Design and Synthesis of Novel Diisopropyloxalamide Derivatives and Their Docking Studies for COX Inhibitions

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Abstract

Inflammation has long been recognized as a localized protective reaction to irritation, injury or infection, characterized by pain, redness, swelling, and sometimes loss of function. There has been a new awareness of its role in a wide variety of diseases, including cancer. Several pro-inflammatory gene products have been identified that mediate a critical role in suppressing apoptosis, proliferation, angiogenesis, invasion, and metastasis. Recently, the role of cyclooxygenase (COX) inhibition in carcinogenesis has become more pronounced. It affects apoptosis, angiogenesis, and invasion and plays a role in the production of carcinogens. Generally, high levels of COX-2 expression are found in cancer cells. However, in some cancers such as prostate or breast cancer, low COX-2 expression is observed. This phenomenon is quite surprising and should influence new anticancer drug development designs.

In recent years, it is reported that thalidomide directly inhibits COX-1/COX-2 with efficacy comparable to that of the representative drug, aspirin. In our previous study, we investigated the effects of thalidomide-like molecules on TNF-α and IL6 from proinflammatory cytokines and anticancer properties.We envisage that COX might be another anticancer-related molecular target of thalidomide. In here, we investigate our new thalidomide-like molecules for COX inhibitions.

Keywords*: *Thalidomide, inflammation, oxalamide derivatives, COX inhibitions

Introduction

Tumor necrosis factor-alpha (TNF-α) and cyclooxygenase-2 (COX-2) are proteins that have key roles in immune cell activation, inflammation and cognitive function in the brain.[1]

Recent advances have shown that TNF-α and COX have also been investigated to play a key role in many different types of cancer.[2] For example, thalidomide is effective for the treatment of certain kinds of cancers, such as colon and prostate cancers, probably because of its TNF-α production-inhibiting activity and antiangiogenic activity.[3]

Prostaglandin and thromboxane biosynthesis occurs after a multi-step reaction of arachidonic acid by interacting with COX enzymes.[4]To date, COX-1 and COX-2 are known to be well defined. While COX-1 has been reported to be constitutive in many organs or tissues, COX-2 can be induced by various stimulating agents. However, molecular biological studies have shown that there are many exceptions to this simple paradigm. COX-2 has been over-stimulated in various tumors and has been shown to play a role in carcinogenesis and angiogenesis.[5,6] The effects of COX-2 inhibitors such as celecoxib, rofecoxib, and sulindac for the chemoprevention of various cancers, including colon and prostate cancers, have been investigated.[7,8]

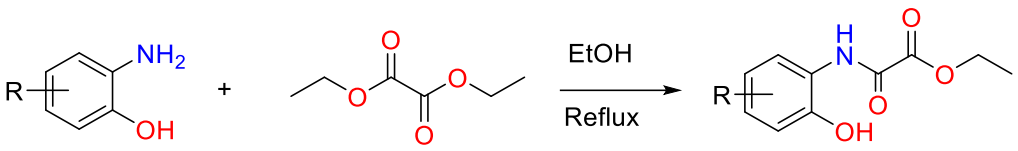
A similar situation for COX-1, experimental results showed a possible involvement of COX-1 in pain and cancer development, thereby providing a rationale for the development of selective COX-1 inhibitors.[9] Therefore, COX enzymes are thought to be a promising therapeutic target for cancer.

However, the severe side effects of COX inhibitors that can be used for this purpose indicate that the desired level of molecules has not been reached yet. For example, the clinical studies of rofecoxib, a COX-2 selective inhibitor, have recently been discontinued and it was withdrawn from the market because, in the treatment group, it caused cardiovascular diseases such as heart attack and stroke compared to the placebo group. Therefore, serious side effects of existing COX inhibitors have led to the need to investigate new molecules.

Thalidomide inhibits lipopolysaccharide-induced COX-2 expression.[10] In addition, it has recently been found that thalidomide directly inhibits COX-1 / COX-2 with comparable efficacy to representative drug aspirin.[11] As part of our ongoing research into structural development as multiple templates for the discovery of thalidomide-leading molecules, we report here molecules that may be novel COX inhibitors, which are derived from thalidomide, focusing on COX-1- and COX-2-inhibitory activities.

