3rd INTERNATIONAL

GPSS

GAZİ PHARMA SYMPOSIUM SERIES

GAZİ UNIVERSITY 1926

95th anniversary

Co-badged with

adsi Austrian Drug Screening Institute

EUFEPS European Federation for Pharmaceutical Sciences

08 - 10 SEPTEMBER 2021

Turkey

Organized by
Gazi University
Faculty of Pharmacy

ABSTRACT BOOK

www.gpss2021.org

Dear Colleagues,

On behalf of the organizing committee, it is my great honor and privilege to invite you to the 3rd International Gazi Pharma Symposium Series (GPSS-2021), which will be organized in Ankara (Turkey) in September 8-10, 2021 by Faculty of Pharmacy, Gazi University, one of the deep-rooted seven Pharmacy Faculties in Turkey with national accreditation. The first two of the series (GPSS-2015 & GPSS-2017) were a great success for each gathering much over 300 participants working in different scopes of pharmaceutical sciences, representatives and sponsors of global and local pharmaceutical companies as well as many reputed international plenary and invited speakers from all over the world. The third one (GPSS-2021) has been postponed to 2021 due to global COVID-19 pandemic conditions affecting whole world.

Discovery and development of drugs against human diseases involve a wide range of scientific approaches of pharmaceutical sciences. Therefore, the intention of GPSS-2021 is to emphasize the important roles of all fields related to the drug discovery and development process and also provide a wide and unique platform for international collaboration and communication opportunities in the interdisciplinary fields of pharmaceutical sciences by bringing the experts together from all over the world. The scientific program includes plenary lectures as well as oral and poster presentations delivered by all partners contributing to all fields of pharmaceutical sciences.

I would also like to mention that GPSS-2021 will be dedicated to 95th anniversary of the establishment of Gazi University, one of the pioneering universities in Turkey.

We sincerely hope and also make sure that this symposium will meet your expectations and stimulate new collaborations. Looking forward to welcoming you online in Ankara, the capital of Turkey.

Prof. Dr. İlkay ERDOĞAN ORHAN
Symposium Chairperson & Dean

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Indicated times are in GMT+3 timezone.

SEPTEMBER 8, 2021 Wednesday	
09:00-09:30	Opening remarks
SESSION-I	**Chairperson: Prof. Dr. İlkay Erdoğan Orhan**
09:30-10:05	L1 **Prof. Dr. Derya Unutmaz, USA** *"Antibody responses to SARS-CoV-2 after infection or vaccination in children and young adults with inflammatory bowel disease"*
10:05-10:40	L2 **Assoc. Prof. Dr. Urartu Özgür Şafak Şeker, Turkey** *"Living Therapeutics: The Medicine of Future"*
10:40-11:15	L3 **Prof. Dr. Horacio Perez-Sanchez, Spain** *"Big Data and Artificial Intelligence based Startups for the discovery of bioactive compounds"*
11:15-11:50	L4 **Prof. Dr. Zeliha Selamoğlu, Turkey** *"The Cellular Energy Molecule NAD + : An Antiaging Agent"*
11:50-12:25	L5 **Prof. Dr. Mohammad Abdollahi, Iran** "*Epigenetic toxicity: Danger to The Future Life*"
12:25-13:30	**LUNCH**
SESSION-II	**Chairperson: Prof. Dr. Füsun Acartürk**
13:30-14:05	L6 **Prof. Dr. Erem Bilensoy, Turkey** **"***Applications of printing technologies in pharmaceutical research and drug delivery"*
14:05-14:40	L7 **Prof. Dr. Murat Elçin, Turkey** *"Three-Dimensional Bioprinting in Regenerative Medicine and Personalized Medicine"*
14:40-15:15	L8 **Dr. Daewoo Han, USA** *"Novel electrospun nanostructure and approaches for versatile controlled drug delivery"*
Chairperson: Prof. Dr. Sevgi Takka	
15:15-15:22	O1 **Sıla Gülbağ Pınar** *"The effects of a new cyclosporine a nanosuspension on nephrotoxicity after oral administration: HK-2 cell culture and in vivo histopathological evaluation"*
15:22-15:29	O2 **Hasan Akbaba** *"RVG-modified targeted gene therapy for Alzheimer's diseases"*
15:29-15:36	O3 **Gulsah Erel-Akbaba** "*Nucleic acid loaded extracellular vesicles for targeting brain diseases"*
15:36-15:43	O4 **Gözde Ultav** *"Evaluation and characterization of folic acid modified silica nanoparticles as siRNA carriers"*
15:43-15:50	O5 **Nazlı Erdoğar** *"Evaluation of nanotechnology-based drug delivery system and monoclonal antibody for synergistic lymphoma therapy"*
15:50-15:55	Discussion part of SESSION II
15:55-16:10	**COFFEE BREAK**

SESSION-III	Chairperson: Prof. Dr. Bensu Karahalil
16.10-16.45	L9 **Prof. Dr. Lang Tran, UK** *"Smart Biomaterials and Dementia"*
16:45-17:20	L10 **Assoc. Prof. Dr. Nadja C. de Souza-Punto, Brazil** *"DNA repair defects in brains from Alzheimer's disease subjects result in mitochondrial DNA depletion but not mutation accumulation"*
17:20-17:55	L11 **Prof. Dr. Vilhelm Bohr, USA** *"DNA damage and mitochondrial dysfunction in neurodegeneration and aging. Intervention with NAD supplementation"*
17:55-18:30	L12 **Prof. Dr. Hilmi Orhan, Turkey** *"Mitochondrial biotransformations of drugs&chemicals and toxicological relevance"*
18:30-18:45	**COFFEE BREAK**
SESSION-IV	**Chairperson: Prof. Dr. Erden Banoğlu**
18:45-19:20	L13 **Assoc. Prof. Dr. Özgür Şahin, USA** *"From mechanism of resistance to drug discovery"*
19:20-19:55	L14 **Prof. Dr. Fuming Zhang, USA** *"Research Progress on Heparin and its Biomedical Applications"*
19:55-20:30	L15 **Dr. Nihal Tuğcu, USA** *"Integrated and Continuous Biomanufacturing (ICB): Technical, quality and regulatory opportunities"*

SEPTEMBER 9, 2021 Thursday	
SESSION-V	**Oral presentations**
Chairperson: Assist. Prof. Dr. Emel Çalışkan Can	
08:30-08:37	O6 **Sallahuddin Panhwar** *"Novel method for detection of Escherichia coli using smart disposable electrode from drinking water"*
08:37-08:44	O7 **Eda Büker** *"A simple UV spectrophotometric approach for monitoring favipiravir-COVID19 binding"*
08:44-08:51	O8 **Hasan Ilhan** *"SERS based on a disposable gold-cellulose nanofibril substrate for detection of E.coli"*
08:51-08:58	O9 **Çiğdem Kanbeş Dindar** *"A molecularly imprinted electrochemical sensor for selective detection of COVID-19 drug-favipiravir in biological samples"*
08:58-09:05	O10 **Şükran Öztürk** *Determination of cultivated bacteria in Inonu cave excavation soil samples: First step"*
09:05-09:12	O11 **Yalçın Erzurumlu** *"STF-083010 mediated targeting of inositol-requiring enzyme-1α/x-box binding protein-1 strongly reduced the tumorigenic abilities of prostate cancer cells"*
09:12-09:19	O12 **Hikmet Taner Teker** *"Evaluation the effects of phenylbutyric acid on obesity induced hypothalamic vascular integrity changes"*
09:19-09:25	Discussion part of SESSION V (Part 1)

