



7th INTERNATIONAL SYMPOSIUM ON PHARMACEUTICAL CHEMISTRY

June 11-14, 2026

Ankara HiltonSA



BOOK OF ABSTRACT

with the supports of



TURKISH
AIRLINES

OFFICIAL AIRLINE OF THE CONGRESS



MAIN SPONSORS



OFFICIAL AIRLINE OF "7TH INTERNATIONAL
SYMPOSIUM ON PHARMACEUTICAL
CHEMISTRY"

ATABAY
Geçmişten Geleceğe Sağlık

BERKO İLAÇ
"sağlıklı yarınlara"



DR. ZEYDANLI
Hayat Bilimleri

IKA

KOLUMAN

LABORİLDAM
1979...Kalite - Güven - İnovasyon

**Majistral
Eczacıları
Derneği**

MENARINI
Türkiye

MSD

NOVAGENIX
BİYOKİMYA İLAÇ AR-GE MERKEZİ

novo nordisk®

PF
POLİFARMA

SARTORIUS



SCIENTIFIC PROGRAM.....	8
COMMITTEES.....	11
PLENARY LECTURES	12
PL1 EPIGENETIC VULNERABILITY IN COLORECTAL CANCER FROM SMALL MOLECULE HDAC INHIBITORS TO HDAC DEGRADERS	
Giuseppe Campiani	13
PL2 STRUCTURE- AND DATA-DRIVEN KINASE INHIBITOR DISCOVERY: INTEGRATING PHARMACOPHORE MODELING, DOCKING, AND MACHINE LEARNING FOR LEAD IDENTIFICATION AND OPTIMIZATION	
Prof. Mutasem Taha.....	14
PL3 REINVENTING AZOLES: NEW TRICKS FROM OLD DRUGS VIA METAL COMPLEXATION	
Sandra Vojnovića, Sanja Škaro Bogojevića, Nevena Lj. Stevanovićb, Mia Stankovićb, Biljana Glišićb, Miloš Đuranb, Jasmina Nikodinović-Runića.....	15
PL4 INTEGRATIVE COMPUTATIONAL, MOLECULAR, AND SYSTEMS-LEVEL APPROACHES TO TARGET MATRIX METALLOPROTEINASES: FROM INHIBITOR DESIGN TO PRECISION MODULATION IN DISEASE	
Sanaa Khaled Bardaweel, Dima A Sabbah, Rima Hajjo	16
PL5 GREEN TECHNOLOGIES IN PHARMACEUTICAL CHEMISTRY: BERBERINE-RICH EXTRACT FOR SUSTAINABLE THERAPEUTIC APPLICATIONS	
Muhammad Ajmal Shah.....	17
PL6 EXPLORING THE MODULATION OF BACTERIAL CARBONIC ANHYDRASES FOR THE PREVENTION AND TREATMENT OF INFECTIOUS DISEASES	
Simone Carradori	17
PL7 CHIRAL DRUGS: CURRENT TRENDS AND ANALYTICAL CHALLENGES	
Bezhan Chankvetadze	17
PL8 ORGANOID TECHNOLOGIES: NEW PERSPECTIVES IN DRUG DEVELOPMENT AND PERSONALIZED MEDICINE	
Fatma Duygu Özel Demiralp	17
PL9 DARIZMETINIB: A PROMISING 1ST-IN-CLASS LIVER REGENERATING DRUG IN PHASE 1B/2A CLINICAL DEVELOPMENT, TARGETING THE STRESS SIGNALING PROTEIN KINASE MKK4	
Stefan Laufer	17
PL10 FROM SELECTIVE TO MULTITARGET-DIRECTED LIGANDS: ENDOCANNABINOID CATABOLISM AS A THERAPEUTIC STRATEGY IN EPILEPSY AND NEUROINFLAMMATORY CONDITIONS	
Stefania Butini.....	18
PL11 THE LIVING SCAFFOLD: DESIGNING ANTI-CANCER T CELL THERAPIES FOR THE MODERN PHARMACOPEIA	

Güneş Esendağlı	18
PL12 FROM MOLECULAR DESIGN TO BIOLOGICAL ACTIVITY: NEW DIRECTIONS IN ANTICANCER AND ALZHEIMER'S THERAPEUTICS	
Reem K. Arafa	18
PL13 INTEGRATED R&D STRATEGIES FOR NITROSAMINE/GTI CONTROL: FROM ROOT CAUSES TO SUSTAINABLE SOLUTIONS	
Manik Reddy Pullagurla	18
PL14 TACC3 INHIBITION AS A PRECISION ONCOLOGY APPROACH FOR AGGRESSIVE SOLID CANCERS	
Erden Banoğlu	18
ORAL PRESENTATIONS	19
OP01	20
OP02 RATIONAL DESIGN, ADMET ANALYSIS, AND SAR EVALUATION OF PYRAZOLE- OXIME HYBRID COMPOUNDS AS ANTICANCER AGENTS AGAINST BREAST CANCER	
Merve Gül, Mehmet Abdullah Alagöz, Ceylan Hepokur, Öztekin Algül	21
OP03 ANTIOXIDANT AND IMMUNOMODULATORY POTENTIAL OF HEXAHYDROQUINOLINE-3-CARBOXYLATE DERIVATIVES: IN VITRO AND IN SILICO STUDIES	
Damiano Iacovozzi, Marialucia Gallorini, Rahime Simsek, Ezgi Pehlivanlar Yavrucu, Gökhan Zengin, Venkatesan Saravanan, Simone Carradori	22
OP04 BIOFILMS ACROSS SECTORS: CHALLENGES AND EMERGING ANTIBIOFILM STRATEGIES TARGETING QUORUM SENSING	
Ayşe Nur Yurdcu, Nefise Akçelik	23
OP05 COMPARATIVE MOLECULAR DOCKING AND STRUCTURE-ACTIVITY RELATIONSHIP ANALYSIS OF FLAVAN-3-OLS AND PROCYANIDIN OLIGOMERS TARGETING FIBRINOLYTIC PROTEINS	
Gizem Deynez, Sümeyra Gültekin	24
OP06 FLUOXETINE DIFFERENTIALLY REDUCES CELL VIABILITY IN MYCN- AMPLIFIED AND NON-AMPLIFIED NEUROBLASTOMA CELLS	
Özge Nur Toprak, Selen Öztürk	26
OP07 DIFLUOROMETHOXY-SUBSTITUTED HEXAHYDROQUINOLINES AS MULTI- TARGET ANTI-INFLAMMATORY AGENTS: MECHANISTIC AND METABOLOMIC INSIGHTS	
Ezgi Pehlivanlar Yavrucu, Ayça Aktaş Şüküroğlu, Meryem Temiz Reşitoğlu, Ozan Kaplan, Esraa Ebraheem Al Jomaa, Taşkın Kalkan, Seyhan Şahan Fırat, Rahime Şimşek	27
OP08 A THREE-CHANNEL ORTHOGONAL REVERSE-SCREENING PIPELINE FOR TARGET DECONVOLUTION OF NOVEL CHALCONE-DERIVED SCAFFOLDS	
Pouria Zarrin, Tasneem S. Hosni, Birsen Tozkoparan Köprücü, Nesrin Gökhan Kelekçi	28
OP09 DESIGN AND EVALUATION OF HYDROGEN PEROXIDE ACTIVATABLE PHOTOSENSITIZER FOR BRAIN TUMOR TARGETED PHOTODYNAMIC THERAPY	
Ecrin Mustanoğlu, Dilek Yigiter, Osman Karaman, Zubeyir Elmazoglu, Gorkem Gunbas	31

OP10 MIXED DONOR SUBSTITUTION IN SELENIUM-CONTAINING XANTHENE
PHOTOSENSITIZERS FOR TUNING SELECTIVITY AND POTENCY IN PDT

Ece Ayça Erdoğan, Osman Karaman, Zübeyir Elmazoğlu, Görkem Günbaş..... 32

OP11 SELECTIVE LITHIATION UNLOCKS A BROMINATED SI-RHODAMINE BASED
PHOTODYNAMIC THERAPY AGENT

Osman Karaman, Naz Özoğul, Deniz Yılmaz, Şafak Tekir, Zübeyir Elmazoğlu, Görkem Günbaş . 33

OP12 ENANTIOSELECTIVE CE-MS/MS ANALYSIS OF MDMA AND MAJOR
METABOLITES: COMPARATIVE PHARMACOKINETICS IN ORAL FLUID, URINE AND
PLASMA

Kardelen Avcı, Saba Jorbenadze, Mehmet Gumustas, Francesco Paolo Busardo, Bezhan
Chankvetadze 34

OP13 35

OP14 DETERMINATION OF SAFINAMIDE IN HUMAN PLASMA BY USING LIQUID
CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY

Sumeyya Koldas, Nesrin Okatan, Elif Basak Tuncer, Gamze Sevinci, Berrak Guney, Onursal Saglam
..... 36

OP15 SYNTHESIS, ANTIPROLIFERATIVE EVALUATION, AND MOLECULAR DOCKING
STUDIES OF NOVEL CHLOROPHENYLPYPERAZINE-HYDROXYPYRIDINONE MANNICH
BASES

Gülşah Karakaya, Beyza Düzleyen, Onurcan Demir, Ünzile Yaman, Canan Sevimli Gür, Mutlu
Dilsiz Aytemir..... 37

OP16 INVESTIGATION OF THE ROLE OF MTOR COMPLEX 2 IN THE INFLAMMATORY
RESPONSE AND OXIDATIVE PROCESSES MEDIATING PERIPHERAL
ISCHEMIA/REPERFUSION INJURY IN RATS

Ayşe Karabulbul, Meryem Temiz Resitoğlu, Esraa Ebraheem Al Jomaa, Taskın Kalkan, Tuba Isik,
Ekrem Can Yaylım, Hatice Oruc Demirbag, Nehir Sucu, Seyhan Sahan Firat 39

POSTER PRESENTATIONS 40

PP01 SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME PYRAZOLE-UREA
DERIVATIVES AS POTENTIAL ANTIMICROBIAL AND ANTIBIOFILM AGENTS

Deniz Lengerli, Gülbeyaz Dökmeci, Berrin Özçelik 41

PP02 GAS-PHASE ION-MOLECULE REACTIONS OF PROTONATED OXIME COMPOUNDS
WITH 2-METHOXYPROPENE IN A LINEAR QUADRUPOLE ION TRAP MASS
SPECTROMETER

Kawthar Z Alzarani, Bright H Adu, Hilka I Kenttamaa 42

PP03 INVESTIGATION OF BACTERIAL AND HUMAN TOPOISOMERASE I INHIBITION
POTENTIAL OF RECALLED DRUGS BY MOLECULAR DOCKING METHOD AND ADME
ANALYSES

Umut Okur, Okan Aykaç, Irem Bozbey Merde 43

PP04 IN SILICO EVALUATION OF A NOVEL BIPHENYL-TRIAZOLE DERIVATIVE AS A
POTENTIAL CYP51 INHIBITOR: A MOLECULAR DOCKING STUDY

Ebru Sert, Harun Uslu, Bünyamin Göktaş, Zeynep Özdemir 44

PP05 DETERMINING THE EFFECTS OF MOLECULES WITH HYDRAZONE AND
PYRIDAZINE STRUCTURES ON LIVER CANCER

Yaren Nur Zenni, Zeynep Özdemir, Neşe Başak Türkmen 45

PP06 NOVEL BENZAZOLE-BENZAMIDE HYBRIDS: SYNTHESIS AND IN VITRO
ANTIPROLIFERATIVE EVALUATION ON BREAST CANCER

Zeynep Sude Yalçın, Mehmet Abdullah Alagöz, Şule Gürsoy, Öztekin Algül..... 46

PP07 EVALUATION OF CARBONIC ANHYDRASE ENZYME INHIBITOR ACTIVITIES OF
TAURINAMIDOBENZENSULFONAMIDE DERIVATIVES

Özlem Akgül, Sema Yılmaz, Andrea Angeli, Gioele Renzo, Fabrizio Carta, Claudiu T. Supuran ... 47

PP08 ANALYSIS OF AFLATOXIN B1 AND M1 IN MEDICAL ENTERAL NUTRITION
PRODUCTS AND INFANT FORMULAS: A CHROMATOGRAPHIC EVALUATION

Sümeyra Albayrak, Ateş Kara 48

PP09 SYNTHESIS AND STRUCTURAL ANALYSIS OF NOVEL OXIME ETHERS BEARING
IMIDAZOLE AND PYRAZOLE RINGS

Melizsa Melizsa, Zeynep Özdemir, Ebru Sert, Zarife Sibel Şahin, Ade Arsianti..... 50

PP10 VIRTUAL SCREENING AND MOLECULAR DYNAMICS-BASED EVALUATION OF AN
ATP-POCKET-TARGETING TNIK HIT CANDIDATE

Selenay Aktemur, Kübra Çalışkan..... 51

PP11 THIOPHENE-TAIL ELONGATION OF OG-001 ENHANCES SELECTIVE DUAL
INHIBITION OF TUMOR-ASSOCIATED HCA IX AND XII: MOLECULAR DYNAMICS
INSIGHTS

Muhammed Trawally, Kübra Demir Yazıcı, Atilla Akdemir, Özlen Güzel Akdemir 52

PP12 DEVELOPMENT AND IN VITRO CHARACTERIZATION OF ORAL DISINTEGRATING
FILMS LOADED WITH A NOVEL HEXAHYDROQUINOLINE COMPOUND

Kutsal Özcan Kosif, Ezgi Pehlivanlar Yavrucu, Rahime Şimşek..... 54

PP13 LABORATORY-SCALE SYNTHESIS OF ANHYDROUS ALUMINUM CHLORIDE FOR
FRIEDEL-CRAFTS APPLICATIONS UNDER MOISTURE-FREE CONDITIONS

Ural Ufuk DEMIREL, Remziye Azra KARTOP..... 55

PP14 ROLE OF CD36 ON CANCER AND METASTASIS

Irem CELIK, Ural Ufuk DEMIREL, Behiye OZTURK SEN..... 56

PP15 ANTI-CANCER EFFECT OF OLEUROPEIN

Fatmanur TUNA, Ural Ufuk DEMIREL, Behiye OZTURK SEN..... 57

PP16 APPLICATION OF PVA HYDROGELS IN DRUG DELIVERY SYSTEM

Berfin DIREKCI, Behiye OZTURK SEN, Ural Ufuk DEMIREL..... 58

PP17 ANTIBACTERIAL MECHANISM OF HYDROGELS FOR THE TREATMENT OF
INFECTIONS

Basant GHALAB, Behiye OZTURK SEN, Ural Ufuk DEMIREL 59

PP18 DESIGN, SYNTHESIS, CHARACTERIZATION, AND MOLECULAR DOCKING
STUDIES OF NOVEL ISATIN-BASED SULFONAMIDE DERIVATIVES AS POTENTIAL
ANTICANCER AGENTS

Marjan AKBARI, Ural Ufuk DEMIREL	60
PP19 COMPUTER-AIDED DESIGN OF ROR γ (ROR GAMMA) AGONIST (RETINOIC ACID RECEPTOR-RELATED ORPHAN NUCLEAR RECEPTOR γ) AND NOVEL DERIVATIVES AS THERAPEUTIC TARGETS IN PROSTATE CANCER	
Mahmut Haluk ÖZÇİLENK, Asiye MERİÇ	61
PP20 NOVEL THIAZOLE-ACRYLONITRILE DERIVATIVES: SYNTHESIS AND EVALUATION AS ANTIMICROBIAL AGENTS	
Rumeysa Yonar, Keriman Özadalı Sarı, Şeyma Nigiz	63
PP21 NOVEL BENZOXAZOLINONE THIOSEMICARBAZIDES TARGETING ALZHEIMER'S DISEASE	
Hayrünnisa Taşci, Ahmet Avcı, Nadire Özenver, Begüm Nurpelin Sağlık, Birsen Tozkoparan, Nesrin Gökhan Kelekçi	64
PP22 SYNTHESIS, ANTIMICROBIAL, AND ANTIPROLIFERATIVE EVALUATION OF A NOVEL PIPERONYL-PIPERAZINE-HYDROXYPYRANONE DITHIOCARBAMATE	
Ilayda Kılıç, Gülşah Karakaya, Yamaç Tekintaş, Şahika Cıngır Köker, Mutlu Dilsiz Aytemir	65
PP23 SYNTHESIS AND ANTIBACTERIAL PROFILING OF A NOVEL 3-HYDOXYPYRIDINONE DERIVATIVE	
Beyza Düzleyen, Gülşah Karakaya, Yamaç Tekintaş, Mutlu Dilsiz Aytemir	66
PP24 FROM VIRTUAL SCREENING TO NANOMOLAR HITS: IDENTIFICATION AND CHARACTERIZATION OF JANUS KINASE 1/2 INHIBITORS	
Ahmet Avcı, Hayrünnisa Taşci, Begüm Nurpelin Sağlık Özkan, Birsen Tozkoparan, Nesrin Gökhan Kelekçi	67
PP25 DISCOVERY OF POTENT MONOAMINE OXIDASE INHIBITORS: BENZYLIDENE-THIAZOLIDINEDIONE-ACETANILIDE HYBRIDS	
Aylin Balaban, Ahmet Avcı, Begüm Nurpelin Sağlık Özkan, Nesrin Gökhan Kelekçi, Birsen Tozkoparan	69
PP26 SYNTHESIS OF NEW CHALCONE COMPOUNDS AND IN VITRO EVALUATION OF THEIR ACTIVITY FOR MULTI-TARGETED ALZHEIMER'S DISEASE THERAPY	
Ezgi Pehlivanlar Yavrucu, İnci Kazkayası Bölük, Vahap M. Kutluay, Rahime Şimşek	71
PP27 NOVEL FLURBIPROFEN-DERIVED HYBRIDS WITH COX-1/COX-2 INHIBITORY ACTIVITY	
Tasneem Hosni, Ahmet Avcı, Begüm Nurpelin Sağlık Özkan, Birsen Tozkoparan, Nesrin Gökhan Kelekçi	72
PP28 DESIGN, SYNTHESIS, AND SPECTROSCOPIC CHARACTERIZATION OF THYMOL- AND CARVACROL-BASED HYDRAZONE DERIVATIVES AS POTENTIAL ANTIBACTERIAL AGENTS	
Mislina Daniştı, Miyase Gözde Gündüz	73
PP29 PYRANO[2,3-D]PYRIMIDINE DERIVATIVES: SYNTHESIS AND EVALUATION OF ANTICANCER AND CALCIUM CHANNEL BLOCKING ACTIVITY	
Ayşe Karagüzel, Münevver Baran, Gözde Özge Önder, Sun Huang, Gerald Zamponi, Miyase Gözde Gündüz	75

PP30 NOVEL DITHIOCARBAMATE DERIVATIVES AS POTENTIAL CHOLINESTERASE INHIBITORS: DESIGN, SYNTHESIS, AND MOLECULAR DOCKING STUDIES	
Ebru Koçak Aslan.....	76
PP31 DESIGN, SYNTHESIS, AND EVALUATION OF 4-(4-FLUOROBENZYL)-6-METHYLPYRIDAZIN-3(2H)-ONE DERIVATIVES AS TYROSINASE INHIBITORS	
Merve Zengin, Esin Akdemir Yılmaz, Suna Sabuncuoğlu, Oya Ünsal Tan	77
PP32 DESIGN, SYNTHESIS, AND CHARACTERIZATION OF NOVEL BENZIMIDAZOLE DERIVATIVES FOR POTENTIAL FLAP INHIBITION	
Azize Gizem Ergül, Paul Mike Jordan	78
PP33 PREPARATION AND CHARACTERIZATION OF HNO ₃ -MODIFIED GRAPHENE-REINFORCED 2-HYDROXYETHYL CELLULOSE NANOCOMPOSITE HYDROGELS FOR CONTROLLED DOXORUBICIN DELIVERY	
İlayda Hatice Çakmak, Nursel Pekel Bayramgil	79
PP34 SYNTHESIS AND CHARACTERIZATION OF 1-PHENYL-4-(4-((2-PHENYLHYDRAZONO)METHYL)PHENYL)PIPERAZINE DERIVATIVES	
Cemre Yıldız, Ezgi Pehlivanlar Yavrucu, Rahime Şimşek.....	80
PP35 SYNTHESIS AND CHARACTERIZATION OF 1,3-DIPHENYLPROP-2-EN-1-ONE DERIVATIVES	
Sude Naz Tulgar, Ezgi Pehlivanlar, Rahime Şimşek.....	81
PP36 GRAPHENE-DOPED ELECTROSPUN HYDROXYPROPYLCELLULOSE (HPC) NANOFIBERS FOR TAILORING TERRAMYCIN RELEASE PROFILES	
Sündüz Alemdar, Nursel Pekel Bayramgil	82
PP37 ENGINEERING ACRIDINE CHROMOPHORES INTO NIR PHOTSENSITIZERS: A FIRST-IN-CLASS STRATEGY FOR PHOTODYNAMIC THERAPY	
Muhammed Ali Civaz, Çağatay Dönmez, Osman Karaman, Görkem Günbaş.....	83
PP38 DESIGN, SYNTHESIS, AND STRUCTURAL CHARACTERIZATION OF NOVEL HYBRID COMPOUNDS CONTAINING INDANONE AND TETRAZOLE MOIETIES	
Zeliha Bilgel, Ayşenur Işgüzar, Doğan Doyduk	84
PP39 DISCOVERY OF NOVEL PYRANO[3,2-b]PYRAN DERIVATIVES AND EVALUATION OF TYROSINASE INHIBITOR ACTIVITY	
Mutlu Dilsiz Aytemir, Rahime Şimşek, Ezgi Pehlivanlar, Eren Çaltekin.....	86
AUTHOR INDEX.....	87

SCIENTIFIC PROGRAM

June 11, 2026, Thursday

13:00-14:00 Registration

14:00-15:00 Opening Ceremony Performance

15:00-15:30 Coffee Break

15:30-17:30 PANEL

Moderator: Prof. Dr. Ateş Kara

Türkiye'de Farmasötik Etkin Madde (API) ve Aşı Üretiminin Güncel Durumu ve Gelecek Stratejileri

- **Prof. Dr. Mutlu Aytemir**
Hacettepe Üniversitesi Eczacılık Fakültesi Dekanı
- **Uzm. Ecz. Taner Ercanlı**
Türk Eczacılar Birliği Genel Sekreteri
- **Guilhem Granier**
Head of EURASIA MCO & Gen. Man. Turkey - VACCINES, SANOFI
- **Turgay Kaçar**
Atabay Biyoteknoloji - ATABAY İLAÇ
- **Dr. Kimyager A. Neşe Kayran**
Stratejik Portföy ve Projeler Müdürü - NOBEL İLAÇ
- **Dr. Ecz. Abdullah Uslu**
Gebze Arge ve Biyoteknoloji Müdürü- NOBEL İLAÇ

17:30-19:30 WELCOME RECEPTION

June 12, 2026, Friday

09:00-10:30 SESSION – 1

Chair Persons: Prof. Dr. Öztekin Algül, Prof. Dr. Miyase Gözde Gündüz

Small Molecule Inhibition And Protein-Targeted Degradation Of Class I HDACs As Effective Therapeutic Strategies, *Prof. Dr. Giuseppe Campiani*

From Molecular Design to Biological Activity: New Directions in Anticancer and Alzheimer's Therapeutics, *Prof. Dr. Reem K. Arafa*

10:30-11:00 Poster Session (PP01-PP20) & Coffee Break

11:00-11:45 SATELLITE SYMPOSIUM - 1 (NOVO NORDISK)

Moderator & Speaker: Işıl Canset Cantürk Üçtuğ

Synthetic Products Referencing Biologically Produced Peptides

Speaker: *Morten Hach* & Panelist: *Jens Heisterberg*

11:45-12:45 SESSION - 2

Chair Persons: Prof. Dr. Seyhan Fırat Şahan, Assist. Prof. Dr. Deniz Lengerli

TACC3 Inhibition as a Precision Oncology Approach for Aggressive Solid Cancers, *Prof. Dr. Erden Banoğlu*

Exploring the Modulation of Bacterial Carbonic Anhydrases for the Prevention and Treatment of Infectious Diseases, *Assoc. Prof. Dr. Simone Carradori*

12:45-13:45 Lunch

13:45-14:30 SATELLITE SYMPOSIUM - 2 (TERRA)

timsOmni - a Revolutionary Tool for Top-Down Protein Characterization and beyond

Speaker: *Daniel Vlačil*

14:30-15:30 SESSION - 3

Chair Persons: Prof. Dr. Kadriye Benkli, Assoc. Prof. Dr. Harun Uslu

Chiral Drugs: Current Trends and Analytical Challenges, *Prof. Dr. Bezhan Chankvetadze*

Structure- and Data-Driven Kinase Inhibitor Discovery: Integrating Pharmacophore Modeling, Docking, and Machine Learning for Lead Identification and Optimization, *Prof. Dr. Mutasem O. Taha*

15:30-16:00 Coffee Break

16:00-17:00 SESSION - 4

Chair Person: Prof. Dr. Sevda enel

Invited speaker: *Prof. Dr. Burak Civelek*

Organoid Teknolojileri: İlaç Geliştirme ve Kişiselleştirilmiş Tedavide Yeni Perspektifler, *Prof. Dr. Fatma Duygu Özel Demiralp*

17:00-17:10 Break

17:10-17:40 Oral Presentations (OP01-OP03) - 1

Chair Persons: Prof. Dr. Reem K. Arafa, Assist. Prof. Dr. Muhammad Ajmal Shah

June 13, 2026, Saturday

09:00-10:30 SESSION - 5

Chair Persons: Prof. Dr. Birsen Tozkoparan Köprücü, Assoc. Prof. Dr. Özlem Akgül

Darizmetinib: A Promising 1st-in-Class Liver Regenerating Drug in Phase 1b/2a Clinical Development, Targeting the Stress Signaling Protein Kinase MKK4, *Prof. Dr. Stefan Laufer*

From Selective to Multitarget-Directed Ligands: Endocannabinoid Catabolism as a Therapeutic Strategy in Epilepsy and Neuroinflammatory conditions, *Prof. Dr. Stefania Butini*

10:30-11:00 Poster Session (PP21-PP39) & Coffee Break

11:00-12:00 SESSION - 6

Chair Persons: Assist. Prof. Dr. Dilan Özmen Özgün, Assoc. Prof. Dr. Simone Carradori

The Living Scaffold: Designing Anti-cancer T Cell Therapies for the Modern Pharmacopoeia, *Prof. Dr. Güneş Esendağlı*

Integrative Computational, Molecular, and Systems-Level Approaches to Target Matrix Metalloproteinases: From Inhibitor Design to Precision Modulation in Disease, *Prof. Dr. Sanaa K. Bardaweel*

12:00-13:00 Lunch

13:00-13:30 SESSION - 7

Chair Persons: Assoc. Prof. Dr. Keriman Özadalı Sarı, Assist. Prof. Dr. Merve Zengin

Integrated R&D Strategies for Nitrosamine/GTI Control: From Root Causes to Sustainable Solutions, *Dr. Manik Reddy Pullagurla*

13:30-14:00 Coffee Break

14:00-15:00 SESSION - 8

Chair Persons: Prof. Dr. Miyase Gözde Gündüz, Assist. Prof. Dr. Muhammed Trawally

Reinventing azoles: New Tricks from Old Drugs Via Metal Complexation, Prof. Dr. Sandra Vojnović

Green Technologies in Pharmaceutical Chemistry: Berberine-Rich Extract for Sustainable Therapeutic Applications, *Prof. Dr. Muhammad Ajmal Shah*

15:00-15:10 Break

15:10-15:50 Oral Presentations - 2 (OP04 - OP07)

Chair Persons: Prof. Dr. Sanaa K. Bardaweel, Prof. Dr. Mutasem O. Taha

15:50-16:00 Break

16:00-16:50 Oral Presentations - 3 (OP08 - OP12)

Chair Persons: Prof. Dr. Stefania Butini, Prof. Dr. Güneş Esendağlı

16:50-17:00 Break

17:00-17:20 Short Oral Presentations (OP13- OP16)

Chair Person: Prof. Dr. Sandra Vojnović

17:20-17:45 Closing Ceremony Performance

The International Symposium on Pharmaceutical Chemistry (ISPC) series is a well-established scientific event initiated by the Department of Pharmaceutical Chemistry at Hacettepe University Faculty of Pharmacy and has been internationally recognized in the fields of pharmaceutical and medicinal chemistry since 1997.