Results and Discussion

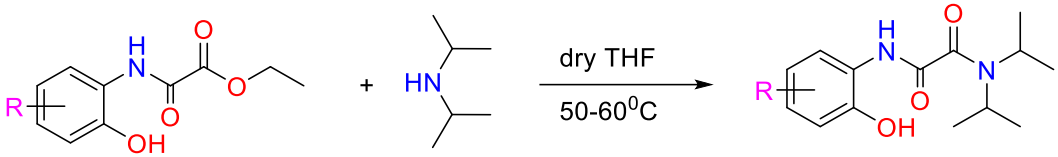
General Procedure for intermediates



R: H, CH_3,Cl, NO_2

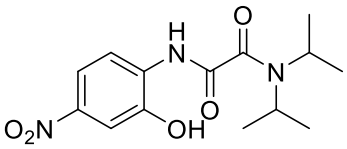
2-Aminophenol derivatives (5 mmol) were dissolved in 10 ml ethanol and diethyloxalate (7.5 mmol) was added to the reaction mixture. The mixture was refluxed for 6 hours and reaction completion was controlled with the TLC method. The reaction flask was cooled to room temperature, after observing that the starting material was finished. The solidification occurs in the solution reaching the room temperature and precipitate was filtered and washed 10 ml ethanol. The obtained solid material was dried in over 60°C overnight. All of the obtained compounds templates without any purification.

General Procedure for Diisopropyloxalamide derivatives



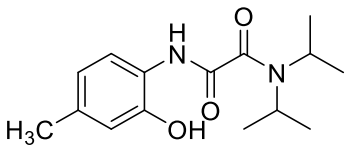
The obtained intermediates (0.5 mmol) were dissolved in 7 ml dry THF (tetrahydrofuran) by heating and diisopropylamine amine (1.2 mmol) was added to reaction mixture. The reaction flask was heated from room temperature to 50-60°C and reaction completion was controlled with TLC method. The reaction mixture was cooled to room temperatureand evaporated for under vacuum. The obtained gel material was washed with diethylether to get solid material. All of the compounds were purified with column chromatography (n-hexane:ethylacetate, 5:1).

***N^1*-(2-hydroxy-4-nitrophenyl)- *N^2*,*N^2*—diisopropyloxalamide**



Orange solid, mp: 235-240°C decomp, Yield: 92%. ^{1}H NMR (400 MHz, d_6-DMSO) δ = 10.35 (bs, 1H, OH), 8.43 (d, J=8.89 Hz, 1H, Ar-H), 7.75-7.70 (m, 2H, Ar-H), 3.33 (h, J=6.49 Hz, 2H, -CH-), 1.20 (d, J=6.49 Hz, 12H, -CH_3).^{13}C NMR (100 MHz, d_6-DMSO) δ= 163.4, 162.3, 146.9, 142.5, 133.8, 117.2, 115.8, 109.2, 46.6, 19.2.

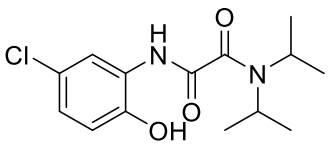
***N^1*-(2-hydroxy-4-methylphenyl)- *N^2*,*N^2*-diisopropyloxalamide**



Gray solid, mp:206-209°C, Yield: 79%. ^{1}H NMR (400 MHz, d_6-DMSO) δ =9.92 (bs, 1H, -NH), 8.72 (bs, 1H, -OH), 8.03 (d, J=8.24 Hz, 1H, Ar-H), 6.66 (d, J=1.41 Hz, 1H, Ar-H), 6.55 (dd, J=1.41, J=8.24 Hz, 1H, Ar-H), 3.32 (h, J=6.47 Hz, 2H, -CH), 2.16 (s, 3H, Ar-

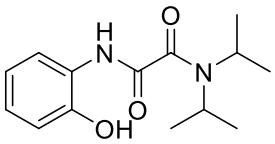
CH_3), 1.19 (d, J=6.47 Hz, 12H, -CH_3). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 163.2, 163.0, 146.4, 132.8, 124.7, 119.8, 118.7, 155.8, 46.5, 21.2, 19.2.