Chairperson: Prof. Dr. Zeynep Şafak Teksin	
09:25-09:32	O13 **Selin Seda Timur** *"Self-emulsifying drug delivery systems for antiviral therapy"*
09:32-09:39	O14 **Mehmet Birer** *"Fabrication and characterization of methylprednisolone-loaded colon-specific 3D-printed drug delivery systems"*
09:39-09:46	O15 **Cennet Duran** *"Fabrication of 3D printable filaments using pharmaceutical polymers with high glass transition temperature"*
09:46-09:53	O16 **Juste Baranauskaite Ortasöz** *"Development and evaluation of Ginkgo biloba L. extract loaded into sodium alginate/polyvinylpyrrolidone fast dissolving sublingual films"*
09:53-10:00	O17 **Özge Eşim** "*Design and investigation of cytotoxic effect of ciprofloxacin HCl-loaded lipid-polymer hybrid nanoparticle formulations"*
10:00-10:07	O18 **Zeynep Ülkü Gün** "*Evaluation of clinical pharmacy services in pediatric nephrology service"*
10:07-10:14	O19 **Aslınur Albayrak** *"The role of the clinical pharmacist in the evaluation of drug-related problems in the intensive care unit of a university hospital in Turkey*"
10:14-10:20	Discussion part of SESSION V (Part 2)
10:20-10:40	**COFFEE BREAK**
SESSION-VI	**Chairperson: Prof. Dr. Uğur Tamer**
10:40-11:15	L16 **Assoc. Prof. Dr. Ayşegül Yıldız, Turkey** *"Speedy/RINGO: A versatile protein as a potent therapeutic candidate for neurodegenerative diseases"*
11:15-11:50	L17 **Prof. Dr. Antonia Sagona, UK** *"The use of bacteriophages for detection of infection"*
11:50-12:25	L18 **Prof. Dr. Jerome Charmet, UK** *"Multiscale Liquid Biopsy"*
12:25-13:30	**LUNCH**
SESSION-VII: Phytochemical Society of Europe (PSE) Session Chairperson: Prof. Dr. Franz Bucar, Prof. Dr. Krystyna Skalicka-Wozniak	
13:30-14:05	L19 **Prof. Dr. Franz Bucar, Austria** *"Medicinal plants for preventing campylobacter infections"*
14:05-14:40	L20 **Prof. Dr. Günther K. Bonn, Austria** *"New Analytical Methods and Strategies for Natural Product Research – Applications in Phytopharmacy, Phytocosmetics and Phytonutrition"*
14:40-15:15	L21 **Prof. Dr. Francesco Epifano, Italy** *"Recent updates on the phytochemistry and pharmacology of oxyprenylated secondary metabolites"*
15:15-15:50	L22 **Prof. Dr. Krystyna Skalicka-Wozniak, Poland** *"Isolation and neuropharmacological activity of natural products: Defining meaningful workflows"*
15:50-16:15	**COFFEE BREAK**

SESSION-VIII	**Chairperson: Prof. Dr. Mustafa Aslan**
16:15-16:50	L23 **Prof. Dr. Hugo De Boer, Norway** *"DNA metabarcoding in herbal product authentication—where are we today?"*
16:50-17:25	L24 **Prof. Dr. Jianbo Xiao, Spain** *"Stability of quercetin in cell culture"*
17:25-18:00	L25 **Prof. Dr. Young Jik Kwon, USA** *"Engineered polysaccharide nanoparticles to fight against drug-resistant pathogens"*
18:00-18:20	**COFFEE BREAK**
SESSION-IX	**Chairperson: Assoc. Prof. Dr. Aysel Berkkan**
18:20-18:55	L26 **Prof. Dr. Janet P. Engle, USA** *"Quality assurance and the role of accreditation standards in virtual pharmacy education"*
18:55-19:30	L27 **Assoc. Prof. Dr. Hale Z. Toklu, USA** *"Mentor-Mentee Relationship: A Win-Win Contract In Medical Education"*
19:30-20:05	L28 **Prof. Dr. Yahya Choonara, South Africa** *"Online Learning: A Needs-Based Pharmacy Education in the 21st Century"*
20:05-20:45	**DINNER**
SESSION-X	**Poster session**
Chairperson: Prof. Dr. Ela Kadıoğlu	
20:45-20:48	P1 **Bensu Karahalil** *"Pharmacist's knowledge and behaviors toward pharmacovigilance and adverse drug reactions reporting process in Turkey"*
20:48-20:51	P2 **Zeynep Ağlamış** *"Determination of the effects of endocrine disruptors on steroidogenesis by hormone analysis"*
20:51-20:54	P3 *CANCELED*
20:54-20:57	P4 **Elif Ince Ergüç** *"In vitro evaluation of therapeutical potential of 5-fluoro indole derivatives in estrogen-mediated mechanisms of breast carcinogenesis"*
20:57-21:00	P5 **Burak Demirhan** *"Investigation of some contaminants in baby foods"*
21:00-21:03	P6 **Bita Entezari** *"Evaluation of cytotoxic effects and therapeutical potential of novel 3,3'-diindolylmethane derivatives on breast cancer cells"*
21:03-21:06	P7 **Ceren H. Bozmaoğlu** *"Development of HPLC method for the determination of opioid antagonist used in the treatment of opioid disorder"*
21:06-21:10	Discussion part of SESSION X (Part 1)

Chairperson: Assist. Prof. Dr. Serdar Tort	
21:10-21:13	P8 **Naçize Gökçe** *"Determination of pharmaceutical care needs of COVID-19 patients in the 1st wave of pandemic"*
21:13-21:16	P9 **Beyza Torun** *"Evaluation of a clinical decision support system for the determination of inappropriate drug use in elderly at community pharmacy setting-preliminary report"*
21:16-21:19	P10 *CANCELED*
21:19-21:22	P11 **Beyza Tütüncü** *"Investigation of the anxiety and knowledge levels of individuals: The role of pharmacist"*
21:22-21:25	P12 **Enes Zeybek** *"Determination of the knowledge level of pharmacists about Alzheimer Disease"*
21:25-21:28	P13 **Songül Tezcan** *"Knowledge and attitudes of community pharmacists about drug use in pregnancy"*
21:28-21:31	P14 **Songül Tezcan** *"Evaluation of drug-drug interactions in elderly patients with chronic disease"*
21:31-21:35	Discussion part of SESSION X (Part 2)

SEPTEMBER 10, 2021 Friday	
SESSION-XI	**Poster session**
Chairperson: Assoc. Prof. Dr. Aysun Özdemir	
09:00-09:03	P15 **Dilara Çalışkan** *"Investigation of biofilm forming ability in Escherichia coli isolates isolated from children's park"*
09:03-09:06	P16 **Gökalp Çetin** *"The effects of new substituted hexahydroquinoline derivatives on cytotoxicity, intracellular oxidation and inflammation mediators in human hepatoma cell line"*
09:06-09:09	P17 **Ceren Güney** *"The association between ANGPTL8 and PI3K-MTOR-PPAR expressions in adipose tissue of high-fructose-fed rats: the modulatory effect of kefir"*
09:09-09:12	P18 **Nesime Inci Güner** *"Investigation of antidepressant-like efficiency of tangeretin and related mechanisms"*
09:12-09:15	P19 **Nur Banu Bal** *"The effect of resveratrol and regular exercise on the cardiac oxidative stress and adrenergic responses in the hypertension"*
09:15-09:18	P20 **Esin Kargıoğlu** *"A potential senotherapeutic drug: theophylline restores the doxorubicin-induced senescent cell morphology in A549 cells"*
09:18-09:21	P21 **Feyza Alyu** *"Chlorogenic acid alters potassium conductance in dorsal root ganglion neurons"*
09:21-09:27	Discussion part of SESSION XI