As one of the most prestigious meetings in Türkiye in this field, ISPC aims to strengthen interdisciplinary academic interaction and to promote scientific collaboration at both national and international levels.

Organized six times between 1997 and 2010 with great success, the symposium has gained a strong position in the field through its expanding scientific scope, deepening academic content, and broad participant profile.

The seventh ISPC will be held in June 2026 in Ankara, in collaboration with the Vaccine Institute of Türkiye (TAE) and the Health Institutes of Türkiye (TÜSEB).

The scientific program will particularly focus on fundamental and applied research areas including, but not limited to:

- * Drug discovery and development processes
- * Modern strategies targeting therapeutic pathways
- * Molecular design, synthesis, structure–activity relationships, and mechanistic studies
- * Vaccine development and next-generation vaccine Technologies

The symposium is expected to host world-renowned scientists, international API manufacturers, advanced research institutions, industry representatives, and public authorities.

Particular emphasis will be placed on supporting young researchers by fostering direct interaction with international experts and contributing to their scientific communication networks and career development.

On the final day, a special panel session will be held with the participation of international health authorities and policymakers, focusing on global drug and vaccine strategies.

We would be honored to welcome you to this significant scientific event.

Prof. Dr. Rahime ŞİMŞEK

Symposium Chair

*Hacettepe University Faculty of Pharmacy
Department of Pharmaceutical Chemistry*

Prof. Dr. Ateş KARA

Symposium Chair

*Hacettepe University Faculty of Medicine
Division of Pediatric Infectious Diseases
Vaccine Institute of Türkiye*

Symposium Chairs

Prof. Rahime Şimşek

Prof. Ateş Kara

Symposium Organizing Committee

Prof. Mutlu Aytemir

Prof. Nesrin Gökhan Kelekçi

Prof. Miyase Gözde Gündüz

Prof. Ateş Kara

Prof. Ümit Kervan

Prof. Erhan Palaska

Prof. Sevda Şenel

Prof. Rahime Şimşek

Prof. Birsen Tozkoparan Köprücü

Prof. Oya Ünsal Tan

Assoc. Prof. Keriman Özadalı Sarı

Assoc. Prof. Murat Sarğın

Assoc. Prof. Suat Sarı

Assist. Prof. Ebru Koçak Aslan

Assist. Prof. Merve Zengin

Symposium Scientific Secretariat

Assist. Prof. Ebru Koçak Aslan

Symposium Scientific Board

Prof. Hülya Akgün

Prof. Reem K. Arafa (Egypt)

Prof. Erden Banoğlu (Türkiye)

Prof. Sanaa K. Bardaweel (Jordan)

Prof. Barkın Berk (Türkiye)

Prof. Stefania Butini (Italy)

Prof. Giuseppe Campiani (Italy)

Prof. Bezhan Chankvetadze

(Georgia)

Prof. Burak Civelek (Türkiye)

Prof. Malgorzata Dukat (USA)

Prof. Hakkı Erdoğan (Türkiye)

Prof. Güneş Esendağlı (Türkiye)

Prof. Meriç Köksal Akkoç (Türkiye)

Prof. Stefan Laufer (Germany)

Prof. Fatma Duygu Özel Demiralp

(Türkiye)

Prof. Selma Saraç Tarhan (Türkiye)

Prof. Cihat Şafak (Türkiye)

Prof. Mutasem O. Taha (Jordan)

Prof. Sandra Vojnović (Serbia)

Prof. Mine Yarım Yüksel (Türkiye)

Assoc. Prof. Simone Carradori (Italy)

Assoc. Prof. İnci Selin Doğan

(Türkiye)

Assist. Prof. Bahadır Bülbül

(Türkiye)

Assist. Prof. Gökalep Çetin (Türkiye)

Assist. Prof. Gülşah Karakaya

(Türkiye)

Assist. Prof. Hayrünnisa Taşçı

(Türkiye)

Assist. Dr. Muhammad Ajmal Shah

(Pakistan)

Dr. Ahmed Elkamhawy (Kazakhstan)

Dr. Manik Reddy Pullagurla (India)

PLENARY LECTURES

PL1

EPIGENETIC VULNERABILITY IN COLORECTAL CANCER FROM SMALL MOLECULE HDAC INHIBITORS TO HDAC DEGRADERS**Giuseppe Campiani**Department of Biotechnology, Chemistry and Pharmacy
University of Siena IT

Colorectal cancer (CRC) ranks among the most prevalent malignancies worldwide, accounting for approximately 10% of all cancer diagnoses and standing as the second leading cause of cancer-related mortality, surpassed only by lung cancer. Despite advances in screening campaigns and treatment regimens, the prognosis for patients with advanced or metastatic CRC remains poor, largely due to the development of resistance to standard-of-care therapies.

The emergence of drug resistance to 5-fluorouracil (5-FU) and biologics like cetuximab significantly limits their long-term efficacy, underscoring the urgent need for novel therapeutic approaches. Tumorigenesis results from genetic mutations and epigenetic dysregulation, including DNA methylation changes, histone modifications, and altered microRNA expression that trigger CRC progression. Furthermore, histone modifications have been identified as prognostic CRC markers, fueling interest in the development of novel epidrugs. Overexpression of HDACs and in particular

HDAC3 has been linked to poor prognosis in CRC, highlighting HDACs as promising epigenetic targets in CRC treatment. More recently the impact of HDAC10 in cancer cells and cancer immunity in CRC has been reported and HDAC10 has been classified as a key prognostic biomarker, overexpressed in CRC and correlated with poor prognosis and resistance to immunotherapy. Reversing epigenetic vulnerability and overcoming therapeutic resistance in colorectal cancer (CRC) remain major clinical challenges, highlighting the need for strategies targeting epigenetic drivers. The research followed two different trajectories; one based on development of occupancy-directed ligands and the other based on identification of event-driven degrading tools for specific interaction with class I HDACs and with HDAC10. The antitumor efficacy of the new HDAC inhibitor *COLRESTAT* and of the new degraders was proved in patient-derived colon cancer organoids and in vivo in the CRC CAM model.

PL2

STRUCTURE- AND DATA-DRIVEN KINASE INHIBITOR DISCOVERY: INTEGRATING PHARMACOPHORE MODELING, DOCKING, AND MACHINE LEARNING FOR LEAD IDENTIFICATION AND OPTIMIZATION

Prof. Mutasem Taha

Protein kinases remain central therapeutic targets in oncology, yet their discovery is complicated by conserved ATP-binding sites, conformational plasticity, activity cliffs, resistance mutations, and the need for novel chemotypes. This presentation summarizes an integrated structure- and data-driven workflow developed across several published kinase inhibitor discovery studies, combining pharmacophore modeling, molecular docking, QSAR, machine learning, and experimental validation.

The strategy integrates ligand-based and structure-based pharmacophores, docking-derived pharmacophores, docking-based comparative intermolecular contact analysis, ligand–receptor contact fingerprints, and molecular-dynamics- or stochastic-deformation-derived pharmacophoric contacts. Pharmacophore fit values,

physicochemical descriptors, docking scores, and contact fingerprints are selected using genetic-function-algorithm-guided QSAR/ML, while SHAP analysis supports mechanistic interpretation and pharmacophore extraction from predictive models. Data augmentation through multiple conformers or docked poses improves model robustness and enables efficient hit prioritization. Representative applications include TTK, CLK4, Aurora A, HER2, STAT3, CDK16, and PI3KC2 α . Virtual screening of chemically diverse databases, including the NCI repository and OpnMe, yielded experimentally confirmed low-micromolar, sub-micromolar, and nanomolar hits with novel chemotypes. Overall, this work demonstrates a scalable, interpretable platform for scaffold hopping, hit identification, and lead optimization against challenging kinase targets.

Keywords: kinase inhibitors; pharmacophore modeling; molecular docking; QSAR; machine learning; ligand–receptor contact fingerprints; virtual screening; scaffold hopping.

PL3

REINVENTING AZOLES: NEW TRICKS FROM OLD DRUGS VIA METAL COMPLEXATION

Sandra Vojnović^a, Sanja Škaro Bogojević^a, Nevena Lj. Stevanović^b, Mia Stanković^b, Biljana Glišić^b, Miloš Đuran^b, Jasmina Nikodinović-Runić^a

^aUniversity of Belgrade, Institute of Molecular Genetics and Genetic Engineering, Vojvode Stepe 444a, 11042 Belgrade, Serbia

^bUniversity of Kragujevac, Faculty of Science, Department of Chemistry, R. Domanovića 12, 34000 Kragujevac, Serbia

Azole antifungals have been used in clinical practice for decades as cornerstone therapies for invasive fungal infections. Nevertheless, their long-term use has led to increasing resistance, alongside limitations in toxicity and bioavailability. To address these challenges, we explored a metal-based drug optimization strategy and initiated the development of novel antifungal metal-based drugs by synthesizing metal (zinc, copper, silver, and gold) complexes with azoles: imidazole (im), clotrimazole (ctz), econazole (ecz), tioconazole (tcz), miconazole (mcz), itraconazole (icz), fluconazole (fcz), and voriconazole (vcz).

These metal complexes were synthesized, characterized using spectroscopic and crystallographic methods, and biologically evaluated. Their antifungal activity was tested against various *Candida* spp., along with their ability to inhibit the yeast-to-hyphae transition and induce reactive oxygen species in *C. albicans*. In addition to *in vitro* toxicity assays, the zebrafish (*Danio rerio*) model was employed both for toxicity evaluation and as a model of lethal disseminated candidiasis to assess the therapeutic profile of selected metal complexes.

In most cases, metal complexes of clinically used azoles demonstrated greater antimicrobial activity and improved therapeutic safety compared to the corresponding free azoles. Among these, silver(I)–azole complexes were particularly notable, with silver(I)–vcz complexes exhibiting the highest antifungal activity against the tested *Candida* spp. Furthermore, most metal–azole complexes significantly inhibited filamentation and the formation of *C. albicans* biofilms at subinhibitory concentrations. Especially silver(I)–icz complexes inhibited the yeast-to-hyphae transition in more than 90% of *C. albicans* cells. Mechanistically, the primary mode of action remains linked to ergosterol biosynthesis inhibition, as supported by docking studies, while metal coordination appears to amplify cellular stress responses, including reactive oxygen species generation.

Overall, this work demonstrates that metal–azole complexation represents a powerful strategy to revitalize existing antifungal drugs, offering enhanced efficacy, reduced toxicity, and new avenues to combat antifungal resistance.

PL4

INTEGRATIVE COMPUTATIONAL, MOLECULAR, AND SYSTEMS-LEVEL APPROACHES TO TARGET MATRIX METALLOPROTEINASES: FROM INHIBITOR DESIGN TO PRECISION MODULATION IN DISEASE

Sanaa Khaled Bardaweel¹, Dima A Sabbah², Rima Hajjo²

¹Department of Pharmaceutical Sciences, School of Pharmacy, University of Jordan, Amman 11942, Jordan

²Department of Pharmacy, Faculty of Pharmacy, Al-Zaytoonah University of Jordan, P.O. Box 130, Amman 11733, Jordan

Matrix metalloproteinases (MMPs) are key regulators of the tumor microenvironment, with functions extending beyond extracellular matrix degradation to include modulation of cytokines, growth factors, and signaling pathways that drive cancer progression. Their roles in invasion, metastasis, angiogenesis, and immune regulation have made them attractive therapeutic targets. However, despite strong rationale, clinical efforts to inhibit MMPs have largely failed, reflecting challenges related to limited selectivity, functional redundancy, and the context-dependent nature of MMP activity.

In this talk, I will present an integrative approach to re-evaluating MMPs as targets in cancer, combining computational drug design, molecular

characterization, and systems-level analysis. Structure- and ligand-based strategies are used to guide the development of targeted inhibitors, while bioinformatics approaches provide insight into MMP regulation and function within the tumor microenvironment.

Emphasis will be placed on the limitations of conventional inhibition strategies and the need for precision-based approaches that account for the spatial and temporal dynamics of MMP activity. By integrating medicinal chemistry with systems-level insights, this work highlights emerging opportunities for selective and context-specific modulation of MMPs in cancer therapy.

Keywords: Matrix Metalloproteinases, Cancer, Bioinformatics, Network analysis, Drug design

PL5

**GREEN TECHNOLOGIES IN PHARMACEUTICAL CHEMISTRY: BERBERINE-RICH EXTRACT
FOR SUSTAINABLE THERAPEUTIC APPLICATIONS**

Muhammad Ajmal Shah

Hazara University, Mansehra, Pakistan

PL6

**EXPLORING THE MODULATION OF BACTERIAL CARBONIC ANHYDRASES FOR THE
PREVENTION AND TREATMENT OF INFECTIOUS DISEASES**

Simone Carradori

University of Chieti-Pescara, Italy

PL7

CHIRAL DRUGS: CURRENT TRENDS AND ANALYTICAL CHALLENGES

Bezhan Chankvetadze

Ivane Javakhishvili Tbilisi State University, Georgia

PL8

**ORGANOID TECHNOLOGIES: NEW PERSPECTIVES IN DRUG DEVELOPMENT AND
PERSONALIZED MEDICINE**

Fatma Duygu Özel Demiralp

Turkish Health Institutes Presidency, Head of the Turkish Biotechnology Institute, Türkiye

PL9

**DARIZMETINIB: A PROMISING 1ST-IN-CLASS LIVER REGENERATING DRUG IN PHASE 1B/2A
CLINICAL DEVELOPMENT, TARGETING THE STRESS SIGNALING PROTEIN KINASE MKK4**

Stefan Laufer

Eberhard Karls University Tübingen, Germany

PL10

**FROM SELECTIVE TO MULTITARGET-DIRECTED LIGANDS: ENDOCANNABINOID
CATABOLISM AS A THERAPEUTIC STRATEGY IN EPILEPSY AND NEUROINFLAMMATORY
CONDITIONS**

Stefania Butini

University of Siena, Italy

PL11

**THE LIVING SCAFFOLD: DESIGNING ANTI-CANCER T CELL THERAPIES FOR THE MODERN
PHARMACOPEIA**

Güneş Esendağlı

Hacettepe University, Türkiye

PL12

**FROM MOLECULAR DESIGN TO BIOLOGICAL ACTIVITY: NEW DIRECTIONS IN ANTICANCER
AND ALZHEIMER'S THERAPEUTICS**

Reem K. Arafa

Zewail City of Science and Technology, Egypt

PL13

**INTEGRATED R&D STRATEGIES FOR NITROSAMINE/GTI CONTROL: FROM ROOT CAUSES TO
SUSTAINABLE SOLUTIONS**

Manik Reddy Pullagurla

Biophore, India

PL14

**TACC3 INHIBITION AS A PRECISION ONCOLOGY APPROACH FOR AGGRESSIVE SOLID
CANCERS**

Erden Banoğlu

Gazi University, Türkiye

ORAL PRESENTATIONS



OP01

OP02

RATIONAL DESIGN, ADMET ANALYSIS, AND SAR EVALUATION OF PYRAZOLE–OXIME HYBRID COMPOUNDS AS ANTICANCER AGENTS AGAINST BREAST CANCER

Merve Gül¹, Mehmet Abdullah Alagöz¹, Ceylan Hepokur², Öztekin Algül³

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Inonu University, Malatya, Türkiye

²Department of Biochemistry, Faculty of Pharmacy, Sivas Cumhuriyet University, Sivas, Türkiye

³Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Mersin University, Mersin, Türkiye; Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Erzincan Binali Yıldırım University, Erzincan, Türkiye

Introduction: Breast cancer remains the most frequently diagnosed malignancy among women and ranks second in cancer-related mortality due to its propensity for widespread metastasis. Insufficient selectivity and elevated cytotoxicity of current therapeutic agents constitute a fundamental clinical challenge, underscoring the need for compounds capable of targeting tumor cells while preserving healthy tissue. Pyrazole-based scaffolds have attracted growing interest in anticancer drug discovery, supported by well-documented antiproliferative activity across various tumor models. A novel series of 1-(4-chlorophenyl)-2-(4-methylpyrazol-1-yl)ethanone oxime derivatives was designed to address the dual criteria of potency and selectivity.

Materials-Methods: Five novel compounds (5–9) were synthesized and structurally characterized by ¹H-NMR, ¹³C-NMR, and mass spectrometry. *In vitro* cytotoxic activity was evaluated against MCF-7 breast cancer and SH-SY5Y neuroblastoma cell lines, with the latter serving as a neuronal reference model. ADMET profiles

and structure–activity relationships were subsequently analyzed.

Results-Conclusion: Cytotoxic potency was assessed via IC₅₀ (μM) values against doxorubicin as reference. Compound 7 showed the highest MCF-7 activity (IC₅₀: 26.49 μM), while the lowest SH-SY5Y cytotoxicity was observed for compound 6 (IC₅₀: 186.39 μM). All compounds complied with Lipinski's rule of five, and oral bioavailability — confirmed by QPPCaco and percent human oral absorption parameters — was markedly superior to doxorubicin. *In silico* toxicity assessment revealed no mutagenic, tumorigenic, or reproductive toxic potential, supporting their drug candidate suitability. SAR analysis confirmed the 4-methylpyrazole core as a favorable scaffold, and further functionalization of the O-alkyl oxime moiety may facilitate development of highly potent therapeutic candidates.

Keywords: 4-methylpyrazole, ADMET, breast cancer, oxime ether, SAR

OP03

ANTIOXIDANT AND IMMUNOMODULATORY POTENTIAL OF HEXAHYDROQUINOLINE-3-CARBOXYLATE DERIVATIVES: IN VITRO AND IN SILICO STUDIES

Damiano Iacovozzi¹, Marialucia Gallorini¹, Rahime Simsek², Ezgi Pehlivanlar Yavrucu², Gökhan Zengin³, Venkatesan Saravanan⁴, Simone Carradori¹

¹Department of Pharmacy, "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy

²Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Hacettepe University, Sıhhiye, Ankara, Türkiye

³Department of Biology, Science Faculty, Selçuk University, Konya, Türkiye

⁴School of Pharmacy, SBV Chennai, Sri Balaji Vidyapeeth (Deemed to be university), Pondicherry, India

Introduction: Hexahydroquinoline-3-carboxylates, structural analogs to 1,4-dihydropyridines, represent a scaffold of interest for therapeutics against inflammation. This study explores the antioxidant and immunomodulatory potential of twelve previously reported derivatives using human macrophages to model the cellular response to immunoinflammation.

Materials-Methods: Antioxidant capacity was evaluated using six *in vitro* assays, including radical-scavenging (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), 2,2-diphenyl-1-picrylhydrazyl (DPPH)), reducing-power (cupric ion reducing antioxidant capacity (CUPRAC), ferric reducing antioxidant power (FRAP), phosphomolybdenum (PBD)), and metal chelating activity (MCA) assays. Human monocytes were differentiated into macrophages using phorbol-12-myristate-13-acetate (PMA) and subsequently exposed to compounds (0.1-100 μ M) under pro-inflammatory conditions induced by lipopolysaccharide (LPS) from *Escherichia coli*. Cellular responses were assessed through cell metabolic activity (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay), flow cytometry for polarization markers (CD14, CD80, CD163), mitochondrial superoxide detection, and Western blotting for HSP70, HIF1A, COX2, and

TGFBR2 expression. *In silico* target prediction and 100 ns molecular dynamics simulations were conducted to evaluate protein-ligand interactions and stability.

Results-Conclusion: Compounds **1b** and **3c** consistently exhibited the strongest antioxidant activity, with structure-activity relationships indicating that potency decreases as the R¹ alkyl chain size increases. In LPS-stimulated macrophages, low concentrations (0.1-10 μ M) of **1a-c** and **3c** mitigated metabolic spikes and restored mitochondrial superoxide levels. While immunophenotyping confirmed a M1 pro-inflammatory phenotype (high CD80, baseline CD163), compounds **1a** and **1c** significantly ($p < 0.01$) upregulated the protective stress protein HSP70. Molecular dynamics simulations confirmed that **1c** and **2a** form stable complexes within the HSP70 nucleotide-binding domain, primarily anchored by Arg303. The hexahydroquinoline-3-carboxylate derivatives demonstrated strong antioxidant properties and the ability to modulate macrophage responses under inflammatory stress. The upregulation of HSP70, supported by computational binding studies, suggests a protective mechanism that warrants further investigation for treating chronic inflammatory conditions. The expression of HIF1A, COX2, and TGFBR2 is expected to follow the trend of HSP70.

Keywords: antioxidant, macrophages, HSP70, inflammation, molecular dynamics

OP04

BIOFILMS ACROSS SECTORS: CHALLENGES AND EMERGING ANTIBIOFILM STRATEGIES TARGETING QUORUM SENSING

Ayşe Nur Yurdcu¹, Nefise Akçelik²

¹Health Institutes of Türkiye - Türkiye Vaccine Institute

²Ankara University - Biotechnology Institute

Biofilms are highly organized microbial communities that adhere to biotic and abiotic surfaces and are embedded within a self-produced extracellular polymeric substance (EPS) matrix, conferring enhanced tolerance to environmental stressors, disinfectants, and antimicrobial agents. Their persistence poses significant challenges across diverse sectors, including healthcare, industrial systems, maritime environments, automotive manufacturing, and food processing, where they are associated with chronic infections, increased morbidity, biofouling, corrosion, contamination, and substantial economic losses. The limited efficacy of conventional antimicrobial approaches against biofilms has driven the exploration of alternative strategies targeting the regulatory mechanisms underlying biofilm development. Among these, quorum sensing (QS), a cell-density-dependent intercellular communication system, plays a central role in coordinating virulence factor production, biofilm maturation, and adaptive responses. This review

systematically examines current literature on biofilm-associated challenges and emerging antibiofilm strategies, with a particular focus on QS-targeted approaches within medicinal chemistry. Quorum sensing inhibitors (QSIs) disrupt bacterial communication by interfering with signal synthesis, signal reception, or downstream regulatory pathways, thereby attenuating pathogenicity without directly affecting microbial viability and potentially reducing selective pressure for resistance development. Accumulating evidence demonstrates that QSIs can effectively inhibit biofilm formation, destabilize established biofilms, and enhance the efficacy of conventional antimicrobial agents across both clinical and industrial settings. In conclusion, QS-targeted antibiofilm strategies represent a promising and rapidly evolving approach for mitigating biofilm-associated challenges across sectors, offering significant potential for the development of next-generation antimicrobial interventions.

Keywords: Antivirulence, Bacterial Communication, Biofilm Inhibition, Quorum Sensing, Quorum Sensing Inhibitors

OP05

COMPARATIVE MOLECULAR DOCKING AND STRUCTURE-ACTIVITY RELATIONSHIP ANALYSIS OF FLAVAN-3-OLS AND PROCYANIDIN OLIGOMERS TARGETING FIBRINOLYTIC PROTEINS

Gizem Deynez¹, Sümeyra Gültekin²

¹Department of Analysis and Control Laboratories, Turkish Medicines and Medical Devices Agency (TITCK),
Ministry of Health, Ankara, Türkiye

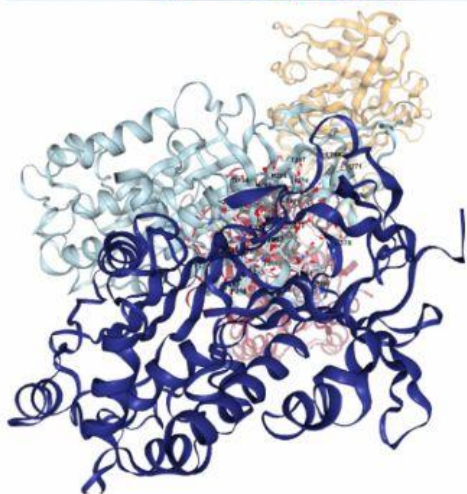
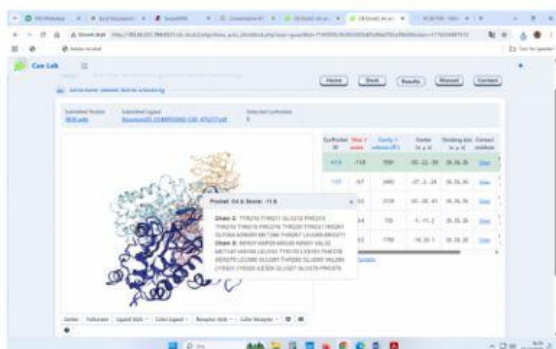
²Department of Biotechnology, Field Crops Central Research Institute, Ministry of Agriculture and Forestry,
Ankara, Türkiye

Introduction: The fibrinolytic system plays a crucial role in maintaining hemostatic balance, and its dysregulation is associated with thrombotic disorders. Polyphenolic compounds have been suggested to modulate fibrinolysis; however, their target selectivity and underlying molecular mechanisms remain unclear. This study aimed to investigate the structure-activity relationship (SAR) and target selectivity of selected polyphenols using a comparative molecular docking approach.

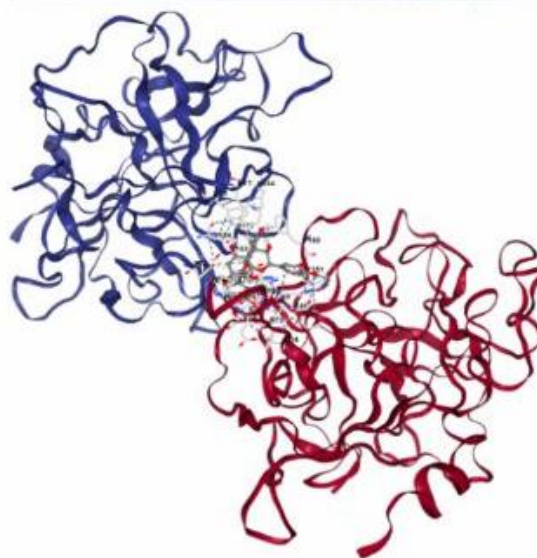
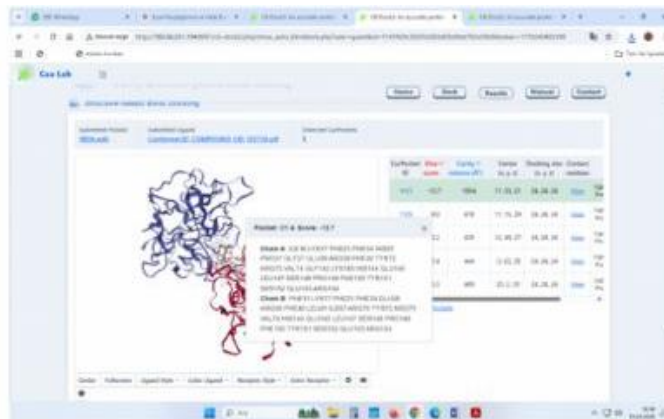
Materials-Methods: A series of polyphenolic compounds with varying structural features, including differences in polymerization degree, A-type interflavan linkages, B-type linkage structures, and gallate substitution, were analyzed. Molecular docking simulations were performed using AutoDock Vina against key fibrinolytic targets, plasminogen activator inhibitor-1 (PAI-1) and tissue plasminogen activator (t-PA). Binding affinities (kcal/mol), ligand-protein interactions, and conformational binding modes were evaluated. Additionally, ADME properties were assessed through in silico bioavailability radar analysis.

Results-Conclusion: Binding affinities ranged from -8.6 to -12.7 kcal/mol, indicating generally strong interactions with both targets. Comparative analysis revealed structure-dependent and target-selective binding behavior. The observed interaction patterns indicate that tannins may exhibit structure-dependent and target-selective binding rather than non-specific interactions. Cinnamtannin B1 showed the highest affinity for PAI-1 (-11.8 kcal/mol), whereas procyanidin B2, characterized by a B-type linkage, exhibited the strongest binding to t-PA (-12.7 kcal/mol), indicating that linkage type plays a critical role in determining target selectivity. Gallate-containing compounds (EGCG and epicatechin gallate) demonstrated enhanced affinity toward PAI-1, while epicatechin showed comparatively weaker and non-selective binding. Increased polymerization degree and the presence of A-type interflavan linkages contributed to stronger and more stable interactions. ADME analysis indicated that oligomeric compounds, despite higher binding affinities, possess lower oral bioavailability potential due to increased molecular weight and polarity. Overall, these findings demonstrate that polyphenols exhibit structure-dependent and target-selective interactions with fibrinolytic proteins, providing mechanistic insights into their potential role in fibrinolysis; however, further experimental validation is required.

