sorular doğurmaktadır. Dolayısıyla, bu alandaki araştırmalar yalnızca teknik fizibiliteye değil, aynı zamanda etik sınırların belirlenmesine ve disiplinler arası iş birliklerine gereksinim vardır.

Anahtar Kelimeler : MAOA geni, genetik modifikasyon, agresif davranışlar.

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KÖPEKLERDE PARVOVİRÜS ENFEKSİYONLARININ GÜNCEL TEDAVİ YÖNTEMLERİ

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ÖZET

Köpek parvoviral enteriti dünya çapında genç köpeklerde morbidite ve mortalitenin en yaygın nedenlerinden biridir. Kanin parvovirüs (CPV) Protoparvovirüs cinsine ait olan Parvoviridae ailesinin bir üyesidir. Akut CPV-2 enteritisi, her ırk, yaş ve cinsiyetteki köpeklerde görülebilir fakat 6 hafta ile 4 ay arasındaki yavruların bu enfeksiyona karşı daha duyarlı oldukları bildirilmektedir. **Hastalığa yatkın hale getiren predispozisyon faktörler koruyucu immunitenin eksikliği, hayvanların barınaklarda aynı kafeslerde bir arada bulunması ile hijyen kurallarına uyulmaması ve stresli çevre şartları olarak sıralanabilir.** Yutulduktan sonra, enfeksiyonun ilk 2 günü boyunca orofarenkste viral replikasyon meydana gelir ve kan dolaşımı yoluyla diğer organlara yayılır. Üçüncü ila beşinci günlerde viremi belirginleşir. Genellikle enterik hastalık olarak ortaya çıksada, parvoviral enfeksiyon sistemiktir. Virüs oral yolla alındıktan sonra ilk başta orofaringeal ve mezenterial lenf nodülleri, timusta replike olmaktadır. Virüs bağırsak lümeninden ziyade kan dolaşımından bağırsak mukozasına ulaşır. CPV enteritis intestinal, kardiyak ve generalize hastalık olmak üzere 3 farklı formda şekillenebilmektedir. Kesin tanı en kolay şekilde dışkıda köpek parvovirüsünün gösterilmesiyle yapılır, bu akut vakalarda mevcut virüs miktarı nedeniyle nispeten basit bir iştir. Tedavi yöntemleri olarak sıvı elektrolit tedavi, antimikrobiyal tedavi, antioksidan tedavi, antiviral tedavi, immunterapi ve antiemetik yöntemleri sayılabilir.

Anahtar Kelimeler: Parvovirüs, Tedavi Yöntemleri, Enfeksiyon

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1. GİRİŞ

Köpek parvoviral enteriti dünya çapında genç köpeklerde morbidite ve mortalitenin en yaygın nedenlerinden biridir (Mylonakis et al., 2016). Kanin parvovirüs (CPV) Protoparvovirüs cinsine ait olan Parvoviridae ailesinin bir üyesidir. CPV küçük, zarfsız ve tek sarmallı bir DNA virüsüdür. Filogenetik analizlerde CPV'nin kedi, gelincik, rakun, rakun köpeği, kutup tilkisinde enfeksiyon oluşturan virüsle ortak bir soydan geldiğine inanılmaktadır (Miranda & Thompson, 2016). Etken canine parvovirus tip 2 (CPV-2)'dir. Parvoviridae ailesi içerisinde yer alan, tek iplikçikli DNA (ssDNA) kapsayan oldukça küçük (18-26 nm) bir virustur. Birçok memelide hastalığa sebep olmalarının yanı sıra tür spesifiktirler (Goddard & Leisewitz, 2010). Akut CPV-2 enteritisi, her ırk, yaş ve cinsiyetteki köpeklerde görülebilir fakat 6 hafta ile 4 ay arasındaki yavruların bu enfeksiyona karşı daha duyarlı oldukları bildirilmektedir. Düşük vücut ağırlığının ölüm oranını artırdığı bildirilmiştir. CPV yalnızca köpekleri etkilemekte, insanlara veya diğer türlere bulaşmamaktadır. Bir köpek hastalandıktan sonra ilk 4 günde hayatta kalırsa, genellikle hızlı bir şekilde iyileşmektedir. Ancak, birçok köpek yavrusu da tıbbi müdahale yapılamadan ölmektedir. CPV hastalığını geçiren ya da bu hastalığa karşı aşılanan köpeklerde uzun süreli bağışıklık meydana gelmektedir. Yavru köpekler kolostrum aldığı sürece (hayatın ilk birkaç haftası boyunca), anneden aldığı maternal antikorlar tarafından enfeksiyona karşı korunur (annede CPV'ye spesifik antikorların olduğu varsayılarak). Bu tür yeni doğanlarda hastalık nadiren görülür. Bununla birlikte, parvovirus için maternal antikorun yarılanma ömrü yaklaşık 10 gündür. Maternal antikor titresinde meydana gelen düşüş yavruları enfeksiyona duyarlı hale getirmektedir. Enfekte olmuş tüm köpekler klinik belirtiler göstermeyebilirler, ancak enterik ateşin akut fazı sırasında virusu dışkı ile saçabilirler ve serum antikor titrelerinde önemli artışlar gösterebilirler (Nandi et al., 2010), Miranda et al., 2016), Schoeman et al., 2013), Schoeman et al., 2013b).

1.1 Predispozisyon faktörler

Hastalığa yatkın hale getiren predispozisyon faktörler koruyucu immunitenin eksikliği, hayvanların barınaklarda aynı kafeslerde bir arada bulunması ile hijyen kurallarına uyulmaması ve stresli çevre şartları olarak sıralanabilir (Reddy et al., 2015). Labrador, Alman çoban köpeği, American Staffordshire Terrier ve Alaska kızak köpek ırklarının CPV enteritise karşı duyarlı ırklar olduğu ifade edilmesine rağmen yakın zamandaki araştırmalarda ise ırk predispozisyonuna rastlanılmamaktadır (Godsall et al., 2010; Iris Kalli et al., 2010). Köpeklerde CPV enteritisin risk faktörlerinin araştırıldığı bir çalışmada ise hastalığın her mevsim görülebildiği, cinsiyet olarak erkek köpeklerde ve yaş olarak 2-4 aylık yaştaki yavru köpeklerde görülme insidansının daha yüksektir (Mustafa et al., 2011).

2. PATOFİZYOLOJİSİ

Yutulduktan sonra, enfeksiyonun ilk 2 günü boyunca orofarenkste viral replikasyon meydana gelir ve kan dolaşımı yoluyla diğer organlara yayılır. Üçüncü ila beşinci günlerde viremi belirginleşir. Genellikle enterik hastalık olarak ortaya çıksada, parvoviral enfeksiyon sistemiktir. Virüs oral yolla alındıktan sonra ilk başta orofaringeal ve mezenterial lenf nodülleri,

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timusta replike olmaktadır. Virüs bağırsak lümeninden ziyade kan dolaşımından bağırsak mukozasına ulaşır (P. C. Meunier, Cooper, Appel, & Slauson, 1985; P. C. Meunier, Cooper, Appel, Lanieu, et al., 1985). Daha sonra virüs bağırsak epitel kriptleri, kemik iliği, dil epiteli, oral kavite, kalp miyositleri ayrıca akciğer, dalak, karaciğer ve böbrekler gibi hücreleri hızlı bir şekilde bölünen organları etkilemektedir (Ford et al., 2017). Bağırsak cidarı etkilendiğinden dolayı bağırsak yüzeyinde kanamalar şekillenebilmekte ve bunun sonucunda kusma ve hemorajik bir diyare, nutrisyonel malabsorbsiyon, bakteriyel translokasyon şekillenebilmektedir. Timusta viral etkenlerin yerleşmesi sonucu timusun korteksinde yıkımlanma oluşabilmektedir. Ayrıca kemik iliğinin etkilenmesi sonucu lökositlerin yıkımlanmasıyla lökopeni şekillenebilmektedir (Decaro et al., 2012). İmmun sistemin bozulması sonucu bağırsak bakterileride sekonder olarak enfeksiyona katılır ve bu durumda da septik şok, sistemik inflamatuar yanıt sendromu (SIRS), çoklu organ yetmezliği ve ölüm meydana gelebilmektedir (Mazzaferro, E. M.,2020).

3. KLİNİK BULGULAR

CPV enteritis intestinal, kardiyak ve generalize hastalık olmak üzere 3 farklı formda şekillenebilmektedir. İntestinal form; lökopeni, kusma ve yaklaşık 8 aylık köpek yavrularında hemorajik diyarenin görüldüğü formdur. Depresyon (laterji ve anoreksi), ateş, kusma ve mukoid ya da şiddetli hemorajik ishal ile birlikte seyreden ciddi enteritisler gözlenir. İshala bağlı dehidrasyon şekillenebilir. Kardiyak formda ise 3-8 haftalık yaştaki yavru köpeklerde solunum ve kardiyovasküler yetmezlik sonucu nonsuppuratif miyokarditis ve ani ölümler görülebilmektedir. Hastalığın generalize formu ise 2 haftadan daha küçük yaştaki yavru köpeklerin dokularında fokal nekrozislerin şekillendiği form olarak nitelendirilmektedir (Lenghaus & Studdert, 1984; “Infectious Diseases of Wild Mammals,” 2001, Decaro et al., n.d.)

4. LABORATUVAR BULGULARI

CPV enteritiste geçici bir lenfopeniye ek olarak total lökosit sayısının düşmesi en çok görülen hematolojik bulgular arasındadır (Ling et al., 2012). Anemi intestinal hemoraji ve rehidrasyon tedavisinin etkisinden dolayı hastalığın şiddetli seyrettiği durumlarda hastalığın son aşamasında görülebilen bir durumdur (Jacobs et al., 1981). Biyokimyasal bulgular CPV enteritiste nonspesifiktir. Hastalığa bağlı olarak anoreksi, kusma ve diyareden dolayı yoğun hipokalemi şekillenebilmektedir. CPV enteritiste hiponatremi ve hipokloremiye kusma ve diyareden dolayı rastlanılmaktadır (Nappert et al., n.d.). 12 ile 24 saat içerisinde yüksek C reaktif protein (CRP) seviyesi ise mortalite oranındaki artışla ilişkilendirilmektedir (Kocaturk et al., 2010; McClure et al., 2013). CPV ile enfekte köpeklerde serum total kolesterol seviyesi ve yüksek yoğunluklu lipoprotein seviyesinde düşme görülmesi, trigliserid seviyesinde artışın şekillenmesi CPV enteritisin şiddetinin bir markırı olarak kullanılabileceği ifade edilmektedir (Yilmaz et al., 2007).

CPV enteritisli köpeklerde intestinal ve kardiyak ilişkili biyomarkırların araştırıldığı bir çalışmada CPV enteritisli köpeklerde kontrol grubuna göre kan gazı hidrojen iyon

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konsantrasyonu, parsiyal oksijen basıncı, sodyum, bikarbonat, oksijen saturasyon seviyeleri ve total lökosit sayısında azalma şekillendiği, intestinal yağ asidi bağlayıcı protein-1, trefoil faktör-3, claudin-3, kalp tipi yağ asidi bağlayıcı protein, cTn-I ve CK-MB düzeylerinde ve trombosit sayılarında ise artışın şekillendiği ifade edilmiştir (Gulersoy et al., 2020).

5. TANI

Kesin tanı en kolay şekilde dışkıda köpek parvovirüsünün gösterilmesiyle yapılır, bu akut vakalarda mevcut virüs miktarı nedeniyle nispeten basit bir iştir. Tanı laboratuvarlarında çeşitli yöntemler mevcuttur- viral izolasyon, dışkı hemaglütinasyonu, elektron mikroskobu vb. (Pollock et al., n.d.). CPV enteritisin hızlı tanısında ELISA antijen snap testler ticari olarak mevcuttur. Bu testlerin duyarlılığı bir çalışmada CPV-2a, 2b ve 2c altiplerine göre sırasıyla %80.4, %78.0 ve %77.0 olarak belirlenmiştir (Decaro et al., 2010). Hastalığın başlangıç aşamasında viral saçılım düşük olabileceğinden dolayı bu zamanda yapılan ELISA testleriyle yapılan analizler yanlış negatif sonuçlar verebilmektedir. Böyle durumlarda hastalıktan şüphe edilmesi durumunda test tekrarlanmalıdır. Ayrıca modifiye canlı CPV aşıları ile aşılanan köpeklerde aşılama sonrası 5-15 gün arasında yanlış pozitif sonuçlar belirlenebilmektedir (Schmitz et al., 2009). Şayet CPV enteritisten şüphelenilmesi ve ELISA testi sonucunun negatif çıkması durumunda moleküler yöntem olarak Polimeraz Zincir Reaksiyonu (PCR) testleri önem arzetmektedir. PCR, köpek dışkısında düşük yoğunlukta bulunabilen etkenleri belirleyebilecek yüksek duyarlılığa sahiptir (Bird et al., 2013).

6. TEDAVİ YÖNTEMLERİ

CPV enteritisin tedavisinde birçok tedavi denemesi yapılmıştır.