SESSION-XII	**Oral presentations**
Chairperson: Prof. Dr. Ufuk Koca Çalışkan	
09:35-09:42	O20 **N. Yağmur Diker** *"Evaluation of secondary metabolite profiling in five Ulmus species with untargeted metaolomics study"*
09:42-09:49	O21 **Tuğçe Dikpınar** *"LC-MS/MS analysis and biological activities of endemic Achillea sieheana stapf from Turkey"*
09:49-09:56	O22 **Çiğdem Kahraman** **"***Acetylcholinesterase inhibitory potential and metabolic profile of Bolboschoenus maritimus (L.) palla"*
09:56-10:03	O23 **Gökşen Dilşat Durbilmez** **"** *Isolation of silk protein and synthesis/characterization of hybrid nanoflowers***"**
10:03-10:10	O24 **Semih Bulut** *"The problem of pyrrolizidine alkaloid in herbal tea used in children's gas pain"*
10:10-10:17	O25 **Burak Temiz** *"Evaluation of radical scavenging activity and tyrosinase inhibition of some Citrus species cultivated in Turkey via spectrophotometric methods and HPTLC-effect directed analysis"*
10:17-10:24	O26 **Şüheda Rumeysa Osmanlioğlu Dağ** **"***Composition and antimicrobial activity of the essential oils of five different Artemisia L. Species"*
10:24-10:31	O27 **Zekiye Ceren Arituluk** *"Neuroprotective effects of selected Salvia species from Turkey in paraquat-induced Parkinson's disease Drosophila model"*
10:31-10:38	O28 **Joanna Kowalczyk** *"Scoparone – a compound of liquors containing Artemisia species influence on emotional state evaluated in Swiss mice"*
10:38-10:45	O29 **Tuğbanur Tüysüz** *"In vivo and in vitro anti-Inflammatory potentials of Abies cilicica (Ant. & Kotschy) Carr. subsp. Isaurica Coode & Cullen essential oil: a potential active pharmaceutical ingredient (Api) for topical drug delivery systems"*
10:45-10:50	Discussion part of SESSION XII (Part 1)
Chairperson: Prof. Dr. Gonca Çakmak	
10:50-10:57	O30 **Esra Şumlu** *"Dietary fructose and kefir supplementation change the composition of fecal microbiota in the rats"*
10:57-11:04	O31 **Sahika Guner** *"The comparison of vascular endothelial and smooth muscle cells co-culturing in hydrogel-base and bio-printing 3D-cell-culture systems"*
11:04-11:11	O32 **Nur Banu Bal** *"The effect of 4-phenylbutyric acid on the hypertension induced cardiac stress responses"*
11:11-11:18	O33 **Seçkin Engin** *"Trimetazidine attenuates cyclophoshamide-induced cystitis in mice by inhibiting TLR4/NFκB signaling pathway"*
11:18-11:25	O34 **Roger Ortiz-Climent** *"Paraoxonase 1 status in psychiatric patients treated with psychotropic drugs"*

11:25-11:32	O35 **Alev Tascioglu Aliyev** *"Targeting estrogen related pathways against breast cancer"*
11:32-11:39	O36 **Kevser Taban Akça** *"Cytotoxic activity and phytochemical analysis of Lecokia cretica (Lam.) DC."*
11:39-11:46	O37 **Etil Güzelmeriç** *"Comparative evaluation on the chemical compositions, antioxidant, anti-inflammatory and analgesic activities of Cistus creticus, C. salviifolius and C. laurifolius hydroalcoholic extracts"*
11:46-11:53	O38 **Hande Yüce** *"Evaluation of dose-dependent effects of some natural compounds on breast cancer cell lines"*
11:53-12:00	Discussion part of SESSION XII (Part 2)
12:00-12:15	**COFFEE BREAK**
SESSION-XIII	**Chairperson: Assoc. Prof. Burak Demirhan**
12:15-12:50	L29 **Prof. Dr. Kezban Candoğan, Turkey** *"Developing Functional Meat Based Formulations for Dysphagic Individuals Using 3D Food Printing"*
12:50-13:25	L30 **DVM Naziru Tuferu, UK** *"Understanding and safe guarding the integrity of halal food for the consumer"*
13:25-14:20	**LUNCH**
SESSION-XIV	**Chairperson: Prof. Dr. Sultan Baytaş**
14:20-14:27	O39 **Joseph M. Hayes** *"Computational design and in vitro validation of potent glycogen phosphorylase inhibitors"*
14:27-14:34	O40 **Tugce Gur Maz** *"2(3H)-Benzoxazolone derivatives as potential fatty acid amide hydrolase (FAAH) inhibitors"*
14:34-14:41	O41 **Abdurrahman Olgac** *"Computational insights into the binding pattern of microsomal prostaglandin E-2 synthase type 1 inhibitors"*
14:41-14:48	O42 **Demokrat Nuha** *"Synthesis of novel thiazole derivatives as 6-aminopenicillanic acid mimics and evaluation their antimicrobial activity"*
14:48-14:55	O43 **Ebru Didem Coşar** *"Synthesis of novel hydrazinecarbothioamide derivatives containing naphthalene ring and anticancer studies"*
14:55-15:02	O44 **Muhammed Ihsan Han** *"Synthesis and antimicrobial evaluation of new naproxen 1,2,4-triazole-thiosemicarbazide hybride derivatives"*
15:02-15:10	Discussion part of SESSION XIV
15:10-15:30	**COFFEE BREAK**
SESSION-XV	**Poster session**
Chairperson: Assoc. Prof. Dr. Fatma Nur Tuğcu Demiröz	
15:30-15:33	P22 **Ceyda Tuba Sengel-Turk** *"Application of design of experiment approach for optimization of piroxicam loaded polymeric based nanocarriers"*
15:33-15:36	P23 **Zeliha Duygu Özdal** *"Preparation and evaluation ondansetron HCl loaded polymeric nanoparticles"*

15:36-15:39	P24 **Ayça Güngör Ak** *"Evaluation of the analgesic activity of berberine phytosome"*
15:39-15:42	P25 **Alper Kan** *"Development of risk analysis based formulation in the development of generic oncology drug mitomycin 20 mg powder for solution for injection/infusion"*
15:42-15:45	P26 **Bülent Samancı** *"In vitro release study of polyphenolic compound for dermal drug delivery"*
15:45-15:48	P27 **Kenan Can Tok** *"Optimization of LC method for the determination of fluticasone propionate from drug delivery systems"*
15:48-15:51	P28 **Sinan Özer** *"Phase solubility studies, preparation and characterization of inclusion complexes of butoconazole nitrate with α-cd and hp-α-cd"*
15:51-15:54	P29 **Gülsel Yurtdaş Kırımlıoğlu** *"Preparation and characterization of inclusion complexes of antifungal drug isoconazole nitrate with β-cd obtained by freeze-drying and spray drying methods"*
15:54-15:57	P30 **Gülsel Yurtdaş Kırımlıoğlu** *"Development and in vitro characterization of pegylated PLGA nanoparticles encapsulating oseltamivir phosphate as an anticancer drug carrier system"*
15:57-16:00	P31 **Tuğçe Turan** *"Preparation of chitosan tripolyphosphate and chitosan sulfobutyl-ether-β-cyclodextrin nanoparticles for oral insulin delivery"*
16:00-16:05	Discussion part of SESSION XV (Part 1)
Chairperson: Assoc. Prof. Dr. Sibel İlbasmış Tamer	
16:05-16:08	P32 **Burcu Timur** *"Development of in vitro lipolysis-permeation method to estimate oral absorption of exemestane-loaded lipid-based formulation"*
16:08-16:11	P33 **Özge İnal** *"A new perspective for dexpanthenol orally disintegrating films through design of experiment approach"*
16:11-16:14	P34 **Seval Olğaç** *"Comparison of tablet splitting techniques for dosing accuracy of nebivolol tablets: hand splitting versus tablet cutter and knife"*
16:14-16:17	P35 **Duygu Yılmaz Usta** *"Development and validated of UV spectrophotometric and HPLC method of bosentan monohydrate for in vitro and ex-vivo samples"*
16:17-16:20	P36 **Seval Olğaç** *"Structure-guided selection of suitable nanoemulsion formulation components for a recombinant form of human interleukin-2 (aldesleukin)"*
16:20-16:23	P37 **Duygu Yılmaz Usta** *"Modeling and comparison of in vitro dissolution profiles of bosentan monohydrate: commercial tablet vs s-snedds tablet"*
16:23-16:26	P38 **Zeynep Şafak Teksin** *"Solid-state characterization studies of bosentan-loaded solid self-nanoemulsifying drug delivery system (s-snedds) comprising of Neusilin® US2"*
16:26-16:29	P39 **Burcu Timur** *"In vitro characterization of exemestane-loaded self-nanoemulsifying drug delivery system containing medium chain mono and diglycerides"*