N^1-(5-chloro-2-hydroxyphenyl)-N^2,N^2-diisopropyloxalamide



Dark yellow solid, mp:203-205°C decomp., Yield: 86%. ^{1}H NMR (400 MHz, d_6-DMSO) δ = 10.04 (s, 1H, -NH), 9.26 (bs, 1H, -OH), 8.27 (d, J=2.38 Hz, 1H, Ar-H), 6.93-6.88 (m, 2H, Ar-H), 3.31 (h, J=6.49 Hz, 2H, -CH), 1.19 (d, J=6.49 Hz, 12H, -CH_3). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 163.0, 162.7, 145.9, 128.1, 123.2, 122.4, 117.9, 116.1, 46.5, 19.2.

N^1-(2-hydroxyphenyl)- N^2,N^2-diisopropyloxalamide

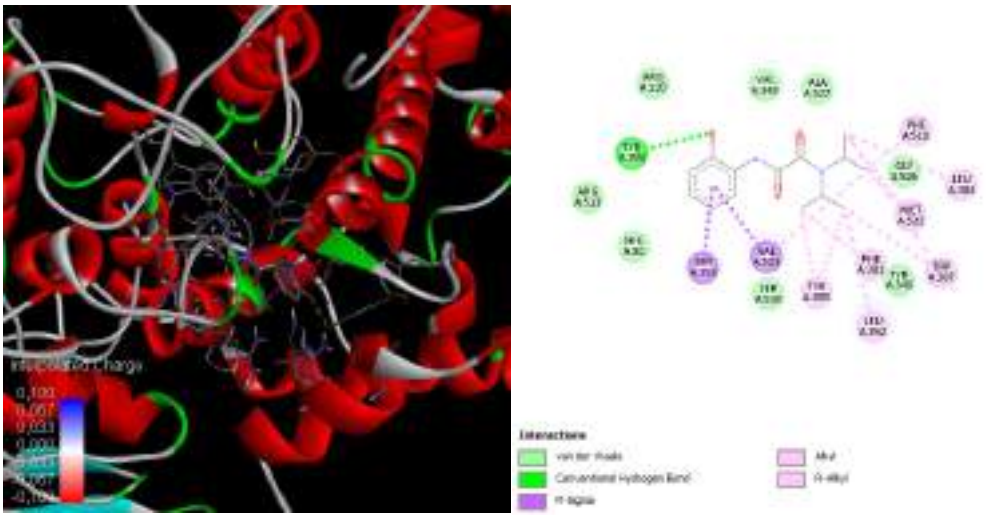


White solid, mp:204-205°C, Yield: 69%. ^{1}H NMR (400 MHz, d_6-DMSO) δ = 10.00 (s, 1H, -NH), 8.78 (bs, 1H, -OH), 8.18 (d, J=7.65 Hz, 1H, Ar-H), 6.90-6.79 (m, 2H, Ar-H), 6.77-6.69 (m, 1H, Ar-H), 3.33 (bs, 1H, -CH), 1.20 (bs, 12H, -CH_3). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 163.2, 163.0, 146.5, 127.1, 123.7, 119.4, 118.8, 115.1, 46.5, 19.2.

We have designed and synthesized new thalidomide-like derivatives based on our previous studies.[12] We performed in silico studies since different substituted diisopropyloxalamide derivatives may be effective in COX inhibition. We designed molecular docking studies to understand the ligand-protein interactions in detail (PDB code: 1CX2). By molecular docking studies with COX-2 inhibition, this showed that these compounds present the pharmacophoric requisites for COX-2 inhibition.

According to the docking results, our ligand, COX-2 active region in co-crystalline celecoxib analog in interaction with the enzyme's active residues Trp387, Try385 and Val523 with van der Waals interaction, TYR355 and hydrogen bonding was observed.
By substituting the phenyl group on the molecule, it is possible to interact simultaneously with His90 and Arg513, which can specifically inhibit COX-2.

Indeed molecular docking studies further supported the potent inhibitory activity of these molecules and further help understanding the various interactions between the ligands and enzyme active sites in detail and thereby helped to design novel potent inhibitors.



Scheme 1. 3D and 2D interactions between diisopropyloxalamide derivative and active side of the enzyme (PDB: 1CX2)

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The scientific program includes invited lectures, oral presentations, poster presentations and workshops. In particular, short oral presentations will also be exhibited as posters and thus, mutual information sharing environment will be established with more participants. In order to provide information exchange and discussion environment to the participants of the congress, it has been planned to make all poster presentations for a total of four hours during the two days of the event and to award the successful posters with the evaluation to be made by the referee committee.

Young academicians have the opportunity to present their work as "Full Text". Moreover, full-text papers to be prepared as "congress articles, will be included in the electronic congress book after the expert referees evaluate them.