6.1. Sıvı- Elektrolit Tedavisi

Asit-baz ve elektrolit dengesizliklerine ilaveten hidrasyon ve onkotik basıncın dengelenmesi CPV enteritisin tedavisinde önemli bir kısmı oluşturmaktadır. Aşırı dehidre hayvanlarda kan sirkülasyonu bozulduğu için subkutan sıvı uygulaması yerine venöz veya intraosseoz sıvı uygulaması sıvı tedavisinin etkinliği açısından son derece önemlidir (Lobetti et al., 2002). CPV enteritiste büyük miktarlarda protein kayıpları şekillenebilmektedir. Periferal ödem (subkutan, konjuktival, pleural veya abdominal efüzyon), hipoalbuminemi (< 2 g/ dL) veya hipoproteinemi (< 4 g/dL) şekillendiği zaman kolloid bir sıvı desteğinin sağlanması gerekmektedir (Davis et al., 2013).

6.2. Antimikrobiyal Tedavi

Antimikrobiyal ilaçlar veya ilaç kombinasyonları hem gram negatif bakteriler hem de anaerobik bakterileri bertaraf etmek için kullanılmaktadır. CPV enteritisin semptomatik tedavisinde antibiyotik olarak enjektabl ampisilin veya sefazolin birçok köpek için yeterli olabilmektedir. Ancak köpeklerde hemorajik diyare veya SIRS belirtileri olduğu zaman ise penisilin+ florokinolon veya penisilin+ aminoglikozid kombinasyonlarının kullanılması tavsiye edilmektedir (Sykes, 2013).

6.3. Antioksidan Tedavi

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CPV enteritisin tedavisinde destekleyici tedaviye ek olarak N-asetilsisteinin (NAC) etkisinin araştırıldığı çalışmada sağlıklı gruba göre CPV enteritisli köpeklerde belirgin bir şekilde hemokonsantrasyon, lökopeni, nötropeni ve oksidatif stresin arttığı ifade edilmiştir. NAC alan grupta ise sadece destek tedavisi alan gruba göre zamanla lökosit, nötrofil, monosit ve eozinofil sayılarında belirgin bir düzelmenin olduğu bildirilmiştir. Ayrıca aynı çalışmada NAC alan grupta glutasyon S transferaz aktivitesinin arttığı, nitrik oksit ve malondialdehit konsantrasyonunun ise belirgin bir şekilde düştüğü bildirilmiştir (Gaykwad et al., 2018). CPV enteritisli köpeklerin tedavisine yönelik yapılan çalışmada antibiyotik tedavisine ek olarak vitamin C ile NAC'ın tedaviye eklendiği gruptaki köpeklerde sadece antibiyotik alan köpeklere nazaran hemato-biyokimyasal parametrelerde daha hızlı bir düzelmenin şekillendiği bildirilmiştir (Kataria et al., n.d.).

6.4. İmmunterapi

CPV enteritisli köpek yavrularında fekal mikrobiyata tranferinin tedavideki etkinliğinin araştırıldığı çalışmada standart tedaviye ek olarak fekal mikrobiyata uygulanan hayvan grubunda diyarenin daha kısa sürede düzeldiği ve daha kısa hospitalizasyon zamanın oluştuğu bildirilmiştir. Ayrıca aynı çalışmada mortalite oranının standart tedaviye göre ek olarak fekal mikrobiyata uygulanan grupta daha düşük seyrettiği ifade edilmiştir (Pereira et al., 2018). CPV enteritisin tedavisinde heterojen immunglobulin Y (Ig Y)'nin etkinliğinin araştırıldığı bir çalışmada Ig Y'nin 6 gün süresince verildiği ve 7. günde Ig Y verilen köpeklerin hepsinin iyileştiği bildirilmiştir. Çalışmanın sonucunda CPV enteritisli köpeklerin tedavisinde Ig Y'nin etkili olduğu belirtilmiştir (Naveenkumar et al., n.d.). CPV enteritisli bir köpekte destek tedavisine ilave olarak CPV enteritise karşı spesifik immunglobulinin kullanılmasının hastalığın şiddetini azalttığını ve klinik belirtileri iyileştirdiğini rapor etmişlerdir. CPV enteritisli köpeklerde probiyotik bakterilerinin terapötik etkisinin araştırıldığı bir çalışmada semptomatik tedaviye kıyasla semptomatik tedaviye ek olarak probiyotik tedavisi başlanan (Lactobacillus casei, Lactobacillus plantarum, Lactobacillus acidophilus, Lactobacillus delbrueckii spp bulgaricus, Bifidobacterium longum, Bifidobacterium breve, Bifidobacterium infantis ve Streptococcus salivarus spp thermophilus) grupta daha yüksek bir sağ kalma oranı (%90) elde edildiği, lökosit ve lenfosit sayılarının semptomatik tedavi grubuna göre daha hızlı bir şekilde düzeldiği ve probiyotik ilavesinin iyileşme zamanını kısalttığı bildirilmiştirV(Arslan et al., n.d.). Meunier ve ark. deneysel olarak CPV ile enfekte olan köpeklerde CPV hiperimmunplazmanın uygulanmasıyla kusma ve diyare insidansının azaldığını ve sağ kalma oranının yükseldiğini bildirmişlerdir (Meunier, Cooper, Appel, Lanieu, et al., 1985b).

6.5. Antiviral Tedavi

Schaudien ve ark. (87) CPV enteritisli köpeklerde oseltamivirin 2 mg/kg dozda peros 5 gün süreyle kullanılmasının çalışmadaki plasebo grubuna göre vücut ağırlığındaki kayıpları ve ayrıca hemotolojik parametrelerdeki patolojik durumu düzelttiğini bildirmişlerdir. CPV enteritis üzerine asiklovirin profilaktik etkisinin araştırıldığı başka bir çalışmada asiklovir verilen gruptaki köpek yavrularında rektal svap örneklerinde CPV replikasyonunun bulunmamasıyla asiklovirin tedavide etkili bir antiviral olduğu belirtilmiştir (Albaz et al., 2015; Schaudien et al., 2010). CPV enteritis üzerine antiviral ilaçların inhibitör etkilerinin araştırıldığı çalışmada Nitazoksanit, Closantel Sodyum ve Closantel'in CPV replikasyon sürecini hızlı bir şekilde inhibe ettiği bildirilmiştir. Bu ilaçların Western blot testinin sonucunda üç CPV varyantının farklı alt tipleri karşısında geniş bir antiviral özelliğinin olduğu belirtilmiştir (Zhou et al., 2019).

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6.6. Antiemetik Tedavi

CPV enteritisli köpeklerde şekillenen kusmanın önlenmesinde metoklopramid, ondansetron ve maropitantın karşılaştırmalı etkisinin araştırıldığı bir çalışmada CPV enteritise bağlı kusmanın sıklığını ve yoğunluğunu azaltmada üç antiemetik ilacında eşit bir şekilde etkili olduğu bildirilmiştir (Yalcin et al., 2017).

7. KORUNMA

Köpeklerde seyreden subklinik enfeksiyon özellikle kalabalık alanlarda ve temizlik kurallarına uyulmayan barınaklarda diğer köpekler için bir bulaş kaynağı oluşturmaktadır (Tupler et al., 2012). Hastalığı önlemenin en etkili yöntemi sağlıklı olan yavru köpeklerin hastalardan izolasyonudur. Hayvan sahiplerine hastalığın yetişkin hayvanlardan yavru köpeklere geçebileceği bilgisinin verilmesi hastalığın yayılımını önlemede oldukça önemlidir. Hayvanların toplu bakımının yapıldığı yerlerde çalışan personelin kullandığı malzemelerin belirli periyotlarda dezenfeksiyonu ve hijyen kurallarına uyulması hastalığın sağlıklı hayvanlara bulaşmasını önlemede son derece önemlidir (… & 2020, n.d.). Yakın zamandaki bir çalışmada 20 haftalıktan daha küçük yaştaki yavru köpeklerin inaktif aşılarla aşılanmasının modifiye canlı aşılara nazaran daha düşük bir immunite gösterdiği ifade edilmiştir (Altman et al., 2017). Tekrar aşılamanın 1 yaşında uygulanması ve bundan sonrada her 3 yılda bir tekrar aşılama yapılması önerilmektedir (… & 2020, n.d.).

8. SONUÇ

CPV enteritis morbidite ve mortalite oranı yüksek, bulaşıcı ve özellikle yavru köpekleri etkileyen bir hastalıktır. Sağaltımda semptomatik tedavinin yanı sıra immun sistemin immunmodülatörler, sitokinler, interferonlar ve antioksidan maddeler, enteral besleme ile desteklenmesi bu hastalıktan dolayı oluşabilecek mortalite oranını önemli oranda azaltmaktadır. Tedavinin yanı sıra hastalıktan korunma önemini korumaktadır. Bunun için kalabalık ve farklı yaştaki köpek popülasyonunun bir arada bulundurulmasından kaçınılması, hijyen kurallarına uyulması, sağlıklı hayvanların hasta hayvanlarla bir arada bulundurulmaması, iç parazit uygulamaları ve CPV enfeksiyonuna yönelik hazırlanmış aşılarla hayvanların immunize edilmesi son derece önemlidir.

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KEDİLERDE HERPES VİRÜS ENFEKSİYONLARININ OKSİDATİF STRES PARAMETRELERİ ÜZERİNE GÜNCEL ARAŞTIRMALARI

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ÖZET

Kedilerde yaygın bir viral enfeksiyon olan Feline Herpesvirüs Tip 1 (FHV-1), üst solunum yolu hastalıklarına neden olur. Bu enfeksiyon, oksidatif stresi artırabilir ve hücrelerde hasara neden olabilir. Malondialdehit (MDA) ve 4-hidroksinonenal (4-HNE) gibi biyobelirteçler oksidatif stresin değerlendirilmesinde kullanılır. Protein karbonilasyonu seviyeleri ve 8-hidroksi-2'-deoksiguanozin (8-OHdG) ise hasarı yansıtır. Antioksidanlar, özellikle E ve C vitaminleri, oksidatif hasarı azaltabilir. Dengeli bir diyet, bağışıklık sistemini güçlendirirken çevresel stres faktörlerinin azaltılması da önemlidir. Antioksidan tedavi stratejilerinin etkinliği daha fazla araştırılmalıdır. Kedilerde FHV-1 enfeksiyonlarını yönetmek, yaşam kalitesini artırabilir ve hastalığın seyrini olumlu yönde etkileyebilir. Ayrıca antioksidan dengenin bozulması saprofit enfeksiyonların oluşmasına neden olabilecektir. Oksidatif stresin erken teşhisi ve izlenmesi için daha hassas biyobelirteçler geliştirilmelidir.

Anahtar Sözcükler: FHV-1, Oksidatif stres, Enfeksiyon, Herpes

1. GİRİŞ

Feline Herpesvirus Tip 1 (FHV-1), kedilerde tipik olarak üst solunum yolu enfeksiyonlarına neden olan yaygın bir viral patojendir. Virüs, kedilerin burun, ağız ve göz çevresinde enfeksiyonlara yol açabilir ve hastalığın şiddeti kedilerin bağışıklık durumuna ve stres seviyelerine bağlıdır (Binns vd., 2000). Kedilerde FHV-1'in belirtileri arasında burun akıntısı, öksürük, göz akıntısı, gözlerde ülserler, hapşırma ve genel halsizlik yer alır. FHV-1 için spesifik bir antiviral ilaç henüz keşfedilmemiştir, ancak semptomatik tedavi sıklıkla uygulanmaktadır (Doğan vd., 2019). FHV-1'in yayılmasını önlemek için genç kedilerde ve büyük gruplar halinde yaşayanlarda aşılama özellikle önemlidir. Sağlık üzerindeki etkilerini azaltmanın kritik öncülleri arasında virüsün erken teşhisi, semptomatik tedavi ve aşılama yer almaktadır (C. J. Gaskell vd., 1982).

1.1. Feline Herpesvirüs Tip 1 (FHV-1) ve Önemi

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Kedi herpes virüsü, herpesvirüs alt familyası Alphaherpesvirinae'nin Varicellovirus cinsinin bir üyesidir. Diğer herpesvirüsler gibi FeHV-1 de çift sarmallı DNA içerir ve bir glikoprotein-lipit zarfı vardır (R. Gaskell vd., 2007; Scott, 1980). Diğer alfaherpesvirüslerde olduğu gibi, iyileşen kedilerin neredeyse tamamı latent olarak enfekte taşıyıcılar haline gelir ve özellikle stres dönemlerinden sonra tespit edilebilir virüs dökülmesi (yeniden aktivasyon) aralıklı atakları meydana gelir. Bu tür ataklar sırasında bulaşıcı virüs oronazal ve konjunktival salgılarda bulunur ve diğer kedilere enfeksiyon kaynağı olarak etki eder (R. M. Gaskell ve Povey, 1977, 1982). FeHV-1 göz, burun ve ağız salgılarıyla yayılır ve bulaşma büyük ölçüde enfekte bir kediyle doğrudan temasla gerçekleşir. Akut olarak enfekte hayvanlar açıkça virüsün en önemli kaynaklarından biridir, ancak latent olarak enfekte olmuş taşıyıcı kediler de virüs saçabilir ve duyarlı kedileri enfekte edebilir (R. M. Gaskell ve Povey, 1982). Kedilerin %90'ından fazlasının bu virüse karşı seropozitif olduğu, enfekte bireylerin en az %80'inin yaşam boyu latent olarak enfekte kaldığı (Maggs vd., 1999) ve latent olarak enfekte kedilerin yaklaşık %45'inin yaşamları boyunca virüsü yaydığı tahmin edilmektedir (R. M. Gaskell ve Povey, 1977).