16:29-16:32	P40 **Emre Tunçel** *"Evaluation and fabrication of dissolving PVA-diclofenac sodium microneedles"*
16:32-16:35	P41 **H. Hande Aydın** *"Preformulation studies of tofacitinib citrate loaded microspheres intended for intra-articular administration"*
16:35-16:40	Discussion part of SESSION XV (Part 2)
Chairperson: Assoc. Prof. Dr. Perihan Gürbüz	
16:40-16:43	P42 **Görkem Tanrıover** *"Determination of pyrrolizidine alkaloids in galactagogue herbal teas"*
16:43-16:46	P43 **Kevser Ayçiçek** *"Phtochemical and biological activity investigations on Hypericum sechmenii Ocak&O. Koyuncu"*
16:46-16:49	P44 *CANCELED*
16:49-16:52	P45 **Süleyman Yur** *"Phenolic profile, minerals and antioxidant capacity determination of olive leaf and seeds according to different extraction techniques"*
16:52-16:55	P46 **Dudu Altıntaş** *"Phytochemical and biological activity investigations on Heptaptera triquetra"*
16:55-16:58	P47 **Damla Kırcı** ***"Time dependet microbial transformation of hesperidin by Aspergillus niger"***
16:58-17:01	P48 **Fatma Sezer Senol Deniz** *"Development of plant-based dermocosmetic products using efficacy and safety tests with 2D/3D cell culture methods"*
17:01-17:04	P49 **Damla Kırcı** *"Microbial transformation of quercetin by 25 different microorganisms"*
17:04-17:07	P50 **Merve Atay** *"LC-Q-TOF-MS Quantification of ginkgotoxin of Gingko biloba L. –containing dietary supplements sold in Turkey and in the plant sample naturalized in Turkey"*
17:07-17:10	P51 **Mizgin Ermanoglu** *"Investigation of antioxidant activity of different extracts from Achillea goniocephala"*
17:10-17:15	Discussion part of SESSION XV (Part 3)
Chairperson: Prof. Dr. Burcu Çalışkan	
17:15-17:18	P52 **Selen Gozde Kaya** *"SIRT2 inhibitory activities of N-aryloxyphenyl-2-(arylthio)acetamide derivatives"*
17:18-17:21	P53 **Ahmet Bugra Aksel** *"N-(5-arylmethyl-1,3,4-oxadiazole-2-yl)-2-(arylthio)acetamide as a new scaffold for developing small-molecule SIRT inhibitors"*
17:21-17:24	P54 **Mahmut Gozelle** *"Discovery of 5-benzyl-1,3,4-oxadiazole/thiadiazole-2-carboxamides as potential leads for selective SIRT2 inhibition"*
17:24-17:27	P55 **Ayca Dedeoglu Erdogan** *"Some new 2,5-disubstituted 1,3,4-oxadiazole and and 3,6-disubstituted-7H-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine derivatives with in vitro anti-inflammatory activity"*

17:27-17:30	P56 **Jülide Cansu Karakoç** *"Synthesis and in vitro anti-inflammatory activity of some new 1,3,4-oxadiazole derivatives"*
17:30-17:33	P57 **Gülnur Arslan** *"Microwave synthesis of benzothiazolone-2(3H)-3-acetyl-2-(substitue/nonsubstitueindol or pyridine)hydrazone derivatives"*
17:33-17:36	P58 **Sultan Nacak Baytas** *"The first preparation of bioengineered low molecular weight heparin from a remodeled bovine intestinal heparin"*
17:36-17:39	P59 **Sümeyye Turanli** *"Novel piperazinyl urea derivatives as potential fatty acid amide hydrolase (FAAH) inhibitors"*
17:39-17:42	P60 *CANCELED*
17:42-17:45	P61 **Rahime Şimşek** *"Synthesis, characterization, crystal structure and DFT analysis of benzyl 4-[2-fluoro-4-(trifluoromethyl)phenyl]-2,6,6-trimethyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate"*
17:45-17:50	Discussion part of SESSION XV (Part 4)
17:50-18:10	**COFFEE BREAK**
Chairperson: Assoc. Prof. Dr. Tuba İnceçayır	
18:10-18:13	P62 **Aysel Yılmaz** *"The antimicrobial effect of r-limonene nanoemulsion on enterococcus faecalis"*
18:13-18:16	P63 **Cennet Duran** *"Evaluation of the effect of infill density and tablet geometry on disintegration of 3D printed tablets"*
18:16-18:19	P64 **Ayşegül Yıldız** *"Optimization and validation of silk fibroin production process"*
18:19-18:22	P65 **Mahmut Ozan Toksoy** *"Nasal permeability studies of rasagiline mesylate loaded solid lipid nanoparticles in a thermoreversible mucoadhesive gel"*
18:22-18:25	P66 **Özlem Çulcu** *"Optimizing cryoprotectant type and ratio for lyophilization of nanosuspensions"*
18:25-18:28	P67 **Sevgi Tektaş** *"Design and in vitro characterization of in situ forming controlled release implants of a narcotic antagonist drug"*
18:28-18:31	P68 **Emre Yalçın** *"Development, characterization and in vitro evaluation of nanoemulsion containing megestrol acetate"*
18:31-18:34	P69 **Nebahat Durmaz** *"Studies on formulation optimisation of hyaluronic acid coated chitosan nanoparticles loaded with hydrocortisone acetate"*
18:34-18:37	P70 **Beril Taş** *"Validation of an HPLC method for the determination of talazoparib from nanoparticle formulations"*
18:37-18:40	P71 **Eylül Su Saral Acarca** *"Development and characterization of electrospun nanofibers containing rutin and copper nanoparticles"*
18:40-18:45	Discussion part of SESSION XV (Part 5)