The main objective of the congress is to take part in more actively and to share the knowledge and experience of the scientists involved in all processes related to medicine, that is, from drug design to its use.

It is also planned to hold a meeting in which representatives of private sector and public institutions working in this field and universities are brought together in order to conduct research and development activities more efficiently, effectively and successfully.

The "Project Collaboration Platform" which has been initiated in previous congresses and will be studied intensively in this congress, will be established to increase these collaborations.

The results of the workshop on “Where are we in the localization of medicine and what can we do? What are the duties of the stakeholders?” with the participation of the relevant institutions and organizations will be presented as a declaration.

With the awareness of the importance of the supply chain in R & D and production, we expect the suppliers of chemicals, devices and equipment that serve the sector and universities to sponsor the congress and to become an important stakeholder of this congress by informing the participants about the innovations with the workshops they will organize; and we invite them to our congress.

We hope to see you at the 8th International Congress of Drug Chemistry: Design, Synthesis, Production and Standardization of Pharmaceutical Active Substances which will be held on 27 February – 01 March 2020 at Mirage Park Resort Hotel in Kemer, Antalya and we wish that the congress will make an important contribution to all research and production scientists and to all stakeholders working in this field.

ORAL PRESENTATION PROGRAMME

Presentation Hall: Phoenix I		
POSTER NO	**Author**	**Title**
OP1	Hatice BEKÇİ	*The Effect of Sistein Carbon Dots on Cell Survival of A549 and Beas-2b Cell Lines*
OP3	Gizem DİNLER DOĞANAY	*Phosphorylation dependent interaction of pro-survival Bag-1 isoforms with MAPkinases*
OP4	Jale YILDIZ	*Identification of the Recurrent VUSs in CHEK2 Gene in Breast Cancer Patients*
OP6	Zeliha Nur YILMAZ	*In silico Molecular Docking, ADME and Druglikeness Properties of Aromatic Schiff Bases*
OP8	Gozde YENİCE CAKMAK	*Synthesis, and Molecular Docking Studies of Some Novel Benzothiazoles as HDAC Inhibitors*
OP9	Sergen GÜL	*Catalyst-free and green chemistry approach for unknown fused tetraheterocyclic skeleton*
OP10	Beyza SIMSEK	*Synthesis and Evaluation of In vitro Antiproliferative Activity of Some Bisbenzazol Derivatives as Topoisomerase Enzyme Inhibitors*
OP11	Serdal KAYA	*A New Strategy for the Synthesis of Beta- and Gamma-Carbolines*
OP12	Dilek AKBASLAR	*Synthesis and Evaluation of Antimicrobial Properties of Some Indolyl Chalcone Derivatives*
OP13	Dilek AKBASLAR	*Synthesis of Tetrasubstituted Pyrroles and Pyrrole-Based Chalcones and Investigation of Their Cytotoxic Effects on MCF-7 Cell Line*
OP14	Havva KURT	*An Investigation For New Topical Antiseptic Solution with Unknown Agents*
OP15	Yakup BUDAK	*Synthesis, characterization of hydroxyapatite and comparison with commercial hydroxyapatite sample*
OP16	Yakup BUDAK	*Anti-fungal activities of Marrubium vulgare L. different solvent extracts against plant pathogenic fungi*

OP17	Nebih LOLAK	*1,3,5-Triazin Türevi Üreido Benzen Sülfonamitlerin Sentezi, Antioksidan, Asetilkolinesteraz, Bütirilkolinesteraz ve Tirozinaz Enzim Aktivitelerinin Araştırılması*
OP18	Karina I S AMUDİ	*New Synthetic Route For Pyrazolo[1,5-a]pyrazine-2-carbohydrazide Derivative*
OP19	Büşra ÖZTÜRK AYDIN	*Synthesis Of N-Alkylated Pyrazolo[3,4-d]pyrimidin Derivatives*
OP20	İrfan KOCA	*Experimental and theoretical characterization and molecular docking studies of novel sulfonamide derivatives*
OP21	Gizem Tuğçe ULU	*The Challenges of Drug Application in Targeted Cancer Treatment and Differentiation of Cell Morphology*
OP22	Fatma ALBAYRAK	*Synthesis of Maleimide-Based Heterocyclic Molecules and Investigation of Their Anti-Cancer Activities*
OP23	Ömer Tahir GUNKARA	*Synthesis of Substituted Bis(heteroaryl)maleimide Derivatives as Glycogen Synthase Kinase-3β Inhibitors With Potential Role as Anticancer Agents*
OP24	Yaren CABBUR	*Synthesis of bicyclic aldehyde derivatives from quasi favorskii reaction; Investigation of their antioxidant activities*