1.2. Oksidatif Stresin Tanımı, Önemi ve FHV-1 Enfeksiyonu ile İlişkisi

Oksidatif stres, vücutta serbest radikaller ve reaktif oksijen türlerinin (ROS) aşırı üretimi ile antioksidan savunma sistemleri arasındaki dengenin bozulması durumudur. Serbest radikaller, yüksek reaktiviteye sahip moleküllerdir (Sies, 1985). Hücre içinde proteinler, lipitler ve DNA gibi organellere bağlanarak bozunmasına neden olaiblmektedir. Normal koşullar altında, vücut bu zararlı molekülleri etkisiz hale getirmek için antioksidan savunma sistemini aktif hale getirir (Sies, 1997). Ancak, oksidanların antioksidanlarda fazla olması durumunda denge bozulur ve oksidatif stres meydana gelir. Serbest radikallerin hücrelerde artması ile oksidatif hasar oluşur (Sies ve Jones, 2007). Bu durum, hücre işlevlerinde bozulmalara ve hastalıkların gelişimine zemin hazırlayabilir. Enfeksiyon durumlardında ise ya serbest radikal miktarında artış meydana gelir ya da antioksidanlar bu artışa karşın yeterli seviyede üretilemez ve oksidatif stres şekillenir (Sugeçti, 2021; Yisak vd., 2021).

Birçok kronik hastalığın patogenezinde oksidatif stres önemli rol oynar. Kardiyovasküler hastalıklar, kanser, nörodejeneratif hastalıklar ve diyabet gibi yaygın sağlık sorunlarının oksidatif stres ile ilişkili olduğu bilinmektedir (Teleanu vd., 2022). Feline Calicivirus (FCV) enfekte kedilerde PON-1 seviyesinde düşüş olduğu oksidatif stress geliştiği bildirilmiştir (Gökçe ve Sarıkaya, 2021).

FHV-1 (Feline Herpsevirus -1) ve FCV (Feline Calicivirus), evcil kedilerde özellikle üst solunum yolu problemlerinde yaygın olarak tespit edilen iki önemli etkendir (Binns vd., 2000). FHV-1, Herpesviridae familyasının Alphaherpesvirinae alt familyasının Varicellovirus cinsinde yer alan, dsDNA içeren zarflı bir virüstür. Ajan üst solunum yolu ve göz epitelinde çoğalır ve rinit ve konjonktivitin yaygın olduğu üst solunum yolu ve göz enfeksiyonlarına neden olabilir (Doğan vd., 2019). Her iki hastalığın da semptomları birbiri ile benzer seyretmektedir. FHV-1, kedilerde üst solunum yolu enfeksiyonlarına ve göz hastalıklarına neden olur. Virüsün aktif olduğu dönemlerde, kedinin bağışıklık sistemi serbest radikallerin üretimini artırabilir ve bunun da oksidatif strese yol açması beklenmektedir. Oksidatif stres, enfeksiyonun şiddetini artırarak semptomların daha ağır seyretmesine neden olabilir (Sykes, 2022). Bu nedenle,

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oksidatif stresi azaltacak antioksidan takviyeleri ve beslenme programları, FHV-1 enfeksiyonlarının yönetiminde önemli bir rol oynayabilir.

1.3. **Oksidatif Stres Parametreleri**

Hücrelerde ROS oluşumunun ana kaynağı, elektron taşıma zincirlerinden elektron kaçışıdır. Mitokondrilerden geçen oksijenin %90 ila %95'inin suya dönüştüğü ve kalan %5 ila %10'unun ROS oluşturduğu tahmin edilmektedir (Hoffmann vd., 2004). Oluşan ROS'a karşı antioksidan savunma sistemi devreye girer ve radikalleri süpürme görevini yerine getirir (Cooke vd., 2003; Williams ve Jeffrey, 2000). Endojen antioksidan savunma mekanizmaları arasında albümin, haptoglobulin, ferritin ve seruloplazmin gibi antioksidan proteinler; SOD, katalaz ve glutatyon peroksidaz gibi enzimatik antioksidanlar ve suda çözünen antioksidanlar (askorbik asit, ürik asit, bilirubin, glutatyon, çinko ve selenyum) ile yağda çözünen antioksidanlar (tokoferoller, β-karoten, ubikinol-10 ve likopen) bulunmaktadır. Albümin, plazmadaki bolluğu nedeniyle en önemli antioksidan protein olarak kabul edilir (Fang vd., 2002).
Oksidatif stresin değerlendirilmesi, reaksiyon ürünlerinin ölçülmesini, ROS'un ölçülmesini veya endojen antioksidanların miktarının belirlenmesi sayesinde gerçekleşebilmektedir. Lipidler, ROS'un saldırısına uğrayan yaygın bir substrat olup, oksidasyonun belirteçleri olarak hizmet edebilir. Malondialdehit, konjuge dienler, kısa zincirli alkanlar ve lipid hidroperoksitler lipid peroksidasyonunun bozunma ürünleridir. Özellikle MDA lipit peroksidasyonunun sonucu oluşan bir yan üründür ve serumda veya dokularda artışı lipit peroksidasyonunun göstergesi olarak kullanılabilmektedir (Yoshioka vd., 1979).

1.4. FHV-1 Enfeksiyonlarında Oksidatif Stres Parametreleri

Oksidatif stres, pet hayvanları pratiğinde çok sayıda hastalıkta tanımlanmıştır. Hem enfeksiyöz hem de enfeksiyöz olmayan etiyolojiler oksidatif stres mekanizmalarının zararlı etkileriyle ilişkilendirilmiştir. Yüksek oksidan yan ürün ve antioksidan muadillerinin azalması durumu oksidatif stres olarak bilinir (N Y Salem vd., 2020). Malondialdehit (MDA), vücuttaki oksidan kolunu değerlendirmek için genellikle ölçülen bir lipid peroksidasyon yan ürünüdür (Abdel-Saeed ve Salem, 2019), toplam antioksidan kapasite (TAK) ise vücuttaki antioksidan sistemin durumunu kaba bir şekilde tahmin etmek için kullanılır (Elsayed vd., 2020). Yapılan bir araştırmada kornea ülseri bulunan kedilerde yapılan otology PRP'nin oksidatif stress parametrelerdeki değişiklikler araştırılmıştır. Çalışmada kedilerdeki kornea ülseri vakasının esas olarak FHV-1 enfeksiyonundan kaynaklandığı tespit edilmiştir. Alınan gözyaşı örneklerinde MDA ve TAK değerlerinde artış CAT'de ise azalma görülmüştür. Buna bağlı olarak oksidatif stres varlığı saptanmış, tedaviden sonra ise normal seviyelere gelmiştir (Farghali vd., 2021).
Reaktif oksijen türleri (ROS) üretimi ile bunları ortadan kaldırma kapasitesine sahip antioksidanların dengesi bozulduğunda, oksidatif stres başlar, bu da hücresel hasara ve hücre zarında lipid peroksidasyonuna yol açar (Cejka ve Cejkova, 2015; Noha Y Salem vd., 2016).

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ROS birikimi, antioksidan sistemi aşırı yükler ve göz dokusunda ROS artışı şekillenir (Ankamah vd., 2019).

MDA seviyesindeki artış, ROS üretimindeki artışa veya antioksidanlardaki azalmaya bağlı olabilir (N Y Salem vd., 2020). Kornea hidrasyonundaki değişiklikler, oksidatif stresin oluşumunda rol oynar (Kubota vd., 2011). Kedilerdeki birçok kornea ülseri vakasının esas olarak FHV-1 enfeksiyonundan kaynaklandığı varsayılmaktadır (Di Martino vd., 2007; Low vd., 2007; Maggs, 2005). Ülseratif keratitiste, artmış MDA seviyeleri ve azalmış CAT ve süperoksit dismutaz (SOD) seviyeleri enfeksiyonla ilişkilendirilmiştir (Ruban vd., 2019). CAT, H_2O_2'yi suya dönüştürerek göz dokusunu korur; CAT ve SOD birlikte hareket ederek ROS'u ortadan kaldırmada kritik rol oynar (Scandalios, 2005). TAK, kornea ülserlerinde morfolojik durumlarından bağımsız olarak anlamlı bir azalma göstermektedir ve vücuttaki antioksidan seviyelerinin genel bir göstergesidir (Abdel-Saeed ve Salem, 2019). TAK'nin azalması, antioksidan sistemin öncülerinin birinci savunma hattı olarak hareket etmesinden kaynaklanır (Abdulaziz vd., 2019). TAK, antioksidan sistemlerin genel durumunu değerlendirmek için basit bir araç olabilir (Mancino vd., 2011). Deneysel keratit, korneada oksidatif stres ile ilişkilidir ve bu durum, görme algısının azalmasından görme kaybına kadar değişen ciddi kornea bozukluklarına yol açabilir (Cejka ve Cejkova, 2015). FHV-1 enfeksiyonlarında oluşan kornea bozukluklarından dolayı da oksidatif stres oluşması beklenmektedir.

2. SONUÇLAR VE DEĞERLENDİRME

FHV-1 enfeksiyonları, kedilerde önemli oksidatif stres kaynaklarından biridir ve bu durum gözlemlenen oksidatif stres parametreleri ile doğrulanmıştır. Enfekte kedilerin gözyaşı örneklerinde artmış malondialdehit (MDA) seviyeleri ve azalmış toplam antioksidan kapasite (TAK) ve katalaz (CAT) seviyeleri, enfeksiyonun hücresel hasar ve lipid peroksidasyonuna yol açtığını göstermektedir. Bu parametreler, ROS üretiminin arttığını ve antioksidan savunma mekanizmalarının yetersiz kaldığını işaret etmektedir. Oksidatif stres, kornea hidrasyonunun bozulmasına ve görme fonksiyonlarının azalmasına neden olabilir. CAT, hidrojen peroksiti suya dönüştürerek ROS'u ortadan kaldırmada önemli bir rol oynar ve süperoksit dismutaz (SOD) ile birlikte antioksidan savunma sisteminin kritik bileşenleridir. TAK ise, vücuttaki tüm antioksidanların kolektif etkisini temsil eder ve genel antioksidan kapasitenin değerlendirilmesinde kullanılır. TAC seviyelerindeki azalma, oksidatif stresin varlığını doğrular niteliktedir. Enfeksiyon sırasında gözlenen MDA seviyelerindeki artış ve TAK ile CAT seviyelerindeki azalma, ROS üretiminin arttığını ve antioksidan savunma mekanizmalarının yetersiz kaldığını göstermektedir. Bu durum, hücresel hasar ve lipid peroksidasyonu ile sonuçlanmakta, kornea hidrasyonunun bozulmasına ve görme fonksiyonlarının azalmasına yol açmaktadır. Tedavi sonrasında gözlemlenen MDA seviyelerindeki azalma ve TAK ile CAT seviyelerindeki artış, tedavinin oksidatif stresi azalttığını ve antioksidan savunma mekanizmalarını desteklediğini göstermektedir. Bu nedenle, FHV-1 enfeksiyonlarıyla mücadelede antioksidan tedavilerin rolü üzerinde durulması gerektiği sonucuna ulaşılmıştır. FHV-1 enfeksiyonlarının neden olduğu oksidatif stresin kontrol altına alınması, hücresel hasarın ve görme kaybının önlenmesinde kritik öneme sahiptir. Bu bağlamda, gelecekteki çalışmaların, farklı antioksidan tedavi stratejilerinin etkinliğini

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araştırarak kedilerde FHV-1 kaynaklı oksidatif stresin yönetimine yönelik yeni yaklaşımlar geliştirilmesine odaklanması gerekmektedir. Sonuç olarak, kedilerde herpes virüs enfeksiyonlarının yol açtığı **oksidatif stresin yönetimi, antioksidan savunma mekanizmalarının desteklenmesi ve uygun tedavi stratejilerinin uygulanması ile** mümkündür. Bu yaklaşımlar, enfeksiyonun neden olduğu hücresel hasarın azaltılması ve görme fonksiyonlarının korunmasında önemli rol oynayacaktır.

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CONTRIBUTION OF ARTVİN (TÜRKİYE) BROWN BEAR POPULATIONS TO THE MOLECULAR PHYLOGENY OF *Ursus arctos*

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ABSTRACT

This study aimed to contribute to the molecular phylogeny of the brown bear (*Ursus arctos*) populations in Artvin (Türkiye) by analysing partial sequences of the mitochondrial *COI* gene, which is widely used as a DNA barcode marker. The analyses were conducted using 559 base pair-long partial *COI* sequences from two Artvin specimens, along with sequences retrieved from GenBank. The results revealed that the Artvin specimens shared the same haplotype with previously reported specimens from Poland and Tibet. Evolutionary dating analysis based on Bayesian inference, in agreement with previous studies, indicated that *Ursus arctos*, *Ursus maritimus*, and *Ursus americanus* began diverging from their common ancestor approximately 5.95 million years ago, while the genetic differentiation between *U. arctos* (including the Artvin specimens) and *U. maritimus* commenced around 1.36 million years ago. Furthermore, the Artvin, Tibet, and Poland specimens were found to have diverged from Russian specimens approximately 243,000 years ago. These findings are consistent with earlier reports suggesting an adaptive radiation of the Ursidae family beginning in the Pliocene. In addition, the results support the phylogeographic continuity of *U. arctos* across Europe and Asia, highlighting that individuals from Türkiye are part of this broader genetic network.