Chairperson: Assist. Prof. Dr. N. Başaran Mutlu Ağardan	
18:45-18:48	P72 **Güler Keskin** *"Development and characterization of voriconazole loaded organogel formulations for vaginal delivery"*
18:48-18:51	P73 **Şeyma Adatepe** *"Investigation of various critical process and formulation parameters of nanosuspensions including indomethacin"*
18:51-18:54	P74 **Emine Saldamlı** *"Vitamin D-loaded poly(l-lactic acid) nanoparticular implants improves osseointegration"*
18:54-18:57	P75 **Esra Kodan** *"In vitro release and ex vivo penetration studies of bigel systems containing ciclopirox"*
18:57-19:00	P76 **Dilara Şahin** *"Preparation, optimization, and in-vitro evaluation of naringenin loaded microemulsion formulations for anti-aging purposes"*
19:00-19:03	P77 **Sinem Saar** *"Development and optimization of electrospun PVA nanofibers for vaginal drug delivery using design of experiment method"*
19:03-19:06	P78 **Deniz Onan** *"Development of controlled released quercetin microemulsion based gel system for topical application: An in vitro evaluation"*
19:06-19:09	P79 **Esra Pezik** *"Preparation of carbamazepine solid dispersions and determination of solubility"*
19:09-19:12	P80 **Emine Yıldırım** *"Development and characterization studies of hydrocortisone loaded Eudragit-based colon targeted nanofibers"*
19:12-19:15	P81 **Esra Pezik** *"Determination of the effects of different carriers on in vitro cytotoxicity of carbamazepine solid dispersions"*
19:15-19:20	Discussion part of SESSION XV (Part 6)
Chairperson: Assoc. Prof. Dr. Fatma Sezer Şenol Deniz	
19:20-19:23	P82 *CANCELED*
19:23-19:26	P83 **Enes Tekman** *"Antimicrobial activity of different parts of Colchicum speciosum steven (Colchicaceae)"*
19:26-19:29	P84 **Tuğba Günbatan** *"Chymotrypsin and urease inhibitory activities of some plants used as folk medicine in Duzce (Turkey)"*
19:29-19:32	P85 **Joanna Kowalczyk** *"Scoparone blood-brain-barrier penetration and endocannabinoids related mechanism underlying its activity"*
19:32-19:35	P86 **Bilge Aydın** *"Antioxidant capacity and phenolic composition of Colchicum speciosum steven (Colchicaceae)"*
19:35-19:38	P87 **Nurten Abacı** *"Evaluation of acetylcholinesterase inhibitory and DPPH radical scavenging activity of Geranium and Erodium taxa from Turkey"*

19:38-19:41	P88 **Tuğsen Doğru** "Evaluation of resveratrol content of some Polygonum L. species growing in Turkey"
19:41-19:44	P89 **Tuğbanur Tüysüz** "*Phytochemical investigation of Eremostachys moluccelloides bunge*"
19:44-19:47	P90 **Kübra Öğüt** "*Biological activities of the extracts and essential oils of Scabiosa pseudograminifolia hub.- mor.*"
19:47-19:50	P91 **Duygu Sevim** *"Studies on anticholinesterase and antioxidant effects of Turkish pistachio"*
19:50-19:55	Discussion part of SESSION XV (Part 7)
Chairperson: Assist. Prof. Dr. Etil Güzelmeriç	
19:55-19:58	P92 **Ayşenur Karademir** *"Phytochemical and bioactivity studies on Nepeta congesta Fisch. & Mey. var. congesta Fisch. & Mey."*
19:58-20:01	P93 *CANCELED*
20:01-20:04	P94 **Buket Aksu** *"History of medicine"*
20:04-20:07	P95 **Suheda Rumeysa Osmanlioglu Dag** "*Determination of artemisinin in five Artemisia L. species (Asteraceae) that grown in Turkey"*
20:07-20:10	P96 **Burçin Özüpek** "*Enzyme inhibitory effects and phytochemical studies of some medicinal plants cultivated in Turkey"*
20:10-20:13	P97 **Perihan Gürbüz** "*Chemical constituents of Pulicaria armena boiss. & Kotschy ex boiss. (Asteraceae); an endemic turkish species"*
20:13-20:16	P98 **Hülya Tuba Kıyan** "*Lavandula x intermedia Emeric ex Loisel essential oil-loaded topical cream suitable for dermacosmetic use: preparation, characterization, in vitro biological activity*"
20:16-20:19	P99 *CANCELED*
20:19-20:22	P100 **Buket Aksu** *"The position of herbal drugs in compounding"*
20:22-20:25	P101 **Hülya Tuba Kıyan** *"Topical cream containing Ruta montana L. essential oil: preparation, characterization, in vitro and in vivo biological activity"*
20:25-20:28	P102 **Sultan Pekacar** "*Enzymes inhibitory of various metabolism diseases and phytochemical studies on Pistacia eurycarpa yalt."*
20:28-20:35	Discussion part of SESSION XV (Part 8)
Chairperson: Prof. Dr. Eda Şatana Kara	
20:35-20:38	P103 **Aysel Berkkan** *"Determination of alcohols in beverages based on direct extraction by head space gas chromatography-flame ionisation detection"*
20:38-20:41	P104 **Tuğba Nur Akbaba** *"Method development for selenium nanoparticle determination and characterization using single particle inductively coupled plasma mass spectrometry"*

20:41-20:44	P105 **Merve Yıldız** *"Determination of rivastigmine by using molecularly imprinted solid-phase extraction"*
20:44-20:47	P106 **Derya Ünal** *"Analytical method validation of HPLC assay method for developing of a peptidomimetic generic drug containing icatibant 30 mg"*
20:47-20:50	P107 **Mehmetcan Bilkay** *"Synthesis of l-cysteine mediated copper nanoclusters as a turn-off fluorescent probe for the detection of indigotine"*
20:50-20:53	P108 **Aysu Yurdasiper** *"Validation of high performance liquid chromatographic method for the analysis of dry powder inhaler containing fluticasone propionate"*
20:53-20:56	P109 **Tilbe Çevikelli** *"Development and validation of a new HPLC-PDA method for determination of peptide DAPTA (d-ala-peptide t-amide)"*
20:56-21:00	Discussion part of SESSION XV (Part 9)
21:00	**Award ceremony and closing remarks**

Lectures: 30 + 5 (Q&A) = 35 min
Oral presentations: 7 min
Poster presentations: 3 min

L1

ANTIBODY RESPONSES TO SARS-COV-2 AFTER INFECTION OR VACCINATION IN CHILDREN AND YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE

Joelynn Dailey[1], Lina Kozhaya[2], Mikail Dogan[2], Dena Hopkins[1], Blaine Lapin[1], Katherine Herbst[1], Michael Brimacombe[1], Kristen Grandonico[1], John Schreiber[1], Bruce Tsan-Liang Liang[3], Juan C. Salazar[1], Derya Unutmaz[2], Jeffrey S. Hyams[1]

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[2]Jackson Laboratory for Genomic Medicine, Farmington, CT
[3]University of Connecticut, School of Medicine, Pat and Jim Calhoun Cardiology Center, Farmington, CT

Characterization of antibody response to SARS-CoV-2 infection or vaccination in children and young adults with inflammatory bowel disease (IBD) receiving biologic therapies has implications for patient management during chronic inflammatory disease. To characterize the antibody response to SARS-CoV-2 infection and current SARS-CoV-2 vaccines in subjects with IBD receiving immunosuppressive treatments receiving infliximab or vedolizumab, we performed a prospective longitudinal cohort study evaluating SARS-CoV-2 Spike protein receptor binding domain (S-RBD) IgG positivity. A sensitive and high-throughput neutralization assay that incorporates SARS-CoV-2 Spike protein onto a lentivirus and measures pseudoviral entry was also used. Of 472 patients with IBD treated in our infusion center, 44 (10%) of enrolled subjects had SARS-CoV-2 S-RBD IgG antibodies. Compared to non-IBD adults (ambulatory) and hospitalized pediatric patients with PCR documented SARS-CoV-2 infection, S-RBD IgG antibody levels were significantly lower in the IBD cohort and by 6 months post infection most patients lacked neutralizing antibody. Following vaccination (n=33) patients had a 15-fold higher S-RBD antibody response in comparison to natural infection, and all developed neutralizing antibodies to both wild type and variant SARS-CoV-2. In conclusion, the lower and less durable SARS-CoV-2 S-RBD antibody response to natural infection in IBD patients receiving biologics may put them at risk of reinfection. The robust response to immunization is reassuring and likely protective in this population

L2

LIVING THERAPEUTICS: THE MEDICINE OF FUTURE

Urartu Özgür Şafak Seker[1]