Presentation Hall: Phoenix II

POSTER NO	Author	Title
OP25	Aişe ÜNLÜ	*Antimicrobial Effect of Green Synthesis of Silver Nanoparticles Using Pomegranate Peel Extract*
OP26	Burak KUZU	*Design and Synthesis of Novel 4-Methylaminopiperidine-Substituted Imidazopiridine Derivatives and Investigation of Their Antimicrobial Activities*
OP27	Burak KUZU	*Design and Synthesis of Novel Diisopropyloxalamide Derivatives and Their Docking Studies for COX Inhibitions*
OP28	Osman Nuri ASLAN	*Synthesis and anticancer activity of novel urea derivatives*
OP29	Osman Nuri ASLAN	*Synthesıs, Characterızatıon And Investıgatıon Of Bıoactıve Propertıes Of Urea Based New Hybrıd Molecules*
OP30	Mesut ŞENTÜRK	*Cytotoxic and Antiproliferative Activity of N- (4-Chlorophenyl) -1 H-Indole-2-Carboxamide on Prostate and Osteosarcoma Cell Lines.*

OP31	Saffet ÇELİK	*Determination 42 Amino Acids in Royal Jelly from Different Regions of Turkey*
OP32	Bunyamin OZGERİS	*Synthesis of Some Carbamates From Substituted Phenethylamines*
OP33	Mustafa Kemal GÜMÜŞ	*1,3-nükleofil olarak 3-amino-1,2,4-triazol'ün modifiye Biginelli reaksiyonları*
OP34	Zekiye Şeyma SEVİNÇLİ	*Design, Synthesis And In Vitro Applications Of New Types Of Cell Imaging Agents: Imidazopyridine Skeleton*
OP35	Burçin TÜRKMENOĞLU	*Synthesis of Heterocyclic Compounds and 4D-QSAR Study*
OP36	Zehra ÖKSÜZ	*Evaluation of Reverse Transcriptase Inhibitor Nucleoside Analogue Resistance Profile in HBV Patients with HCMV/EBV Coinfection*
OP37	Ufuk ATMACA	*A Safe Alternative for The Synthesis of Primary Carbamates From Alcohols*
OP38	Hamdi ÖZKAN	*1-(2-(5-(4-Sübstitüefenil)-1H-tetrazol-1-il)etil)amin Bileşiklerinin Sentezi Karakterizasyonu ve Biyolojik Özelliklerinin Araştırılması*
OP39	Ali Enis SADAK	*Live Cell Imaging*
OP40	Özge ÇAĞLAR	*Activity and stability enhancement by chemical modification of the Candida rugosa Lipase*
OP41	Elif ÖZYİLMAZ	*Immobilization of Candida rugosa lipase on Calix[4]aren functionalized water-soluble iron oxide magnetite nanoparticles for enzymatic resolution of (R,S)-Naproxen methyl ester*
OP42	Murat KIRANŞAN	*Removal of Antibiotic Drug Wastes from Aqueous Solutions by Photocatalytic Ozonation Process*
OP43	Murat KIRANŞAN	*A review on the Removal of Pharmaceutical Wastes from Aqueous Solutions under the Effect of Different Nanocomposite Catalysts of Sonocatalytic Degradation*
OP44	Mehmet KUZUCU	*Synergistic Anti-proliferative and Anti-Cancer Effects of Gambogic Acid with Capecitabine in MDA-MB-453 Human Breast Cancer Cells*
OP45	Alim SUSAM	*Towards a multi-emissive drug*
OP46	Arzu GÖBEK	*Synthesis of Flouro-Substituted Bis-Chalcone Derivatives as an Antiproliferative Agent*