Keywords : *Ursus arctos*, mitochondrial *COI* sequences, phylogeny, molecular dating, Türkiye

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SHILAJIT, SIÇANLARDA ANTİOKSİDAN VE SİRTUİN YOLLARI ARACILIĞIYLA 5-FLOROURASİL İLE OLUŞAN HEPATOTOKSİSİTEYİ AZALTIR

SHILAJIT ATTENUATES 5-FLUOROURACIL-INDUCED HEPATOTOXICITY THROUGH ANTIOXIDANT AND SIRTUIN PATHWAYS IN RATS

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ÖZET

5-Florourasil (5-FU), ciddi hepatotoksisiteye neden olduğu bilinen yaygın olarak kullanılan bir kemoterapötik ajandır. Shilajit, Himalayalar ve çevresindeki dağlık bölgelerde oluşan, fenolik bileşikler, dibenzo-α-pironlar ve çeşitli eser elementler içeren doğal bir mineral reçinesidir ve geleneksel tıpta hepatoprotektif, antioksidan ve anti-inflamatuar özellikleriyle bilinir. Bu çalışmada, bir sıçan modelinde 5-FU kaynaklı karaciğer hasarına karşı Shilajit'in koruyucu etkileri araştırılmıştır. Sıçanlar dört gruba ayrıldı (her grup için n=5): Kontrol (0.05% salin), 5-FU (7. günde 200 mg/kg i.p.), Shilajit (7 gün boyunca 200 mg/kg oral) ve Shilajit+5-FU (ilk 6 gün Shilajit, 7. günde eş zamanlı 5-FU uygulandı). 5-FU uygulaması oksidatif ve nitrozatif stres belirteçlerini (MDA, NO ve 8-OHdG), proinflamatuar sitokinleri (TNF-α, IL-1β, IL-6 ve NF-κB) ve ADA aktivitesini artırırken, antioksidan parametreleri (SOD, CAT, GSH) ve SIRT2/3 ekspresyonunu azaltmıştır. Shilajit tedavisi bu değişiklikleri önemli ölçüde iyileştirerek redoks dengesini ve mitokondriyal fonksiyonu geri kazandırmıştır. Yapısal karakterizasyon (NMR, FTIR, ICP-MS), fenolik grupların ve eser elementlerin (Zn, Cu, Fe) varlığını ortaya koymuştur. Bu bulgular, Shilajit'in oksidatif stresi, inflamasyonu ve sirtuin aracılı yolları düzenleyerek 5-FU kaynaklı toksisiteye karşı hepatoprotektif etkiler gösterdiğini göstermektedir.

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Anahtar Kelimeler: Shilajit, 5-florourasil, hepatotoksisite, oksidatif stres, sirtuinler, inflamasyon.

ABSTRACT

5-Fluorouracil (5-FU) is a widely used chemotherapeutic agent known to cause severe hepatotoxicity. Shilajit is a natural mineral resin formed in the Himalayan and surrounding mountainous regions, containing phenolic compounds, dibenzo-α-pyrones, and various trace elements, and is known in traditional medicine for its hepatoprotective, antioxidant, and anti-inflammatory properties. This study investigated the protective effects of Shilajit against 5-FU-induced liver injury in a rat model. Twenty Sprague-Dawley rats were divided into four groups:(n=5 each): Control (0.05% saline), 5-FU (200 mg/kg i.p. on day 7), Shilajit (200 mg/kg orally for 7 days), and Shilajit+5-FU (Shilajit for 6 days followed by simultaneous 5-FU on day 7). Administration of 5-FU increased oxidative and nitrosative stress markers (MDA, NO and 8-OHdG), pro-inflammatory cytokines (TNF-α, IL-1β, IL-6 and NF-κB), and ADA activity, while reducing antioxidant parameters (SOD, CAT, GSH) and SIRT2/3 expression. Shilajit treatment significantly ameliorated these alterations, restoring redox balance and mitochondrial function. Structural characterization (NMR, FTIR, ICP-MS) revealed the presence of phenolic groups and trace elements (Zn, Cu, Fe). These findings demonstrate that Shilajit exerts hepatoprotective effects against 5-FU-induced toxicity by modulating oxidative stress, inflammation, and sirtuin-mediated pathways.

Keywords: Shilajit, 5-fluorouracil, hepatotoxicity, oxidative stress, sirtuins, inflammation.

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INVESTIGATION OF THE CAUSES OF *EUCALYPTUS CAMALDULENSIS* SEEDLINGS MORTALITY IN TARSUS FOREST NURSERY

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ABSTRACT

To investigate the causes of desiccation in eucalyptus seedlings grown in Tarsus Forest Nursery, root and root collar samples were taken from ten eucalyptus seedlings and ten soil of the same seedlings was also carried out. *Phytopythium* and *Pythium* isolates were obtained using selective media, from ten plant and ten soil samples collected from the nursery. Oomycetous pathogens were identified by molecular tools, using ITS, LSU, and *coxII* primers. *Pythium ultimum* did not produced necrosis as large as *Pp. helicoides* and *Pp. litorale* when inoculated on to young seedlings. In this study, six specific miRNAs (miR156, miR159, miR398, miR482, miR156, and miR159) were identified in the root and root collar tissues of *Eucalyptus camaldulensis* infected with *Phytopythium* and *Pythium* species (*Pp. litorale*, *Pp. helicoides*, and *P. ultimum*) were analysed on day 15. The findings revealed that miRNA expression profiles showed significant differences depending on the pathogen species.

Keywords: Forest diseases, gene expression, oomycetes

INTRODUCTION

Eucalyptus (Family= Myrtaceae) is an important tree species widely found and planted around the world (Richardson and Rejmánek, 2011). Almost all species of this tree originate from

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Australia (Williams and Woinarski, 1997). In Türkiye, *Eucalyptus camaldulensis* Dehnh. is cultivated for commercial purposes. Eucalyptus is developing especially in the southern region of Türkiye and has an important role in the forest industry (Toker, 2014).

Eucalyptus was first introduced in Türkiye in 1885 at the Adana-Mersin station for ornamental purposes. Later, it was planted in this region by the General Directorate of Forestry in 1939 to drain the Tarsus-Karabucak swamp (Adalı, 1944). *Eucalyptus* species have faced various fungal diseases. One of the most important in the world affecting eucalyptus trees is Mycosphaerella leaf disease (MLD) (Wingfield et al., 2008, Branco et al., 2014, Silva et al., 2009). Some of the other diseases threatening eucalyptus plantations are eucalyptus rust caused by *Puccinia psidii* G. Winter, Ceratocystis wilt caused by *Ceratocystis* spp, certain canker-causing agents such as *Chrysoporthe cubensis* (Bruner) Hodges (=*Cryphonectria cubensis*), and species of *Botryosphaeriaceae* Theiss. & P. Syd. (Coutinho et al., 1998, Gryzenhout et al., 2004, Roux & Wingfield, 2009, Slippers et al., 2009).

In other studies, it has been reported that some genera such as *Botryosphaeria*, *Lasiodiplodia* and *Neofusicoccum* cause dieback and mortality in this species (Old et al., 1990, Smith et al., 1994; Mohali et al., 2005). In addition to these diseases, soil-borne agents also affect *Eucalyptus* species. *Phytophthora cinnamomi* Rands and *Phytophthora multivora* P.M. Scott & T. Jung are an important pathogen threatening *Eucalyptus* species in Western Australia (Scott et al., 2009; Davison, 2018; Podger, 1972). Soil-borne species such as *Phytophthora* and *Pythium* affect herbaceous and woody plants, including forest trees, causing root rot (Jung et al., 1996). According to Shearer and Smith (2000), *Pythium* species are predominantly associated with damping-off in seedlings. The only known case of plantation diseases caused by *Pythium* involves *Pythium splendens*, which was reported to cause root and collar rot in *Eucalyptus grandis* (W. Hill ex Maiden) in South Africa (Linde et al., 1994).

Contamination of nurseries, natural forests and plantation areas with these species has been reported by many researchers worldwide (Lehtijarvi et al., 2017; Jung et al., 2015; Çakar et al., 2025). Numerous studies have also identified *Pythium* species as key pathogens affecting young saplings, particularly in nursery systems (Ertek and Bayraktar, 2025; Çakar et al., 2025; Lehtijarvi et al., 2017). *Phytopythium* species are an economically important group of Oomycetes that live in soil and water (Li et al., 2014; Park et al., 2019). *Phytopythium helicoides* (Drechsler) Abad, de Cock, Bala, Robideau, Lodhi & Lévesque causes root, stem and root collar rot in susceptible plants, especially in seedlings (Benfradj et al. 2017; Ishiguro et al. 2014; Yang et al., 2013; Spies et al., 2011). This species has been reported to cause diseases in many hosts (Ghimire and Gürel-Baysal, 2023). *Phytopythium vexans* (de Bary) Abad, de Cock, Bala, Robideau, Lodhi & Lévesque is an emerging soil borne and aquatic pathogen reported to infect a wide range of plant hosts across multiple families and geographic regions (Gürel-Baysal and Ghimire, 2023). *Eucalyptus* species have been reported to be infected with the pathogen *Phytopythium vexans* (de Bary) Abad, de Cock, Bala, Robideau, Lodhi & Lévesque (Linde et al., 1994).

MicroRNAs (miRNAs), also known as single-stranded RNAs, are short, non-coding RNAs that range in length from 18 to 24 nucleotides. miRNAs are essential for many biological activities

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that occur in both plants and animals (Iwakawa and Tomari, 2015). They feature a helical secondary structure and are formed from single stranded (SS)-RNA. RNA polymerase II interactions are typically used by plants to transcribe miRNAs from distinct MIR genes, producing 5' capped, 3' polytailed miRNA molecules. After pri-miRNAs are synthesized into catalyst miRNAs by Dicer-like 1 (DCL1) proteins, other DCL1 proteins identify the catalyst miRNAs and combine them to form miRNA/miRNA* duplexes. AGO protein is integrated into a duplex miRNA strand by the RNA-induced silencing complex (RISC), which catalyses the interactions of miRNAs with target transcripts. This facilitates sequence complementarity, which aids in the AGO's attachment to targets (Pagano et al., 2021).

miRNAs have been demonstrated to be involved in morphogenesis, growth and development, hormone production, signal transduction, and responses to biotic-abiotic stresses. Additionally, agronomic properties are strongly linked to the post-transcriptional regulation of genes (Bej and Basak, 2014; Islam et al., 2024). Each year, several pathogens, including bacteria, fungus, viruses, and oomycetes, cause plant diseases that severely harm forests and destroy crops. The complex relationship between miRNAs and their targets in disease resistance has proven difficult to dissolve (Gupta et al., 2020; Zhang et al., 2022). However, a growing number of miRNAs responding to biological stresses have been identified, and details about their expression levels, targets, and mode of action in response to bacteria, fungi, and viruses in various plants are becoming clear thanks to advancements in high-throughput technologies. As a result, over the past several years, a number of regulatory circuits that use miRNAs in plant defense against various pathogens have been discovered (Chandan et al., 2020).

This study aims to determine the expression levels of six specific miRNAs (miR156, miR159, miR398, miR482, miR167, and miR393) in the root and root collar tissues of *Eucalyptus* species infected with *Phytopythium* and *Pythium* species (*Pp. litorale, Pp. helicoides*, and *P. ultimum*) and the causes of dieback and mortality on eucalyptus seedlings grown in Tarsus Forest Nursery.

MATERIALS AND METHODS

The study material consisted of ten seedlings and ten soil obtained from Tarsus Forest Nursery, where eucalyptus seedlings were grown, which had started to dry, and dieback was observed.

Samplings

In Tarsus Forest Nursery, sampling studies were carried out in areas showing signs of desiccation. In the nurseries, individuals showing desiccation or dieback were checked and root samples were taken from those showing signs of disease (Figure 1). Tissue samples were taken from seedlings that were infected, and the seedlings were not completely dried, but showed necrosis of the root collar, and from the junction of intact tissue and necrosed tissue.

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Figure 1 Completely dead eucalyptus seedlings were observed in the nursery

Isolation of Oomycetes from the Seedlings

To isolate *Phytopythium* and *Pythium* species, samples were aseptically collected from necrotic lesions on the root collar and fine roots (Figure 2) and placed on P_5ARPNH selective medium. P_5ARPNH medium (mg/L) contained pimaricin 5, ampicillin 200, rifampicin 10, quintozen 50, nystatin 50 and hymexazole 50. In this selective medium, carrot grated agar (CGA) (40 g grated carrot, 18 g agar and 1000 mL water) was used as the base medium. Cultures were incubated at 20 ± 1ºC in the dark. *Phytopythium* spp. and *Pythium* sp. colonies were purified by transferring small pieces of developing hyphae tips to CGA medium. CGA medium (in mg/L; β-sitosterol 30, thiamine hydrochloride, 20) supplemented with isolates was used to promote oospore and sporangium formation (Wilcox and Ellis, 1989). Cultures were incubated at 20 ± 1ºC in the dark and examined at intervals of 2-8 days.