Cinnamtannin B1



Procyanidin B2



Molecular Docking Results of Polyphenols Targeting PAI-1 and t-PA

Compound	PAI-1 Vina score (kcal/mol)	tPA Vina score (kcal/mol)
Cinnamtannin B1	-11.8	-9.5
Procyanidin B2	-10.0	-12.7
Epigallocatechin gallate	-10.3	-8.8
Epicatechin gallate	-9.9	-8.9
Epicatechin	-8.9	-8.6

Keywords: Molecular docking, Structure–activity relationship, Flavan-3-ols, Fibrinolytic system, PAI-1/t-PA

OP06

FLUOXETINE DIFFERENTIALLY REDUCES CELL VIABILITY IN MYCN-AMPLIFIED AND NON-AMPLIFIED NEUROBLASTOMA CELLS

Özge Nur Toprak¹, Selen Öztürk²

¹Medical Laboratory Techniques Program, Vocational School of Health Services, Ankara University, Ankara, Türkiye; Department of Biology, Faculty of Science, Hacettepe University, Ankara, Türkiye

²Department of Biology, Faculty of Science, Hacettepe University, Ankara, Türkiye

Introduction: Fluoxetine, a selective serotonin reuptake inhibitor (SSRI), has emerged as a promising candidate for drug repurposing in oncology. Increasing evidence indicates that fluoxetine disrupts mitochondrial function, induces oxidative stress, and activates apoptotic pathways in cancer cells, including neuroblastoma. However, its differential impact on neuroblastoma subtypes with distinct biological features, particularly MYCN amplification status, remains insufficiently characterized. To investigate the antiproliferative effects of fluoxetine in SH-SY5Y (non-MYCN amplified) and Kelly (MYCN-amplified) human neuroblastoma cell lines.

Materials-Methods: SH-SY5Y and Kelly cells were treated with fluoxetine, and cell viability was assessed using MTT and Neutral Red uptake assays, reflecting mitochondrial metabolic activity and lysosomal integrity. Total cellular protein levels were quantified using the BCA assay as an indicator associated with cell mass and proliferative capacity. Comparative analyses

were performed between the two cell lines.

Results-Conclusion: Fluoxetine induced a robust and consistent reduction in cell viability in both SH-SY5Y and Kelly cells. Notably, Kelly cells exhibited a greater sensitivity to fluoxetine, reflected by a relative leftward shift in dose-response behavior and an apparent reduction in IC₅₀ compared to SH-SY5Y cells. These findings were supported by concordant decreases observed across MTT and Neutral Red assays, as well as reduced total protein content. The enhanced susceptibility of Kelly cells may be associated with their MYCN-amplified, high-risk phenotype. Fluoxetine demonstrates a potent antiproliferative effect in neuroblastoma cells, with differential sensitivity linked to tumor subtype characteristics. The observed shift in response profiles suggests that MYCN amplification status may influence fluoxetine susceptibility, supporting its potential as a repositioned therapeutic candidate in high-risk neuroblastoma.

Keywords: Fluoxetine, SH-SY5Y, Kelly Cells, Cell Viability, Antiproliferative Effect

OP07

DIFLUOROMETHOXY-SUBSTITUTED HEXAHYDROQUINOLINES AS MULTI-TARGET ANTI-INFLAMMATORY AGENTS: MECHANISTIC AND METABOLOMIC INSIGHTS

Ezgi Pehlivanlar Yavrucu¹, Ayça Aktaş Şüküroğlu², Meryem Temiz Reşitoğlu³, Ozan Kaplan⁴, Esraa Ebraheem Al Jomaa³, Taşkın Kalkan³, Seyhan Şahan Fırat³, Rahime Şimşek¹

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey

²Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Mersin University, Mersin, Turkey

³Department of Pharmacology, Faculty of Pharmacy, Mersin University, Mersin, Turkey

⁴Department of Analytical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey

Introduction: Chronic inflammation is driven by persistent activation of signaling pathways such as NF- κ B and sustained production of pro-inflammatory mediators, contributing to the progression of several disorders including cancer, diabetes, and neurodegenerative diseases. Although current anti-inflammatory drugs are effective, their long-term use is limited by adverse effects and insufficient efficacy in chronic settings. In this study, difluoromethoxy-substituted hexahydroquinoline (HHQ) derivatives were designed as conformationally restricted 1,4-dihydropyridine analogues and evaluated as potential multi-target anti-inflammatory agents in LPS-stimulated RAW 264.7 macrophages.

Materials-Methods: A series of 2-, 3-, and 3,4-difluoromethoxy-substituted HHQ derivatives were synthesized via a modified Hantzsch reaction and structurally characterized by IR, NMR, and HRMS. Cytotoxicity was assessed using the MTT assay in RAW 264.7 macrophages at 24 and 48 h. The most cytocompatible compounds (3b, 3c, and 3d) were further evaluated in LPS-stimulated macrophages for their

effects on NF- κ B p65 phosphorylation and inflammatory mediators (TNF- α , IL-6, IL-10, COX-2, iNOS, MCP-1, and TGF- β 1) by Western blotting. Molecular docking was performed against NF- κ B, COX-2, iNOS, and TNF- α , and untargeted metabolomics was applied to investigate treatment-related metabolic alterations.

Results-Conclusion: Among the synthesized derivatives, compounds 3b, 3c, and 3d showed acceptable cytocompatibility, with compound 3b emerging as the most active analogue. Compound 3b significantly suppressed NF- κ B activation and reduced TNF- α , IL-6, COX-2, iNOS, MCP-1, and TGF- β 1 expression, indicating a broad anti-inflammatory effect. Docking studies supported its favorable multi-target binding profile, particularly toward COX-2 and iNOS. Metabolomic analysis further demonstrated that 3b modulated LPS-induced metabolic reprogramming, especially pathways related to purine, taurine, glutathione, and lipid metabolism. Overall, difluoromethoxy-substituted HHQ derivatives, particularly 3b, represent promising multi-target anti-inflammatory scaffolds for further optimization.

Keywords: Antiinflammatory, multi-target, synthesis, hexahydroquinoline, metabolomics

OP08

A THREE-CHANNEL ORTHOGONAL REVERSE-SCREENING PIPELINE FOR TARGET
DECONVOLUTION OF NOVEL CHALCONE-DERIVED SCAFFOLDS**Pouria Zarrin, Tasneem S. Hosni, Birsen Tozkoparan Köprücü, Nesrin Gökhan Kelekçi**

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Türkiye

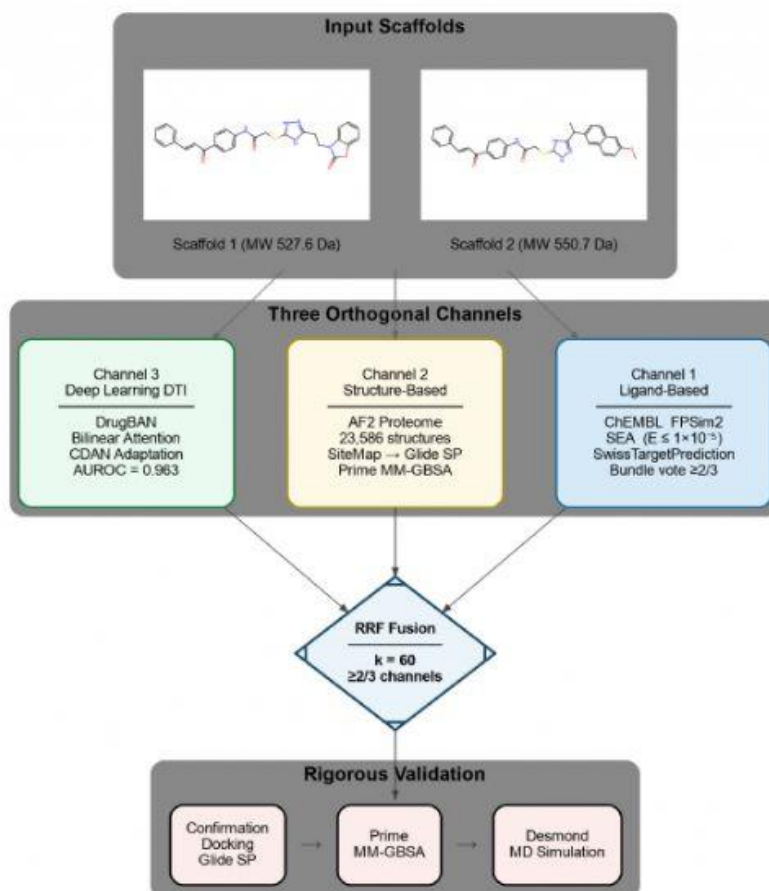
Introduction: Chalcones (1,3-diaryl-2-propen-1-ones) constitute a privileged scaffold in medicinal chemistry, with well-documented inhibitory activity against monoamine oxidases,¹ cytochrome P450 1B1,² ABC efflux transporters,³ and tubulin polymerization,⁴ underscoring their broad pharmacological versatility.⁵ Yet systematic multi-target deconvolution of novel chalcone-derived chemical entities has not been demonstrated in the literature. Here we present a three-channel orthogonal reverse-screening pipeline integrating ligand-based similarity, structure-based proteome docking, and deep-learning drug–target interaction prediction to identify and rank protein targets for two novel chalcone-derived triazoline scaffolds, extending the drug-repurposing paradigm⁶ to new chemical entity target deconvolution.

Materials-Methods: Two novel chalcone-derived triazoline scaffolds (MW 527.6 and 550.7 Da, sharing a trans-cinnamoyl-anilide core) were profiled through the pipeline. Channel 1 (ligand-based): ChEMBL⁷ fingerprint similarity (FPSim2), Similarity Ensemble Approach (SEA, $E \leq 1 \times 10^{-5}$),⁸ and SwissTargetPrediction,⁹ with bundle consensus ($\geq 2/3$ methods). Channel 2 (structure-based): the AlphaFold2¹⁰ human proteome (23,586 structures) was screened by

SiteMap binding-site detection, Glide SP docking, and Prime MM-GBSA rescoring (Schrödinger Suite 2025-4).¹¹ Channel 3 (deep-learning DTI): DrugBAN, a bilinear attention network with CDAN domain adaptation trained on BindingDB (AUROC 0.963).¹² Per-channel rankings were integrated by Reciprocal Rank Fusion (RRF, $k=60$),¹³ requiring ≥ 2 -channel agreement for consensus nomination, following the multi-method consensus strategy of Mayr et al.¹⁴

Results and Conclusion: The pipeline identified novel, previously unreported targets for this scaffold class. AKR1C3 and AKR1B10, aldo-keto reductases overexpressed in multiple malignancies, emerged as top-ranked hits (Glide SP -11.37 and -10.74 kcal/mol), alongside FAAH (-10.65 kcal/mol), EPHX2 (-8.77 kcal/mol), and RIPK2 (-8.60 kcal/mol). Prime MM-GBSA rescoring and Desmond molecular dynamics confirm favorable binding free energies and stable binding modes for all top hits. These findings establish that three-channel orthogonal integration driven by RRF rank fusion surfaces pharmacologically relevant targets beyond those predictable from scaffold class alone, providing a broadly applicable strategy for early-stage target deconvolution of novel chalcone-derived chemical series

Three-Channel Orthogonal Reverse-Screening Pipeline



Architecture of the three-channel orthogonal reverse-screening pipeline. Two novel chalcone-derived triazoline scaffolds (left) are simultaneously profiled through three independent channels: Channel 1 (ligand-based, blue) combining ChEMBL fingerprint similarity, SEA, and SwissTargetPrediction with bundle vote ($\geq 2/3$); Channel 2 (structure-based, yellow) screening the AlphaFold2 human proteome (23,586 structures) via SiteMap $\rightarrow$ Glide SP $\rightarrow$ Prime MM-GBSA; and Channel 3 (deep-learning DTI, green) using the DrugBAN bilinear attention network (AUROC = 0.963). Channel rankings are integrated by Reciprocal Rank Fusion ($k=60$; diamond) requiring $\geq 2/3$ channel consensus, followed by confirmation docking, Prime MM-GBSA, and Desmond MD validation (right).

References

- (1) Chimenti, F.; Bolasco, A.; Manna, F.; Granese, A.; Orallo, F.; Yanez, M.; Ortuso, F.; Alcaro, S.; Secci, D. Chalcones: A Valid Scaffold for Monoamine Oxidases Inhibitors. *Journal of Medicinal Chemistry* 2009, 52, 1601–1604. <https://doi.org/10.1021/jm801590u>.
- (2) Horley, N. J.; Beresford, K. J. M.; Chawla, T.; McCann, G. J. P.; Ruparelia, K. C.; Gatchie, L.; Sonawane, V. R.; Williams, I. S.; Tan, H. L.; Joshi, P.; Bharate, S. S.; Kumar, V.; Bharate, S. B.; Chaudhuri, B. Discovery and Characterization of Novel CYP1B1 Inhibitors Based on Heterocyclic Chalcones: Overcoming Cisplatin Resistance in CYP1B1-Overexpressing Lines. *European Journal of Medicinal Chemistry* 2017, 130, 151–166. <https://doi.org/10.1016/j.ejmech.2017.02.016>.
- (3) Silbermann, K.; Shah, C. P.; Sahu, N. U.; Juvale, K.; Stefan, S. M.; Kharkar, P. S.; Wiese, M. Novel Chalcone and Flavone Derivatives as Selective and Dual Inhibitors of the Transport Proteins ABCB1 and ABCG2. *European Journal of Medicinal Chemistry* 2019, 164, 572–592. <https://doi.org/10.1016/j.ejmech.2018.12.019>.

- (4) Mirzaei, H.; Emami, S. Recent Advances of Cytotoxic Chalconoids Targeting Tubulin Polymerization: Synthesis and Biological Activity. *European Journal of Medicinal Chemistry* 2016, 121, 610–639. <https://doi.org/10.1016/j.ejmech.2016.05.067>.
- (5) Zhuang, C.; Zhang, W.; Sheng, C.; Zhang, W.; Xing, C.; Miao, Z. Chalcone: A Privileged Structure in Medicinal Chemistry. *Chemical Reviews* 2017, 117 (12), 7762–7810. <https://doi.org/10.1021/acs.chemrev.7b00020>.
- (6) Pushpakom, S.; Iorio, F.; Eyers, P. A.; Escott, K. J.; Hopper, S.; Wells, A.; Doig, A.; Williams, T.; Latimer, J.; McNamee, C.; Norris, A.; Sanseau, P.; Cavalla, D.; Pirmohamed, M. Drug Repurposing: Progress, Challenges and Recommendations. *Nature Reviews Drug Discovery* 2019, 18, 41–58. <https://doi.org/10.1038/nrd.2018.168>.
- (7) Zdrazil, B.; Felix, E.; Hunter, F.; Manners, E. J.; Blackshaw, J.; Corbett, S.; Veij, M. de; Ecker, G. F.; Jacoby, E.; Loewe, S.; Mutowo, P.; Naz, R.; Scheiber, J.; Schneider, G.; Westen, G. J. P. van; Leach, A. R. The ChEMBL Database in 2023: A Drug Discovery Platform Spanning Multiple Bioactivity Data Types and Time Periods. *Nucleic Acids Research* 2024, 52 (D1), D1180–D1192. <https://doi.org/10.1093/nar/gkad1004>.
- (8) Keiser, M. J.; Roth, B. L.; Armbruster, B. N.; Ernsberger, P.; Irwin, J. J.; Shoichet, B. K. Relating Protein Pharmacology by Ligand Chemistry. *Nature Biotechnology* 2007, 25, 197206. <https://doi.org/10.1038/nbt1284>.
- (9) Daina, A.; Michielin, O.; Zoete, V. SwissTargetPrediction: Updated Data and New Features for Efficient Prediction of Protein Targets of Small Molecules. *Nucleic Acids Research* 2019, 47 (W1), W357–W364. <https://doi.org/10.1093/nar/gkz382>.
- (10) Jumper, J.; Evans, R.; Pritzel, A.; Green, T.; Figurnov, M.; Ronneberger, O.; Tunyasuvunakool, K.; Bates, R.; Židek, A.; Potapenko, A.; Bridgland, A.; Meyer, C.; Kohl, S. A. A.; Ballard, A. J.; Cowie, A.; Romera-Paredes, B.; Nikolov, S.; Jain, R.; Adler, J.; Back, T.; Petersen, S.; Reiman, D.; Clancy, E.; Zielinski, M.; Steinegger, M.; Pacholska, M.; Berghammer, T.; Bodenstein, S.; Silver, D.; Vinyals, O.; Senior, A. W.; Kavukcuoglu, K.; Kohli, P.; Hassabis, D. Highly Accurate Protein Structure Prediction with AlphaFold. *Nature* 2021, 596, 583–589. <https://doi.org/10.1038/s41586-021-03819-2>.
- (11) Luo, J.; Bhatt, D. L.; Ge, W.; Zou, A.; Li, X.; Liu, H.; Guo, Z.; Chen, G.; Xu, L.; Cheng, X.; Zhong, J.; Luo, M. Benchmarking Reverse Docking Through AlphaFold2 Human Proteome. *Protein Science* 2024, 33, e5167. <https://doi.org/10.1002/pro.5167>.
- (12) Bai, P.; Miljković, F.; John, B.; Lu, H. Interpretable Bilinear Attention Network with Domain Adaptation Improves Drug–Target Prediction. *Nature Machine Intelligence* 2023, 5, 126–136. <https://doi.org/10.1038/s42256-022-00605-1>.
- (13) Cormack, G. V.; Clarke, C. L. A.; Büttcher, S. Reciprocal Rank Fusion Outperforms Condorcet and Individual Rank Learning Methods. In *Proceedings of the 32nd international ACM SIGIR conference on research and development in information retrieval*; 2009; pp 758759. <https://doi.org/10.1145/1571941.1572114>.
- (14) Mayr, F.; Möller, G.; Garscha, U.; Fischer, J.; Rodríguez Castaño, P.; Inderbinen, S. G.; Temml, V.; Waltenberger, B.; Schwaiger, S.; Hartmann, R. W.; Gege, C.; Martens, S.; Odermatt, A.; Pandey, A. V.; Werz, O.; Adamski, J.; Stuppner, H.; Schuster, D. Finding New Molecular Targets of Familiar Natural Products Using in Silico Target Prediction. *International Journal of Molecular Sciences* 2020, 21 (19), 7102. <https://doi.org/10.3390/ijms21197102>.

Keywords: drug repurposing, chalcone scaffold, target deconvolution, reverse screening, structure-based docking

OP09

DESIGN AND EVALUATION OF HYDROGEN PEROXIDE ACTIVATABLE PHOTSENSITIZER FOR BRAIN TUMOR TARGETED PHOTODYNAMIC THERAPY

Ecirin Mustanoglu¹, Dilek Yigiter², Osman Karaman¹, Zubeyir Elmazoglu³, Gorkem Gunbas¹

¹Middle East Technical University, Department of Chemistry, Ankara, Turkey

²Middle East Technical University, Department of Biochemistry, Ankara, Turkey,

³Ankara Medipol University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Turkey

Introduction: Brain tumors remain one of the most challenging cancers to treat due to the protective blood-brain barrier (BBB) and the limitations of conventional therapies. Photodynamic therapy (PDT) offers a minimally invasive alternative by using light, a photosensitizer (PS), and molecular oxygen to generate reactive oxygen species (ROS). However, for effective treatment, PS agents must have a low molecular weight to cross the BBB and absorb in the near-infrared (NIR) "therapeutic window" (600–850 nm) for deep tissue penetration.

Materials-Methods: In this study, we report the synthesis of an acridine-based photosensitizer, DDAO-Br. To enhance selectivity, targeting group attachment is also studied. This handle contains a hydrogen peroxide-activated group, a boronic ester. DDAO-Br is applied to glioblastoma (U87MG) and neuroblastoma (SHSY5Y) cells, as well as healthy SVGp12 and HMC3 cells. Their

responses are observed in dark and irradiated conditions.

Results-Conclusion: The absorption maxima of DDAO-Br are reported at 648nm in a pH 7.4 PBS buffer. According to photophysical experiments, PS undergoes a Type I mechanism, which generates radical ROS. No significant toxicity is observed in the dark; however, after 2h of irradiation, selective cytotoxicity occurred. The IC₅₀ values were 16 μ M in glioblastoma and 8 μ M in neuroblastoma. Ongoing photophysical and biological (in vitro and in vivo) studies aim to evaluate the targeting capability and H₂O₂-responsive activation efficiency. Findings highlight the potential of DDAO-Br as a promising platform for ROS-responsive, targeted PDT of brain tumors.

Keywords: Acridine, Photodynamic therapy, Glioblastoma, Neuroblastoma, Photosensitizer

OP10

MIXED DONOR SUBSTITUTION IN SELENIUM-CONTAINING XANTHENE PHOTOSENSITIZERS FOR TUNING SELECTIVITY AND POTENCY IN PDT

Ece Ayça Erdoğan¹, Osman Karaman¹, Zübeyir Elmazoğlu², Gökrem Günbaş¹

¹Department of Chemistry, Middle East Technical University, Ankara 06800, Türkiye

²Faculty of Pharmacy, Ankara Medipol University, Ankara 06050, Türkiye

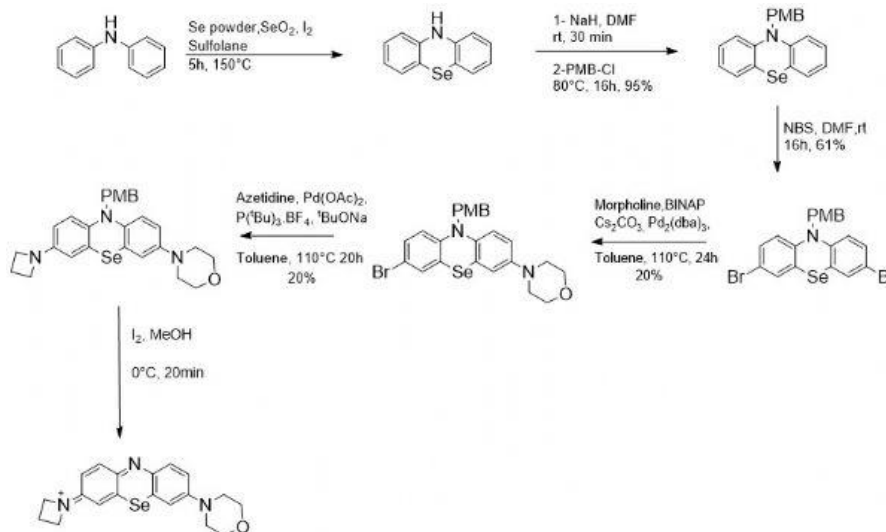
Introduction: Photodynamic therapy (PDT) is a promising strategy for cancer treatment due to its minimally invasive nature and reduced side effects. Recently, our group reported selenium-containing xanthene photosensitizers with near-infrared (NIR) absorption and low molecular weight properties, where donor substituents were shown to drastically influence PDT behavior. In these systems, morpholine-containing derivatives displayed improved selectivity, while azetidine-containing analogues exhibited significantly enhanced phototoxic potency. Building on these findings, we designed an unsymmetrical selenium-containing xanthene photosensitizer incorporating both morpholine and azetidine donor groups to investigate the effect of mixed donor substitution on PDT properties.

Materials–Methods: The mixed donor photosensitizer was synthesized through stepwise donor substitution starting from a dibrominated selenium-xanthene intermediate, followed by oxidative deprotection. The compound was characterized by NMR, HRMS, and UV–

Vis spectroscopy. Preliminary photophysical studies were performed to evaluate absorption behavior in the visible/NIR region, while biological studies are currently ongoing.

Results–Conclusion: Preliminary results revealed strong absorption in the red/NIR region, supporting the suitability of the mixed donor system for PDT applications. The hybrid donor design is expected to provide insight into the relationship between donor asymmetry, selectivity, and phototoxic potency. Ongoing biological evaluations aim to determine whether combining morpholine and azetidine donors within the same scaffold can balance the favorable selectivity associated with morpholine-containing systems and the enhanced potency observed for azetidine analogues. This study may contribute to the development of tunable low-molecular-weight photosensitizers for PDT.

Reaction Scheme



Keywords: Photodynamic therapy (PDT), Xanthene photosensitizers, Selenium-containing dyes, Mixed donor substitution, Near-infrared absorption

OP11

SELECTIVE LITHIATION UNLOCKS A BROMINATED SI-RHODAMINE BASED PHOTODYNAMIC THERAPY AGENT

Osman Karaman¹, Naz Özoğul¹, Deniz Yılmaz¹, Şafak Tekir¹, Zübeyir Elmazoğlu², Görkem Günbaş¹¹Department of Chemistry, Middle East Technical University, 06800, Ankara, Türkiye²Department of Pharmacology, Ankara Medipol University, 06050, Ankara, Türkiye

Introduction: Photodynamic therapy (PDT) enables spatially controlled cancer treatment; however, its broader clinical application is limited by insufficient light penetration and the limited availability of near-infrared (NIR)-absorbing photosensitizers that combine efficient reactive oxygen species (ROS) generation with favorable biological properties. Si-rhodamines are widely used NIR fluorophores in bioimaging but remain largely unexplored in PDT due to the absence of viable strategies for direct heavy-atom functionalization of their electronically sensitive core. This study aims to develop a general synthetic strategy to convert Si-rhodamine fluorophores into efficient NIR photosensitizers and to comprehensively evaluate their photophysical properties and *in vitro* photodynamic efficacy.

Materials-Methods: A regioselective lithiation approach was employed to enable direct heavy-atom incorporation into the Si-rhodamine scaffold, affording a brominated derivative (**SiR-Br**). Photophysical properties, ROS generation, and biological activity were systematically evaluated using spectroscopic methods, ROS-sensitive probes, and *in vitro* assays in glioblastoma cell lines.

Results: **SiR-Br** retains strong NIR absorption ($\lambda_{\text{abs}} = 653 \text{ nm}$) and aqueous solubility while exhibiting enhanced intersystem crossing. The photosensitizer shows suppressed fluorescence ($\Phi_F = 1.6\%$) and efficient ROS generation, with a singlet oxygen quantum yield of 45% alongside significant Type I activity, indicating dual photodynamic behavior. *In vitro* studies reveal negligible dark toxicity ($\text{IC}_{50} > 16 \mu\text{M}$) and pronounced light-induced cytotoxicity, with IC_{50} values of $2.45 \mu\text{M}$ (U87MG), $2.78 \mu\text{M}$ (U118MG), and $4.45 \mu\text{M}$ (T98G) after 2 h of incubation. Confocal imaging indicates predominant mitochondrial localization. Mechanistic studies demonstrate a time-dependent shift from initial singlet oxygen production to sustained Type I ROS involvement, consistent with mitochondria-mediated cell death pathways.

Conclusion: This work establishes a general strategy for transforming Si-rhodamine imaging agents into functional PDT photosensitizers via direct core modification. These findings expand the applicability of Si-rhodamines for NIR-activated cancer theranostics and highlight their potential for advanced photodynamic therapy.

Keywords: Photodynamic Therapy, Glioblastoma, Lithiation, Si-Rhodamine, Theranostics

OP12

ENANTIOSELECTIVE CE-MS/MS ANALYSIS OF MDMA AND MAJOR METABOLITES: COMPARATIVE PHARMACOKINETICS IN ORAL FLUID, URINE AND PLASMA

Kardelen Avcı¹, Saba Jorbenadze^{2,3}, Mehmet Gumustas^{1,4}, Francesco Paolo Busardo³, Bezhan Chankvetadze²

¹Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, Ankara, Türkiye

²Institute of Physical and Analytical Chemistry, School of Exact and Natural Sciences, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

³Department of Excellence-Biomedical Sciences and Public Health, Università Politecnica delle Marche, 60121 Ancona, Italy

⁴Ankara University, Integrated Technologies Research Center (BÜTAM), Ankara, Türkiye

3,4-Methylenedioxymethamphetamine (MDMA) is a chiral psychoactive substance whose enantiomers exhibit different pharmacological, toxicological, and pharmacokinetic properties. Therefore, enantioselective analytical methods are required to investigate its metabolism and disposition. This study presents a capillary electrophoresis–tandem mass spectrometry (CE-MS/MS) method was developed for the simultaneous enantioselective analysis of MDMA and its major phase-I metabolites, namely 3,4-methylenedioxyamphetamine (MDA), 4-hydroxy-3-methoxymethamphetamine (HMMA), and 4-hydroxy-3-methoxyamphetamine (HMA).