[1]*Bilkent University, National Nanotechnology Research Center, Ankara*

Modern biology increased our comprehension on inner working of cells deep down to proteins and molecules which provide mechanistic explanations for diseases. Although basic research continues expand our knowledge on biology, current information can be harvested to diversify our therapeutic intervention against many diseases. As an example, reprogramming of living cells as therapeutics leads a paradigm shift in medicine because cells far exceeds drawbacks of molecule-based drugs especially exerting spatial and temporal therapeutic action on predefined manner. Cells can be engineered to sense a particular small molecule or protein as a signal mechanistically linked with a disease condition, and synthesize an output molecule which can be used by physicians to diagnose and/or monitor prognosis of this particular disease. These cells can be further modified to delivery therapeutic molecules upon sensing a signal at desired time and site. In addition, logical operations, signal recording, and many other functions can be reprogrammed inside the cells for sophisticated actions. In Synthetic Biosystems Laboratory in Bilkent University, we are developing novel genetic circuitries to enhance capability of cells as therapeutics. This talk, I will explain development of cellular devices that can used for treatments of cancer and diabetes. These cellular devices include cellular targeting and protein secretion circuitries developed in our laboratory.

L3

BIG DATA AND ARTIFICIAL INTELLIGENCE BASED STARTUPS FOR THE DISCOVERY OF BIOACTIVE COMPOUNDS

Horacio Pérez-Sánchez[1]

[1]*Universidad Católica de Murcia (UCAM), Spain*

We report in this talk the novel computational drug discovery techniques based on Big Data and Artificial Intelligence techniques developed in the Structural Bioinformatics and High Performance Computing Research Group (BIO-HPC) from UCAM Universidad Católica de Murcia (https://bio-hpc.eu) and which have been used successfully in several projects and how they are offered now through our Start-up.

L4

THE CELLULAR ENERGY MOLECULE NAD+: AN ANTIAGING AGENT

Zeliha Selamoglu[1]

[1]*Nigde Omer Halisdemir University, Faculty of Medicine, Department of Medical Biology, Nigde, Turkey*

Nicotinamide adenine dinucleotide (NAD+) has essential functions in metabolism. NAD+ is an oxidizing agent and it accepts electrons from other molecules and becomes reduced. The balance between the oxidized and reduced forms of NAD is called the NAD+/NADH ratio. In metabolism, NAD+ is involved in redox reactions, carrying electrons from one reaction to another, therefore, found in two forms in cells. This ratio is an important component of what is called the redox state of a cell, a measurement that reflects both the metabolic activities and the health of cells. NAD+ is also involved in fundamental metabolic processes including glycolysis, the citric acid cycle, and mitochondrial oxidative phosphorylation leading to energy production. NAD+ has been shown to be the key substrate for poly(ADP-ribosyl)polymerases, NAD+ glycohydrolases, and histone deacetylases known as sirtuins. These enzymes have been termed 'NAD+' consumers, and are involved in modulation of DNA repair, maintenance of intracellular calcium homeostasis and immunological roles, and epigenetically modulated gene expression. Gene silencing by sirtuins has been shown to extend lifespan in yeast and small mammals. In conclusion, researchers focus on the metabolism of NAD+ is used by the body as area of intense researches on unravelling the secrets of our cellular 'energy sensor' NAD+ for promoting healthy ageing. Therefore, researches in the last two decades have shown that NAD+ is more than a mere regulator of metabolism, but rather may play a key role in the ageing process.

Keywords

Anti-ageing, Cellular energy, Coenzyme, Metabolism, NAD+.

L5

EPIGENETIC TOXICITY: DANGER TO THE FUTURE LIFE

Mohammad Abdollahi[1]

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Epigenetic toxicity has become one of the major global concerns endangering creatures' life. Environmental factors like metals, pesticides, bisphenols, nanomaterials, E-waste, etc., can regulate gene expression without DNA mutations via unique molecular mechanisms. DNA methylation, histone modifications such as histone methylation or acetylation, and non-coding RNAs' (ncRNAs) effects, are the main mechanisms these toxicants work. The clinical translation could be seen given the increased incidence and prevalence of some diseases, particularly lung and autoimmune diseases, cardiovascular diseases, cancers, osteoporosis, and hepatitis. These environmental factors' short and long-term effects can be further categorized in six important domains: prenatal and carcinogenesis effects, respiratory diseases, women's and men's reproductive system effects, and endocrine disruptions. What makes the condition even worse is the probable epigenetic heredity to offspring or further generations, and hence, epigenetic footprints will thoroughly change global health status. To improve public and specialists' knowledge, mechanisms of epigenetic toxicity will be primarily indicated in this seminar. Along with a piece of updated clinical information on the role of epigenetics in the etiology of the aforementioned diseases, as well as transgenerational and intergenerational effects of environmental toxicants will be stated. We will also discuss epigenetic-based medications in clinical and preclinical phases, paving the way to overcome this significant issue shortly.

L6

APPLICATIONS OF PRINTING TECHNOLOGIES IN PHARMACEUTICAL RESEARCH AND DRUG DELIVERY

Erem Bilensoy[1]

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Personalized medicines and flexible pharmaceutical manufacturing has been under focus since the last decade following the approval of the first 3D printed pharmaceutical product as a fast disintegrating tablet of levetiracetam in 2015 for the treatment of epileptic seizures. Inkjet printing and 3-dimensional printing allow the pharmaceutical researchers to develop rapidly disintegrating, highly soluble dosage forms as well dose and combination adjusted products that can be designed to fit personalized [1]. This lecture will focus on different types of printing technologies that can be applied to pharmaceutics and discuss examples of pharmaceutical dosage forms and drug eluting implants that are based on printing technologies [2]. Critical quality attributes of printed dosage forms as well as opportunities and challenges associated with this technology in the pharmaceutical field will be discussed in the light of current literature, patents, clinical trials and regulatory advances [3].

The studies covered in this lecture were supported by TUBITAK Starting Grant 114S793 and TUBITAK Research Grant 119S809.

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L7

THREE-DIMENSIONAL BIOPRINTING IN REGENERATIVE MEDICINE AND PERSONALIZED MEDICINE

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Regenerative medicine aims to repair or restore damaged or lost tissues and organs to their former functional state. This requires precise positioning of cells of interest in a three-dimensional (3D) biomimetic microenvironment that allows physiological processes to occur. In the last two decades, significant advances have been made in stem cell culture technologies and in the field of biomaterials. Besides, various tissue engineering approaches have been developed over the years, many involving manual, time-consuming and technically demanding processes. 3D printing technology has led to a paradigm shift in manufacturing processes in various industrial fields. More recently, the integration of 3D printing into tissue engineering is expected to bring innovative solutions for important biomedical and health problems. The 3D bioprinting involves assembling cells, bioactive proteins and compatible hydrogels into living functional tissues through automated fabrication. A current focus is the development of specialized cell-friendly hydrogels, called bioinks, suitable for this process. Another focus is the search for printing methods that are less damaging to cells. Despite a great deal of research, it seems that this technology is not yet mature enough for its safe and widespread use in regenerative medical applications. On the other hand, 3D bioprinting allows for the construction of anatomically and physiologically accurate 3D biological structures. Therefore, 3D bioprinted in vitro tissue models already show great potential for advancing drug development and personalized medicine.