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Figure 2 Root with necrotic lesion (a), root collar lesions (b)

Isolation of Oomycetes from Soil Samples

Phytopythium and *Pythium* isolations were carried out according to Akıllı et al. (2012). Trapping studies from eucalyptus soil samples were carried out at 18 ± 1ºC using carnation leaves. For this purpose, approximately 400 g of soil samples were placed in one kg freezing containers and saturated with pure water to a level one cm above the soil level. Organic material was removed, and carnation leaves were placed on top of the water. The baits were incubated under diurnal day light illumination at 18 ± 1ºC and the leaves showing watery lesions were plated on the P_5ARPNH selective medium. Edge of hyphae suspected to be *Phytopythium* and *Pythium* were then removed and supplemented CGA medium was used to stimulate oospore and sporangium formation.

Identification of Oomycetes

The morphological and cultural characteristics of the isolates were determined by growth on Corn Meal Agar (CMA; Difco), and supplemented CGA media. Sporangium growing on CMA and supplemented CGA media were identified according to previous studies (Akıllı et al., 2012; Uzuhashi et al., 2010) and culture discs of isolates grown on these media were incubated in sterile and non-sterile soil extract at 22 ± 1ºC in daylight. For different heterothallic species, oospores developed on supplemented CGA media in the dark for 4 days were checked (Wilcox and Ellis, 1989).

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DNA Isolation

For DNA isolation of the species, the isolates were grown in petri dishes in appropriate media for 2-4 days. Mycelium was then collected from the culture surface for DNA isolation. DNA was isolated from 100 mg of fresh mycelium using a plant DNA kit (Qiagen DNeasy Plant Mini Kit) and stored at -80°C until use. These studies were conducted at Çankırı Karatekin University/ Department of Biology.

PCR

For the molecular identification of isolates, primers ITS6/ITS4 for the internal transcribed spacer (ITS) region (Cooke et al., 2000, White et al., 1990), NL1/NL4 for the Large subunit (LSU) region of rDNA (O'Donnell, 1993) and FM58/FM66 for the cytochrome c oxidase subunit II (*coxII*) gene region (Martin and Tooley, 2003) were used (Table 1).

PCR amplifications were performed with the selected primers in 50 µL of reaction mixture containing 40 ng DNA, 1× FirePol PCR buffer BD [0.8 M Tris-HCl, 0.2 M (NH_4)], 10 µM each primer, 200 µM dNTPs, 1 U FIREPol Taq DNA polymerase (Solis Biodyne, Tartu, Estonia). The reaction was started in an Arctic™ Thermal Cycler (Thermo Fisher Scientific, Waltham, MA, USA) at 94°C for 5 minutes for initial denaturation and completed with 45 cycles, denaturation at 94°C for 45 seconds, anneling temperature (melting temperature) varying depending on the primers (ITS: 55°C; NL1/NL2: 55°C; FM58/FM66: 52°C) for 45 seconds, extension at 72°C for 90 seconds and final extension at 72°C for 10 minutes.

The raw sequence data were processed with the MEGAX program (Kumar et al., 2018) and the closest species were identified by BLAST search in the GenBank database (http://blast.ncbi.nlm.nih.gov/) and compared with the NCBI nucleotide collection.

Table 1 Primers used in this study

Gene regions	Used primers	Sequences (5'-3')	References
ITS	ITS6	GAAGGTGAAGTCGTAACAAGG	Cooke et al. (2000)
	ITS4	TCCTCCGCTTATTGATATGC	White et al. (1990)
LSU	NL1	GCATATCAATAAGCGGAGGAAAAG	O'Donnell (1993)
	NL4	GGTCCGTGTTTCAAGACGG	
coxII	FM58	CCACAAATTTCACTACATTGA	Martin and Tooley (2003)
	FM66	TAGGATTTCA AGATCCTGC	

Pathogenicity Test

Pathogenicity studies were carried out by root collar inoculation of one-year-old *Eucalyptus* seedlings. For inoculation, 0.5 cm sterile cork borer was used and 5-day-old the isolates developed in CGA medium were used by making holes in the root collar of the seedlings with a cork borer. After inoculation, the treatment areas were wrapped with moist cotton and parafilm. Isolates of *Pp. litorale* (FTP_05, FTP_06), *Pp. helicoides* (FTP_02, FTP_04), *P.*

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ultimum (FTP_1.1, FTP_2.1) were used for pathogenicity test. A total of 90 seedlings were used, 10 seedlings for each isolate and control.

Collection of Tissue Samples and RNA Isolation

Root collar tissue and fine root samples were collected 15 days after inoculation. The tissue samples were flash frozen with liquid nitrogen and stored at -80°C until the time of analysis. Total RNA isolation was performed according to the protocol of mirVana™ miRNA Isolation Kit (Thermo Fisher Scientific, USA). The amount and purity of RNA was determined by NanoDrop™ spectrophotometer and integrity was confirmed by 1.5% agarose gel electrophoresis.

cDNA Synthesis and miRNA Expression Analysis

Primers specific for the 6 miRNAs (miR156, miR159, miR398, miR482, miR167, miR393) examined in the study were designed based on the sequences of *Eucalyptus* species registered in the miRBase (v22) database. cDNA synthesis was performed using TaqMan™ MicroRNA Reverse Transcription Kit according to commercial instructions. Quantitative PCR (qRT-PCR) analysis was performed on an Applied Biosystems™ QuantStudio™ 5 instrument with SYBR® Green I dye system. Reaction conditions were pre-denaturation at 95 °C for 10 min, followed by 40 cycles of 95 °C for 15 s and 60 °C for 1 min. U6 snRNA was used as an internal reference gene.

Statistical Analyses

Kruskal Wallis test ($P<0.05$) and Dunn test were used to compare the pathogenicity of isolates obtained from the forest nursery. The relative expression level of each miRNA was calculated by $2^{-\Delta\Delta Ct}$ method. Statistical analyses were performed with SPSS v25.0 software and data were evaluated by analysis of variance (ANOVA).

RESULTS

Oomycetous Pathogens Determined

Among the 10 lesioned root and root collar samples examined; *Pp. litorale* was detected in two seedling, *Pp. helicoides* in two seedling, *P. ultimum* in three seedlings (Figure 3).

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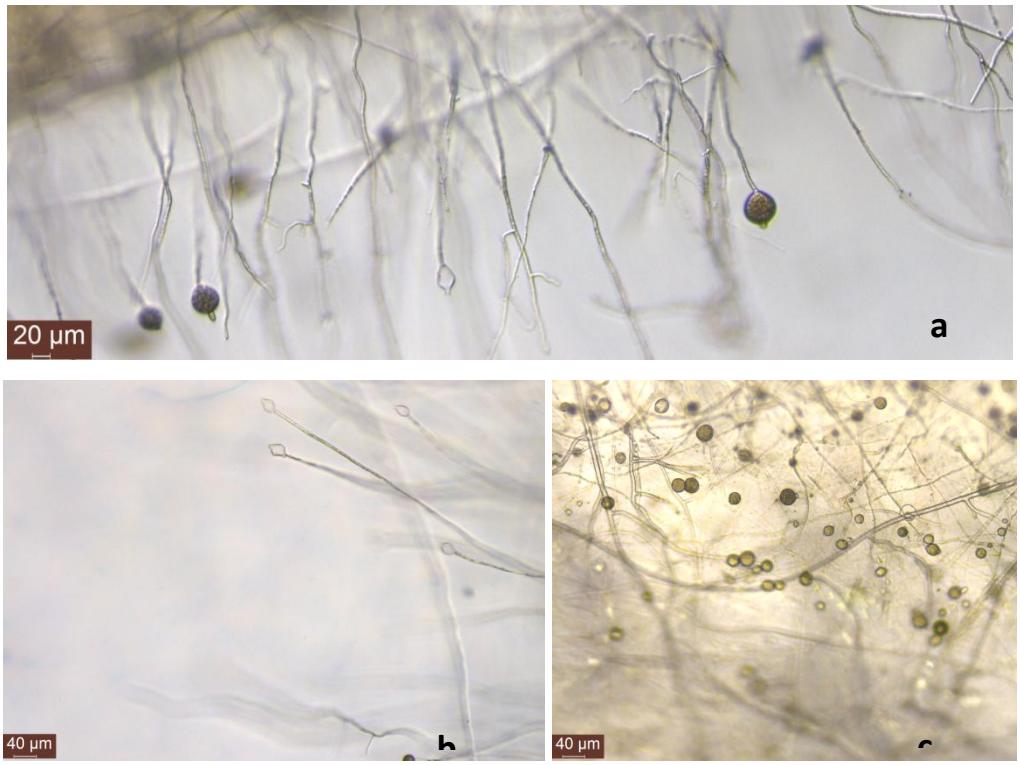

Figure 3 Papillate sporangium and sporangium with discharge tube in *Pp. helicoides* (a), sporangium with discharge tube in *Pythium* sp. (b), hyphal swellings in *P. ultimum* (c)

Molecular Identification of the Obtained *Phytopythium*

For molecular identification of *Phytopythium* species, ITS, LSU and *coxII* gene regions were studied. Sequences of the relevant gene regions were obtained, and the sequences were compared with the closest species by blast search in NCBI. The sequence data of *Pp. litorale* and *P. ultimum* species based on the LSU region showed similarity with the GenBank accession number MM197634 and HQ665103 in the NCBI database, with 99.61% and 99.60% similarity, respectively, as a result of the BLAST search. *Pp. helicoides*, on the other hand, showed a 99.71% match with the GenBank accession number PV849203 in the NCBI database based on ITS region sequence data as a result of a BLAST search.

Pathogenicity of *Phytopythium* spp.

Phytopythium litorale (FTP_05, FTP_06), *Pp. helicoides* (FTP_02, FTP_04), *P. ultimum* (FTP_1.1, FTP_2.1) pathogenicity test results were presented in Figure 4, 5.

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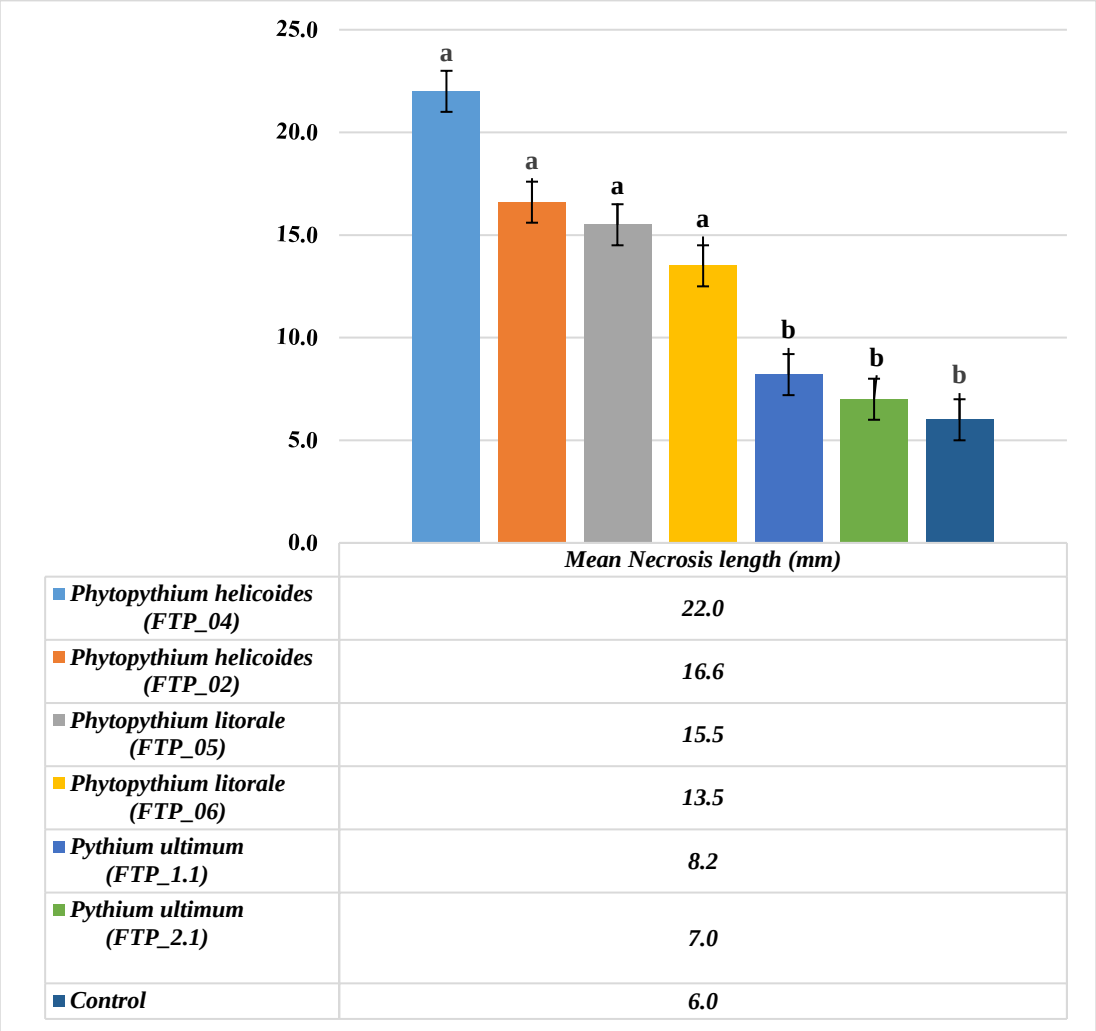

	Mean Necrosis length (mm)
Phytopythium helicoides (FTP_04)	***22.0***
Phytopythium helicoides (FTP_02)	***16.6***
Phytopythium litorale (FTP_05)	***15.5***
Phytopythium litorale (FTP_06)	***13.5***
Pythium ultimum (FTP_1.1)	***8.2***
Pythium ultimum (FTP_2.1)	***7.0***
Control	***6.0***

Figure 4 Mean sizes of the necrosis (mm) on the seedlings after 15 days of inoculation by *Phytopythium* spp. Vertical bars indicate standard error. Sharing the same letters are not significant (Kruskal Wallis test p= 0.00<0.05).