Presentation Hall: Mirage I-II		
POSTER NO	**Author**	**Title**
OP47	Mehmet OGUZ	*The Synthesis of Cationic Calix[4]arene Derivatives and Evaluation of Their Cytotoxic Potential for Human Cancerous Cells*
OP48	Mehmet ERŞATIR	*Novel Coumarin-Selenophene Hybrids as Potential Antiproliferative Agents: Synthesis and Biological Evaluation*
OP49	Özgür YILMAZ	*α-C-H cyanation of tertiary amines with a new method*
OP50	Erdin DALKILIÇ	*Synthesis of Novel Molecular Clip Based on Norbornadiene Framework*
OP51	Bilal NİŞANCI	*Transition Metal Nanoparticles Supported on Metallic Aluminum Nanoparticles Intercalated Two-Dimensional Carbon Support Materials as Catalysts for the New Generation of Transfer Hydrogenation Reactions*
OP52	Bilal NİŞANCI	*A Facile and Highly Efficient Dehalogenation of Halides Catalyzed by Palladium Nanoparticles Supported on Mesoporous Graphitic Carbon Nitride*
OP53	Yusuf AKBABA	*Synthesis of Novel Symmetrical Sulfamides Derived 2-Aminotetralins*
OP54	Sinem ÜMİT	*Synthesis of bicyclic haloalcohols from ketene addition reaction; Investigation of their antioxidant activities*
OP55	İrfan ÇAPAN	*Synthesis of Potential Biologically Active Molecules; Thiosemicarbazide and 1,2,4-Triazole Derivatives Having the Carbazole Hybrid.*
OP56	Gönül YAPAR	*Based Imine Compounds*
OP57	Gönül YAPAR	*Synthesis of New Bis-Schiff Base Podands and Investigation of Their Antioxidant Activity, Biological and Anion Sensor Properties*
OP58	Nalan İmamoğlu	*The Contrast Effects of Pre- and Post- Treatment with Dexamethasone on the Expressions of Interleukin (IL)-6, IL-8 and Eotaxin-1 in Lipopolysaccharide-Stimulated BEAS-2B Cells*
OP59	Onur DEMİRKOL	*Extraction of Furanocoumarin and Coumarins by Subcritical Water Extraction from Ruta chalepensis*

OP60	Sinan BİLGİNER	*Synthesis, Cholinesterase Inhibition and Molecular Docking Studies of Novel Mannich Bases of Banzoxazolone Chalcone Compounds*
OP61	Burak ARABACI	*Determination of Sapropterin Dihydrochloride in Solid Dosage Forms by Visible Spectroscopy*
OP62	Aysun DEGIRMENCI	*Polymer Drug Conjugates for Pancreatic Cancer Therapy*
OP63	Enfal ÖZER	*Antibody-Drug Conjugates As Targeted Drug Delivery Agents*
OP64	Ümit BABACAN	*Variations of Ferulic Acid in Traditional Turkish Wheat Species*
OP65	Ümit BABACAN	*Cell Viability Effects of Ferulic Acid on Melanoma Cell Line (SK-MEL-30)*
OP66	Ümit BABACAN	*A Sensitive Determination of Cannabidiol (CBD) by HPLC*
OP67	İrem NAMLI	*An Approach for Solubility Enhancement of Poorly Water-Soluble Drug Cefdinir with Polyvinyl Alcohol*
OP68	Ülkü ÇAYKÖYLÜ	*A Review of Quantum Dot Based Nano-Biosensors*

Presentation Hall: Mirage I-II

POSTER NO	**Author**	**Title**
OP69	Salli GÜR	*Antibody Polymer-Drug Conjugates As Targeted Chemotherapy Agents*
OP70	Erbay KALAY	*Palladium Nanoparticles Assembled on Mesoporous Graphitic Carbon Nitride: A Highly Efficient Heterogeneous Catalyst for the Stille Coupling Reaction*
OP71	Malak ALIZADA	*The Synthesis of Calixarene Based Non-Toxic Fluorogenic and Colorimetric Dual-Channel Chemo-sensor and its Applications in Bioimaging*
OP72	Meltem TAN	*Novel Synthesis Method For 5,6-Substitue Heterobicyclic Compounds*
OP73	Meltem TAŞ	*Anadolu Kestane ve Narenciye Ballarının Glisemik İndeksleri*
OP74	Begüm Hazar ÇİFTÇİ	*Liquidambar orientalis reçinesinin üreaz enzim inhibisyon aktivitesi*