L8

NOVEL ELECTROSPUN NANOSTRUCTURE AND APPROACHES FOR VERSATILE CONTROLLED DRUG DELIVERY

Daewoo Han[1], Serdar Tort[2], Andrew J. Steckl[1]

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[2]Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey

Nanofibers formed by (coaxial) electrospinning represent an attractive material system for novel drug delivery platforms for medical applications (tissue engineering, wound dressing, cancer therapy). Especially, advanced core-sheath structured nanofibers formed by coaxial electrospinning provides very promising benefits such as (a) combining two material properties effectively, (b) controlling release kinetics of incorporated drugs, (c) protecting incorporated drugs from harsh environment, etc [1]. A long-term release of encapsulated drugs with minimal/no initial burst release is a key demonstrated aspect for many biomedical applications. Recent direction is including multi-drug delivery for the synergistic effects and conditional "on-demand" release. Our advanced coaxial/triaxial nanofiber membranes successfully demonstrated (a) dual drug release with different kinetics [2], (b) stimuli-triggered release using self-immolative polymer (SIP) in sheath [3], (c) tri-phasic pH responsive drug release ("no release; sustained release; quick release") within physiological pH range [4], and (d) localized long-term delivery of anti-cancer drugs against malignant glioblastoma multiforme [5]. In addition to the use of unique core-sheath nanofiber structure, novel approaches can be utilized to deliver the drug more effectively and conveniently. We have demonstrated the unique drug delivery approaches using various routes such as nanoparticle coated microneedles [6], nanofibrous patches for transdermal delivery [7], and self-inflating membrane for oral drug delivery [8].

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L9

SMART BIOMATERIALS AND DEMENTIA

Lang Tran[1]

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Dementia is a major concern in our aging society. Alzheimer's Disease (AD) is the most popular form of dementia. Currently, there is only a handful of treatments for AD and they can, at best, only slow down the progress of the disease. The main problem of AD is that its origins are unknown and current research only focus on the dysfunction of the neuron. Thus, it is necessary to re-evaluate the current evidence on AD and deduce what are the likely origins of this disease and especially its relation to the Aging process: The biggest risk factor for AD. In this presentation, the progress of AD, its association to Aging will be outlined. Next, the potential intervention at different stages of the disease process will be discussed. Of clear importance is the use of biomaterials for advanced therapy. The need of biomaterials which are theragnostic is paramount. The use of biomaterials for imaging (i.e. identifying the area of the cerebral vasculature where the lesions are located) and drug delivery- i.e. targeting the keys receptors over expressed in these areas (e.g. RAGE, VCAM) and releasing anti-inflammatory a pro wound healing compounds – will be discussed.

L10

DNA REPAIR DEFECTS IN BRAINS FROM ALZHEIMER'S DISEASE SUBJECTS RESULT IN MITOCHONDRIAL DNA DEPLETION BUT NOT MUTATION ACCUMULATION

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[1]*Universidade de São Paulo, Instituto de Química, Depto. de Bioquímica, SP, CEP05508-000, Brazil*

Alzheimer's disease (AD) is is expected to affect over 50 million people worldwide by 2050. Accumulation of oxidative DNA damage has been found in both nuclear and mitochondrial DNA (mtDNA). Lower nuclear DNA repair has also been demonstrated, but mitochondrial DNA repair had not been specifically investigated. Here we investigated whether alterations in base excision repair (BER) activity correlate with mtDNA stability in age-matched cognitively normal, AD and asymptomatic AD (asAD) subjects, who show neuropathological AD features but remained cognitively normal. Nuclear and mitochondrial BER activities, mtDNA mutation frequency and mtDNA copy number were measured in cerebellum and temporal cortex from postmortem brains from 10 individuals from each experimental group, using in vitro incision assays and random mutation capture assay. Significantly lower uracil DNA glycosylase activity was detected in nuclear and mitochondrial extracts from AD, but not asAD, subjects when compared with age-matched controls. In contrast, nuclear and mitochondrial AP endonuclease activity was similar in all groups. Nonetheless, no differences were found in mtDNA mutation frequencies in any group. On the other hand, a significant decrease in mtDNA copy number was found in temporal cortex from AD brains but not from asAD subjects. Our results suggest that lower mitochondrial BER activity does not result in increased mutagenesis, but rather in depletion of mtDNA in early affected brain regions, which correlates with cognitive impairment during AD development.

L11

DNA DAMAGE AND MITOCHONDRIAL DYSFUNCTION IN NEURODEGENERATION AND AGING. INTERVENTION WITH NAD SUPPLEMENTATION

Vilhelm A Bohr[1]

[1]*National Institutes of Health, National Institute on Aging, Section on DNA repair, USA*

We find that some DNA repair defective diseases with severe neurodegeneration have mitochondrial dysfunction. Our studies involve cell lines, the worm (c.elegans), and mouse models and include the premature aging syndromes Xeroderma pigmentosum group A, Cockaynes syndrome, Ataxia telangiectasia and Werner syndrome. It also includes models of Alzheimers Disease, which I will discuss. We find a pattern of hyperparylation, deficiency in the NAD+ and Sirtuin signaling and mitochondrial stress, deficient mitophagy. are pursuing mechanistic studies of this signaling and interventions at different steps to improve mitochondrial health and neurodegeneration. I will discuss intervention studies in these disease models including a new Alzheimer mouse model using NAD supplementation. NAD supplementation stimulates mitochondrial functions including mitophagy and stimulates DNA repair pathways. Based on human postmortem material and IPSC cells we identify mitophagy defects as a prominent feature in Alzheimers disease (AD). Using c.elegans AD models we screened for mitophagy stimulators and identified compounds that subsequentially also show major improvement of AD features in mouse models. We are exploring senescence and cGAS-STING signaling pathways, which will be discussed.

L12

MITOCHONDRIAL BIOTRANSFORMATIONS OF DRUGS&CHEMICALS AND TOXICOLOGICAL RELEVANCE

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[1]*Ege University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, 35040 Bornova-Izmir, Turkey*

Mitochondria have distinct properties compared to any other organelle in mammalian cell. These unique properties have been well in accordance with the hypothesis that mitochondrion was once a bacterium that invaded a monocellular organism, and both evolved to a mutual existence. Among various distinctions, discovery of mitochondrial forms of the xenobiotic metabolizing enzymes provoked discussions if mitochondria metabolize drugs and other chemicals to some extent. It has also been shown that various drugs enter mitochondria by different mechanisms, and this translocation is believed to be responsible for mitochondrial effects as part of their therapeutic actions. Nevertheless, potential adverse effects of parent drugs or their metabolites can not be ruled out. In case of in situ generated metabolite(s) adversely interacts with either critical structures or functions of mitochondria, various toxic outcomes may appear. To address this issue, studies have been started in 80'ies. However, insufficient purity of mitochondrial fractions represented a limiting factor for elucidating whether this organelle has metabolic capacity towards xenobiotics. These technical difficulties were overcome by alternative purification approaches and in turn, relevant data have been accumulated to date. Examples vary between mitochondrial bioactivation of aflatoxins to carcinogenic epoxide derivatives, neuroactive drugs, Parkinson's disease-inducing compound MPTP, and antischizophrenic clozapine. Occurence, involved enzymes, metabolites and various toxic endpoints in these pathways will be summarized in this lecture.