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Figure 5. Lesions formed by *Phytopythium helicoides* (a, b) on eucalyptus seedlings 15 days after inoculation.

miRNA Expression Analysis

In this study, the expression levels of six specific miRNAs (miR156, miR159, miR398, miR482, miR167 and miR393) were analyzed in root and root collar tissues of *Eucalyptus* species on the 15th day of infection with *Phytopythium* pathogens (*Pp. litorale*, *Pp. helicoides* and *P. ultimum*). The findings revealed that miRNA expression profiles showed significant differences depending on the pathogen species.

miR156 and miR159 were induced at high levels, especially in seedlings infected with *Pp. litorale* and *Pp. helicoides*. A 3-4-fold increase was observed compared to the control group, and it is thought that this increase may be related to the regulation of SPL transcription factors involved in the biosynthesis of defense metabolites. In *P. ultimum* infections, the increase in these miRNAs was more limited.

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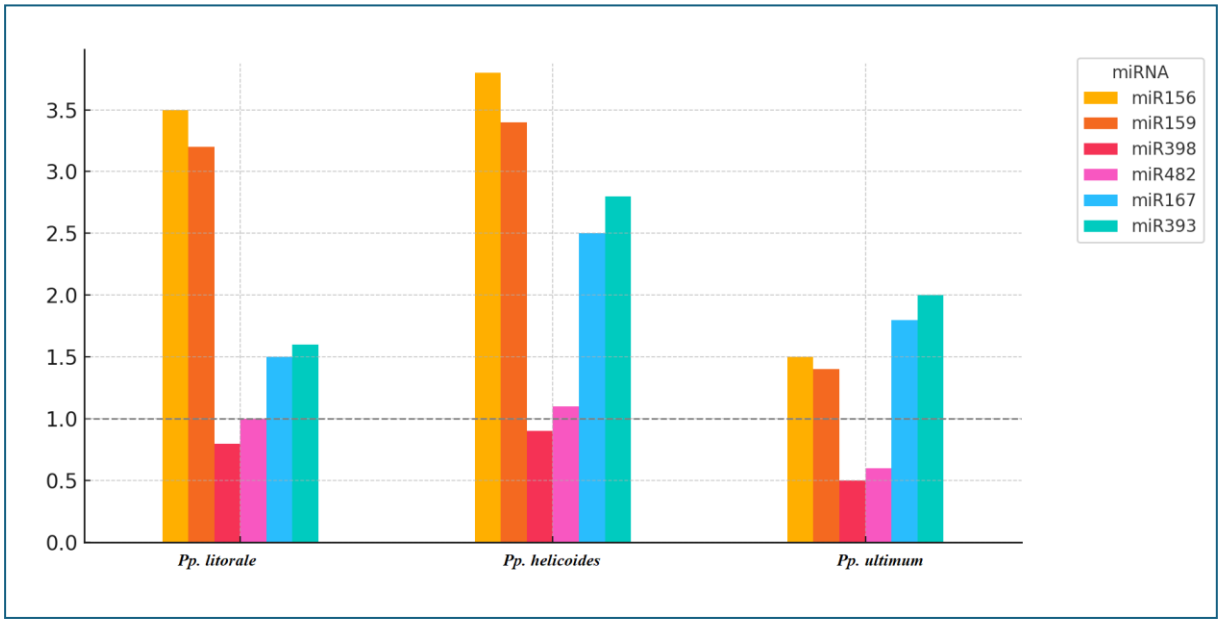

Figure 6. Relative expression levels of miRNAs in three different *Phytopythium* species

The most pronounced repression of miR398 was observed in *P. ultimum* infections. This repression may contribute to increased reactive oxygen species (ROS) production by allowing higher levels of expression of Cu/Zn-SOD genes involved in the oxidative stress response. In *Pp. litorale* and *Pp. helicoides* infections, miR398 expression was slightly suppressed. miR482 showed a similar suppression trend as miR398 in *P. ultimum* infections. This suggests a strategy of the pathogen to suppress the immune response by targeting R-gene-mediated resistance mechanisms. Limited changes in miR482 expression were recorded in *Pp. litorale* and *Pp. helicoides* infections. miR167 and miR393 were significantly increased, especially in *Pp. helicoides*-infected samples. This increase may be associated with the re-regulation of the auxin signaling pathway and the pathogen's strategy to affect plant developmental processes. There was a similar upward trend in *P. ultimum* infections, but statistically not as strong as in *Pp. helicoides* infections.

Overall, the day 15 data suggest that miRNAs play a critical role in the generation of pathogen species-specific defense responses. In *Pp. litorale* and *Pp. helicoides* infections, miR156/miR159 induction was predominant, whereas in *P. ultimum* infections, miR398 and miR482 repression associated with the oxidative stress response was more prominent. These different response profiles point to both the biological characteristics of the pathogen and the diversity of the plant's defense strategies in the *Eucalyptus-Phytopythium* interaction.

DISCUSSION

In this study, three *Phytopythium* species were associated with desiccation of eucalyptus seedlings. These species were *Pp. litorale*, *Pp. helicoides*, and *P. ultimum*. This is the first time these species have been reported on eucalyptus seedlings in Türkiye. Species of *Phytophthora* and *Pythium* are the most frequent oomycet associated with root rot in *Eucalypts* (Shearer and Smith, 2000). At least thirteen *Pythium* species have been reported in natural eucalyptus forests (Shearer and Smith, 2000). In our study, *Phytopythium* species were detected and pathogenicity

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studies of these species showed that the pathogenicity of *Pp helicoides* was higher. According to the statistical evaluation, a statistically significant result was found when the pathogenicity of the factors was compared to the control seedlings.

In a study conducted in Portugal, two species of *P. cinnamomi*, *P. alticola* were associated with *E. globulus* root rot and dieback (Diogo et al., 2023). *P. cinnamomi*, which is associated with mortality in eucalyptus trees (Podger, 1972), was not isolated from root and stem lesions in this study.

Ertek and Bayraktar (2025) reported *Pp. litorale* on walnuts for the first time in walnut nurseries in Bursa and Isparta provinces. Derviş et al. (2020) reported that *Pp. litorale* was the cause of root and root collar rots, trunk and branch cancers in *Platanus orientalis* L. trees, while Mert et al. (2020) associated the agent with dieback in apple trees. Çakar et al. (2025) frequently isolated *Pp. litorale* from chestnut saplings in forest nurseries. It was also confirmed to be a pathogen in seedlings. *Pp helicoides* causes stem and root rot in many plants (Tkaczyk, 2020). In this study, it was similarly found to be pathogenic on eucalyptus seedlings.

According to Moein et al. (2019), elevated irrigation regimes significantly increased disease severity in apple seedlings infected with *Phytopythium* species such as *Pp. irregulare*, *Pp. ultimum*, and *Pp. sylvaticum*. *P. ultimum* isolates used in our study were measured the least lesions against to other species.

This study reveals species-wise differences in the expression levels of specific miRNAs in response to *Phytopythium* infection in *Eucalyptus* species. miR156 and miR159 were induced at high levels, especially in *Pp. litorale* and *Pp. helicoides* infections, suggesting that these miRNAs may trigger secondary metabolite biosynthesis by activating transcription factors (such as SPL) involved in the early defense response (Zheng et al, 2019). Suppression of miR398 may lead to overexpression of Cu/Zn-SOD genes, strengthening the oxidative stress signaling pathway. This suppression is more pronounced in *p. ultimum* infections, suggesting that this pathogen strongly activates the oxidative stress-based defense response (Jiang et al., 2021).

The decrease of miR482 family in *Pp. ultimum* infections may reflect the pathogen's strategy to suppress the R-gene-mediated resistance mechanism (Shivaprasad et al., 2012). In addition, the increase of miR167 and miR393 in *Pp. helicoides* infections may be related to the reorganization of the auxin signalling pathway and the pathogen's strategy to influence plant developmental processes (Navarro et al., 2006). In conclusion, this study demonstrates that miRNA-based defence responses against *Phytopythium Pythium* pathogens in Eucalyptus species vary depending on both pathogen species and tissue type, suggesting that miRNAs play critical roles in the pathogen recognition-defense activation chain. These data may provide a scientific basis for future studies to improve pathogen resistance in Eucalyptus through miRNA-based biotechnological approaches.

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VIRTUAL BIOLOGY LABORATORY FOR ENHANCED STUDENT LEARNING

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Abstract
Virtual biology laboratories offer a transformative approach to learning, enhancing student engagement and understanding through immersive digital environments. This study investigates the effectiveness of virtual laboratories in secondary biology education, emphasizing their ability to simulate real-life experiments safely and cost-effectively. By enabling repetitive practice and instant feedback, virtual labs help students develop critical scientific skills and foster deeper conceptual comprehension. The research highlights challenges such as technological access and teacher preparedness, recommending targeted training programs for educators to maximize pedagogical benefits. Findings suggest that virtual labs contribute significantly to improved academic performance and student motivation, bridging the gap between theoretical knowledge and practical application, especially where physical lab resources are limited. Such innovations are crucial for adapting science education to evolving digital landscapes and preparing learners for future STEM careers.

Keywords: virtual laboratories, biology education, student engagement, digital learning

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INTEGRATING ONLINE LABORATORIES INTO SECONDARY BIOLOGY EDUCATION IN KAZAKHSTAN

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Abstract
The integration of online laboratories into Kazakhstan's secondary biology curriculum offers substantial educational benefits, addressing constraints related to laboratory access and practical training. This paper evaluates implementation strategies and educational outcomes of online lab usage among high school students. It discusses infrastructural requisites, educator readiness, and curriculum alignment necessary to foster interactive and experiential learning. Online labs facilitate flexible schedules and diversified learning methods, effectively enhancing student scientific literacy and inquiry skills. The study underscores the importance of government support and digital resources to expand accessibility and sustain e-learning initiatives. Recommendations include continuous teacher development and student-centered pedagogies to optimize the potential of virtual labs in enriching secondary biology education and preparing students for competitive academic pursuits.

Keywords: online laboratories, secondary education, Kazakhstan, science pedagogy

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BIOLOGICALLY INSPIRED REACTIVE AGENT MODELING USING X-MACHINES

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Abstract
This research develops biologically inspired reactive agent models using X-machines to simulate complex biological interactions and behaviors. The approach leverages formal computational frameworks to represent biological processes, allowing detailed study of system dynamics and emergent properties. Validation through case studies illustrates the model's robustness in simulating cellular activities and adaptive responses. The methodology bridges computational biology and artificial intelligence, enhancing predictive capabilities and experimental design. Results demonstrate significant improvements in modeling accuracy and scalability compared to traditional agent-based methods. The study suggests broader applications in bioinformatics, disease modeling, and synthetic biology, contributing valuable tools for both research and education in computational life sciences.

Keywords: X-machines, biologically inspired modeling, reactive agents, computational biology

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CRYPTOGENIC FRESHWATER FISH BIODIVERSITY IN BANGLADESH

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Abstract
The cryptogenic freshwater fish biodiversity of Bangladesh reflects complex historical and ecological factors influencing species distribution and conservation status. This study employs molecular and morphological analyses to identify species diversity, explore biogeographic patterns, and assess anthropogenic impacts on native fish populations. Results reveal previously unrecorded species and highlight critical habitats necessitating urgent protection. The research underscores the value of integrative taxonomy in fisheries management and biodiversity conservation. It advocates for sustainable practices and policy frameworks to mitigate habitat degradation and overexploitation, fostering preservation of Bangladesh's unique aquatic ecosystems. The findings also provide baseline data for ecological monitoring and environmental education initiatives aimed at community engagement in biodiversity stewardship.

Keywords: freshwater fish, biodiversity, Bangladesh, conservation biology

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UNIFIED MODELS IN GENOME REARRANGEMENT AND SORTING PRIMITIVES IN BIOINFORMATICS

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Abstract
Genome rearrangement plays a pivotal role in evolutionary biology and comparative genomics. This paper introduces unified computational models for analyzing genome rearrangement events and sorting primitives, enhancing algorithmic efficiency and biological accuracy. Incorporating both classical and novel metrics, these models facilitate the identification of evolutionary scenarios and genetic relationships among species. Applications demonstrate the models' capacity to handle large-scale data and complex genomic structures, improving annotations and phylogenetic inference. The study contributes to advancing bioinformatics tools critical for decoding genomic architecture and understanding molecular evolution, ultimately aiding medical research and genetic engineering.