In the CE-MS/MS method, enantioselective separation was achieved using a dual chiral selector system consisting of highly sulfated β -cyclodextrin (HS- β -CD) and highly sulfated γ -cyclodextrin (HS- γ -CD). To ensure compatibility with mass spectrometric detection and prevent contamination of the ion source by non-volatile chiral selectors, a segmental partial filling approach was employed. Method optimization was performed using a 20 mM ammonium formate background electrolyte at pH 2.1 in a bare fused-silica capillary (100 cm effective length, 50 μ m i.d.). Separations were carried out at an applied voltage of 30 kV, and samples were introduced

hydrodynamically at 50 mbar for 8 s. Under the optimized conditions, the combination of 1 mg/mL HS- β -CD and 15 mg/mL HS- γ -CD enabled successful enantioselective separation of MDMA and its major phase-I metabolites.

The developed method was applied to plasma, oral fluid, and urine samples collected from volunteers following controlled MDMA administration. Pharmacokinetic evaluation of the three biological matrices demonstrated stereoselective metabolism of MDMA and its metabolites. In all matrices, S-(+)-MDMA was metabolised and eliminated faster than R-(–)-MDMA, resulting in an increase in the relative abundance of the R-enantiomer over time. A similar stereoselective pattern was observed for the major metabolites. These findings were consistently observed across the investigated biological matrices.

The developed CE-MS/MS method provides a reliable and environmentally friendly approach for the simultaneous enantioselective analysis of MDMA and its metabolites in biological samples and contributes to pharmacokinetic and forensic toxicology studies involving chiral drugs.

Keywords: capillary electrophoresis, enantioselective analysis, green analytical chemistry



OP13

OP14

DETERMINATION OF SAFINAMIDE IN HUMAN PLASMA BY USING LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY

Sumeyya Koldas, Nesrin Okatan, Elif Basak Tuncer, Gamze Sevici, Berrak Guney, Onursal Saglam

Novagenix Bioanalytical R&D Centre, 06970, Akyurt, Ankara, Turkey

A liquid chromatography tandem mass spectrometry (LC-MS/MS) method was developed and validated for the determination of safinamide (SAF) in human plasma. Protein precipitation was used for sample preparation. The analyte and internal standard (safinamide-d3 (SAFD3)) were separated on a GL Sciences Inert Sustain C18 column (50x4.6mm, 5 μ m (UP)). Multiple reaction monitoring detection was performed by electrospray ionization in the positive ion mode. The MRM transitions of m/z 303.000>215.100 for SAF and

306.000>215.100 for SAFD3 were used for quantification. The standard curve was found to be linear in the range of 2-2500 ng/mL for safinamide. The method was validated in accordance with EMA, FDA and ICH guidelines and proved suitable for bioequivalence and pharmacokinetic studies. The validated method was successfully applied to a bioequivalence study and demonstrated high sensitivity, robustness, and suitability for high-throughput pharmacokinetic applications.

Keywords: Safinamide, Safinamide -d3, human plasma, LC-MS/MS

OP15

SYNTHESIS, ANTIPROLIFERATIVE EVALUATION, AND MOLECULAR DOCKING STUDIES OF NOVEL CHLOROPHENYLPYPERAZINE-HYDROXYPYRIDINONE MANNICH BASES

Gülşah Karakaya¹, Beyza Düzleyen¹, Onurcan Demir², Ünzile Yaman³, Canan Sevimli Gür⁴, Mutlu Dilsiz Aytemir⁵

¹İzmir Kâtip Çelebi University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İzmir, Türkiye

²İzmir Kâtip Çelebi University, Faculty of Pharmacy, İzmir, Türkiye

³İzmir Kâtip Çelebi University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, İzmir, Türkiye

⁴İzmir Kâtip Çelebi University, Faculty of Pharmacy, Department of Basic Sciences, İzmir, Türkiye

⁵Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Türkiye

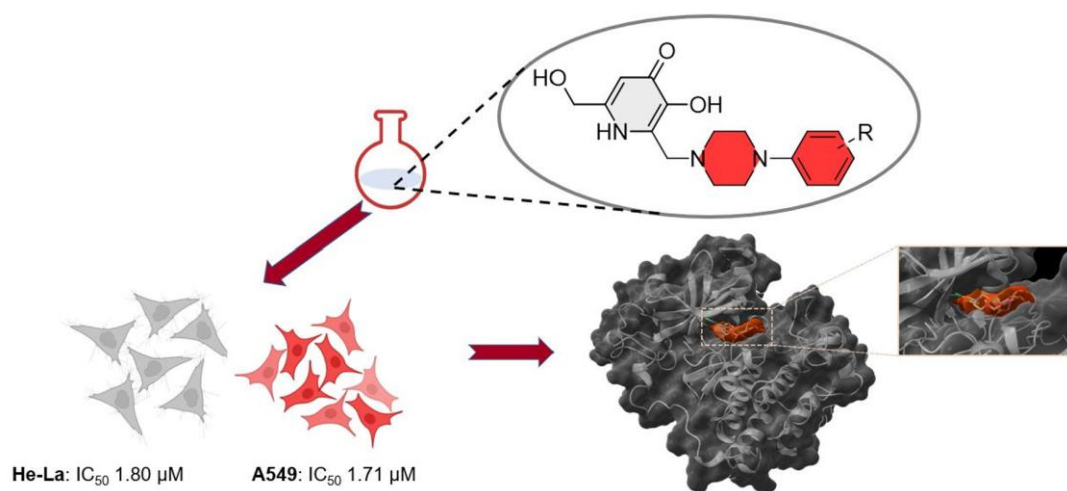
Introduction: Several compounds possessing hydroxypyranone and hydroxypyridinone moieties have been reported to show potent anticancer activity (He, 2021). Herein, we designed novel Mannich bases and evaluated their cytotoxicities against A549, HeLa, HepG2, HT29, and SK-Br3 cancer cell lines, as well as the non-cancerous Vero cell line. Coupled with the selective cytotoxicity observed in EGFR-driven A549 and HeLa cells, these findings led us to hypothesize that the intracellular kinase domain of EGFR might serve as a plausible target for this novel scaffold.

Materials/Methods: The synthesis involved the benzylation of kojic acid, followed by ring transformation to pyridine via aqueous ammonia. After deprotection by catalytic hydrogenation, the compounds were synthesized through a multicomponent Mannich reaction. The cytotoxic potential was evaluated by the MTT assay (Karakaya, 2026). The docking studies were performed to explore the binding interactions with the wild-type EGFR protein (PDB: 9QXN), using AutoDock-GPU. To assess the stability of the lead compound-EGFR complex under physiological

conditions, molecular dynamics simulations were conducted using GROMACS 2025.4 with the CHARMM36 force field.

Results-Conclusion: The targeted compounds were successfully synthesized and characterized by spectral analyses. In vitro cytotoxicity evaluations revealed a pronounced SAR dependent on the halogenation pattern of the phenyl ring. While the mono-chlorinated derivatives remained inactive at the tested concentrations, the 3,4-dichlorophenyl substituted derivative emerged as the active lead. According to the docking results, the lead demonstrated strong binding affinity to the active site of the EGFR, yielding an average of -9.30 kcal/mol. The primary interactions within the active site are two hydrogen bonds formed by the nitrogen of the hydroxypyridinone, a salt bridge involving the piperazine ring, and two hydrogen bonds formed by the hydroxyl group, significantly supported by prominent lipophilic interactions. These results highlighting the potential of this novel chlorophenylpiperazine-hydroxypyridinone hybrid as a promising targeted intracellular EGFR inhibitor.

Keywords: Hydroxypyridinone, EGFR, Antiproliferative Activity, Molecular Dynamics



References

1. He, M., Fan, M., Peng, Z., & Wang, G. (2021). European Journal of Medicinal Chemistry, 221, 113546.
2. Karakaya, G., Gür, C. S., & Aytemir, M. (2026). Fabad Eczacılık Bilimler Dergisi, 51(1), 163-174.

OP16

INVESTIGATION OF THE ROLE OF MTOR COMPLEX 2 IN THE INFLAMMATORY RESPONSE AND OXIDATIVE PROCESSES MEDIATING PERIPHERAL ISCHEMIA/REPERFUSION INJURY IN RATS

Ayşe Karabulbul¹, Meryem Temiz Resitoglu¹, Esraa Ebraheem Al Jomaa¹, Taskın Kalkan¹, Tuba Isik¹, Ekrem Can Yaylim², Hatice Oruc Demirbag², Nehir Sucu³, Seyhan Sahan Firat¹

¹Mersin University, Faculty of Pharmacy, Department of Pharmacology, Mersin, Turkey

²Mersin University, Faculty of Medicine, Department of Histology and Embryology, Mersin, Turkey

³Mersin University, Faculty of Medicine, Department of Cardiovascular Surgery, Mersin, Turkey.

Introduction: In this study, we investigated the contribution of mTOR complex 2 to inflammatory response and oxidative stress induced by peripheral ischemia/reperfusion (I/R) injury in rats and how pro-inflammatory cytokines and oxidative stress markers are regulated via rictor/Akt (protein kinase B; PKB)/inhibitory κ B kinase α (inhibitory κ B- α kinase; IKK α)/inhibitory κ B α (inhibitory κ B α ; I κ B- α)/nuclear factor κ B (nuclear factor κ B; NF- κ B) signaling pathway change using selective mTORK2 inhibitor JR-AB2-011.

Materials-Methods: Rats were divided into 5 groups: (1) Control group, (2) I/R group, (3) JR-AB2-011 group (1 mg/kg), (4) I/R + JR-AB2-011 group (1 mg/kg), and (5) DMSO group (0.5-5% DMSO; 4 ml/kg, i.p.). No treatment was applied to animals in the control group. In the I/R group, ischemia was created in both hind limbs at the trochanter major level with a tourniquet for 4 hours, followed by 4 hours of reperfusion. JR-AB2-011 was administered 1 hour before reperfusion. At the end of the experiment, the animals were sacrificed; blood, kidney, and gastrocnemius muscles were collected. Rictor, Akt, IKK α , I κ B- α , NF- κ B p65, TNF- α , IL-1 β , MMP9,

gp91phox, p22phox, α -sarcomeric actin, and β -actin protein expression and/or phosphorylation and MPO levels were measured in serum and tissue samples. Superoxide formation was assessed by DHE and cellular localization by DAPI staining.

Results-Conclusion: Peripheral I/R resulted in an increase in mTORK2 activity and expression and/or phosphorylation of rictor, Akt, IKK α , I κ B- α , NF- κ B, TNF- α , IL-1 β , MMP9, gp91phox, p22phox, and MPO levels and superoxide formation in all tissues. These changes by I/R were prevented by mTORK2 inhibitor JR-AB2-011. JR-AB2-011 alone had no effect on the parameters. Our results demonstrate the significant role of mTORK2 in the damage caused by inflammatory responses and oxidative stress in kidney and gastrocnemius muscle in a peripheral I/R model in rats, and specific inhibition of mTORK2 has a protective effect on this injury.

Keywords: peripheral ischemia/reperfusion, mTORC2, inflammation, oxidative stress, DHE

POSTER PRESENTATIONS

PP01

SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME PYRAZOLE-UREA DERIVATIVES AS POTENTIAL ANTIMICROBIAL AND ANTIBIOFILM AGENTS

Deniz Lengerli¹, Gülbeyaz Dökmeci², Berrin Özçelik²

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gazi University, Yenimahalle, 06560 Ankara, Turkey

²Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Gazi University, Yenimahalle, 06560 Ankara, Turkey

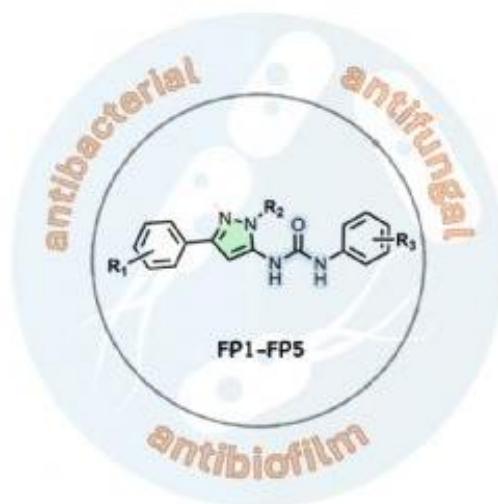
Introduction: Infections associated with microbial biofilms are difficult to treat due to increased pathogen persistence and reduced susceptibility to antimicrobial agents. Therefore, the development of new small molecules with both antimicrobial and antibiofilm potential is an important objective in medicinal chemistry. In this context, the present study aimed to synthesize a series of pyrazole-urea derivatives (FP1–FP5) and evaluate their bioactivity against selected bacterial and fungal strains.

Materials-Methods: FP1-FP5 were synthesized through the reaction of aminopyrazole derivatives with appropriate isocyanates, and their chemical structures were confirmed by ¹H-NMR, ¹³C-NMR, and HRMS. Antimicrobial activities were evaluated using the broth microdilution method and antibiofilm activities were

assessed using a colorimetric microdilution assay based on the resazurin microplate assay (REMA). The assays were performed using reference antimicrobial agents [1–4].

Results-Conclusion:

The final compounds exhibited antimicrobial activity with MIC values ranging from 8 to 64 µg/ml, and antibiofilm activity with IC₅₀ values between 4 and 40 µg/ml, depending on the tested strain. In the antifungal evaluation, selected derivatives showed activity against yeast-like fungi and dermatophytes, displaying MIC values of 8–16 µg/ml and IC₅₀ values of 5–12 µg/ml. Overall, these findings suggest that pyrazole-urea derivatives may serve as promising starting points for further optimization as antimicrobial and antibiofilm agents.



References

1. Karakaya, Gülşah et al., J Enzyme Inhib Med Chem, 2013;28(3):627-638.
2. Ustun, Osman et al., Pharmacogn Mag, 2016;12(Suppl 1):S82-S85.
3. Süntar, İpek et al., Pharm Biol, 2016;54(6):1065-1070.
4. Dökmeci, Gülbeyaz, et al., J Res Pharm, 2026;30(1):51-59.

Keywords: Antimicrobial, antibiofilm, pyrazole, urea

PP02

GAS-PHASE ION-MOLECULE REACTIONS OF PROTONATED OXIME COMPOUNDS WITH 2-METHOXYPROPENE IN A LINEAR QUADRUPOLE ION TRAP MASS SPECTROMETER

Kawthar Z Alzarieni¹, Bright H Adu², Hilikka I Kenttamaa²

¹Department of Medicinal Chemistry and Pharmacognosy, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid, Jordan

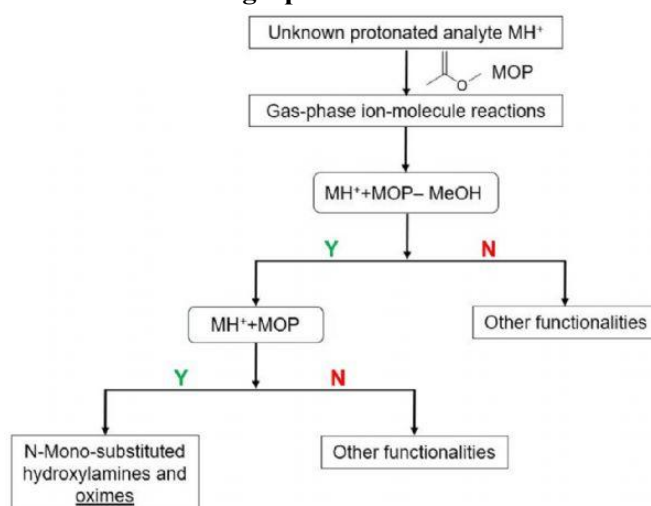
²James Tarpo Jr. and Margaret Tarpo Department of Chemistry, Purdue University, West Lafayette, Indiana, USA

Introduction: Gas-phase ion-molecule reactions of protonated analytes with selective neutral reagents provide a valuable means for probing for the presence of specific functional groups in analytes, which is often inaccessible by conventional collision-activated dissociation (CAD) experiments. In this study, the gas-phase reactivity of protonated oximes toward 2-methoxypropene (MOP) was examined using a linear quadrupole ion trap (LQIT) mass spectrometer.

Materials-Methods: Ketoxime and aldoxime model compounds, encompassing both aliphatic and aromatic structures, were protonated by atmospheric pressure chemical ionization (APCI), isolated in the ion trap, and allowed to react with MOP for various reaction times.

Results: All oximes (M) were found to react with MOP to produce three ions: $\text{MOP}+\text{H}^+$, MH^++MOP and, importantly $\text{MH}^++\text{MOP-methanol}$. Previous studies on the reactivity of structurally related protonated analytes have shown that only N-monosubstituted hydroxylamines form all three product ions. Other functionalities react only through proton transfer or not at all, including 1° N-oxides, 2° N-oxides, 3° aliphatic N-oxides, and amides. In contrast, 3° aromatic N-oxides, C-nitroso compounds, and N-disubstituted hydroxylamines form both the proton-transfer product ion and the adduct. Nitrosamines also yield proton-transfer and adduct products, although the adduct subsequently loses 2-propenol. Quantum chemical calculations were employed to evaluate the feasibility of the proposed reaction mechanisms and to support interpretation of the experimental results.

Biographical abstract



Keywords: Oximes, Tandem mass spectrometry, 2-Methoxypropene, Gas-phase ion-molecule reaction

PP03

INVESTIGATION OF BACTERIAL AND HUMAN TOPOISOMERASE I INHIBITION POTENTIAL OF RECALLED DRUGS BY MOLECULAR DOCKING METHOD AND ADME ANALYSES**Umut Okur, Okan Aykaç, Irem Bozbey Merde**

Inonu University Faculty of Pharmacy Department of Pharmaceutical Chemistry

Topoisomerase enzymes are critical targets in DNA metabolism and have an important position in both antibacterial and anticancer drug development^{1,2}. Given the ongoing pharmacoeconomic appeal of drug repositioning³, This study investigated the potential for repositioning drugs withdrawn from the market due to safety or efficacy issues. The interactions of the molecules with bacterial topoisomerase I (PDB ID: 4RUL) and human topoisomerase I (PDB ID: 1K4T) enzymes were investigated by molecular docking method using MzDOCK 2025.24.

As a result of docking analyses, it was determined that some withdrawn drugs localized to the active sites of topoisomerases with strong binding energies and

established hydrophobic interactions with critical amino acids by hydrogen bonding. Pharmacokinetic and toxicity evaluations were performed with SwissADME and pkCSM tools and it was found that some molecules showed high gastrointestinal absorption potential and favorable lipophilicity profile^{4,5}. However, candidates with risk factors such as hepatotoxicity and CYP450 inhibition were also identified.

In conclusion, this study suggests that withdrawn drugs may be repositioned against topoisomerase targets. The findings may shed light on the development of new candidates, especially in antibacterial resistance and cancer therapies.

References

1. Pommier Y., Drugging Topoisomerases: Lessons and Challenges, ACS Chemical Biology, 2013, 8(1), 82–95.
2. Tse-Dinh Y.C., Targeting bacterial topoisomerases: how to counter mechanisms of resistance, Future Medicinal Chemistry, 2016, 8(10), 1085–1100.
3. Kulkarni, V. S., et al. "Drug repurposing: an effective tool in modern drug discovery." Russian journal of bioorganic chemistry 49.2,2023:
4. Kabier M, Gambacorta N, Trisciuzzi D, Kumar S, Nicolotti O, Mathew B. MzDOCK: A free ready-to-use GUI-based pipeline for molecular docking simulations. J Comput Chem.
5. Daina A., Michielin O., Zoete V., SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules, Scientific Reports
6. Pires D.E.V., Blundell T.L., Ascher D.B., pkCSM: predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures

Keywords: Docking, Drug Repurposing, Recalled Drugs

PP04

IN SILICO EVALUATION OF A NOVEL BIPHENYL-TRIAZOLE DERIVATIVE AS A POTENTIAL CYP51 INHIBITOR: A MOLECULAR DOCKING STUDY

Ebru Sert¹, Harun Uslu², Bünyamin Göktaş², Zeynep Özdemir³

¹Department of Pharmaceutical Chemistry, Institute of Health Sciences, İnönü University, Malatya, Türkiye

²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Fırat University, Elâzığ, Türkiye

³Department of Pharmaceutical Chemistry, Faculty of Pharmacy, İnönü University, Malatya, Türkiye

Introduction: Azole antifungals function by blocking fungal lanosterol 14 α -sterol demethylase (CYP51), a crucial enzyme in ergosterol production. The rising resistance to current azole antifungals and the advent of new pathogenic strains, especially among non-albicans *Candida* species, underscore the critical necessity for innovative CYP51 inhibitors. Computer-aided drug design methodologies provide an effective means for discovering potential candidates before synthesis. This study presents the in silico assessment of a new biphenyl-triazole derivative, 1-(2-([1,1'-biphenyl]-4-yl)-2-(benzyloxy)ethyl)-1H-1,2,4-triazole (BTE1), as a prospective antifungal drug aimed at CYP51.

Materials-Methods: The three-dimensional crystal structure of CYP51 (PDB ID: 1EA1) was obtained from the Protein Data Bank. The candidate chemical BTE1 was constructed and energy-optimized via ChemOffice. Molecular docking simulations were conducted utilizing AutoDock and AutoDock Vina, with a minimum of 50

iterations per molecule. Fluconazole (TPF) served as the reference ligand for validation; the RMSD value achieved during re-docking was <0.99 Å, thereby affirming the trustworthiness of the docking process. Binding interactions were depicted utilizing Maestro.

Results and Conclusion: BTE1 exhibited a superior AutoDock docking score of -10.14 kcal/mol relative to fluconazole (-7.07 kcal/mol), with an estimated inhibitory constant (K_i) of 36.74 nM compared to 6.58 μ M for the reference drug. BTE1 engaged with crucial active site residues such as TYR76, PHE78, PHE83, and PHE255 by π - π stacking, HEM460 via π -cation contact, and ALA256 through hydrogen bonding—an interaction profile aligned with established CYP51 inhibitors. The results indicate that BTE1 is a potential candidate for subsequent antifungal medication development. The synthesis and biological assessment of BTE1 and its derivatives are presently in progress.

Keywords: Azole antifungals, CYP51, molecular docking

PP05

DETERMINING THE EFFECTS OF MOLECULES WITH HYDRAZONE AND PYRIDAZINE STRUCTURES ON LIVER CANCER

Yaren Nur Zenni¹, Zeynep Özdemir¹, Neşe Başak Türkmen²

¹Inonu University Department of Pharmaceutical Chemistry

²Inonu University Department of Pharmaceutical Toxicology

Introduction: Liver cancer continues to be one of the leading causes of cancer-related deaths worldwide. Late diagnosis, high recurrence rate, and limited treatment options are several reasons why studies in this area are so important. Although targeted agents and multikinase inhibitors used clinically are effective in patients, developing resistance mechanisms and side effect profiles demonstrate the need for the development of new and more effective molecules.

Materials-Methods: The compounds in this study are in the form of two groups: 2-(aminoglycyl)-6-benzylpyridazin-3(2*H*)-one and 2-(aminoglycyl)-6-(4-(2-fluorophenyl)piperazin-1-yl)pyridazin-3(2*H*)-one. In addition to unsubstituted benzaldehyde, benzaldehyde derivatives containing methyl, chloro bromo, fluoro, and methoxy substituents at various positions were used in the synthesis of the derivatives in this study, and the contributions of these groups to the activity were investigated. The structures of the obtained compounds were validated using ¹H-NMR, ¹³C-NMR, and mass spectrum data. The MTS assay, which we use to measure cell viability, was used after incubation for 24-48 hours.

The selective killing of cancerous cells without harming healthy cells by the test agents is of great importance in chemotherapy. Therefore, the cytotoxic effects of the newly synthesized hydrazone compounds on cancerous cell lines were evaluated in comparison with healthy fibroblast cells.

Results-Conclusion: In this study, 8 compounds containing hydrazone and pyridazine rings were resynthesized, and the biological activities of these compounds on liver cancer cell lines were evaluated. The obtained results were analyzed in terms of structure-activity relationship, contributing to the identification of potential candidate molecules. The highest antiproliferative activity among the compounds in question was observed in compound 6-benzyl-2-(((4-bromobenzylidene)amino)glycyl)pyridazin-3(2*H*)-one, coded S6, with a value of 16.1 μ M. The data obtained show that hydrazone, particularly the S6-coded one, and its pyridazinone derivative may be promising compounds for liver cancer treatment and should be supported by further in vivo studies.

Keywords: Hydrazone, Pyridazine, Hep3B, Cytotoxicity, Anticancer agent

PP06

NOVEL BENZAZOLE-BENZAMIDE HYBRIDS: SYNTHESIS AND IN VITRO ANTIPROLIFERATIVE EVALUATION ON BREAST CANCER

Zeynep Sude Yalçın¹, Mehmet Abdullah Alagöz¹, Şule Gürsoy², Öztekin Algül³

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Inonu University, Malatya, Türkiye;

²Department of Biochemistry, Faculty of Pharmacy, Erzincan Binali Yıldırım University, Erzincan, Türkiye

³Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Mersin University, Mersin, Türkiye

Introduction: Breast cancer is a major health concern worldwide, and there is ongoing interest in the discovery of new small-molecule agents with improved activity. Benzazole and benzamide scaffolds are known for their diverse biological properties; however, hybrid molecules combining both motifs have not been extensively explored against breast cancer.

Materials-Methods: In this work, a new series of N-(benzazol-2-yl)-4-substituted benzamide derivatives was synthesized and fully characterized by ¹H NMR, ¹³C NMR, and IR spectroscopy. The antiproliferative activity of the synthesized compounds was evaluated against the human breast cancer cell line MCF-7 and the normal fibroblast cell line L929 using the MTT assay.

Results-Conclusion: All compounds were obtained in good to excellent yields (70–85%). Several derivatives exhibited strong growth-inhibitory effects, with IC₅₀ values ranging from 2.11 to 10.39 µM against MCF-7 cells. Among the tested compounds, compounds 3 and 4 showed the most significant cytotoxic activity, with compound 4 being the most promising candidate for further studies. Notably, the compounds displayed lower cytotoxicity against normal L929 cells, indicating selective antiproliferative effects. These findings provide initial structure–activity insights and identify benzazole–benzamide hybrids as a promising scaffold for further development of anti-breast cancer agents.

Keywords: benzazole-benzamide hybrids, scaffold hybridization, breast cancer

PP07

EVALUATION OF CARBONIC ANHYDRASE ENZYME INHIBITOR ACTIVITIES OF
TAURINAMIDOBENZENSULFONAMIDE DERIVATIVES**Özlem Akgül¹, Sema Yılmaz¹, Andrea Angeli², Gioele Renzo², Fabrizio Carta², Claudiu T. Supuran²**¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ege University, 35100 Bornova, İzmir-Turkey.²Università degli Studi di Firenze, Laboratorio di Chimica Bioinorganica, Rm. 188, Via della Lastruccia 3, I-50019 Sesto Fiorentino (Firenze), Italy

Introduction: Drug discovery is progressively transitioning from conventional approaches toward precision medicine, a paradigm centered on the identification of disease-specific biomarkers and enzymatic targets. Carbonic anhydrase (CA; EC 4.2.1.1) enzymes have emerged as valuable molecular targets for the development of precision medicine tools. Carbonic anhydrases (CAs) are a family of metalloenzymes found in numerous organisms that catalyze the reversible hydration of carbon dioxide to bicarbonate and protons. Among the 15 human CA isoforms, the transmembrane isoforms CA IX and CA XII are predominantly expressed in hypoxic tumors, show limited distribution in normal tissues, and are mainly regulated by hypoxia-inducible factor-1 α (HIF-1 α). These characteristics make CA IX and CA XII reliable targets in drug development studies.