OP75	Göksun DEMIREL	*Metamfetamin Bağımlılığın Tedavisinde Terapötik Aday :mikroRNA- Let7b-3p*
OP76	Mine BUĞA	*Synthesis of Benzimidazole-2-Phenyl with Alkyl / Alkyloxy linker Derivatives and Their Investigation of Antiproliferative Effect*
OP77	E. Vildan BURGAZ	*Yeni 7,11-diaril-3-tiyookso-2,4-diazaspiro[5,5]undekan-1,5,9-trion Bileşiklerinin Sentezi*
OP78	Pelin VURAL	*Selectıng "Worst Case" For Equıpment Cleanıng Valıdatıon*
OP79	Efe Doğukan DINCEL	*Novel 4-thiazolidinones and 1,3,4-oxadiazoles: Synthesis, theoretical evaluation of ADME properties and docking study*
OP80	Ersin DEMIR	*The electrochemical behaviour and determination of bupivacaine ophthalmic drug by square wave voltammetry on glassy carbon electrode*
OP81	Emre ÜNLÜ	*Determination of anthrax by strong luminescence of lanthanide phosphorescence*
OP82	Şeyma OCAKÇI	*Design and synthesis of a new chemiluminogenic probe for hypochlorite*
OP83	M. Fatih POLAT	*Design, Synthesis and Determination of Bisbenzazol Derivatives for Antiproliferative and Antimicrobial Activity*
OP84	Tansu DOĞAN	*Development of Practical Electrochemical System for Phenytoin Detection*
OP85	Tansu DOĞAN	*Preparation and Characterization of Metal Oxide Nanoparticles Modified Carbon Nanotube-Conducting Polymers Based Composite Electrode For Simultaneous Determination Of Melatonin And Caffeine*
OP86	Nilgun KARASU	*Effect Of Tamoxifen-Gambogic Acid Combinations on Antiproliferative Activity in Estrogen Receptor-Positive Breast Cancer Cells*
OP87	Eren BOSTANCI	*Investigation of the Effects of BK369 Compound on Breast Cancer*
OP88	Yakup KAPTAN	*Synthesis of 3,5-Diarylsubstituted İsoxazoles as an Anticancer Agent*
OP89	Derya AKTAŞ ANIL	*Synthesis and Investigation of Anticancer Properties Fluoro Substitued Bis-Chalcone Derivatives*

OP90	Derya AKTAŞ ANIL	*Elucidation of Chemical Structures of Some Chalcones Compounds by NMR Spectroscopy*

POSTER PRESENTATION PROGRAMME

Poster No	Author	Title
P2	Hatice BEKÇİ	*The Effect of Pt-Au Bimetalic nanoparticules of Curcuma Longa extract Cell Survival of A549 and Beas-2b Cell Lines*
P5	Gizem DİNLER DOĞANAY	*Development of a Practical Capillary Zone Electrophoresis Method to Determine Charge Variant Profiles Under Forced Degradation Conditions for Monoclonal Antibodies*
P7	Zeliha Nur YILMAZ	*Investigation of Functional Models for the Catalase, Catecholase and Phenoxazinone Synthase Enzymatic Activities*
P91	Muhammed TUNEĞ	*Aromatik Yapıya Sahip Bis-Sülfonamit Schiff Bazı Türevlerinin Sentezi, Antioksidan, Asetilkolinesteraz ve Bütirilkolinesteraz Aktivitelerinin Araştırılması*
P92	Eylem Esin YÜCESOY	*Astım İlaç Etken Maddesi Olan Tomelukast'ın Benzer Bileşiklerinin Sentezi ve Yapılarının Aydınlatılması*
P93	Burçin KIVANÇ	*Comparison of Sink Condition Solubility Studies of A Direct Factor Xa Inhibitor Molecule By Traditional Solubility Methodology And Compendial Apparatus*
P94	Yonca TARAMAN	*Artvin Yöresinde Yetişen Bazı Yenilebilir Mantarların Metal Konsantrasyonu ve Toplam Fenolik İçeriğinin Belirlenmesi*
P95	Canan ALTUNTAŞ	*Yeni triazol-salisiliden Schiff bazı türevlerinin çevreye duyarlı sentezi ve yapılarının aydınlatılması*
P96	Elif Tuğçe ERDEVE	*Molecular modelling studies to identify novel inhibitors of the human 26S proteasome complex*
P97	Özlen GÜZEL AKDEMİR	*The Ongoing Quest for Selective hCA IX/XII Inhibitors*
P98	Serenay AKYOL	*Development of a Reversed Phase UHPLC Method As an Alternative of Normal Phase HPLC Method For Vitamin D3 (Cholecalciferol) 50000 IU/15 ml Oral Drop Assay Analysis*