Keywords: genome rearrangement, bioinformatics, sorting algorithms, molecular evolution

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MOLECULAR IDENTIFICATION AND DIVERSITY ASSESSMENT OF AGRICULTURAL PESTS USING DNA BARCODING

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Abstract
DNA barcoding offers a precise molecular approach for identifying agricultural pest species and assessing genetic diversity, crucial for effective pest management and crop protection. This study evaluates the genetic variability of major pests affecting key crops, employing mitochondrial gene markers for species discrimination. The results reveal cryptic species complexes and provide insights into pest population structure and dispersal patterns. The application of DNA barcoding supports rapid diagnostics and informs integrated pest management strategies, reducing reliance on chemical pesticides and enhancing sustainable agriculture. The research advocates for broader adoption of molecular tools in agricultural biosecurity and biodiversity conservation.

Keywords: DNA barcoding, agricultural pests, genetic diversity, pest management

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ADVANCED MICROFLUIDIC TECHNIQUES FOR BIOMEDICAL AND BIOHEALTH APPLICATIONS

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Abstract
Microfluidics technology has revolutionized biomedical research by enabling precise manipulation of fluids at microscale, facilitating innovative diagnostic and therapeutic applications. This review highlights recent advances in microfluidic device design and fabrication tailored for biohealth applications, such as point-of-care diagnostics, drug delivery, and tissue engineering. Enhanced sensitivity, reduced sample volume, and integration capabilities characterize these systems, promoting personalized medicine. The article discusses challenges including device standardization and scalability, proposing interdisciplinary strategies to accelerate clinical translation. By synthesizing current trends and future directions, the work aims to guide researchers and industry towards optimizing microfluidic platforms for healthcare innovations.

Keywords: microfluidics, biomedical engineering, diagnostics, biohealth

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EVALUATING THE EFFECTIVENESS OF INTERPROFESSIONAL SIMULATION TRAINING ON COLLABORATIVE SKILLS AMONG HEALTHCARE UNDERGRADUATES

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Abstract
Interprofessional simulation training (IPST) enhances collaborative skills among healthcare undergraduates by providing realistic, hands-on learning environments that mimic clinical settings. This study measures the impact of IPST on communication, teamwork, and decision-making abilities in multidisciplinary teams. Mixed-method assessments, including surveys and focus groups, indicate significant improvements in students' confidence and competence post-training. The findings support integrating simulation-based interprofessional education into healthcare curricula to foster effective teamwork and improve patient outcomes. Challenges such as resource allocation and faculty training are discussed, with recommendations for sustainable implementation. The research underscores IPST as a vital pedagogical tool for preparing future healthcare professionals in complex clinical environments.

Keywords: interprofessional education, simulation training, collaborative skills, healthcare education

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IMPACT OF INTEGRATED REHABILITATION STRATEGIES ON FUNCTIONAL RECOVERY AND FALL PREVENTION FOLLOWING HIP FRACTURE SURGERY IN CLINICAL PRACTICE

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Abstract
Hip fractures are a major cause of morbidity and mortality among the elderly population, often resulting in significant functional decline and increased risk of falls post-surgery. This study evaluates the effectiveness of integrated rehabilitation strategies, combining multidisciplinary care including physical therapy, occupational therapy, nutritional support, and fall prevention programs. Patients undergoing hip fracture surgery were enrolled in a comprehensive rehabilitation program initiated early postoperatively and continued in community settings. Key interventions included progressive resistance training, balance exercises, and assisted ambulation. Outcomes measured were improvements in mobility, muscle strength, balance, and reduction in fall incidence. Results demonstrated significant functional recovery, enhanced quality of life, and decreased healthcare costs associated with complications resulting from falls. The integrated approach emphasizes early mobilization, continuous therapy, and multidisciplinary coordination to optimize rehabilitation outcomes. These findings support the implementation of structured rehabilitation protocols in clinical practice to improve recovery trajectory and patient safety post-hip fracture surgery.

Keywords: Hip fracture, rehabilitation, functional recovery, fall prevention, elderly care

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INVESTIGATION OF OCCUPATIONAL STRESS AND BURNOUT AMONG MEDICAL STAFF IN A NORTH AFRICAN UNIVERSITY HOSPITAL

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Abstract
Healthcare workers are exposed to numerous stressors that may lead to occupational burnout, adversely affecting their health and the quality of patient care. This study explores the prevalence of occupational stress and burnout syndrome among medical staff in a tertiary university hospital in North Africa. Using validated questionnaires assessing emotional exhaustion, depersonalization, and personal accomplishment, data were collected from physicians, nurses, and allied health professionals. The analysis identified high levels of stress associated with long working hours, workload, and emotional demands. Factors contributing to burnout included lack of social support, inadequate resources, and organizational inefficiencies. The study emphasizes the need for institutional interventions focusing on stress management, work environment improvement, and psychosocial support to mitigate burnout and sustain healthcare workforce well-being. Recommendations include regular screening, training in coping strategies, and administrative reforms to enhance job satisfaction and retention.

Keywords: Occupational stress, burnout, healthcare workers, hospital staff, North Africa

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THE IMPACT OF LOW-INTENSITY BALANCE EXERCISE ON MUSCLE STRENGTH, MOBILITY, AND WELL-BEING IN OLDER ADULTS UNDERGOING HEMODIALYSIS

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Affiliation: Department of Rehabilitation Medicine, National Taiwan University, Taiwan

Abstract
Older adults with end-stage renal disease undergoing hemodialysis face challenges including muscle weakness, limited mobility, and decreased quality of life. This study assesses the effects of a low-intensity balance exercise program administered over 12 weeks on muscle strength, functional mobility, and psychological well-being. Participants followed a supervised regimen emphasizing balance, coordination, and gentle strength training during dialysis sessions. Outcome measures included muscle torque assessed by dynamometry, gait speed, balance tests, and validated questionnaires evaluating mental health status. Findings revealed statistically significant improvements in lower limb strength, enhanced mobility, and reduced depressive symptoms, indicating the efficacy of integrating low-intensity exercise within routine dialysis care. The program was well-tolerated with high adherence and no adverse events, suggesting feasibility for widespread clinical adoption. This intervention offers a valuable strategy to address physical and mental health decline in this vulnerable population.

Keywords: Hemodialysis, balance exercise, muscle strength, mobility, older adults

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KNOWLEDGE, ATTITUDE AND PRACTICE OF EXPECTANT MOTHERS TOWARD MATERNAL HEALTH SERVICES AT GOVERNMENT HOSPITALS IN ADEN CITY

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Abstract
Maternal health service utilization is critical for ensuring positive pregnancy outcomes, yet barriers persist in several regions. This cross-sectional study investigates the knowledge, attitudes, and practices regarding maternal healthcare among expectant mothers attending government hospitals in Aden City. Data were collected through structured interviews covering awareness of antenatal care (ANC), perceptions of healthcare quality, and adherence to recommended visits. Results demonstrate an overall moderate level of knowledge but highlight misconceptions and cultural barriers influencing late or inadequate ANC attendance. Positive attitudes correlated with higher educational levels and prior obstetric experiences. Recommendations include targeted community education programs, enhanced provider-patient communication, and culturally sensitive health policies to increase maternal service uptake and reduce pregnancy-related complications. The study underscores the importance of empowering expectant mothers with accurate information and supportive healthcare environments.

Keywords: Maternal health, antenatal care, expectant mothers, healthcare utilization, Yemen

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CHALLENGES AND ENABLERS IN ACCESSING CHILDHOOD IMMUNIZATION SERVICES AMONG UNREGISTERED MIGRANT FAMILIES IN EASTERN INDONESIA: A QUALITATIVE STUDY

Assoc. Prof. Dr. Putri Anindya Santoso, Mohammad Rizal Fauzi, Lec. Siti Rahmah Hidayat
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Abstract
Vaccination programs are essential to reducing childhood morbidity and mortality, yet unregistered migrant families often face barriers in accessing immunization services. This qualitative study explores the challenges and facilitators experienced by migrant communities in Eastern Indonesia through in-depth interviews and focus groups. Barriers identified include lack of official documentation, language difficulties, misinformation, limited healthcare infrastructure, and discrimination. Enablers involved supportive community networks, mobile health clinics, and targeted outreach by local health workers. The study advocates policy reforms promoting inclusivity, simplified registration processes, and the deployment of culturally competent health mediators to improve vaccine coverage among marginalized groups. Findings highlight the pivotal role of community engagement and health system adaptability to achieve equitable immunization access.

Keywords: Childhood immunization, migrant families, healthcare access, vaccination barriers, Indonesia

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INTERDISCIPLINARY COLLABORATION IN PALLIATIVE CARE SYSTEMS ACROSS URBAN AND RURAL AREAS

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Abstract
Palliative care requires coordinated efforts among diverse healthcare professionals to address complex patient needs effectively. This study examines interdisciplinary collaboration within palliative care systems comparing urban and rural settings. Surveys and interviews with physicians, nurses, social workers, and chaplains reveal disparities in resource availability, communication, and role clarity impacting care quality. Urban centers demonstrated structured team approaches with regular interdisciplinary meetings, whereas rural areas faced challenges including workforce shortages and fragmented service delivery. Strategies to enhance collaboration encompass formalized communication protocols, mutual education programs, and telemedicine integration. Outcomes suggest that strengthening interdisciplinary teamwork improves patient-centered care, symptom management, and family support. The research informs policy recommendations to bridge rural-urban gaps and optimize palliative care delivery.

Keywords: Palliative care, interdisciplinary collaboration, rural health, urban health, healthcare teams

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EVALUATING THE PHYSIOLOGICAL AND PSYCHOLOGICAL STRESSORS AND COPING MECHANISMS IN HEMODIALYSIS PATIENTS

Assoc. Prof. Dr. Leila M. Hassan, Reem A. Al-Farhan, Assis. Prof. Dr. Omar S. Rahman, Lec. Nour T. Aziz
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Abstract
Hemodialysis imposes considerable physiological and psychological stress on patients, affecting treatment adherence and quality of life. This mixed-method study assesses stressors including fatigue, anxiety, depression, and social isolation among chronic hemodialysis patients, alongside their coping strategies. Quantitative data were collected via validated psychological scales, while qualitative interviews provided insight into patients' experiences and resilience mechanisms such as spiritual beliefs, social support, and adaptive behaviors. Findings reveal high prevalence of psychological distress with significant correlations to decreased physiological health indicators. Implementation of tailored psychosocial interventions including counseling, peer support groups, and stress management training is recommended to improve patient outcomes. The study emphasizes the holistic approach necessary in hemodialysis care to address both physical symptoms and mental well-being.

Keywords: Hemodialysis, stress, coping mechanisms, psychological distress, patient care

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REGULATION OF EPIGENETIC MODIFICATIONS IN METABOLIC SYNDROME AND DIABETES: MECHANISTIC INSIGHTS AND THERAPEUTIC POTENTIAL

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Abstract
Metabolic syndrome and diabetes are major global health challenges characterized by complex pathophysiological mechanisms involving environmental and genetic factors. Epigenetic modifications, including DNA methylation, histone modification, and non-coding RNAs, play a critical role in the regulation of gene expression in these metabolic diseases. This review explores recent advances in understanding how epigenetic alterations contribute to the onset and progression of metabolic syndrome and diabetes. We detail mechanistic insights into key epigenetic regulators and how these modifications influence insulin resistance, lipid metabolism, and inflammatory responses. The translational potential of targeting epigenetic modulators for therapeutic interventions is highlighted, with emphasis on developing novel epigenetic drugs and personalized medicine approaches. The review also discusses challenges in epigenetic research, such as tissue specificity and dynamic changes in epigenetic marks, underscoring the need for further longitudinal studies to validate novel targets. This comprehensive overview aims to provide a foundation for future research directed at improving diagnosis, prognosis, and treatment strategies for metabolic syndrome and diabetes.

Keywords: epigenetics, metabolic syndrome, diabetes, insulin resistance, therapeutic targets

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ADVANCES IN ENZYME KINETICS AND ALLOSTERIC REGULATION FOR DRUG DEVELOPMENT IN INFECTIOUS DISEASES

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Abstract
Enzyme kinetics and allosteric regulation are pivotal in understanding the biochemical pathways exploited by infectious pathogens. This paper presents recent advancements in the study of enzyme behavior, focusing on allosteric mechanisms that modulate enzymatic activities essential for pathogen survival and virulence. Current drug discovery efforts leverage these kinetic insights to develop inhibitors that specifically target allosteric sites, offering improved selectivity and reduced drug resistance compared to active site-targeted therapies. We review methodologies employed in dissecting enzyme kinetics, including high-throughput screening and computational modeling, and highlight case studies where allosteric modulators successfully disrupt pathogen biology. Challenges such as enzyme flexibility and complex regulatory networks are addressed, alongside future prospects involving integrated systems biology approaches to identify novel drug candidates. This work aims to enhance strategic frameworks in anti-infective drug development by incorporating detailed kinetic and regulatory knowledge of key enzymatic targets.