A major challenge in the development of carbonic anhydrase inhibitors (CAIs) as therapeutic agents has been successfully addressed through the “tail approach” strategy. Our studies focus on the development of CAIs bearing taurine as the main scaffold. According to our previously published results, the

taurinamidobenzenesulfonamide (TBS) core exhibits strong interactions with the amino acid residues constituting the CA active sites.

Materials-Methods: Building on these findings, in the present study, we designed and synthesized a series of TBS derivatives using the “tail approach” strategy. The target compounds were obtained through a five-step synthetic route. The chemical structures of the titled compounds were confirmed by spectroscopic analyses. The compounds were evaluated for their CA inhibitory activity using the stopped-flow CO₂ hydration assay.

Results-Conclusion: According to the activity results, some of the derivatives displayed selectivity toward CA IX over the cytosolic isoforms CA I and CA II. Overall, the CA-targeted taurine derivatives reported in this study displayed promising inhibitory profiles and may be considered valuable candidates for further investigation.

Acknowledgements: This study was supported by the Scientific and Technological Research Council of Turkey (TÜBİTAK117S516) and Ege University Scientific Research Project Coordinatorship (16-ECZ-012).

References

1. Supuran, C. T. *Pharmacol. Rev.* 2025, 77 (1), 100004.
2. Akgül, Ö.; Lucarini, E.; Mannelli, L. D. C.; Ghelardini, C.; D'Ambrosio, K.; Buonanno, M.; Monti, S. M.; De Simone, G.;
3. Angeli, A.; Supuran, C. T.; Carta, F. *Eur. J. Med. Chem.* 2022, 227, 113956.
4. Akgül, O.; Singh, S.; Andring, J. T.; McKenna, R.; Selleri, S.; Carta, F.; Angeli, A.; Supuran, C. T. *Eur. J. Med. Chem.* 2021, 212, 113035.
5. Akgül, Ö.; Angeli, A.; Vullo, D.; Carta, F.; Supuran, C. T. *Bioorg. Chem.* 2020, 103, 104236.

Keywords: Carbonic anhydrase inhibitors, taurinamidobenzenesulfonamide, anticancer drug development

PP08

ANALYSIS OF AFLATOXIN B1 AND M1 IN MEDICAL ENTERAL NUTRITION PRODUCTS AND INFANT FORMULAS: A CHROMATOGRAPHIC EVALUATION

Sümevra Albayrak¹, Ateş Kara²

¹Turkish Vaccine Institute, Health Institutes of Türkiye, Ankara, Türkiye

²Turkish Vaccine Institute, Health Institutes of Türkiye, Ankara, Türkiye; Department of Pediatric Infectious Diseases, Hacettepe University, Ankara, Türkiye

Introduction: Aflatoxins are mycotoxins classified as Group 1 carcinogens by the International Agency for Research on Cancer (IARC). Aflatoxin B1 (AFB1), the most toxic and prevalent type, is metabolized in the liver into a highly active form that binds to DNA and proteins, leading to liver damage and hepatocellular carcinoma. Aflatoxin M1 (AFM1) is characterized by its thermal resistance, as it can persist in the final product even after processes such as pasteurization. Therefore, high-sensitivity analysis is critical for ensuring food safety in these products.

Materials-Methods: Analyses were conducted on eight leading brands, comprising an equal number of Medical Enteral Nutrition Products (MENPs) and infant formulas (IFs) (four of each, three liquid and five powder) using a High-Performance Liquid Chromatography (HPLC) system equipped with a Fluorescence Detector (FLD). For sample preparation, a methanol(MeOH):water (H2O) solvent system was utilized for extraction. Following dissolution via magnetic stirring and

extraction, samples were purified using immunoaffinity cartridges. Chromatographic separation was achieved using a C18 column, with a mobile phase consisting of a mixture of H2O, acetonitrile (ACN), and MeOH.

Results-Conclusion: Data obtained through HPLC confirmed that the calibration curves were linear, with a correlation coefficient of $R^2 > 0.990$. The measurement results indicated that the concentrations of AFB1 in the samples and samples were below the maximum limit of 0.1 ppb, and AFM1 levels were below the maximum limit of 0.025 ppb. Through the application of advanced chromatographic analysis methods, it has been confirmed that the risk of aflatoxin contamination in MENPs and IFs remains within legal limits. The finding that detected values are below legislative thresholds demonstrates that these products meet the required efficacy and safety, regarding AFB1 and AFM1 parameters. Furthermore, the results indicate that this analytical method can be effectively utilized with high accuracy for measurements requiring such sensitivity.

Characteristics and Intended Uses of MENPs and IFs

Code	Product Form	Main Compositional Feature	Recommended Population	Nutritional Purpose/ Clinical Use
MENP1	Powder formula	Amino acid based	Infant	Hypoallergenic
MENP2	Liquid formula	High protein	Above 1 year old & Adolescence	Disease-related malnutrition
MENP3	Powder formula	Low Calorie	Adult	Diabetes
MENP4	Liquid formula	High Energy	Adult	Disease related malnutrition
IF1	Powder formula	High protein-to-energy ratio	Up to 3.5 kg	Preterm and Low Birth Weight
IF2	Liquid formula	scGOS/lcFOS	From Birth	Breastmilk substitute
IF3	Powder formula	High energy, high protein	From birth up to 12 months	Immune system maturation of preterm and low birth weight newborns.
IF4	Powder formula	Synbiotic formulation	From 6 months	Follow-on milk

Keywords: Aflatoxin B1, Aflatoxin M1, Infant Formula, HPLC, Food Safety

PP09

SYNTHESIS AND STRUCTURAL ANALYSIS OF NOVEL OXIME ETHERS BEARING IMIDAZOLE AND PYRAZOLE RINGS

Melizsa Melizsa¹, Zeynep Özdemir², Ebru Sert¹, Zarife Sibel Şahin³, Ade Arsianti⁴¹Department of Pharmaceutical Chemistry, Institute of Health Sciences, İnönü University, Malatya, Türkiye²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, İnönü University, Malatya, Türkiye³Sinop University, Department of Energy System Engineering, 57000, Sinop, Türkiye⁴Department of Medical Chemistry, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia

Introduction: Oximes are nitrogen-containing molecules with the general formula $RR'C=N-OH$ and exhibit a wide range of biological activities (Taktaci, et al., 2025; Fotie, et al., 2023). This specific group of organic compounds is a condensation product of carbonyl and hydroxylamine compounds (Fotie, et al., 2023). Oximes and their ether derivatives are highly effective, low-toxicity compounds widely used in the development of anticancer, antibacterial, herbicidal, insecticidal, antifungal, and antiviral drugs (Fotie, et al., 2023), as well as in the treatment of Alzheimer's disease (Yuan, et al., 2024).

Materials-Methods: Imidazole and hydroxylamine chloride were supplied by Merck. Pyrazole was supplied by Aldrich. 2-bromo-1-(4-fluorophenyl)ethanone (Bostonchem) and 2-bromo-4-(trifluoromethyl)acetophenone was supplied by Bostonchem. Iodomethane and 2-bromopropane from Fluka, bromoethane from Acros and allyl chloride from Aldrich and bromomethyl cyclohexane from Aldrich.

Benzyl chloride was also used. 1-(4-fluorophenyl)-2-(1H-imidazol-1-yl)ethanone, 1-(4-fluorophenyl)-2-(1H-pyrazole-1-yl)ethanone, 2-(1H-imidazol-1-yl)-1-(4-(trifluoromethyl)phenyl)ethanone, and their corresponding oxime and oxime ethers were prepared according to the methods in the literature (Sari et al., 2017; Özdemir, 2010). The aim of this study was to synthesize new imidazole and pyrazole oxime ether compounds (M1–M15). To determine their structures, ¹H-NMR, ¹³C-NMR, and HRMS analyses were performed. In addition, x-ray crystallographic analysis was conducted for M15.

Results-Conclusion: The synthesis steps, including the identification of imidazole and pyrazole binding to ethanone, the oxime formation, and the resulting oxime ether compounds M1–M15 confirmed the successful production of the desired compounds. For compound M15, x-ray crystallography analysis clearly revealed the bonded atoms, consistent with the predicted chemical structures.

Keywords: Oxime ethers, imidazole, pyrazole, x-ray crystallographic

PP10

VIRTUAL SCREENING AND MOLECULAR DYNAMICS-BASED EVALUATION OF AN ATP-POCKET-TARGETING TNIK HIT CANDIDATE

Selenay Aktemur, Kübra Çalışkan

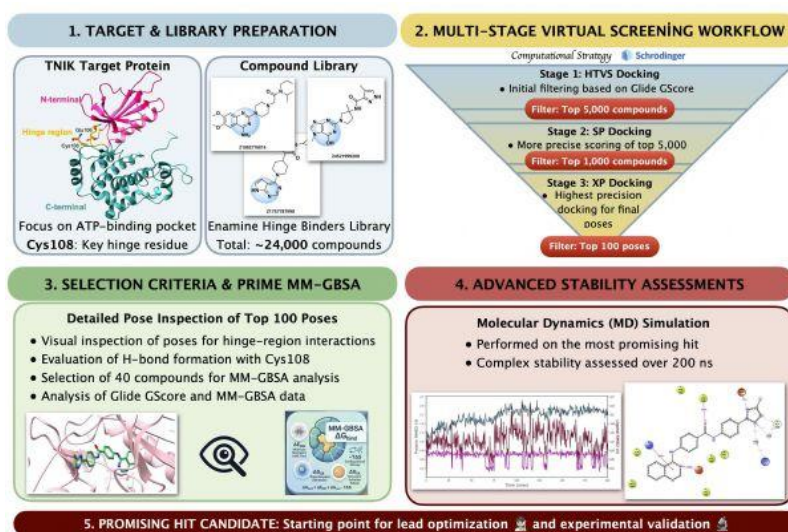
Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gazi University, Ankara, Turkey

Introduction: TRAF2 and NCK-interacting kinase (TNIK) is a serine/threonine kinase involved in signaling pathways associated with cell proliferation, migration, and transcriptional regulation. Owing to its critical role in the Wnt/ β -catenin pathway, TNIK has emerged as a promising therapeutic target, particularly in cancer research. Structurally, the TNIK ATP-binding pocket comprises the hinge region, a solvent-exposed front pocket, and a back hydrophobic pocket shaped by the gatekeeper residue Met105. Key residues, including Glu106 and Cys108 in the hinge region, Lys54 and Glu69 involved in catalytic organization, and Leu160, Val170, Asp171, and Phe172 in the deeper hydrophobic region, contribute to ligand recognition within the ATP pocket. Among these, Cys108 represents a major hinge interaction point for TNIK inhibitors through hydrogen-bond formation, supporting ATP-competitive binding as a rational strategy for hit identification

Materials-Methods: In this study, a structure-based virtual screening workflow was performed to identify a potential TNIK-targeting hit candidate. Compounds from the Enamine Hinge Binder Library were progressively filtered through hierarchical docking

protocols, followed by visual inspection of key binding interactions, particularly hydrogen-bond formation with the hinge residue Cys108. The most promising candidates were further evaluated using Prime MM-GBSA binding free energy calculations. Based on the combined analysis of Glide GScore, MM-GBSA results, and protein-ligand interactions, the leading hit candidate was selected for molecular dynamics (MD) simulation to assess protein-ligand complex stability.

Results-Conclusion: The integrated structure-based screening workflow enabled the prioritization of a promising TNIK-targeting hit candidate. The selected compound showed favorable docking performance, acceptable MM-GBSA binding free energy, and key protein-ligand interactions within the ATP-binding pocket, particularly involving the hinge region. Overall, the identified hit may provide a promising starting point for further lead optimization and experimental validation toward the development of TNIK-targeting compounds.



Keywords: TNIK inhibitors, virtual screening, molecular dynamics

PP11

THIOPHENE-TAIL ELONGATION OF OG-001 ENHANCES SELECTIVE DUAL INHIBITION OF TUMOR-ASSOCIATED hCA IX AND XII: MOLECULAR DYNAMICS INSIGHTS

Muhammed Trawally¹, Kübra Demir Yazıcı¹, Atilla Akdemir², Özlen Güzel Akdemir¹

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Istanbul University, Istanbul, Türkiye.

²Department of Pharmacology, Faculty of Pharmacy, Istanbul Kent University, Istanbul, Türkiye

Introduction:

Human carbonic anhydrases (hCA) are Zn-containing enzymes with 15 isoforms catalyzing CO₂ reversible hydration. Tumor-associated membrane-bound isoforms hCA IX and hCA XII are overexpressed in several solid tumors, playing important roles in hypoxia-induced extracellular acidosis, tumor progression, metastasis, and chemoresistance¹. Selective inhibition of these isoforms has emerged as a promising strategy for cancer therapy. However, achieving selectivity over ubiquitous cytosolic isoforms hCA I and hCA II remains a challenge². OG-001, an indole-based sulfonamide hCA inhibitor, shows subnanomolar inhibition of hCA I (7.5 nM), hCA II (7.2 nM), hCA IX (102 nM), and hCA XII (110 nM) and was crystallized with hCA II (PDB: 3B4F)³. Although OG-001 demonstrates high inhibition of hCA IX and hCA XII, its lack of isoform selectivity limits its potential as a promising lead. This study includes the introduction of a thiophene-methylene tail to the hydrazide moiety of OG-001 to improve its selectivity toward hCA IX and hCA XII, and a subsequent

comparative molecular dynamics simulation to investigate the structural basis of the observed selectivity profile.

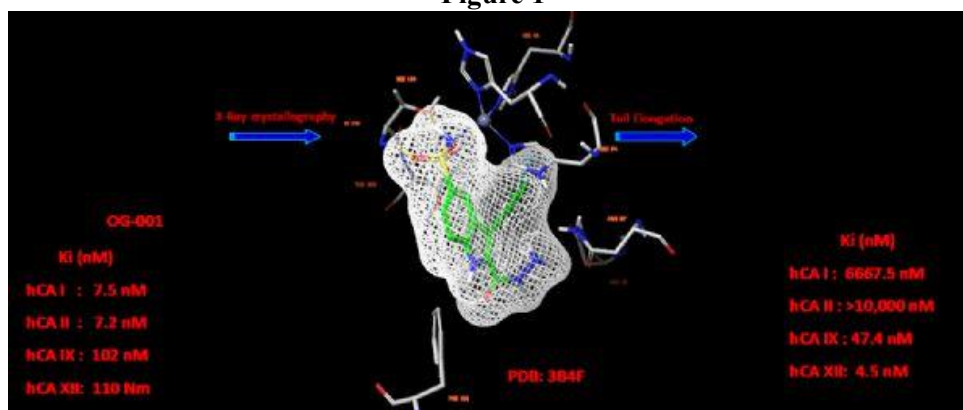
Materials-Methods:

The synthesis of the compound was reported in the literature⁴, and the molecular modeling studies were conducted according to the protocol reported⁵.

Results-Conclusion:

The thiophene-tail-elongated OG-001 analogue displayed an enhanced potency against the tumor-associated hCA IX (47.4 nM) and hCA XII (4.5 nM) with selectivity ratios of 140.7 and >211.0 for hCA IX over hCA I and hCA II, respectively, and selectivity ratios of 1481.7 and >2222.2 over hCA I and hCA II, respectively (Figure 1). Molecular dynamics simulations revealed how the extended thiophene tail favors interactions with the residues present in the outer rim of the isoforms, contributing to improved selectivity.

Figure 1



Tail elongation of OG-001

References

1. Chegwiddden, W. R. The Carbonic Anhydrases in Health and Disease. in *The Carbonic Anhydrases: Current and Emerging Therapeutic Targets* (eds Chegwiddden, W. R. C Carter, N. D.) vol. 75 1–12 (Springer International Publishing, Cham, 2021).
2. Nerella, S. G., Thacker, P. S., Arifuddin, M. C Supuran, C. T. Tumor associated carbonic anhydrase inhibitors: Rational approaches, design strategies, structure activity relationship and mechanistic insights. *European Journal of Medicinal Chemistry Reports* 10, 100131 (2024).
3. Güzel, Ö. *et al.* Carbonic anhydrase inhibitors. Interaction of 2-(hydrazinocarbonyl)-3-phenyl-1*H*-indole-5-sulfonamide with 12 mammalian isoforms: Kinetic and X-ray crystallographic studies. *Bioorganic & Medicinal Chemistry Letters* 18, 152–158 (2008).
4. Demir-Yazıcı, K. *et al.* Indole-Based Hydrazones Containing A Sulfonamide Moiety as Selective Inhibitors of Tumor-Associated Human Carbonic Anhydrase Isoforms IX and XII. *International journal of molecular sciences* 20, (2019).
5. Trawally, M. *et al.* Novel benzenesulfonamide-Thiourea derivatives as potent carbonic anhydrase inhibitors with anticancer activity. *Journal of Sulfur Chemistry* 1–33 (2026) doi:10.1080/17415993.2026.2646550.

Keywords: Sulfonamide, indole, tail-elongation, selectivity, carbonic anhydrase

PP12

DEVELOPMENT AND IN VITRO CHARACTERIZATION OF ORAL DISINTEGRATING FILMS
LOADED WITH A NOVEL HEXAHYDROQUINOLINE COMPOUNDKutsal Özcan Kosif¹, Ezgi Pehlivanlar Yavrucu², Rahime Şimşek³¹Department of Pharmaceutical Technology, Faculty of Pharmacy, Karadeniz Technical University, Trabzon, Turkey²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Karadeniz Technical University, Trabzon, Turkey³Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey

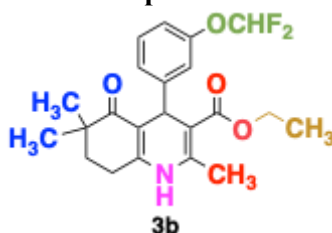
Introduction: Inflammation plays a critical role in the pathogenesis of numerous diseases, and its dysregulation may lead to chronic conditions (Tripathi, 2025). In this context, a hexahydroquinoline derivative compound, coded as 3b, was previously synthesized by our research group, structurally characterized, and evaluated for its anti-inflammatory activity. The compound demonstrated significant anti-inflammatory effects, likely mediated through a multitarget mechanism of action, rather than a single static pathway. The present study represents a continuation of this work and focuses on the development of an optimized formulation of compound 3b to improve its biopharmaceutical properties.

Materials-Methods: ODFs represent an innovative drug delivery system that rapidly disintegrates in the oral cavity without the need for water, thus improving patient compliance and potentially increasing the bioavailability of drug candidates. In this study, ODF formulations containing compound 3b were prepared by the solvent casting method using hydroxypropyl methylcellulose (HPMC) as the film-forming polymer at three different

concentrations: 3%, 4%, and 5% (w/v). Glycerin was used as the plasticizer, while citric acid, sodium saccharin, and peppermint flavor were incorporated to improve palatability and stimulate saliva production.

Results-Conclusion: The prepared films were evaluated by in vitro characterization tests including organoleptic properties, thickness uniformity, pH, water absorption capacity, and disintegration time. Organoleptic evaluation showed that all formulations were homogeneous and transparent in appearance. The pH values of the reconstituted film formulations were found to be 6.15, 6.10, and 6.04 for the films containing 3%, 4%, and 5% HPMC, respectively. In addition, water absorption capacity increased with increasing polymer concentration, consistent with the hydrophilic nature of HPMC. In terms of disintegration performance, the 3% HPMC formulation disintegrated in less than 30 seconds, while the 4% and 5% HPMC formulations exhibited disintegration times between 30 and 60 seconds.

Compound 3b



Keywords: orally disintegrating film, solvent casting, characterization

PP13

LABORATORY-SCALE SYNTHESIS OF ANHYDROUS ALUMINUM CHLORIDE FOR FRIEDEL–CRAFTS APPLICATIONS UNDER MOISTURE-FREE CONDITIONS

¹Ural Ufuk DEMIREL, ¹Remziye Azra KARTOP

¹Faculty of Pharmacy, Altınbaş University, Istanbul, Türkiye

Introduction:

Anhydrous aluminum chloride (AlCl_3) is a highly important Lewis acid catalyst widely used in Friedel–Crafts alkylation and acylation reactions. However, its high cost, limited stability during storage, and extreme sensitivity to atmospheric moisture create challenges for routine laboratory use. In this study, a practical and cost-effective laboratory-scale synthesis of anhydrous AlCl_3 was developed using easily accessible starting materials under strictly dry conditions.

Materials and Methods:

Aluminum foil was used as an aluminum source, while chlorine gas was generated by the controlled addition of sulfuric acid onto sodium chloride using a dropping funnel system. The generated chlorine gas was dried using a CaCl_2 trap before entering the reaction system. All glassware was initially dried with dry air and subsequently flame-dried prior to use. The reaction was carried out at 350–400 °C under moisture-free conditions. The generated AlCl_3 vapor was isolated in a cooler section of the apparatus by sublimation and collected under dry conditions. The synthesized AlCl_3

was subsequently tested as a Lewis acid catalyst in a Friedel–Crafts alkylation reaction.

Results: White crystalline anhydrous aluminum chloride was obtained successfully with an isolated yield of 84%. The synthesized compound exhibited strong hygroscopic behavior upon exposure to atmospheric moisture. The measured melting point was 190–191 °C, consistent with reported literature values for anhydrous AlCl_3 . The sublimation-based isolation method enabled effective purification and separation of the product from the reaction zone. The synthesized AlCl_3 successfully catalyzed the Friedel–Crafts alkylation reaction without observable complications.

Conclusion:

The present study demonstrates an effective, economical, and reproducible laboratory-scale synthesis of anhydrous aluminum chloride using accessible materials and a moisture-controlled setup. The synthesized AlCl_3 was successfully applied as an active Lewis acid catalyst in Friedel–Crafts alkylation, confirming its practical laboratory applicability.

Keywords: Aluminum chloride, Lewis acid, Friedel–Crafts alkylation, Anhydrous synthesis, Sublimation

PP14

ROLE OF CD36 ON CANCER AND METASTASIS

¹Irem CELIK, ¹Ural Ufuk DEMIREL, ¹Behiye OZTURK SEN¹Faculty of Pharmacy, Altınbaş University, Istanbul, Türkiye

CD36 is a type 2 cell surface scavenger receptor, and it is commonly found in many cells of immune and non-immune. Its functions are signaling receptor for DAMPs and PAMPs, also long chain free fatty acid transporter that regulates immune cell metabolism and fate (1). With respect to recent research, it was indicated that CD36 can integrate cell signaling and metabolic pathways via its dual functions and hence affect immune cell differentiation and activation. Its expression contributes to pathogenesis of common diseases, including atherosclerosis and tumor progression (2).

The role of CD36 receptor in tumor development is favoring the lipid intake in cancer cells. It triggers a switch in lipid metabolism in order to supply the increasing energetic demand of the tumor. CD36 has been concerning to tumor growth kinetics and cell proliferation in several types of cancers (3).

It was founded that CD36 expression/activation is correlated with EMT induction in cancer cells. CD36+ cancer cells show the increment in stemness functional properties which suggest CD36, a marker of the cancer stem cell population. Therefore, CD36 has been evaluated as a promising therapeutic target in cancer. Until recent studies, at least three different types of active molecules have been developed for reducing CD36-related functions: small-molecule inhibitors, compounds knocking-down CD36 expression and blocking monoclonal antibodies (4).

In this review study, the role of CD36 in cancer and metastasis processes and especially its role in the human body will be explained via latest research on CD36. Also, the importance of CD36 will be emphasized.

References:

1. Pepino, M. Y., Kuda, O., Samovski, D., & Abumrad, N. A. (2014). Structure-function of CD36 and importance of fatty acid signal transduction in fat metabolism. *Annual review of nutrition*, 34, 281–303. <https://doi.org/10.1146/annurev-nutr-071812-161220>.
2. Chen, Y., Zhang, J., Cui, W., & Silverstein, R. L. (2022). CD36, a signaling receptor and fatty acid transporter that regulates immune cell metabolism and fate. *The Journal of experimental medicine*, 219(6), e20211314. <https://doi.org/10.1084/jem.20211314>.
3. Deng, M., Cai, X., Long, L., Xie, L., Ma, H., Zhou, Y., Liu, S., & Zeng, C. (2019). CD36 promotes the epithelial-mesenchymal transition and metastasis in cervical cancer by interacting with TGF- β . *Journal of translational medicine*, 17(1), 352. <https://doi.org/10.1186/s12967-019-2098-6>.
4. Guerrero-Rodríguez, S. L., Mata-Cruz, C., Pérez-Tapia, S. M., & Velasco-Velázquez, M. A. (2022). Role of CD36 in cancer progression, stemness, and targeting. *Frontiers in cell and developmental biology*, 10, 1079076. <https://doi.org/10.3389/fcell.2022.1079076>.

Keywords: CD36, cancer, metastasis

PP15

ANTI-CANCER EFFECT OF OLEUROPEIN

¹Fatmanur TUNA, ¹Ural Ufuk DEMIREL, ¹Behiye OZTURK SEN¹Faculty of Pharmacy, Altınbaş University, Istanbul, Türkiye

The term cancer comes from the Latin word "cancerand"; Greek "karsinosan"; It is based on words. It is defined as uncontrolled abnormal cell proliferation, in other words, the irresponsible proliferation of cells that have lost their physiological coordination ability. Cancer treatment, control of cancer, and elimination of symptoms caused by cancer are the main goals of anticancer activity (1). For cancer treatment, anticancer drugs or different plant extracts have been used and one of them is oleuropein (2). The term oleuropein derived from the botanical name of the olive tree, *Olea europaea*. Oleuropein is a glycosylated seco-iridoid, a phenolic bitter compound found in green olives, peel, pulp, leaves, argan oil and seeds. Oleuropein is one of the more powerful dominant and world-leading phenolic bioactive compounds circulating in the veins of olive trees. Studies conducted in recent years have revealed that it has anti-cancer effects on cancer cells. In clinical studies conducted on various tumor samples, it has been shown to stop and

reduce the possibility of metastasis by affecting breast, prostate, and colon tumors (3). In vitro and in vivo animal studies have been conducted to investigate the anticancer effect of oleuropein. In many experimental studies, it has been observed that oleuropein has antitumor effects on different cancer cell lines (4). The types of cancer on which oleuropein has an anticancer effect are as follows: Breast cancer, Colon cancer, Liver cancer, Prostate cancer, Pancreatic cancer, Thyroid cancer, Osteosarcoma, Leukemia, Neuroblastoma, Mesothelioma, Glioblastoma (5) and the number of cancer-related studies has increased significantly in recent years.

In this review study, it is aimed to investigate the anticancer effects of oleuropein and, explain on which types of cancer it is mostly effective according to recent studies.

References:

- 1.Greenwell, M., Rahman, P.K.S.M. (2015). Medicinal plants: their use in anticancer treatment. *Int. J. Pharm. Sci. Res.*, 6 (10), 4103–4112. doi: 10.13040/IJPSR.0975-8232.6(10).4103-12.
- 2.Acquaviva, R., Di Giacomo, C., Sorrenti, V., Galvano, F., Santangelo, R., Cardile, V., Gangia, S., D'Orazio, N., Abraham, N. G., & Vanella, L. (2012). Antiproliferative effect of oleuropein in prostate cell lines. *International journal of oncology*, 41(1), 31–38.
- 3.Psaltopoulou, T., Kosti, R. I., Haidopoulos, D., Dimopoulos, M., & Panagiotakos, D. B. (2011). Olive oil intake is inversely related to cancer prevalence: a systematic review and a meta-analysis of 13,800 patients and 23,340 controls in 19 observational studies. *Lipids in health and disease*, 10, 127.
- 4.Nediani, C., Ruzzolini, J., Romani, A., & Calorini, L. (2019). Oleuropein, a Bioactive Compound from *Olea europaea* L., as a Potential Preventive and Therapeutic Agent in Non-Communicable Diseases. *Antioxidants (Basel, Switzerland)*, 8(12), 578. <https://doi.org/10.3390/antiox8120578> doi: 10.3390/antiox8120578
- 5.Shamshoum, H., Vlatcheski, F., & Tsiani, E. (2017). Anticancer effects of oleuropein. *BioFactors (Oxford, England)*, 43(4), 517–528. <https://doi.org/10.1002/biof.1366>

Keywords: Oleuropein, Anti-Cancer, Phenolic Bioactive

PP16

APPLICATION OF PVA HYDROGELS IN DRUG DELIVERY SYSTEM

¹Berfin DIREKCI,¹ Behiye OZTURK SEN ¹Ural Ufuk DEMIREL¹Faculty of Pharmacy, Altınbaş University, Istanbul, Türkiye

Polymeric hydrogels are three-dimensional networks, either chemical or physical, that have a high capacity to absorb and hold water. Such structures are highly desirable for the preparation of materials in biomedical applications due to their great swelling capacity (1).