FULL TEXTS

AUTHORS	TITLE
Burçin TÜRKMENOĞLU	4D-QSAR and Molecular Docking Studies on Some Steroidal Derivatives
Kübra DEMİR YAZICI	Inhibition of the α-class Carbonic Anhydrase from Vibrio cholerae (VchCA) with Novel Sulfonamido-based Hydrazones
Büşra CESUR	Preparation and Safety Evaluation of Nano-niosomes for Biotechnology-derived Medicinal Products and Cosmetics
Zinnet Şevval AKSOYALP	Effects of Vorapaxar Incubation on Human Left Internal Mammary Artery Endothelial Function
Aysun DEGİRMENCİ	Polymer Drug Conjugates for Pancreatic Cancer Therapy
Enfal ÖZER	Antibody-Drug Conjugates As Targeted Drug Delivery Agents
Emine Ülkü ÇAYKÖYLÜ	A Review of Quantum Dot Based Nano-Biosensors
Nalan İMAMOĞLU	The Contrast Effects of Pre- and Post-Treatment with Dexamethasone on the Expressions of Interleukin (IL)-6, IL-8 and Eotaxin-1 in Lipopolysaccharide-Stimulated BEAS-2B Cells
M. Fatih POLAT	Design, Synthesis and Determination of Bisbenzazol Derivatives for Antiproliferative and Antimicrobial Activity
Sinan BİLGİNER	Synthesis, Cholinesterase Inhibition and Molecular Docking Studies of Novel Mannich Bases of Banzoxazolone Chalcone Compounds
Salli GÜR	Antibody Polymer-Drug Conjugates As Targeted Chemotherapy Agents
Murat KIRANŞAN	Removal of Antibiotic Drug Wastes from Aqueous Solutions by Photocatalytic Ozonation Process
Meltem TAN	Novel Synthesis Method For 5,6-Substitue Heterobicyclic Compounds

Büşra ÖZTÜRK AYDIN	Synthesis Of N-Alkylated Pyrazolo[3,4-d]pyrimidin Derivatives
Onur DEMİRKOL	Extraction of Furanocoumarin and Coumarins by Subcritical Water Extraction from Ruta chalepensis
Mehmet ERŞATIR	Novel Coumarin-Selenophene Hybrids as Potential Antiproliferative Agents: Synthesis and Biological Evaluation
Dilek AKBASLAR	Synthesis and Evaluation of Antimicrobial Properties of Some Indolyl Chalcone Derivatives
İrem NAMLI	An Approach for Solubility Enhancement of Poorly Water-Soluble Drug Cefdinir with Polyvinyl Alcohol
Beyza SIMSEK	Synthesis and Evaluation of In vitro Antiproliferative Activity of Some Bisbenzazol Derivatives as Topoisomerase Enzyme Inhibitors
Dilek AKBASLAR	Synthesis of Tetrasubstituted Pyrroles and Pyrrole-Based Chalcones and Investigation of Their Cytotoxic Effects on MCF-7 Cell Line
Mine BUGA	Synthesis of Benzimidazole-2-Phenyl with Alkyl / Alkyloxy linker Derivatives and Their Investigation of Antiproliferative Effect
Zehra ÖKSÜZ	Evaluation of Reverse Transcriptase Inhibitor Nucleoside Analogue Resistance Profile in HBV Patients with HCMV/EBV Coinfection
Ufuk ATMACA	A Safe Alternative for The Synthesis of Primary Carbamates From Alcohols
Efe Doğukan DİNCEL	Novel 4-thiazolidinones and 1,3,4-oxadiazoles: Synthesis, theoretical evaluation of ADME properties and docking study
Ahmet Mesut ŞENTÜRK	Cytotoxic and Antiproliferative Activity of N-(4-Chlorophenyl) -1 H-Indole-2-Carboxamide on Prostate and Osteosarcoma Cell Lines.

Burak KUZU	Design and Synthesis of Novel Diisopropyloxalamide Derivatives and Their Docking Studies for COX Inhibitions
Tansu DOĞAN	Preparation and Characterization of Metal Oxide Nanoparticles Modified Carbon Nanotube-Conducting Polymers Based Composite Electrode For Simultaneous Determination Of Melatonin And Caffeine
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