Keywords: enzyme kinetics, allosteric regulation, drug development, infectious diseases, pharmacology

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MOLECULAR MECHANISMS OF PROTEIN AGGREGATION AND ITS ROLE IN NEURODEGENERATIVE DISORDERS

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Faculty of Biological Sciences, University of Tehran, Iran

Abstract
Protein aggregation is a hallmark of various neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's disease. This review synthesizes current knowledge on the molecular mechanisms driving aberrant protein folding and aggregation, focusing on amyloidogenic pathways and the impact of cellular quality control systems such as proteostasis networks and autophagy. We discuss the role of pathological aggregates in neuronal toxicity, synaptic dysfunction, and neuroinflammation. Emerging therapeutic strategies aimed at modulating aggregation processes by stabilizing native protein conformations or enhancing clearance of aggregates are evaluated. Furthermore, we explore advances in biophysical techniques and animal models that have shed light on the aggregation landscape. Understanding these molecular underpinnings is crucial for developing targeted interventions to alleviate neurodegenerative disease burden.

Keywords: protein aggregation, neurodegeneration, amyloids, proteostasis, therapeutic strategies

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INTERACTION OF NON-CODING RNAS IN GENE EXPRESSION REGULATION AND CANCER BIOLOGY

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Abstract
Non-coding RNAs (ncRNAs) encompass a diverse class of RNA molecules that regulate gene expression post-transcriptionally and epigenetically. This review focuses on the interactions of microRNAs, long non-coding RNAs, and circular RNAs in the context of cancer biology. We examine the mechanisms through which ncRNAs modulate oncogenes and tumor suppressors, influence signaling pathways, and contribute to tumor initiation, progression, and metastasis. Recent developments in high-throughput sequencing and computational tools facilitating ncRNA profiling are discussed alongside therapeutic applications such as ncRNA mimics and inhibitors. Challenges in clinical translation, including delivery systems and off-target effects, are considered. The complex regulatory networks orchestrated by ncRNAs highlight their potential as diagnostic biomarkers and targets for cancer therapy.

Keywords: non-coding RNAs, cancer, gene regulation, microRNAs, therapeutics

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STRUCTURAL BIOLOGY OF MEMBRANE TRANSPORTERS: IMPLICATIONS FOR DRUG RESISTANCE IN BACTERIA

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Abstract
Membrane transporters mediate the influx and efflux of substances across bacterial membranes and play critical roles in antibiotic resistance mechanisms. This review elucidates the structure-function relationships of major bacterial transporter families, including ATP-binding cassette (ABC) transporters and major facilitator superfamily (MFS) proteins. Insights from crystallography, cryo-electron microscopy, and molecular dynamics simulations reveal conformational changes essential for substrate recognition and translocation. We discuss how transporter mutations contribute to multidrug resistance and the potential to exploit structural features for inhibitor development. The review also covers challenges in targeting membrane proteins and advances in allosteric modulation as a therapeutic strategy. Understanding transporter architecture and mechanism is vital for counteracting antimicrobial resistance.

Keywords: membrane transporters, drug resistance, bacteria, structural biology, antibiotic inhibitors

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METABOLOMIC PROFILING AND BIOMARKERS DISCOVERY IN CARDIOVASCULAR DISEASES USING MASS SPECTROMETRY

Dr. Javokhir Khodjaev, Dian Anggraini, Lila Haddad, Dr. Folashade Adeyinka
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Abstract
Cardiovascular diseases (CVD) remain the leading cause of morbidity and mortality worldwide. Metabolomics, through mass spectrometry, offers a powerful platform to identify novel biomarkers for early diagnosis, prognosis, and therapeutic monitoring of CVD. This paper reviews techniques and methodologies in mass spectrometry-based metabolomic profiling, highlighting recent discoveries of metabolic signatures associated with CVD pathogenesis. Analytical challenges such as sample preparation, data analysis, and biomarker validation are addressed. Integrative omics approaches combining metabolomics with genomics and proteomics are discussed to provide a comprehensive understanding of disease mechanisms. The translation of metabolomic biomarkers into clinical practice promises personalized management of CVD patients and improved outcomes.

Keywords: metabolomics, cardiovascular diseases, mass spectrometry, biomarkers, systems biology

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CRISPR-CAS9 APPLICATIONS IN GENOME EDITING: CURRENT CHALLENGES AND FUTURE DIRECTIONS IN THERAPEUTICS

Azizbek Tursunov, Assoc. Prof. Kamal Souilah
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Abstract
The CRISPR-Cas9 system has revolutionized genome editing with its precision, efficiency, and versatility, offering unprecedented therapeutic possibilities. This review outlines current applications of CRISPR-Cas9 technology in correcting genetic defects, treating infectious diseases, and cancer therapy. We discuss technical challenges such as off-target effects, delivery systems, and immune responses, alongside ethical considerations in clinical use. Emerging advancements including base editing and prime editing are evaluated for their potential to overcome current limitations. Regulatory frameworks and ongoing clinical trials highlight the path toward safe and effective therapeutic genome editing. The review underscores CRISPR-Cas9's transformative potential while calling for continued innovation and responsible application.

Keywords: CRISPR-Cas9, genome editing, gene therapy, off-target effects, clinical trials

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ROLE OF MITOCHONDRIAL DYSFUNCTION IN AGING AND AGE-RELATED DISEASES: A MOLECULAR BIOLOGY PERSPECTIVE

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Abstract
Mitochondria are central regulators of cellular metabolism and apoptosis with substantial influence on aging and age-associated pathologies. This paper synthesizes molecular insights into how mitochondrial dysfunction—characterized by altered dynamics, defective oxidative phosphorylation, and increased reactive oxygen species production—contributes to tissue degeneration and disease. Mechanistic pathways linking mitochondrial defects to neurodegenerative diseases, cardiovascular disorders, and metabolic syndromes are thoroughly examined. Therapeutic approaches aimed at restoring mitochondrial function, including pharmacological agents and lifestyle interventions, are reviewed. The integration of mitochondrial biology into aging research offers promising avenues for interventions to delay aging processes and mitigate age-related disease burden.

Keywords: mitochondria, aging, oxidative stress, age-related diseases, molecular biology

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DIFFERENTIATION OF GENE EXPRESSION PROFILES IN LIVER AND KIDNEY TISSUES OF PIGS

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Abstract

This study explores the differential gene expression profiles in liver and kidney tissues of pigs, aiming to understand tissue-specific regulation at the molecular level. Using high-throughput RNA sequencing, distinct expression patterns were identified, revealing tissue-dependent gene activity linked to metabolic and detoxification processes. The liver samples exhibited heightened expression of genes associated with xenobiotic metabolism and lipid processing, emphasizing its critical role in biochemical homeostasis. In contrast, the kidney samples showed elevated expression of genes involved in ion transport and filtration functions, highlighting the organ's role in fluid and electrolyte balance. Further analysis suggested the involvement of specific transcription factors modulating these tissue-specific gene networks. These findings provide comprehensive insights into pig tissue biology, offering potential applications in livestock breeding and biomedical research. Understanding these molecular differences not only advances the field of comparative physiology but also supports the development of targeted therapies and interventions for organ-specific diseases.

Keywords: gene expression, liver, kidney, pigs, tissue specificity

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DECISION TREES FOR PREDICTING RISK OF MORTALITY USING ROUTINELY COLLECTED DATA

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Abstract

Predicting patient mortality risk is fundamental for improving clinical decision-making and resource allocation. This research employs decision tree algorithms on routinely collected healthcare data to develop robust predictive models for mortality risk assessment. Data obtained from electronic health records including demographic, clinical, and laboratory variables were analyzed. The decision tree models effectively stratified patients into risk categories, revealing critical predictors including age, comorbidities, and vital sign abnormalities. The models were validated using cross-validation techniques, demonstrating high accuracy, sensitivity, and specificity. Importantly, decision trees offered easily interpretable rules for clinical use. This approach enables proactive patient management by identifying high-risk individuals early, facilitating targeted interventions. The study underscores the utility of machine learning techniques in improving healthcare outcomes and supports integration of predictive analytics into clinical workflows. Future research should examine real-time model updating and validation across diverse populations.

Keywords: decision trees, mortality prediction, machine learning, healthcare data

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SELENIUM LEVELS IN AGRICULTURAL SOILS AND CROPS OF THE BALKAN REGION

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Abstract

This study investigates selenium concentrations in agricultural soils and staple crops across the Balkan region, assessing potential impacts on human nutrition and environmental health. Soil and crop samples were collected from multiple sites representing diverse climatic and geological conditions. Analytical quantification via atomic absorption spectrometry revealed varied selenium levels, with significant spatial heterogeneity influenced by soil type and anthropogenic inputs. Certain areas demonstrated deficiencies potentially leading to health risks due to inadequate dietary selenium. Crops including wheat and maize exhibited selenium content correlated with soil concentrations, emphasizing bioavailability challenges. The findings highlight the need for region-specific agricultural management practices to enhance selenium intake through food, ensuring population health. Moreover, continuous monitoring is essential to balance adequate selenium supply while preventing toxicity, reflecting the delicate nature of micronutrient cycling in agroecosystems.

Keywords: selenium, soil, crops, Balkans, micronutrients

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MODELING THE COMPLEX INTERACTIONS BETWEEN miRNA DYSREGULATION AND BREAST CANCER PROGRESSION

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Abstract

Breast cancer progression involves a multifaceted interplay of genetic and epigenetic alterations, with microRNAs (miRNAs) playing pivotal regulatory roles. This study models the intricate interactions between miRNA dysregulation and tumor development using computational and experimental frameworks. Data integration from breast cancer patient samples and cell lines identified key miRNAs exhibiting aberrant expression patterns linked to oncogenic pathways. Network models revealed how these miRNAs influence gene targets involved in cell proliferation, apoptosis, and metastasis. Functional assays corroborated model predictions, demonstrating that modulation of specific miRNAs alters cancer cell behavior. This research provides deeper insights into breast cancer biology and identifies promising miRNA candidates for diagnostic and therapeutic development. Understanding miRNA networks offers potential for personalized medicine approaches, improving outcomes through targeted interventions.

Keywords: miRNA, breast cancer, gene regulation, tumor progression

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MODELING THE COMPLEX RELATIONSHIP BETWEEN miRNA DYSREGULATION AND BREAST CANCER PROGRESSION

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Abstract

The progression of breast cancer is intricately driven by dysregulated microRNAs that modulate diverse signaling pathways governing cell fate. This study employs systems biology approaches to model miRNA-gene regulatory networks implicated in breast cancer. Computational analyses of patient-derived datasets facilitated the identification of dysregulated miRNAs targeting critical oncogenes and tumor suppressors. Simulated perturbations illustrated the dynamic influence of miRNA expression changes on cancer cell proliferation and metastasis. Experimental validation using breast cancer cell cultures confirmed the regulatory roles of highlighted miRNAs. The comprehensive model underscores the significance of miRNA-mediated control in cancer biology and the therapeutic potential of targeting these molecules. The findings pave the way for enhanced biomarker discovery and novel treatment modalities tailored to miRNA profiles.

Keywords: breast cancer, miRNA, regulatory networks, systems biology

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PRELIMINARY ANALYSIS OF REAL-TIME HAND MOVEMENT RECOGNITION FOR UPPER-LIMB PROSTHETICS BASED ON ELECTROMYOGRAPHIC SIGNALS

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Abstract
Effective control of upper-limb prosthetics relies heavily on accurate real-time interpretation of electromyographic (EMG) signals corresponding to hand movements. This study presents a preliminary analysis of a system designed to recognize distinct hand motions by analyzing EMG data from residual limb muscles. Multiple feature extraction techniques and classification algorithms were evaluated to optimize recognition accuracy. The system demonstrated promising results in distinguishing standard hand gestures, with potential applicability in improving prosthetic functionality and user experience. Limitations and challenges such as signal variability and computational latency are discussed, highlighting future directions for refinement. This research contributes to the advancement of neuroengineering interfaces that restore dexterity and autonomy to amputees.

Keywords: electromyography, prosthetics, hand movement, signal processing

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ADVANCED SIMULATION PLATFORM FOR MEDICAL IMAGE FUSION AND LEARNING

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Abstract

Recent advancements in medical imaging have emphasized the integration of multi-modal data to enhance diagnostic accuracy and treatment planning. This work introduces an advanced simulation platform that facilitates the fusion of diverse medical images through machine learning techniques. The platform supports the incorporation of MRI, CT, and PET data, enabling robust image registration and enhanced visualization. Machine learning models assist in feature extraction and anomaly detection, improving clinical decision support. Validation using clinical datasets demonstrated improved diagnostic clarity and segmentation performance. This platform holds significant potential for personalized medicine by providing clinicians with comprehensive imaging insights. Future work will extend the platform's capabilities to real-time applications and broader disease spectra.

Keywords: medical imaging, image fusion, machine learning, simulation

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MICROFLUIDIC SYSTEMS FOR ADVANCED BIOMEDICAL ENGINEERING APPLICATIONS

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Abstract

Microfluidic systems represent a cutting-edge technology enabling precise manipulation of fluids at the microscale, with widespread applications in biomedical engineering. This paper reviews recent innovations in microfluidic device design tailored for diagnostics, drug delivery, and tissue engineering. Emphasis is placed on the integration of biosensors and lab-on-a-chip technologies that facilitate rapid and sensitive biological assays. The advantages of microfluidics include reduced reagent consumption, enhanced portability, and improved assay speed. Challenges such as fabrication complexity and device standardization are discussed. Emerging approaches utilizing novel materials and automation are highlighted, underscoring the transformative potential of microfluidics in medical technology development.

Keywords: microfluidics, biomedical engineering, lab-on-a-chip, biosensors