Polyvinyl alcohol (PVA), synthetic and semicrystalline polymer is a biomaterial which has many beneficial qualities, well-known for its biocompatibility, good biodegradability, and high hydrophilicity, ability to form fibers or films, appropriate mechanical properties and hence it has been utilized in biomedical applications for many years (1-4). It has been extensively explored due to its chemical stability, nontoxic, good biocompatibility, biological aging resistance, high water-absorbing capacity, and easy processing (2). Owing to their biocompatibility resemblance to human tissue, amphiphilic nature, and self-assembly characteristic, they are extensively utilized in many applications such as controlled medication release, contact lenses, wound dressings, and biosensors (3).

The use of hydrogels in drug delivery has significantly enhanced the delivery of macromolecular medicines, small compounds. Although there have been difficulties with medication administration utilizing hydrogels, ongoing advancements are being made to determine which hydrogel design is most appropriate for a certain drug delivery system (4). PVA hydrogels have been widely used in medicine and have been shown to significantly improve the therapeutic result of drug delivery.

PVA is also utilized in the production of jellies that quickly dry on the skin, transdermal patches, and formulations for immediate and sustained release tablets. PVA-based hydrogels have also been identified as promising biomaterials.

In this review study, some applications of PVA hydrogels will be discussed in a range of drug delivery systems.

References

- 1.Narayanaswamy, R., & Torchilin, V. P. (2019). Hydrogels and Their Applications in Targeted Drug Delivery. *Molecules (Basel, Switzerland)*, 24(3), 603. <https://doi.org/10.3390/molecules24030603>.
- 2.Wang, M., Bai, J., Shao, K., Tang, W., Zhao, X., Lin, D., Huang, S., Chen, C., Ding, Z., & Ye, J. (2021). Poly(vinyl alcohol) Hydrogels: The Old and New Functional Materials,. *International Journal of Polymer Science*, <https://doi.org/10.1155/2021/2225426>.
- 3.Chen, Y., Li, J., Lu, J., Ding, M., & Chen, Y. (2022). Synthesis and properties of poly (vinyl alcohol) hydrogels with high strength and toughness. *Polymer Testing*, 108, 107516.
- 4.Gajra*, B., Pandya, S. S., Vidyasagar, G., Rabari, H., Dedania, R. R., & Rao, S. (2012). Poly vinyl alcohol hydrogel and its pharmaceutical and biomedical applications: A review. *Int. J. Pharm. Res*, 4, 2026.

Keywords: PVA, hydrogel, drug delivery, biomaterials

PP17

ANTIBACTERIAL MECHANISM OF HYDROGELS FOR THE TREATMENT OF INFECTIONS

¹Basant GHALAB, ¹Behiye OZTURK SEN ¹Ural Ufuk DEMIREL¹Faculty of Pharmacy, Altınbaş University, Istanbul, Türkiye

Bacterial infections, resistance to chemotherapy which are especially caused by drug-resistant bacteria possess major risks for human health and life. Thus, it is necessary to develop new antibacterial agents addressing for the of bacterial infections. In antibacterial applications, biomedical materials having good antimicrobial characteristics can be used.

Hydrogels are important biomaterials due to their good bio-compatibility, mechanical qualities like human soft tissue extracellular matrix, and tissue healing properties (1). They are used in different applications, one of them is antibacterial application. Hydrogels having antibacterial functions are particularly well-suited for dressing applications in skin wound repair (2). Thus, novel antibacterial hydrogel wound dressings have received a lot of attention, due to their component design, preparation of method optimization, and bacterial

resistance reduction strategies. Antibacterial hydrogels are more than simply bandages; they are active battlegrounds where a remarkable interaction of physical and chemical properties defeats bacterial opponents. According to recent studies, these innovative materials hold the potential of a speedier, safer, and more successful future for wound healing (3). Especially, hydrogels have become the focus of biomedical material research owing to their biocompatibility, high hydrophilicity and distinct three-dimensional network structure.

In this review study, it is aimed to learn about types and preparations of antimicrobial hydrogels and understand how antibacterial hydrogels employ a diverse mechanism to combat and prevent infections, offering a promising tool in the fight against antibiotic resistance.

References

- 1.Jia, B., Li, G., Cao, E., Luo, J., Zhao, X., & Huang, H. (2023). Recent progress of antibacterial hydrogels in wound dressings. *Materials today. Bio*, 19, 100582. <https://doi.org/10.1016/j.mtbio.2023.100582>
- 2.Tang, Y., Xu, H., Wang, X., Dong, S., Guo, L., Zhang, S., Yang, X., Liu, C., Jiang, X., Kan, M., Wu, S., Zhang, J., & Xu, C. (2023). Advances in preparation and application of antibacterial hydrogels. *Journal of nanobiotechnology*, 21(1), 300. <https://doi.org/10.1186/s12951-023-02025-8>
- 3.Veiga, A. S., & Schneider, J. P. (2013). Antimicrobial hydrogels for the treatment of infection. *Biopolymers*, 100(6), 637–644. <https://doi.org/10.1002/bip.22412>.

Keywords: Bacterial infections, hydrogels, antibiotic resistance

PP18

DESIGN, SYNTHESIS, CHARACTERIZATION, AND MOLECULAR DOCKING STUDIES OF NOVEL ISATIN-BASED SULFONAMIDE DERIVATIVES AS POTENTIAL ANTICANCER AGENTS

¹Marjan AKBARI, ¹Ural Ufuk DEMIREL

¹Faculty of Pharmacy, Altınbaş University, Istanbul, Türkiye

Introduction: Cancer remains a major global health problem, and the limitations of current chemotherapeutic agents, including toxicity, poor selectivity, and multidrug resistance, necessitate the development of novel anticancer agents. Protein tyrosine kinases (PTKs), particularly VEGF and PDGF receptor kinases, are important molecular targets in cancer therapy. Isatin derivatives and sulfonamide-containing compounds have demonstrated promising anticancer activities in current studies. In this study, novel isatin-based sulfonamide derivatives were designed as potential tyrosine kinase inhibitors, synthesized and characterized.

Materials and Methods: Novel sulfonamide-substituted isatin derivatives were synthesized starting from 5-aminoisatin using various sulfonyl chlorides. The synthesized compounds were purified by ¹H-NMR, and mass spectrometry. Molecular docking studies were performed against VEGF receptor tyrosine kinases using AutoDock Vina 4.2.6. Protein-ligand interactions were analyzed with PyMOL, and in silico ADME predictions were evaluated using SwissADME tools.

Results: Target compounds were successfully synthesized and characterized by spectral methods and the melting point ranges were determined 223–225 °C for 2a, 249–252 °C for 2b, and 228–231 °C for 2c. Molecular docking analyses demonstrated favorable binding affinities of the synthesized derivatives toward

VEGF receptor kinases. The compounds exhibited interaction profiles comparable to the reference tyrosine kinase inhibitors sorafenib and sunitinib. Docking results of compounds 2a and 2b in VEGFR showed binding energies of –9.7 and –8.5 kcal/mol, respectively. Compound 2a formed one hydrogen bond with ASN423 in VEGFR2, whereas compound 2b formed two hydrogen bonds with GLU885 and ASP1046.

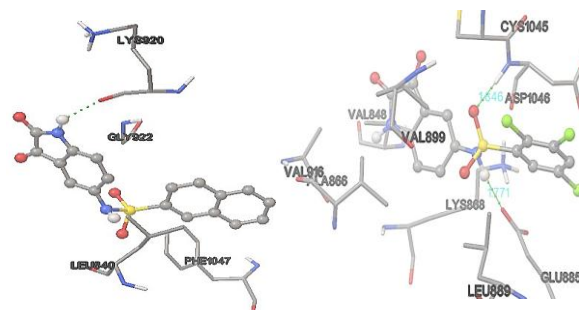
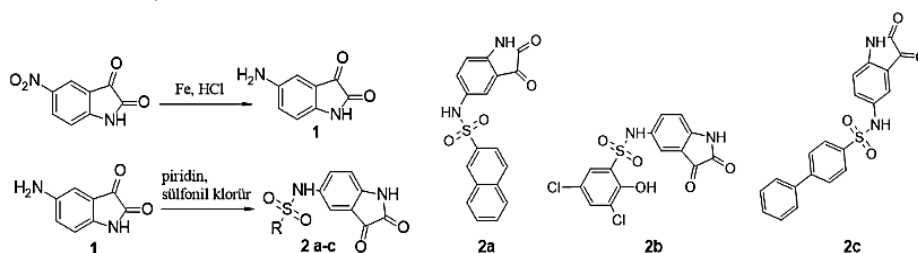


Figure 1. Predicted binding mode of compound 2a (left) compound 2b (right) in the VEGFR active site.

Conclusion: The synthesized novel isatin-based sulfonamide derivatives may represent promising candidates for further development as anticancer agents targeting receptor tyrosine kinases. These findings support the potential of isatin-derived scaffolds in rational anticancer drug design.



Scheme 1. Synthetic pathway for compounds 2a–c.

Keywords: Anticancer agents, isatin derivatives, sulfonamides, tyrosine kinase inhibitors, molecular docking.

PP19

COMPUTER-AIDED DESIGN OF ROR γ (ROR GAMMA) AGONIST (RETINOIC ACID RECEPTOR-RELATED ORPHAN NUCLEAR RECEPTOR γ) AND NOVEL DERIVATIVES AS THERAPEUTIC TARGETS IN PROSTATE CANCER

Mahmut Haluk ÖZÇİLENK¹, Asiye MERİÇ²

²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University,

Introduction: Prostate cancer is a significant public health issue characterized by high incidence and mortality rates among the male population. In this study, based on the critical role of ROR γ , a member of the nuclear receptor superfamily, in prostate cancer pathophysiology, the rational development of novel derivatives using computer-aided drug design methods was aimed. Within the scope of the study, the structural dynamics and pharmacophore characteristics of the receptor's ligand-binding domain were analyzed in light of literature data.

Materials-Methods: During the molecular modeling process, novel original molecules were designed using

MOE, and Schrödinger software, and molecular docking studies were performed to determine the interaction profiles of these molecules with the receptor. Furthermore, the drug-likeness potential, toxicity risks, and physicochemical parameters of all designed derivatives were theoretically analyzed using the Osiris Property Explorer software.

Results-Conclusion: The data obtained from these *in silico* studies provide significant findings indicating that the designed compounds could be potential drug candidates for the treatment of prostate cancer and establish a scientific basis for future research.

References:

- Cook, D. N., Kang, H. S., & Jetten, A. M. (2015). Retinoic Acid-Related Orphan Receptors (RORs): Regulatory Functions in Immunity, Development, Circadian Rhythm, and Metabolism. *Nuclear Receptor Research*, 2, 101185. <https://doi.org/10.11131/2015/101185>
- Fauber BP., & Magnuson, S. (2014). Modulators of the nuclear receptor retinoic acid receptor-related orphan receptor- γ (ROR γ or RORc). *J. Med. Chem.*, 57(14), 5871–5892. <https://doi.org/10.1021/jm401901d>
- Fauber BP, RenéO, Deng Y, DeVoss J, Eidenschenk C, Everett C, Ganguli A, Gobbi A, Hawkins J, Johnson AR, La H, Lesch J, Lockey P, Norman M, Ouyang W, Summerhill S, and Wong H. (2015). Discovery of 1-{4-[3-Fluoro-4-((3S,6R)-3-methyl-1,1-dioxo-6-phenyl-[1,2]thiazinan-2-ylmethyl)-phenyl]-piperazin-1-yl}-ethanone (GNE-3500): a Potent, Selective, and Orally Bioavailable Retinoic Acid Receptor-Related Orphan Receptor C (RORc or ROR γ) Inverse Agonist. *J. Med. Chem.* 58, 5308–5322 DOI: 10.1021/acs.jmedchem.5b00597
- Fukuda, S., Ikenogami, T., Otake, K., Miwa, S., Maeda, K., Yamashita, T., Inami, T., Yokota, M., Lu, Y., Suma, A., Hirono, Y., Ogawa, N., Inoue, T., Harada, K., Yamaguchi, K., Akai, S., Nomura, A., Adachi, T., Terawaki, T., Suzukawa, A., ... Shiozaki, M. (2025). A Concise and Modular Approach to Generate Novel ROR γ Agonists. *J. Med. Chem.*, 68(15), 15849–15871. <https://doi.org/10.1021/acs.jmedchem.5c00872>
- Kojetin, D. J., & Burris, T. P. (2014). REV-ERB and ROR nuclear receptors as drug targets. *Nature reviews. Drug discovery*, 13(3), 197–216. <https://doi.org/10.1038/nrd4100>
- Qin, H.-L., Shang, Z.-P., Jantan, I., Tan, O. U., Hussain, M. A., Sher, M., & Bukhari, S. N. A. (2015). Molecular docking studies and biological evaluation of chalcone based pyrazolines as tyrosinase inhibitors and potential anticancer agents. *RSC Advances*, 5(57), 46330–46338. <https://doi.org/10.1039/C5RA02995C>
- Zhang, Y., Luo, X. Y., Wu, D. H., & Xu, Y. (2015). ROR nuclear receptors: structures, related diseases, and drug discovery. *Acta Pharmacologica Sinica*, 36(1), 71–87. <https://doi.org/10.1038/aps.2014.120>
- Zheng, J., Wang, J., Wang, Q., Zou, H., Wang, H., Zhang, Z., Chen, J., Wang, Q., Wang, P., Zhao, Y., Lu, J., Zhang, X., Xiang, S., Wang, H., Lei, J., Chen, H. W., Liu, P., Liu, Y., Han, F., & Wang, J. (2020). Targeting castration-resistant prostate cancer with a novel ROR γ antagonist elaiophylin. *Acta Pharmaceutica Sinica. B*, 10(12), 2313–2322. <https://doi.org/10.1016/j.apsb.2020.07.001>

Keywords: Prostate Cancer, ROR γ , Agonist, Computer Aided Drug Design

PP20

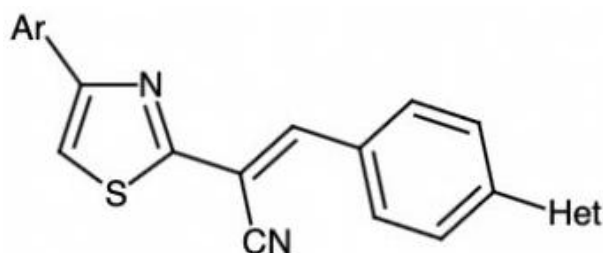
NOVEL THIAZOLE-ACRYLONITRILE DERIVATIVES: SYNTHESIS AND EVALUATION AS
ANTIMICROBIAL AGENTSRumeysa Yonar¹, Keriman Özadalı Sarı², Şeyma Nigiz³¹Ankara Medipol University, Faculty of Pharmacy Department of Pharmaceutical Chemistry, Ankara, Turkey;
Hacettepe University, Faculty of Pharmacy Department of Pharmaceutical Chemistry, Ankara, Turkey²Hacettepe University, Faculty of Pharmacy Department of Pharmaceutical Chemistry, Ankara, Turkey³Hacettepe University, Faculty of Pharmacy Department of Pharmaceutical Microbiology, Ankara, Turkey

Microbial infections are diseases caused by bacteria, fungi, and other microorganisms that can affect human health at various levels. Such infections represent a major global health challenge, particularly due to the rapid emergence and spread of resistance to existing antimicrobial agents. This growing resistance significantly limits the effectiveness of current therapeutic strategies, leading to increased morbidity, mortality, and healthcare burden worldwide. Consequently, there is a continuous need for the development of novel antimicrobial compounds with improved efficacy and reduced potential for resistance development. In this regard, the design and synthesis of structurally diverse molecules have gained considerable

attention in recent research. In this context, the antimicrobial activities of the target compounds against various Gram-positive and Gram-negative bacteria, as well as their antifungal activities against some *Candida* species, were investigated using microdilution methods. Ciprofloxacin and fluconazole were used as reference drugs for the evaluation of antibacterial and antifungal activities, respectively. The obtained results provide important insights into the antimicrobial potential of the synthesized compounds.

This study was supported by a grant of Hacettepe University Scientific Research Projects Coordination Unit (THD-2025-22415).

Chemical structures of the synthesized compounds



Keywords: Antimicrobial, acrylonitrile, thiazole

PP21

NOVEL BENZOXAZOLINONE THIOSEMICARBAZIDES TARGETING ALZHEIMER'S DISEASE

Hayrünnisa Taşci¹, Ahmet Avcı², Nadire Özenver³, Begüm Nurpelin Sağlık⁴, Birsen Tozkoparan², Nesrin Gökhan Kelekçi²

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, EBYU

²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University

³Department of Pharmacognosy, Faculty of Pharmacy, Hacettepe University

⁴Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University

Introduction: Alzheimer's disease is a progressive illness whose prevalence is increasing in society(1). Among the most critical mechanisms involved in the development of the disease are cholinergic activity and monoamine-oxidase-linked oxidative stress (2-4). Cholinesterases (acetylcholinesterase-AChE and butyrylcholinesterase-BuChE) and monoamine oxidases (MAO-A and MAO-B) have long been considered important therapeutic targets for halting the progression of Alzheimer's disease and treating the disease. Given the multiple mechanisms involved in its pathology, it is accepted that targeting multiple factors in the treatment of Alzheimer's disease will provide an advantage for research.

Materials-Methods: In this study, molecules incorporating both benzoxazolinone and thiosemicarbazide moieties were designed using computer-aided drug design approaches. Following the synthesis of 8 novel compounds (4aa'-d'/4ba'-d'), structural elucidation was carried out using infrared (IR) spectroscopy, ¹H nuclear magnetic resonance (NMR),

and electrospray ionization mass spectrometry (ESI-MS). The therapeutic potential of the compounds in Alzheimer's disease was evaluated by assessing their inhibitory effects on Acetylcholinesterase (AChE), Butyrylcholinesterase (BuChE), Monoamine oxidase A (MAO-A), and Monoamine oxidase B (MAO-B), along with their antioxidant activities, under in vitro conditions.

Results-Conclusion: The compounds showed consistent sub-micromolar inhibitory activity across AChE, BChE, MAO-A, and MAO-B in vitro. Several AChE potencies approached the reference donepezil, and selected BChE activities were within an order of magnitude of tacrine. Particularly, 4bd' inhibited three targets (AChE, BChE and MAO-B) and 4ab' showed a balanced profile (AChE, BChE and MAO-A). Protein-ligand interactions of these compounds at the active sites of target enzymes (AChE: 4EY7; MAO-B: 2V5Z) supported the in vitro enzyme inhibition results. In silico ADME (QikProp) indicated compliance with compounds Lipinski's Rule of Five and Jorgensen's Rule of Three.

References

1. In Ganong's Review of Medical Physiology, 25e, McGraw-Hill Education, 2018.
2. Curr Neuropharmacol 2016, 14 (1), 101-115.
3. Curr Med Chem 2004, 11 (15), 1983-1993.
4. Antioxidants (Basel) 2023, 12 (2).

Keywords: Alzheimer's disease, enzyme inhibition, computer-aided drug design, benzoxazolinone, thiosemicarbazide

PP22

SYNTHESIS, ANTIMICROBIAL, AND ANTIPROLIFERATIVE EVALUATION OF A NOVEL PIPERONYL-PIPERAZINE-HYDROXYPYRANONE DITHIOCARBAMATE

İlayda Kılıç¹, Gülşah Karakaya¹, Yamaç Tekintaş², Şahika Cıngır Köker³, Mutlu Dilsiz Aytemir⁴

¹İzmir Kâtip Çelebi University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İzmir, Türkiye

²İzmir Kâtip Çelebi University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, İzmir, Türkiye

³Ufuk University, Faculty of Medicine, Department of Medical Biology, Ankara, Türkiye

⁴Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Türkiye

Introduction: The piperazine core, a versatile nitrogen-containing heterocyclic ring, and the kojic acid, a naturally occurring secondary metabolite, have emerged as promising candidates for the rational design of bioactive agents (Wu et al., 2019; Dong et al., 2026). Furthermore, the incorporation of a dithiocarbamate moiety, known for its strong metal-chelating and antimicrobial properties, into this hybrid system is hypothesized to exhibit enhanced biological potency.

Materials/Methods: Herein, a novel compound containing 1-piperonylpiperazine and hydroxypyranone, linked via a dithiocarbamate moiety, was synthesized, characterized and its antibacterial activity was determined against *Staphylococcus aureus* BAA-44, *Enterococcus faecalis* ATCC 29212, *Salmonella enterica* RSKK 04059, and *Escherichia coli* NCTC 13846 using the broth microdilution method (Öztürk et al., 2025). Also, the antiproliferative effect was evaluated in MDA-

MB-468 triple negative breast cancer cells using the MTT assay after 24, 48, and 72 h of treatment.

Results-Conclusion: The compound exhibited antibacterial activity with minimum inhibitory concentration values of 0.25 mM against *S. aureus*, 2 mM against *E. coli*, and 1 mM against both *E. faecalis*, *S. enterica*. The reduced susceptibility, demonstrated against *E. coli* was likely due to the intrinsic permeability barrier of the outer membrane. The compound may serve as a structural template that can be further optimized to enhance its antibacterial profile. Moreover, the compound reduced MDA-MB-468 cell viability in a concentration- and time-dependent manner, with the strongest antiproliferative effect observed after 72 h, particularly at higher concentrations. These findings suggest that the compound may have broader biological activity beyond its antibacterial profile and warrants further investigation in both antimicrobial and anticancer experimental models.

References:

1. Dong, J., Guo, T., Huang, Y., Ma, Y., Chen, W., Xue, J., Jiang, J., Dong, E., Kong, Y., Ding, H., Zhang, W., & Ma, S. (2026). *Advanced science* (Weinheim, Baden-Wurttemberg, Germany), 13(12), e12859. <https://doi.org/10.1002/advs.202512859>
2. Öztürk, İ., Karakaya, G., Tekintaş, Y., Temel, A., İstanbullu, H., & Aytemir, M. (2025). *İzmir Katip Çelebi Üniversitesi Sağlık Bilimleri Fakültesi Dergisi*, 10(2), 229-237.
3. Wu, Y., Shi, Y. G., Zeng, L. Y., Pan, Y., Huang, X. Y., Bian, L. Q., Zhu, Y. J., Zhang, R. R., & Zhang, J. (2019). *Food science and technology international = Ciencia y tecnologia de los alimentos internacional*, 25(1), 315. <https://doi.org/10.1177/1082013218793075>

Keywords: Antimicrobial, Cytotoxicity, Hydroxypyranone, Piperazine

PP23

SYNTHESIS AND ANTIBACTERIAL PROFILING OF A NOVEL 3-HYDOXYPYRIDINONE
DERIVATIVEBeyza Düzleyen¹, Gülşah Karakaya¹, Yamaç Tekintaş², Mutlu Dilsiz Aytemir³¹İzmir Katip Çelebi University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İzmir, Türkiye²İzmir Katip Çelebi University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, İzmir, Türkiye³Hacettepe University Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Türkiye

Introduction: Hydroxypyridinone (HPO) derivatives are versatile compounds known for their broad spectrum of biological activities, particularly due to their metal-chelating properties (Jiang, 2020). Similarly, dithiocarbamate (DTC) derivatives have gained attention as promising therapeutic agents with notable antimicrobial potential (Shinde, 2020). In this context, hybrid molecules combining multiple bioactive pharmacophores have emerged as a promising strategy to enhance antimicrobial efficacy and overcome resistance mechanisms which is a growing global health concern that reduces the effectiveness of existing antibiotics (Salam, 2023).

Materials-Methods: In the present study, the target compound (Figure) was synthesized from kojic acid as the starting material. Initially, the phenolic hydroxyl group was reacted with benzyl bromide, followed by pyridinone ring formation via reaction with methylamine to transform the pyrone ring to pyridinone. The resulting HPO intermediate was then reacted with sodium 4-nitrophenylpiperazine carbodithioate moiety, and the final product was obtained by crystallization. The structure of the final compound was elucidated using

spectroscopic techniques, including ¹H NMR, ¹³C NMR, and HSQC analyses. The antibacterial activities of the compound were determined against *Staphylococcus aureus* BAA-44, *Enterococcus faecalis* ATCC 29212, *Salmonella enterica* RSKK 04059, and *Escherichia coli* NCTC 13846 using the standard broth microdilution method. Ciprofloxacin was used as the control.

Results-Conclusion: The compound exhibited antibacterial activity with minimum inhibitory concentration (MIC) values of 0.125 mM against *Staphylococcus aureus* BAA-44, 0.5 mM against *Enterococcus faecalis* ATCC 29212 and 1 mM against both *Salmonella enterica* RSKK 04059 and *Escherichia coli* NCTC 13846. These results indicate species-dependent efficacy, with the highest susceptibility observed in *Staphylococcus aureus* BAA-44, while particularly *Escherichia coli* NCTC 13846, exhibited reduced sensitivity, likely due to outer membrane permeability barriers. The compound could be a promising antimicrobial alternative, especially against Gram-positive pathogens.

References

- Jiang, X., Zhou, T., Bai, R., & Xie, Y. (2020). Hydroxypyridinone-Based Iron Chelators with Broad Ranging Biological Activities. *Journal of medicinal chemistry*, 63(23), 14470–14501. <https://doi.org/10.1021/acs.jmedchem.0c01480>
- Salam, M. A., Al-Amin, M. Y., Salam, M. T., Pawar, J. S., Akhter, N., Rabaan, A. A., & Alqumber, M. A. A. (2023). Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *Healthcare (Basel, Switzerland)*, 11(13), 1946. <https://doi.org/10.3390/healthcare11131946>
- Shinde, S. D., Sakla, A. P., & Shankaraiah, N. (2020). An insight into medicinal attributes of dithiocarbamates: Bird's eye view. *Bioorganic chemistry*, 105, 104346. <https://doi.org/10.1016/j.bioorg.2020.104346>
- Öztürk, İ., Karakaya, G., Tekintaş, Y., Temel, A., İstanbullu, H., & Aytemir, M. (2025). Evaluation of Antimicrobial and Antibiofilm Effects of Kojic Acid Derivatives against Bacteria and Fungi. *İzmir Katip Çelebi Üniversitesi Sağlık Bilimleri Fakültesi Dergisi*, 10(2), 229-237. <https://doi.org/10.61399/ikcusbfd.1609257>

Keywords: Hydroxypyridinone, Dithiocarbamate, Antimicrobial activity

PP24

FROM VIRTUAL SCREENING TO NANOMOLAR HITS: IDENTIFICATION AND CHARACTERIZATION OF JANUS KINASE 1/2 INHIBITORS

Ahmet Avcı¹, Hayrünnisa Taşcı², Begüm Nurpelin Sağlık Özkan³, Birsen Tozkoparan¹, Nesrin Gökhan Keleşçi¹

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, 06100, Türkiye

²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, EBYU, Erzincan, 24100, Türkiye

³Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University, Eskişehir, 26470, Türkiye

Introduction: The Janus kinase (JAK)-signal transducer and activator of transcription (STAT) axis represents a central regulatory node in cytokine signaling and a validated therapeutic target across inflammatory and oncological diseases [1-3]. However, the current inhibitor landscape is dominated by a limited set of chemotypes, restricting chemical space exploration and highlighting the need for the identification of structurally diverse and biologically active JAK inhibitor scaffolds with improved selectivity profiles [4,5].

Materials-Methods: An integrated virtual screening workflow was applied to the InterBioScreen (IBS) database. Following drug-likeness filtering, 116,064 compounds were subjected to structure-based molecular docking using the Glide module against JAK1 (PDB ID: 4EI4) and JAK2 (PDB ID: 6VGL) [6-8]. Compounds meeting defined docking thresholds (-8.5 kcal/mol for JAK1 and -9.0 kcal/mol for JAK2) were prioritized based on binding energy and key interactions. Ligand-based methods were not applied at the initial stage to avoid bias toward known chemotypes and enable identification of structurally novel scaffolds. Instead, post-docking shape similarity analysis was performed to

support prioritization. A total of 42 compounds were selected for in vitro kinase assays. Molecular dynamics simulations (100 ns) were conducted to evaluate ligand-protein stability.

Results-Conclusion: Biological evaluation revealed a high success rate, with 20 out of 42 compounds (48%) exhibiting significant inhibitory activity ($IC_{50} < 1 \mu M$), including multiple nanomolar inhibitors, confirming the efficiency of the screening workflow. Molecular dynamics simulations provided mechanistic validation of the predicted binding modes, demonstrating persistent hinge-region interactions and stable conformational profiles throughout the simulation, indicative of a well-maintained and energetically favorable binding state. While the identified compounds retain canonical ATP-competitive binding features, structural analysis revealed multiple chemically distinct scaffolds, including 6-substituted-9H-purine, 2H-chromene, and dihydroquinoxaline frameworks. These findings highlight successful expansion of the JAK inhibitor chemical space and provide biologically validated starting points for further optimization.

References

- [1] Shawky, A.M., et al., A Comprehensive Overview of Globally Approved JAK Inhibitors. *Pharmaceutics*, 2022. 14(5).
- [2] Schwartz, D.M., et al., JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. *Nat Rev Drug Discov*, 2017. 16(12): p. 843-862.
- [3] Schindler, C. and J.E. Darnell, Jr., Transcriptional responses to polypeptide ligands: the JAK-STAT pathway. *Annu Rev Biochem*, 1995. 64: p. 621-51.
- [4] Roskoski, R., Jr., Janus kinase (JAK) inhibitors in the treatment of inflammatory and neoplastic diseases. *Pharmacol Res*, 2016. 111: p. 784-803.
- [5] Quintás-Cardama, A., et al., Janus kinase inhibitors for the treatment of myeloproliferative neoplasias and beyond. *Nat Rev Drug Discov*, 2011. 10(2): p. 127-40.
- [6] Davis, R.R., et al., Structural Insights into JAK2 Inhibition by Ruxolitinib, Fedratinib, and Derivatives Thereof. *J Med Chem*, 2021. 64(4): p. 2228-2241.
- [7] Schrödinger Release 2020-4: Glide, Schrödinger, LLC, New York, NY, 2020.
- [8] Zak, M., et al., Discovery and optimization of C-2 methyl imidazopyrrolopyridines as potent and orally bioavailable JAK1 inhibitors with selectivity over JAK2. *J Med Chem*, 2012. 55(13): p. 6176-93.

Keywords: Janus kinase inhibitors, virtual screening, molecular docking, molecular dynamics, drug discovery

PP25

DISCOVERY OF POTENT MONOAMINE OXIDASE INHIBITORS: BENZYLIDENE-THIAZOLIDINEDIONE-ACETANILIDE HYBRIDS

Aylin Balaban¹, Ahmet Avci¹, Begüm Nurpelin Sağlık Özkan², Nesrin Gökhan Kelekçi¹, Birsen Tozkoparan¹

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, 06100, Türkiye.

²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University, Eskişehir, 26470, Türkiye.

Introduction: Monoamine oxidase-B (MAO-B) is a key enzyme in the oxidative metabolism of neurotransmitters in the central nervous system and an important target for treating neurological disorders such as Alzheimer's and Parkinson's diseases. Nevertheless, the development of selective MAO-B inhibitors remains challenging, as insufficient isoform selectivity may cause unintended MAO-A inhibition, leading to adverse effects such as the tyramine-induced "cheese effect," as well as drug-drug interactions and safety concerns associated with some clinically used agents. Therefore, there is a continuing need for novel MAO-B inhibitors with improved selectivity and safety profiles. In this study, a molecular hybridization strategy was employed based on the reported MAO inhibitory activities of benzylidene-thiazolidinedione and acetanilide pharmacophores. Based on this rationale, a series of 6 novel compounds, which are expected to exhibit selective MAO-B inhibitory activity and possess the general structure of substituted benzylidene-2,4-dioxothiazolidin-3-yl acetamide, were designed and synthesized. (1–6).

Materials-Methods: The target compounds were synthesized via a multi-step pathway initiated from a key

intermediate obtained by the reaction of chloroacetic acid and thiourea in acidic condition and their structures were elucidated by IR, ¹H-NMR, ¹³C-NMR, and HRMS analyses. Molecular docking studies were performed using MAO-A (PDB ID: 2Z5X) and MAO-B (PDB ID: 2V5Z) structures with Glide software, and substituents were rationally selected based on the obtained docking interactions and binding profiles. The in vitro inhibitory activities of the synthesized compounds against MAO-A and MAO-B were evaluated using a fluorometric method, and percentage inhibition as well as IC₅₀ values were determined (7-9).

Results-Conclusion: The inhibitory activities of the synthesized compounds against MAO-A and MAO-B, along with the selectivity indices of the active derivatives, were systematically evaluated. Furthermore, binding modes and molecular interaction analyses were conducted for the most potent compounds. The results suggest that thiazolidinedione-acetamide hybrids represent promising scaffolds for the inhibition of MAO-B enzyme.

References

1. Carroll RT, Dluzen DE, Stinnett H, Awale PS, Funk MO, Geldenhuys WJ. Structure–activity relationship and docking studies of thiazolidinedione-type compounds with monoamine oxidase B. *Bioorganic & medicinal chemistry letters*. 2011;21(16):4798-803.
2. Hagenow J, Hagenow S, Grau K, Khanfar M, Hefke L, Proschak E, vd. Reversible small molecule inhibitors of MAO A and MAO B with anilide motifs. *Drug design, development and therapy*. 2020;371-93.
3. Geldenhuys WJ, Darvesh AS, Funk MO, Van der Schyf CJ, Carroll RT. Identification of novel monoamine oxidase B inhibitors by structure-based virtual screening. *Bioorganic & medicinal chemistry letters*. 2010;20(17):5295-8.
4. Edmondson DE, Binda C, Wang J, Upadhyay AK, Mattevi A. Molecular and mechanistic properties of the membrane-bound mitochondrial monoamine oxidases. *Biochemistry*. 2009;48(20):4220-30.
5. Finberg JP, Gillman K. Selective inhibitors of monoamine oxidase type B and the “cheese effect”. *International review of neurobiology*. 2011;100:169-90.
6. Youdim MB, Weinstock M. Therapeutic applications of selective and non-selective inhibitors of monoamine oxidase A and B that do not cause significant tyramine potentiation. *Neurotoxicology*. 2004;25(1-2):243-50.
7. Son SY, Ma J, Kondou Y, Yoshimura M, Yamashita E, Tsukihara T. Structure of human monoamine oxidase A at 2.2-Å resolution: The control of opening the entry for substrates/inhibitors. *Proceedings of the National Academy of Sciences*. 2008;105(15):5739-44.
8. Binda C, Wang J, Pisani L, Caccia C, Carotti A, Salvati P, vd. Structures of human monoamine oxidase B complexes with selective noncovalent inhibitors: safinamide and coumarin analogs. *Journal of medicinal chemistry*. 2007;50(23):5848-52.
9. Schrödinger Release 2020-4: Glide, Schrödinger, LLC, New York, NY, 2020.

Keywords: Benzylidene-thiazolidinedion, acetanilide, molecular hybridization, MAO inhibitor activity, molecular docking

PP26

SYNTHESIS OF NEW CHALCONE COMPOUNDS AND IN VITRO EVALUATION OF THEIR
ACTIVITY FOR MULTI-TARGETED ALZHEIMER'S DISEASE THERAPY**Ezgi Pehlivanlar Yavrucu¹, İnci Kazkayası Bölük², Vahap M. Kutluay³, Rahime Şimşek¹**¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey²Department of Pharmacology, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey³Department of Pharmacognosy, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey**Introduction:**

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, amyloid- β plaque accumulation, tau hyperphosphorylation, oxidative stress, and neuroinflammation. Because currently available therapies mainly provide symptomatic relief and do not halt disease progression, multitarget-directed ligands (MTDLs) have emerged as a promising strategy for AD treatment. Chalcone derivatives are attractive MTDL candidates due to their structural simplicity, synthetic accessibility, and ability to modulate multiple AD-related targets, including acetylcholinesterase, monoamine oxidase-B, amyloid aggregation, and neuroinflammation. In this study, a new series of chalcone derivatives was designed and evaluated as potential multi-target anti-Alzheimer agents.

Materials-Methods:

A series of novel chalcone derivatives (5a–5j) were synthesized via Claisen–Schmidt condensation and characterized by IR, ¹H-NMR, ¹³C-NMR, and HRMS. In silico drug-likeness and ADMET properties were evaluated using molecular descriptors including molecular weight, LogP, LogS, TPSA, and Veber criteria. Cytotoxicity was assessed in LPS-stimulated BV-2 microglial cells using the MTT assay at 10–250 μ M.

Anti-inflammatory activity was evaluated by measuring nitric oxide (NO) production in LPS-stimulated BV-2 cells using the Griess assay. Compounds were tested across multiple concentrations, and their inhibitory effects on NO production were compared with cell viability profiles to identify the most promising derivatives.

Results-Conclusion: All synthesized chalcone derivatives showed acceptable drug-like properties and favorable predicted CNS compatibility. Most compounds were non-cytotoxic at 10 μ M, while higher concentrations caused variable reductions in BV-2 cell viability. Compounds 5c, 5g, and 5j exhibited the most potent inhibition of LPS-induced NO production, reducing inflammatory response in a dose-dependent manner while maintaining favorable cell viability. Other derivatives showed moderate anti-inflammatory effects, whereas some compounds displayed mild cytotoxicity or non-linear responses at higher concentrations. Overall, the results indicate that chalcone derivatives, particularly 5c, 5g, and 5j, represent promising multitarget scaffolds for further development as anti-Alzheimer agents with anti-neuroinflammatory potential.

Keywords: Chalcone, synthesis, inflammation, docking

PP27

NOVEL FLURBIPROFEN-DERIVED HYBRIDS WITH COX-1/COX-2 INHIBITORY ACTIVITY

Tasneem Hosni¹, Ahmet Avcı¹, Begüm Nurpelin Sağlık Özkan², Birsen Tozkoparan¹, Nesrin Gökhan Kelekçi¹

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, 06100, Türkiye

²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University, Eskişehir, 26470, Türkiye.

Introduction: Nonsteroidal anti-inflammatory drugs remain widely used for the treatment of pain and inflammation, nevertheless, their chronic use is limited by gastrointestinal, cardiovascular, and renal adverse effects. In an effort to identify new anti-inflammatory lead compounds with enhanced activity and improved side-effect profiles, a series of flurbiprofen-based triazole-piperazine hybrids (1-6) was designed through bioisosteric modification of the carboxylic acid moiety followed by Mannich functionalization (1, 2).

Materials-Methods: The target compounds were synthesized from a flurbiprofen-derived precursor via thiosemicarbazide-mediated cyclization and subsequent Mannich reaction with appropriate piperazine compounds (3). Their structures were confirmed by IR, ¹H-NMR, ¹³C-NMR, and HRMS. Molecular docking studies were performed against COX-1 (PDB: 3KK6)(4) and COX-2 (PDB: 5KIR)(5) to support the design and interpret binding profiles. They also were subsequently

evaluated for their in vitro inhibitory activity against both isoenzymes (6).

Results-Conclusion: The synthesized compounds were evaluated for their inhibitory potential against COX-1 and COX-2 enzymes, and their selectivity profiles were assessed based on enzyme activity. The biological results demonstrated that compounds 4 and 5 ($IC_{50} = 0.206 \pm 0.009 \mu M$ and $0.456 \pm 0.020 \mu M$), respectively, exhibited stronger COX-2 inhibitory activity than the reference compound nimesulide ($IC_{50} = 1.684 \pm 0.079 \mu M$). Furthermore, the binding modes of the most active derivatives were investigated through in silico molecular docking studies. Collectively, these results highlight piperazine-functionalized flurbiprofen triazole hybrids as promising starting points for the development of improved anti-inflammatory lead structures.

References

1. Pirlamarla P, Bond RM. FDA labeling of NSAIDs: Review of nonsteroidal anti-inflammatory drugs in cardiovascular disease. Trends in cardiovascular medicine. 2016;26(8):675-80.
2. Akgün H, Aytemir M, Balkan A, Bilgin A, Çalış Ü, Dalkara S, et al. Farmasötik ve Medisinal Kimya. Hacettepe Üniversitesi Yayınları. 2021;27:904-27.
3. Avcı A, Taşci H, Kandemir Ü, Can ÖD, Gökhan-Kelekçi N, Tozkoparan B. Synthesis, characterization, and in vivo pharmacological evaluation of novel mannich bases derived from 1, 2, 4-triazole containing a naproxen moiety. Bioorganic chemistry. 2020;100:103892.
4. Rimon G, Sidhu RS, Lauver DA, Lee JY, Sharma NP, Yuan C, et al. Coxibs interfere with the action of aspirin by binding tightly to one monomer of cyclooxygenase-1. Proceedings of the National Academy of Sciences. 2010;107(1):28-33.
5. Orlando BJ, Malkowski MG. Crystal structure of rofecoxib bound to human cyclooxygenase-2. Structural Biology and Crystallization Communications. 2016;72(10):772-6.
6. Avcı A, Taşci H, Özkan BNS, Telli G, Gökhan-Kelekçi N, Özkay Y, et al. Synthesis and biological evaluation of novel naproxen-phenacetin triazole hybrids as promising anti-inflammatory agents with enhanced gastrointestinal tolerability. Bioorganic Chemistry. 2025:109000.

Keywords: COX inhibition, NSAI, flurbiprofen-hybrids, mannich

PP28

DESIGN, SYNTHESIS, AND SPECTROSCOPIC CHARACTERIZATION OF THYMOL- AND CARVACROL-BASED HYDRAZONE DERIVATIVES AS POTENTIAL ANTIBACTERIAL AGENTS

Mislina Daniştı¹, Miyase Gözde Gündüz²

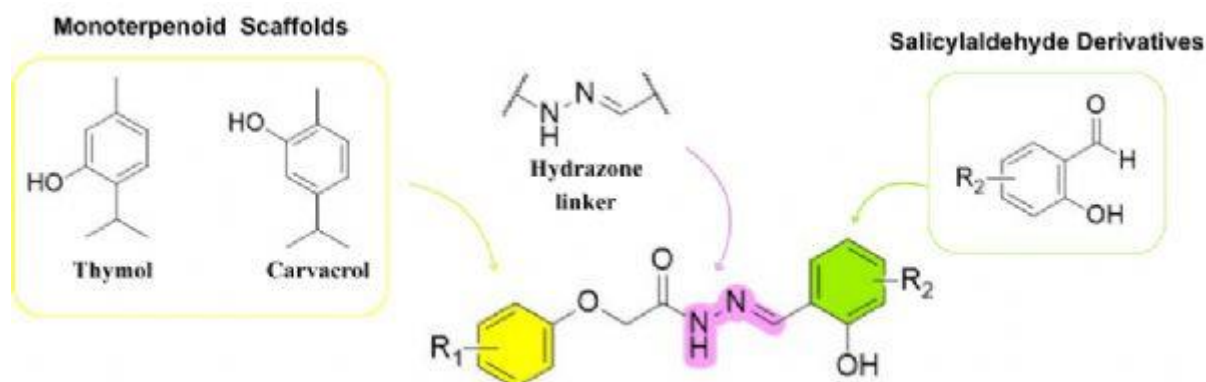
¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey; Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ankara Medipol University, Ankara, Turkey

²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey

Introduction: Bacterial infections have been reported to cause significant morbidity and mortality worldwide. Although a considerable number of compounds are available as antibacterial agents [1], the gradual increase in resistant strains has increased the need for the development of new antibacterial agents [2]. Thymol and carvacrol, two monoterpenoid compounds isolated from plants such as thyme and oregano, which belong to the *Lamiaceae* family, have been reported to exhibit antibacterial activity against various bacterial strains [3]. Similarly, it has been reported in the literature that some hydrazone derivatives of salicylaldehyde also exhibit antibacterial activity [4]. Within the scope of the present study, various salicylaldehyde derivatives linked to carvacrol and thymol through a hydrazone linker were synthesized as

potential antibacterial agents. **Materials-Methods:** The ester derivatives, obtained from the reaction of thymol/carvacrol with ethyl bromoacetate, were treated with hydrazine hydrate to prepare the corresponding hydrazide intermediates. The target compounds were then synthesized by the condensation reaction of the hydrazides with appropriate salicylaldehyde derivatives. The structural characterization of the obtained products was performed using ¹H-NMR and ¹³C-NMR spectroscopy. **Results-Conclusion:** In the present study, hydrazone derivatives of thymol and carvacrol featuring a salicylaldehyde moiety were successfully synthesized as potential antibacterial agents. Furthermore, their proposed chemical structures were confirmed by spectral techniques.

Design strategy of thymol- and carvacrol-based salicylaldehyde hydrazone derivatives



References

- [1] Pedrood K, Azizian H, Montazer MN, Moazzam A, Asadi M, Montazeri H, et al. Design and synthesis of new N-thioacylated ciprofloxacin derivatives as urease inhibitors with potential antibacterial activity. Scientific Reports. 2022; 12(1):13827.
- [2] Chattopadhyay MK, Chakraborty R, Grossart HP, Reddy GS, Jagannadham MV. Antibiotic resistance of bacteria. BioMed Research International. 2015:501658
- [3] Dong H, You Y, Wang N, Wang M, Song T, He Y, et al., Development of amphipathic derivatives of thymol and carvacrol as potent broad-spectrum antibacterial agents. European Journal of Medicinal Chemistry, 2024; 276:116716.
- [4] Pelttari E, Karhumäki E, Langshaw J, Elo H. Carbohydrazones of Substituted Salicylaldehydes as Potential Lead Compounds for the Development of Narrow-Spectrum Antimicrobials. Zeitschrift für Naturforschung C. 2007; 62(7-8):483-486.

Keywords: Antibacterial agents, Salicylaldehyde derivatives, Thymol, Carvacrol

PP29

PYRANO[2,3-*D*]PYRIMIDINE DERIVATIVES: SYNTHESIS AND EVALUATION OF ANTICANCER AND CALCIUM CHANNEL BLOCKING ACTIVITY

Ayşe Karagüzel¹, Münevver Baran², Gözde Özge Önder³, Sun Huang⁴, Gerald Zamponi⁴, Miyase Gözde Gündüz¹

¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey

²Department of Basic Science, Faculty of Pharmacy, Erciyes University, Kayseri, Turkey

³Department of General Surgery, Faculty of Medicine, Erciyes University, Kayseri, Turkey

⁴Department of Clinical Neurosciences, Hotchkiss Brain Institute and Alberta Children's Hospital Research Institute, University of Calgary, Calgary, Canada

Introduction: The development of novel heterocyclic compounds with anticancer potential continues to attract considerable attention in medicinal chemistry. Pyran- and pyrimidine-containing scaffolds are of particular interest due to their diverse biological activities. Pyrimidine derivatives are present in several approved anticancer drugs, while pyran-based compounds have demonstrated promising anticancer effects in preclinical and clinical studies (1,2). In addition, compounds containing pyran and pyrimidine rings have also been reported to exhibit calcium channel blocking activities (3,4). Based on the biological potential of these heterocyclic systems, a series of tetrahydro-2H-pyrano[2,3-*d*]pyrimidine derivatives were synthesized and evaluated for their anticancer and calcium channel blocking activities.

Materials-Methods: The target compounds were synthesized via multicomponent cyclocondensation reaction of substituted aldehydes, malononitrile, and barbituric acid or thiobarbituric acid (2). Their structures

were characterized by ¹H NMR and ¹³C NMR spectroscopy. Anticancer activities of the synthesized compounds were evaluated against HT29, MDA-MB-231, PC3, and HepG2 cell lines, while selectivity profiles were determined using L929 fibroblast cells. In addition, the blocking activities of the compounds against L-type (Ca_v1.2 and Ca_v1.3) and T-type (Ca_v3.2) calcium channels were evaluated using the whole-cell patch-clamp technique.

Results-Conclusion: The chemical structures of the synthesized compounds were confirmed by spectral methods. Among the tested compounds, some derivatives exhibited notable antiproliferative activity against the HepG2 and HT29 cell lines with favorable selectivity profiles toward L929 fibroblast cells. In addition, one of these derivatives showed activity against all tested cancer cell lines. In contrast, the compounds exhibited limited blocking activity against L-type and T-type calcium channels.

Keywords: barbituric acid, thiobarbituric acid, pyrano[2, 3-*d*]pyrimidine

PP30

NOVEL DITHIOCARBAMATE DERIVATIVES AS POTENTIAL CHOLINESTERASE INHIBITORS:
DESIGN, SYNTHESIS, AND MOLECULAR DOCKING STUDIESEbru Koçak Aslan

Ebru Koçak Aslan, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey

Introduction: Alzheimer's disease (AD) is a progressive, age-related neurodegenerative disorder characterized by memory loss, cognitive impairment, and behavioral abnormalities. Since cholinergic dysfunction and reduced acetylcholine levels are among the major pathological features of AD, cholinesterase inhibitors play a crucial role in symptomatic treatment by preventing acetylcholine degradation and enhancing cholinergic neurotransmission. Dithiocarbamates are versatile pharmacophores with a wide range of biological activities. Recent studies suggest that dithiocarbamate-containing compounds may serve as promising cholinesterase inhibitors for the treatment of AD (1,2). In this study, a series of novel dithiocarbamate derivatives were designed and synthesized as potential acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitors for the treatment of Alzheimer's disease, and molecular docking studies were performed to investigate their binding interactions within the active sites of AChE and BChE.

Materials-Methods: N-(4-(benzo[d]oxazol-2-yl)phenyl)-2-chloroacetamide was first prepared via an acetylation reaction. Subsequently, dithiocarbamate intermediates were obtained through the reaction of carbon disulfide with various secondary amines. Finally, the acetylated intermediate and dithiocarbamate derivatives were reacted to afford the target compounds. The structures of the synthesized compounds were confirmed by ¹H-NMR, ¹³C-NMR, and HRMS spectral analyses. Molecular docking studies were performed using AutoDock 4.2 to investigate the binding interactions of the synthesized compounds within the active sites of AChE and BChE. Visualisation of ligand-enzyme interactions was performed using Discovery Studio software.

Results-Conclusion: The dithiocarbamate derivatives were successfully synthesized via a multistep process. Molecular docking studies revealed favorable binding interactions of the compounds within the active sites of AChE and BChE, suggesting their potential as effective cholinesterase inhibitors.

Reference

1. Fu J, Bao F, Gu M, Liu J, Zhang Z, Ding J, et al. Design, synthesis and evaluation of quinolinone derivatives containing dithiocarbamate moiety as multifunctional AChE inhibitors for the treatment of Alzheimer's disease. *J Enzyme Inhib Med Chem*. 2020;35(1):118–28.
2. He Q, Liu J, Lan JS, Ding J, Sun Y, Fang Y, et al. Coumarin-dithiocarbamate hybrids as novel multitarget AChE and MAO-B inhibitors against Alzheimer's disease: Design, synthesis and biological evaluation. *Bioorg Chem*. 2018;81:512–28.

Keywords: Alzheimer's disease, cholinesterase inhibitors, molecular docking

PP31

DESIGN, SYNTHESIS, AND EVALUATION OF 4-(4-FLUOROBENZYL)-6-METHYLPYRIDAZIN-3(2H)-ONE DERIVATIVES AS TYROSINASE INHIBITORS**Merve Zengin¹, Esin Akdemir Yılmaz¹, Suna Sabuncuoğlu², Oya Ünsal Tan¹**¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey.²Department of Toxicology, Faculty of Pharmacy, Hacettepe University, Ankara, Turkey.

Introduction: Melanin is a key pigment responsible for skin, hair, and eye coloration and provides protection against UV-induced damage. Overactivation of tyrosinase, which catalyzes the rate-limiting step in melanin biosynthesis, is associated with dermatological disorders such as hyperpigmentation and may contribute to the development of melanoma. Accordingly, tyrosinase inhibitors have gained significant attention for both cosmetic and therapeutic applications [1]. The 4-fluorobenzyl moiety is an important structural feature that enhances the activity of synthetic tyrosinase inhibitors through interactions with active-site amino acids [2]. Likewise, the pyridazinone scaffold is widely utilized in drug design due to its straightforward synthesis under mild conditions and its ease of structural modification [3]. It is also capable of forming strong and specific interactions within the tyrosinase active site. In this study, novel 4-(4-fluorobenzyl)-6-methylpyridazin-3(2H)-one derivatives were designed and synthesized to evaluate their tyrosinase inhibitory activity. Furthermore, molecular docking studies of the compounds were performed at the active site of the tyrosinase.

Materials-Methods: 6-Methyl-4,5-dihydropyridazin-

3(2H)-one was synthesized from levulinic acid and hydrazine hydrate, followed by condensation with 4-fluorobenzaldehyde to afford 4-(4-fluorobenzyl)-6-methylpyridazin-3(2H)-one. The target 2-(5-(4-fluorobenzyl)-3-methyl-6-oxopyridazin-1(6H)-yl)-N-(aryl)acetamide derivatives were synthesized via alkylation with appropriate 2-chloro-N-arylacetamides under reflux conditions and purified by column chromatography.

The antityrosinase activities of the target compounds were evaluated using L-DOPA as the substrate, with kojic acid as the reference inhibitor. Molecular docking studies were performed using the Molecular Operating Environment with the X-ray crystal structure of mushroom tyrosinase (PDB ID: 2Y9X).

Results-Conclusion: Target compounds were obtained in good yields (70–75%), and their structures were confirmed by IR, ¹H NMR, ¹³C NMR, and mass spectrometry. Docking results supported biological activity findings through prediction of the potential binding modes and interactions of the compounds with tyrosinase enzyme.

Keywords: tyrosinase, 4-(4-fluorobenzyl)piperazine, melanin content, DPPH, molecular docking

PP32

DESIGN, SYNTHESIS, AND CHARACTERIZATION OF NOVEL BENZIMIDAZOLE DERIVATIVES FOR POTENTIAL FLAP INHIBITION

Azize Gizem Ergül¹, Paul Mike Jordan²

¹Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara, Turkey

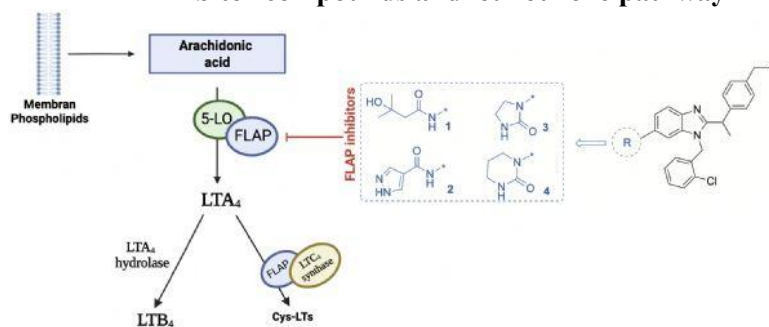
²Friedrich Schiller University Jena, Institute of Pharmacy, Department of Pharmaceutical/Medicinal Chemistry, Jena, Germany

Introduction: Leukotrienes (LTs), key metabolites of the arachidonic acid (AA) cascade, are central drivers in the pathogenesis of inflammatory disorders. 5-lipoxygenase-activating protein (FLAP) plays a critical role in this pathway by organizing AA before the 5-LO enzyme, thereby initiating leukotriene biosynthesis. Inhibition of FLAP offers a strategic advantage over direct 5-LO inhibition as it suppresses pro-inflammatory leukotrienes while allowing the synthesis of pro-resolving mediators that support tissue repair. **Materials-Methods:** Building upon BRP-7 a benzimidazole-based lead previously developed in our laboratory, we designed and synthesized four novel derivatives. Structural modifications focused on the removal of the C(5) substituent and functional diversification at the C(6) position. The structures of the

synthesized compounds were elucidated and confirmed by ¹H-NMR, ¹³C-NMR, ROESY, COSY and HRMS analyses; these analyses enabled the characterization and differentiation of 6-position benzimidazole regioisomers. Biological efficacy was subsequently assessed through leukotriene inhibition assays in human neutrophils at concentrations of 1 μM and 0.1 μM [1, 2].

Results and Conclusion: Our screening identified three derivatives capable of suppressing leukotriene formation by 44–56% at a concentration of 1 μM. These findings highlight the potential of the modified benzimidazole scaffolds as promising templates for further optimization. In conclusion, these derivatives serve as valuable lead compounds for the development of targeted therapies in chronic inflammatory conditions

FLAP inhibitor compounds and leukotriene pathway



References

1. Gür, Z.T., et al., Identification of multi-target inhibitors of leukotriene and prostaglandin E2 biosynthesis by structural tuning of the FLAP inhibitor BRP-7. *European Journal of Medicinal Chemistry*, 2018. 150: p. 876-899.
2. Banoglu, E., et al., Identification of novel benzimidazole derivatives as inhibitors of leukotriene biosynthesis by virtual screening targeting 5-lipoxygenase-activating protein (FLAP). *Bioorganic & Medicinal Chemistry*, 2012. 20(12): p. 3728-3741.

Keywords: FLAP, benzimidazole, inflammation, leukotrienes

PP33

PREPARATION AND CHARACTERIZATION OF HNO_3 -MODIFIED GRAPHENE-REINFORCED 2-HYDROXYETHYL CELLULOSE NANOCOMPOSITE HYDROGELS FOR CONTROLLED DOXORUBICIN DELIVERY

Ilayda Hatice Cakmak, Nursel Pekel Bayramgil

Department of Chemistry, Faculty of Science, Hacettepe University, Ankara, Türkiye

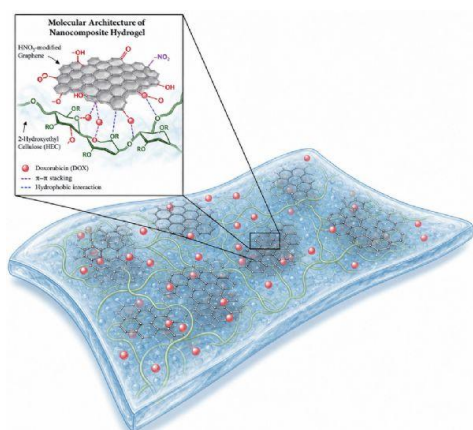
Introduction: Current cancer treatment focuses on developing drug delivery systems that enhance the therapeutic efficacy of chemotherapeutic agents while minimizing systemic side effects and preventing secondary complications. This study aims to develop nitric acid (HNO_3)-modified graphene-reinforced 2-hydroxyethyl cellulose (HEC)-based nanocomposite hydrogel films. These films are designed to overcome the challenges of burst release and systemic toxicity, which are key factors limiting the clinical application of Doxorubicin (DOX).

Materials-Methods: To improve nanoparticle compatibility and ensure homogeneous dispersion within the polymeric matrix, graphene was functionalized via nitric acid treatment. The structural, morphological, mechanical, and thermal properties of the prepared films were comprehensively characterized using FT-IR, XRD, SEM, and TGA. Furthermore, the mechanical performance of the system was determined through

tensile-elongation tests in accordance with ASTM 638 standards. Swelling behavior and in vitro release kinetics were also evaluated to complete the design of the drug delivery platform.

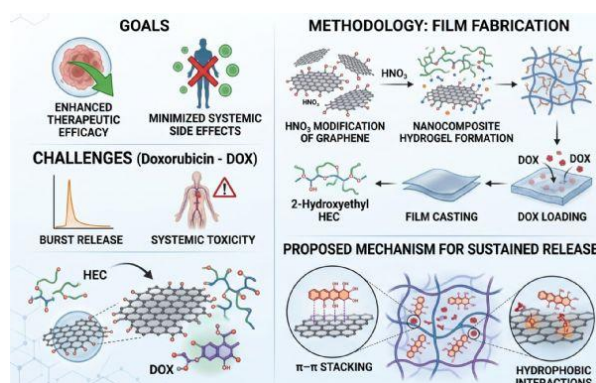
Results-Conclusion: It has been shown that strong π - π stacking interactions and hydrophobic interactions between the aromatic regions of modified graphene and DOX molecules enhance mechanical stability and can regulate the swelling behavior of the hydrogel matrix, enabling sustained drug release. As a result, this study not only presents an HEC-based carrier but also defines a new generation platform that controls polymer-drug interactions at the molecular level thanks to the HNO_3 -modified graphene. This developed 'smart' interface overcomes the systemic toxicity barrier in chemotherapy, offering a strategic solution for sustainable and patient-centered treatment protocols.

Molecular Architecture and Interfacial Interactions



Detailed view of the smart interface within the hydrogel matrix, highlighting the synergistic π - π stacking and hydrophobic interactions that ensure the controlled delivery of doxorubicin.

Research Framework: Goals, Synthesis, and Structural Design



Schematic overview illustrating the target challenges (burst release, toxicity), the step-by-step HNO_3 modification and film casting process, and the foundational release mechanism.

Keywords: doxorubicin, 2-hydroxyethyl cellulose, hydrogel, graphene, drug delivery

PP34

SYNTHESIS AND CHARACTERIZATION OF 1-PHENYL-4-(4-((2-PHENYLHYDRAZONO)METHYL)PHENYL)PIPERAZINE DERIVATIVES

Cemre Yıldız, Ezgi Pehlivanlar Yavrucu, Rahime Şimşek

Hacettepe University Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Ankara

Introduction: This study aimed to develop novel compounds capable of modulating inflammatory processes. In this context, four new hydrazone derivatives, possessing the general structure of 1-phenyl-4-(4-((2-phenylhydrazono)methyl)phenyl)piperazine and not previously reported in the literature, were synthesized, and their potential anti-inflammatory activities were investigated. Furthermore, the drug-likeness of the synthesized compounds was evaluated using in silico methods, and it was aimed to contribute to structure–activity relationship studies.

Materials-Methods: The 4-fluorobenzaldehyde, piperazine, and phenylhydrazine derivatives, as well as the solvents used in this study, were commercially obtained from Sigma-Aldrich and Merck. The target hydrazone derivatives were synthesized via a two-step synthetic procedure. In the first step, 4-fluorobenzaldehyde was reacted with appropriate piperazine derivatives in DMF in the presence of potassium carbonate to afford 4-(4-

phenylpiperazin-1-yl)benzaldehyde intermediates. In the second step, these intermediates were reacted with appropriate phenylhydrazine derivatives in methanol to yield the target hydrazone derivatives. The reactions were monitored by thin-layer chromatography (TLC), and the obtained products were purified by recrystallization. The structural characterization of the synthesized compounds was carried out using IR, ¹H-NMR, ¹³C-NMR, and high-resolution mass spectrometry (HRMS). In addition, molecular docking and in silico modeling studies of the compounds were performed using AutoDock Vina 1.5.7 software.

Results-Conclusion: As a result of the study, 1-phenyl-4-(4-((2-phenylhydrazono)methyl)phenyl)piperazine derivatives were successfully synthesized. Molecular docking studies were performed on tumor necrosis factor-alpha (TNF- α).

Keywords: Anticancer, anti-inflammatory, hydrazone, inflammation, piperazine

PP35

SYNTHESIS AND CHARACTERIZATION OF 1,3-DIPHENYLPROP-2-EN-1-ONE DERIVATIVES

Sude Naz Tulgar, Ezgi Pehlivanlar Yavrucu, Rahime Şimşek

Hacettepe University Pharmaceutical Chemistry Ankara/Türkiye

Introduction: Alzheimer's disease (AD) is a chronic and progressive disorder characterized by the impairment of cognitive functions such as memory, learning, spatial perception, language, comprehension, and reasoning ability. The aim of this study was to structurally characterize novel compounds, not previously reported in the literature, which are expected to exhibit selective MAO-B inhibitory activity by targeting the monoamine catabolism hypothesis, an important mechanism in the treatment of AD. In addition, molecular docking and in silico studies of the synthesized compounds were performed. Future studies will focus on structural modifications based on preliminary screening results and computer-aided modeling studies for the development of more potent molecules.

Materials-Methods: For the synthesis of 1,3-diphenylprop-2-en-1-one derivatives, 1 mmol of the appropriate ketone derivative and 1 mmol of the appropriate aldehyde derivative were reacted in 40% NaOH in the presence of ethanol under cold conditions.

Initially, the ketone was stirred with 0.5–1 mL of 40% NaOH solution for 20 minutes, followed by the addition of the aldehyde, and the reaction mixture was further stirred for 3–4 hours. The resulting solid product was filtered, dried, and recrystallized from suitable solvents. Structural characterization of the synthesized compounds was carried out using IR, ¹H-NMR, ¹³C-NMR, and high-resolution mass spectrometry (HRMS). In addition, molecular docking and in silico modeling studies of the compounds were performed using AutoDock Vina 1.5.7 software.

Results-Conclusion: Within the scope of this study, four compounds were synthesized and their structures were fully elucidated. The drug-likeness properties of the molecules were evaluated through in silico studies, and molecular modeling studies were also performed.

Keywords: Alzheimer's disease, Synthesis, Structural characterization

PP36

GRAPHENE-DOPED ELECTROSPUN HYDROXYPROPYLCELLULOSE (HPC) NANOFIBERS FOR TAILORING TERRAMYCIN RELEASE PROFILES

Sündüz Alemdar, Nursel Pekel Bayramgil

Hacettepe University, Faculty of Science, Chemistry Department, 06800, Beytepe, Ankara, Türkiye

Introduction: Electrospun nanofibers are promising wound dressing materials due to their high surface area, porous architecture, and capacity for controlled drug delivery. In this study, hydroxypropylcellulose (HPC) nanofibers doped with HNO₃-modified graphene were developed as a pH-responsive carrier for terramycin release.

Materials-Methods: HPC and HNO₃-modified graphene were processed by electrospinning using an in situ encapsulation approach. Terramycin-loaded nanofibers were prepared by adding terramycin to the HPC solution before the electrospinning process. The produced nanofibers were characterized by scanning electronmicroscopy (SEM), FT-IR/ATR spectroscopy, X-ray diffraction (XRD), and TGA-DSC analyses. In vitro drug release studies were performed in phosphate-buffered saline at pH 4.5 and pH 7.4 for 24 h at 36.5 °C.

Results-Conclusion: SEM analysis confirmed the formation of uniform, bead-free nanofibers. The average diameter decreased from approximately 250 nm for pure

HPC nanofibers to 186 nm after graphene incorporation, suggesting enhanced jet stretching during electrospinning. FT-IR/ATR spectra confirmed the characteristic functional groups of HPC and graphene-related vibrations, while thermal analysis indicated improved structural stability in the graphene-doped system. Drug release was strongly pH-dependent. At pH 4.5, HPC-modified graphene nanofibers released approximately 63% of terramycin within 24 h, whereas at pH 7.4, graphene incorporation reduced the release to approximately 30%, indicating a more sustained release profile. HNO₃-modified graphene-doped HPC nanofibers provided a structurally stable and pH- responsive platform for terramycin delivery. The controlled release behavior was attributed to hydrogen bonding, π - π interactions, and the barrier effect of graphene sheets within the polymer matrix. These findings suggest that HPC-modified graphene nanofibers may be promising candidates for localized antibiotic delivery in wound dressing applications.

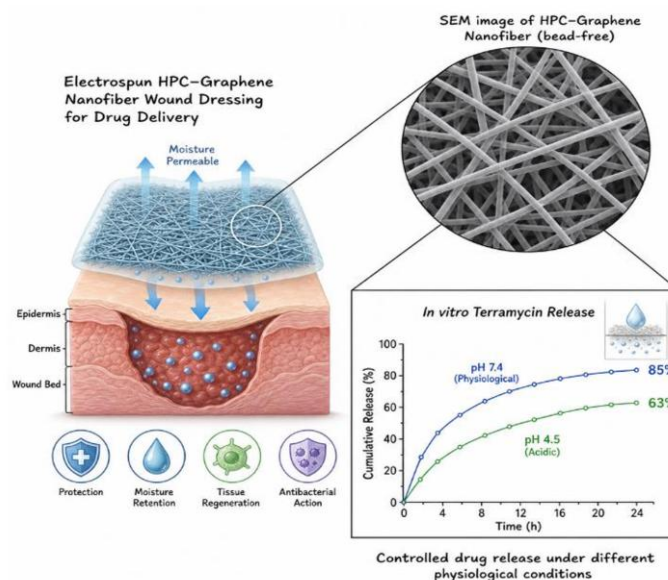


Figure 1. Schematic representation of electrospun HPC-graphene nanofibers wound dressing for controlled terramycin release, including SEM morphology and cumulative release profiles at pH 7.4 and pH 4.5.

Keywords: Electrospinning, Hydroxypropylcellulose, Modified graphene, Terramycin, Drug release

PP37

ENGINEERING ACRIDINE CHROMOPHORES INTO NIR PHOTSENSITIZERS: A FIRST-IN-CLASS STRATEGY FOR PHOTODYNAMIC THERAPY

Muhammed Ali Civaz, Çağatay Dönmez, Osman Karaman, Görkem Günbaş

Department of Chemistry, Middle East Technical University, 06800, Ankara, Türkiye

Introduction: Photodynamic therapy (PDT) is a minimally invasive treatment modality; however, its broader application is limited by the lack of near-infrared (NIR)-absorbing photosensitizers with tunable photophysical properties. Acridine-based chromophores provide a versatile platform for molecular engineering but remain underexplored in PDT applications. This study aims to design and synthesize azetidine-functionalized, brominated acridine derivatives, to investigate their NIR absorption properties, and to evaluate their potential impact on in vitro PDT efficacy.

Materials-Methods: Two azetidine-functionalized acridine derivatives, DDAN-oBr and DDAN-mBr, were synthesized starting from commercially available 9,10-Dihydro-9,9-dimethylacridine via six-step synthetic routes involving halogenation, Boc protection, and Buchwald–Hartwig cross-coupling reactions. Structural modification involves the incorporation of an azetidine donor group and controlled bromination to modulate the electronic properties of the acridine core. The absorption maxima of synthesized acridine derivatives, DDAN-oBr and DDAN-mBr, were measured with a UV-VIS spectrometer.

Results-Conclusion: The monobrominated DDAN-oBr

was obtained in 16.6% overall yield, while the dibrominated DDAN-mBr analogue was synthesized in 3.3% overall yield. Photophysical studies revealed that both derivatives exhibit NIR absorption. DDAN-oBr displayed an absorption maximum at 680 nm, whereas the dibrominated DDAN-mBr analogue showed a bathochromically shifted absorption maximum at 703 nm. Because DDAN-mBr contains an additional bromine substituent relative to DDAN-oBr, the observed red shift likely arises from the combined influence of bromination degree and substitution pattern on the electronic structure.

These findings establish brominated azetidine-functionalized acridines as a previously unexplored class of NIR-active PDT scaffolds. Ongoing studies are focused on comprehensive photophysical characterization, including fluorescence quantum yields, singlet oxygen generation efficiencies, and photostability, followed by evaluation of in vitro PDT efficacy. To decouple the effects of bromination pattern and bromine number, the synthesis of a di-ortho-brominated analog is currently underway, enabling a systematic investigation of structure-property-activity relationships.

Keywords: Photodynamic therapy, Acridine, Near-infrared dyes, Heavy-atom effect, Photosensitizers

PP38

DESIGN, SYNTHESIS, AND STRUCTURAL CHARACTERIZATION OF NOVEL HYBRID COMPOUNDS CONTAINING INDANONE AND TETRAZOLE MOIETIES

Zeliha Bilgel, Ayşenur Işgüzar, Doğukan Doyduk

Department of Chemistry, Faculty of Science, Gazi University, Teknikokullar 06500, Ankara, Turkey

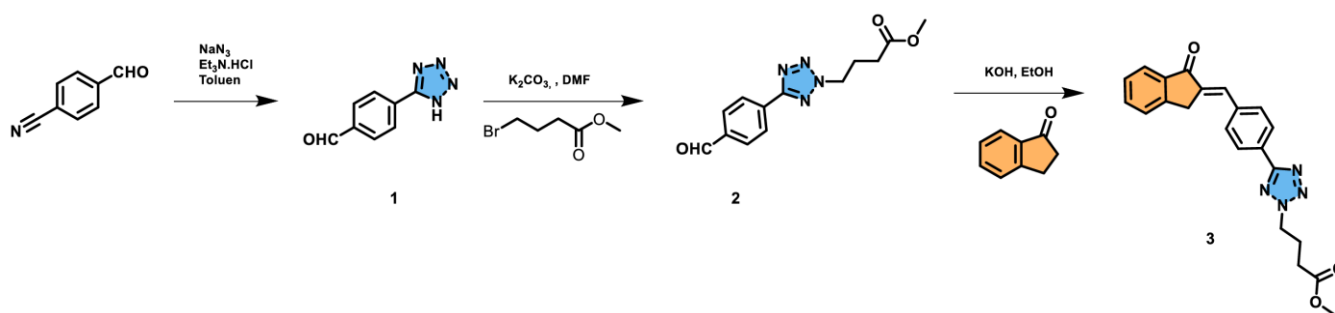
Introduction: Cancer is a disease characterized by uncontrolled cell proliferation with metastatic potential and poses a life-threatening risk if not diagnosed early. In addition to genetic mutations, environmental factors such as tobacco use, unhealthy nutrition, and radiation are among the major causes of cancer [1]. Conventional treatment methods including surgery, chemotherapy, and radiotherapy may also damage healthy cells, leading to severe side effects and decreased quality of life for patients. Therefore, cancer remains a major global health problem and continues to be a central focus of scientific research [2].

Heterocyclic compounds play a crucial role in medicinal chemistry due to their structural diversity and broad spectrum of biological activities [3]. In this context, the present study aims to synthesize novel derivatives containing indanone and tetrazole nuclei based on their known bioactive properties. Tetrazole, a stable heterocyclic ring containing four nitrogen atoms, has been reported to exhibit a wide range of biological

activities including anticancer, antibacterial, antimalarial, antifungal, and antitubercular effects [4]. Owing to its pharmacological importance, the tetrazole ring is present in several FDA-approved drugs such as oteseconazole, cilostazol, and cefamandole [5].

Indanone, an oxygen-containing scaffold frequently found in bioactive natural products, is another highly effective pharmacophore. Previous studies have demonstrated that indanone derivatives possess significant anticancer potential against various cancer cell lines [6].

Results-Conclusion: A novel derivative incorporating both tetrazole and indanone rings was designed and targeted for synthesis. The structure of the synthesized compound will be elucidated using spectroscopic techniques including FT-IR, ¹H NMR, ¹³C NMR, and HR-MS analyses. In future studies, biological activity evaluations will be carried out by relevant research groups.



Scheme 1. Synthetic Pathway for target compound

References

- 1- Yokuş, B., & Çakır, D. Ü. (2012). Kanser Biyokimyası. Dicle Üniversitesi Veteriner Fakültesi Dergisi (1), 718.
- 2- Debela, D. T., Muzazu, S. G., Heraro, K. D., Ndalama, M. T., Mesele, B. W., Haile, D. C., Kitui, S. K., & Manyazewal, T. (2021). New approaches and procedures for cancer treatment: Current perspectives. SAGE open medicine, 9, 20503121211034366

- 3- Hossain, M., Habib, I., Singha, K., & Kumar, A. (2024). FDA-approved heterocyclic molecules for cancer treatment: Synthesis, dosage, mechanism of action and their adverse effect. *Heliyon*, 10(1).
- 4- Zhang, J., Wang, S., Ba, Y., & Xu, Z. (2019). Tetrazole hybrids with potential anticancer activity. *European journal of medicinal chemistry*, 178, 341–351.
- 5- Karati, D., Sen, D., Mahanti, B., Roy, S., & Mukherjee, S. (2025). Indanone derivatives: Emerging frontiers in cancer therapy. *Synthetic Communications*, 1–22.
- 6- Yuan, Y., Li, M., Apostolopoulos, V., Matsoukas, J., Wolf, W. M., Blaskovich, M. A. T., Bojarska, J., & Ziora, Z. M. 2024. “Tetrazoles: A multi-potent motif in drug design”, *European Journal of Medicinal Chemistry*, 279, 116870.
- 7- Leoni, L. M., Hamel, E., Genini, D., Shih, H., Carrera, C. J., Cottam, H. B., & Carson, D. A. 2000. “Indanocine, a Microtubule-Binding Indanone and a Selective Inducer of Apoptosis in Multidrug-Resistant Cancer Cells”, *JNCI: Journal of the National Cancer Institute*, 92(3), 217-224

Keywords: Cancer, tetrazole, indanone, π -bridge

PP39

DISCOVERY OF NOVEL PYRANO[3,2-*b*]PYRAN DERIVATIVES AND EVALUATION OF
TYROSINASE INHIBITOR ACTIVITYMutlu Dilsiz Aytemir, Rahime Şimşek, Ezgi Pehlivanlar Yavrucu, Eren Çaltekin

Introduction: Tyrosinase is a key enzyme in melanin biosynthesis and hyperpigmentation disorders, which are frequently accompanied by chronic oxidative stress and inflammation. Although kojic acid (KA) serves as a potent tyrosinase inhibitor, its clinical application remains limited by stability constraints and toxicity issues. This study aimed to structurally design and evaluate novel KA-derived 2-amino-6-(hydroxymethyl)-8-oxo-4-phenyl-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile derivatives as multi-target agents capable of simultaneous tyrosinase inhibition and inflammatory mediation. Furthermore, extensive *in silico* molecular docking studies were performed to investigate the binding affinities of these novel compounds.

Materials-Methods: For the synthesis of novel pyrano[3,2-*b*]pyran derivatives, malononitrile, KA, and aldehyde derivatives were reacted in ethanol under reflux conditions at 90 °C for 5–6 hours using a triethylamine catalyst. The resulting solid products were filtered, dried, and recrystallized. Structural characterization of the synthesized compounds was carried out using IR, ¹H-NMR, ¹³C-NMR, and high-resolution mass

spectrometry (HRMS). In addition, molecular docking and *in silico* modeling studies of the compounds were performed utilizing Schrödinger Maestro 2025-4 software against the 2Y9X protein structure to accurately determine enzymatic interactions.

Results-Conclusions: Within the scope of this comprehensive study, novel compounds were designed. The drug-likeness properties of the molecules were evaluated through *in silico* studies, confirming zero violations of Lipinski's Rule of Five. Molecular modeling studies demonstrated that compounds EC-12 and EC-13 exhibited superior tyrosinase binding affinities (-5.369 and -5.092 kcal/mol) compared to the standard KA (-4.92 kcal/mol). Moreover, derivatives EC-17 and EC-10 showed remarkable docking scores against TNF- α , highlighting their anti-inflammatory potential. Consequently, modifying the pyrano[3,2-*b*]pyran scaffold significantly enhanced key target interactions. These novel derivatives represent highly promising, safe lead molecules for the treatment of hyperpigmentation and associated inflammatory conditions.

Keywords: Kojic acid, synthesis, tyrosinase inhibition, melasma, anti-inflammatory



AUTHOR INDEX

- A Sabbah D., 16
Akbari M., 60
Akçelik N., 23
Akdemir A., 52
Akdemir Yılmaz E., 77
Akgül Ö., 47
Aktaş Şüküroğlu A., 27
Aktemur S., 51
Alagöz M.A., 21, 46
Albayrak S., 48
Alemdar S., 82
Algül Ö., 21, 46
Angeli A., 47
Arafa R.K., 18
Arsianti A., 50
Avcı A., 67, 69, 72
Avcı A., 64
Avcı K., 34
Aykaç O., 43
Balaban A., 69
Banoğlu E., 18
Baran M., 75
Bardaweel S.K., 16
Bilgel Z., 84
Bozbey Merde I., 43
Butini S., 18
Çakmak İ.H., 79
Çalışkan K., 51
Çaltekin E., 86
Campioni G., 13
Carradori S., 17, 22
Carta F., 47
Çelik I., 56
Chankvetadze B., 17, 34
Cıngır Köker Ş., 65
Civaz M.A., 83
Danıştı M., 73
Demir O., 37
Demir Yazıcı K., 52
Demirel U.U., 55, 57, 58, 59, 60
Deynez G., 24
Dilsiz Aytemir M., 37, 65, 66, 86
Direkçi B., 58
Dökmeci G., 41
Dönmez Ç., 83
Doyduk D., 84
Đuran M., 15
Düzleyen B., 37, 66
Ebraheem Al Jomaa E., 27, 39
Elmazoglu Z., 31
Elmazoğlu Z., 32, 33
Erdoğan E.A., 32
Ergül A.G., 78
Esendağlı G., 18
Gallorini M., 22
Ghalab B., 59
Glišić B., 15
Gökhan Kelekçi N., 28, 64, 67, 69, 72
Göktaş B., 44
Gül M., 21
Gültekin S., 24
Gumustas M., 34
Gunbas G., 31
Günbaş G., 32, 33, 83
Gündüz M.G., 73, 75
Guney B., 36
Gürsoy Ş., 46
Güzel Akdemir Ö., 52
H Adu B., 42
Hajjo R., 16
Hepokur C., 21
Hosni T., 72
Huang S., 75
I Kenttamaa H., 42
Iacovozzi D., 22
İşgüzar A., 84
Isik T., 39
Jorbenadze S., 34
Jordan P.M., 78
Kalkan T., 27, 39
Kaplan O., 27
Kara A., 10, 48
Karabulbul A., 39
Karagüzel A., 75
Karakaya G., 37, 65, 66
Karaman O., 31, 32, 33, 83
Kartop R.A., 55
Kazkayası Bölük İ., 71
Kılıç İ., 65
Koçak Aslan E., 76
Koldas S., 36
Kosif K.Ö., 54
Kutluay V.M., 71
Laufer S., 17
Lengerli D., 41
Lj. Stevanović N., 15
Melizsa M., 50
Meriç A., 61
Mustanoglu E., 31
Nigiz Ş., 63
Nikodinović-Runić J., 15
Okatan N., 36
Okur U., 43
Önder G.Ö., 75
Oruc Demirbag H., 39
Özadalı Sarı K., 63
Özçelik B., 41
Özçilenk M.H., 61
Özdemir Z., 44, 45, 50
Özel Demiralp F.D., 17
Özenver N., 64
Özoğul N., 33
Öztürk S., 26
Öztürk Şen B., 56, 57, 58, 59
Paolo Busardo F., 34
Pehlivanlar Yavrucu E., 22, 27, 54, 71, 80, 81, 86
Pekel Bayramgil N., 79, 82
Pullagurla M.R., 18
Renzo G., 47
S. Hosni T., 28
Sabuncuoğlu S., 77
Sağlam O., 36
Sağlık B.N., 64
Sağlık Özkan B.N., 67, 69, 72
Sahan Fırat S., 39
Şahan Fırat S., 27
Şahin Z.S., 50
Saravanan V., 22
Sert E., 44, 50
Sevici G., 36
Sevimli Gür C., 37
Shah M.A., 17
Şimşek R., 10, 22, 27, 54, 71, 80, 81, 86
Škaro Bogojević S., 15
Stanković M., 15
Sucu N., 39
T. Supuran C., 47
Taha M., 14
Taşci H., 64, 67
Tekintaş Y., 65, 66
Tekir Ş., 33
Temiz Resitoglu M., 39

Temiz Reşitoğlu M., 27
Toprak Ö. N., 26
Tozkoparan B., 28, 64, 67,
69, 72
Trawally M., 52
Tulgar S.N., 81
Tuna F., 57
Tuncer E.B., 36
Türkmen N.B., 45

Ünsal Tan O., 77
Uslu H., 44
Vojnovic S., 15
Yalçın Z.S., 46
Yaman Ü., 37
Yaylim E.C., 39
Yigiter D., 31
Yıldız C., 80
Yılmaz D., 33

Yılmaz S., 47
Yonar R., 63
Yurdcu A. N., 23
Z Alzarieni K., 42
Zamponi G., 75
Zarrin P., 28
Zengin G., 22
Zengin M., 77
Zenni Y.N., 45



with the supports of



OFFICIAL AIRLINE OF THE CONGRESS