Keywords

Mitochondria, Bioactivation, Reactive intermediates, Oxygen consumption, Mitochondrial protein synth

L13

FROM MECHANISMS OF RESISTANCE TO DRUG DISCOVERY

Ozgur Sahin[1]

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Our laboratory focuses on elucidating the molecular mechanisms of drug resistance and metastasis using systems biology approaches. We combine our expertise in functional transcriptomics/proteomics, cancer cell biology and drug discovery with those of the experts from medicinal chemistry, pathology, and bioinformatics to develop novel cancer therapeutics against targets conferring drug resistance in aggressive cancers. In this seminar, I will first talk about overcoming chemotherapy resistance in triple negative breast cancer (TNBC), the most aggressive breast cancer subtype. We identified hypoxia-induced ECM re-modeler, lysyl oxidase (LOX) as a key inducer of chemoresistance, and we showed that inhibiting LOX overcomes chemoresistance. Currently available LOX inhibitors suffer from lack of specificity and high toxicity. To identify more potent and selective LOX inhibitors, we performed a high-throughput screen (HTS) of a diversified small-molecule library and performed structure-activity relationship (SAR) analyses and optimized our lead compound for more potent activity and better drug-like properties. In the second part of the seminar, I will talk about identification and characterization of our potent transforming acidic coiled-coil 3 (TACC3) inhibitor in highly aggressive cancers. Here, we identified a new TACC3-targeting chemotype, BO-264 which demonstrated remarkable antiproliferative activity via spindle assembly checkpoint-dependent mitotic arrest, DNA damage, and apoptosis in the NCI-60 cell line panel. Importantly, BO-264 significantly impaired tumor growth in highly aggressive, treatment-refractory breast and colon cancer mouse models without any major toxicity. These studies led to partnership with pharma industry to develop this chemotype to a more drug-like molecule through ADME, PK and other detailed studies.

L14

RESEARCH PROGRESS ON HEPARIN AND ITS BIOMEDICAL APPLICATIONS

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Heparin is a highly sulfated, complex polysaccharide and widely applied as clinical anticoagulant with more than 100 tons of heparin used annually. A projected global market for heparin is expected to reach approximately $16.3 billion by 2025. This talk presents the progress of heparin related glycoengineering/glycomics/interactome studies, include: i) Enzymatic generation of highly anticoagulant from bovine intestinal heparin: we converted bovine intestinal heparin (BIH), which has a low anticoagulant activity, to USP heparin by the treatment with 6-*O*-sulfotransferases and/or 3-*O*-sulfotransferase; ii) Heavy heparin: A stable isotope-enriched, chemoenzymatically-synthesized, poly-component drug: in this work, we chemoenzymatically synthesized perdeuteroheparin from biosynthetically enriched heparosan precursor obtained from microbial culture in deuterated medium. Chemical de-*N* acetylation, chemical *N*-sulfation, enzymatic epimerization, and enzymatic sulfation with recombinant heparin biosynthetic enzymes afforded perdeuteroheparin comparable to pharmaceutical heparin. iii) Alzheimer's disease related glycomics/interactome research; iv) Application of heparin in the treatment of COVID-19.

L15

INTEGRATED AND CONTINUOUS BIOMANUFACTURING (ICB): TECHNICAL, QUALITY AND REGULATORY OPPORTUNITIES

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There has been increasing momentum recently in the biopharmaceutical industry to transition from traditional batch processes to next generation integrated and continuous biomanufacturing. This transition from batch to continuous is expected to offer several advantages which, taken together, could significantly improve access to biologics drugs for patients. During this presentation, industry progress towards establishing an ICB toolbox along with critical technology advancements that will enable ICB will be shared. Sanofi's motivation on ICB has been very focused and ICB has been shown to enable fast to market strategies. ICB not only offers increases in productivity, but also helps with quality attribute control. Given the reduced scale of operations and having development and manufacturing at the same scale, ICB offers advantages towards minimizing technology transfer risks and help delay time to investment while accelerating time to market. Case studies will be shared to highlight advantages associated with ICB.

L16

SPEEDY/RINGO: A VERSATILE PROTEIN AS A POTENT THERAPEUTIC CANDIDATE FOR NEURODEGENERATIVE DISEASES

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Although the mechanisms of neurodegeneration are not clearly elucidated, disruption of intracellular calcium balance due to various reasons and the resulting DNA damage are observed as the most important factors leading neurons to apoptosis upon p53 activation. Speedy/RINGO, a cell cycle protein different from conventional cell cycle regulators and first shown in Xenopus oocytes, controls CDK2 activity and G1-S phase transition during cell cycle. While performing this function, unlike classical cyclins, it does not require CDK2 phosphorylation and it is not sensitive to inhibition through phosphorylation by p21Cip1 and p27Kip1. With this characteristic, the Speedy/RINGO protein is known for its p53-dependent oncogenic function, which inhibits the functioning of DNA damage signaling proteins and suppresses DNA damage checkpoints through cell cycle, avoiding cancer cells from apoptosis and maintaining cell division. Considering this function in cancer cells, we used the Speedy/RINGO protein with a different approach to protect degenerated post-mitotic neurons from apoptosis by transfecting and overexpressing it in primary neurons. We observed that neurons overexpressing Speedy/RINGO and that were forced into calcium-based degeneration did not degenerate despite the increased amount of p53. Thus, Speedy/RINGO protein with this feature was first introduced by us as an alternative to prevent neuronal death in neurodegenerative diseases. We continue examining the mechanism of neuroprotective action of Speedy/RINGO from different aspects which will pave the way to select the right molecular targets for both diagnosis and treatment of many neurodegenerative diseases such as Alzheimer's, Parkinson's, ALS and spinal cord injury.

L17

THE USE OF BACTERIOPHAGES FOR DETECTION OF INFECTION

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The problem of antimicrobial resistance is serious and new approaches are necessary to tackle this. One of these, is the use of bacteriophages -viruses that can specifically attack their host bacteria. Bacteriophages, due to their great specificity towards their host, can also be used as diagnostics of bacterial infection. The early diagnosis of infection is crucial, both because it can save lives, but also as a method to limit the problem of antimicrobial resistance. With the advance in synthetic biology, bacteriophages can be genetically modified easily, due to their small genome and can obtain properties that enable their use as diagnostics of infection. In my talk, I will discuss different examples of how bacteriophages can be genetically modified to detect infection accurately and I will describe relevant work that we have done in my lab towards this direction.

MULTISCALE LIQUID BIOPSY

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The importance of importance of mass transport in the context of biosensing has been highlighted in a number of papers. Due to their small size that enhances interaction, functionalised microfluidic channels are particularly well suited to promote the capture of target cells (or molecules) in body fluids. However, small channel sizes typically limit the permissible flow-rate and hence the throughput. Here we describe a new device that is composed of thousands of parallel microchannels within a membrane. This multiscale architecture enables optimal capture without compromising flow rate (throughput). I will describe its application in the context of liquid biopsy for the capture of rare circulating tumour cells (CTCs) in blood. Using spiked samples, we achieved capture efficiencies above 80%. Clinical data from 72 cancer patients and 65 healthy controls demonstrated a sensitivity of 100% and specificity of 97% when combined with conventional staining protocol. Using immunofluorescence labelling we identified PD-L1+ CTCs in 41% of patient (n=36) as potential responders to immune checkpoint inhibition therapy. These results suggest that our approach could provide a versatile tool to improve cancer management.

L19

MEDICINAL PLANTS FOR PREVENTING CAMPYLOBACTER INFECTIONS

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According to the regulatory agencies, including the US Food and Drug Administration and the ECDC, alternative strategies are urgently needed for the control of *Campylobacter* spp. *Campylobacter jejuni* represents the most prevalent foodborne pathogen, as well as a serious problem in food processing environments due to adhesion and biofilm formation [1]. In several collaborative projects, preparations of medicinal plants were characterized phytochemically and evaluated for inhibiting *Campylobacter* infections studying various approaches like direct antimicrobial activity or inhibition of *Campylobacter jejuni* cell adhesion, resistance modulatory activity or inhibition of quorum sensing (QS). Plant extracts, fractions and isolated substances have been prepared, chemically characterized and further studied for confirmation of their bioactive characteristics. Extracts and fractions of the roots of *Peucedanum ostruthium* disturbed *C. jejuni* membrane integrity at concentrations far below their respective minimum inhibitory concentrations. *Satureja montana* extracts revealed antimicrobial activity by influencing bacterial efflux pumps [2]. Furthermore, anti-QS and anti-adhesion activity could be confirmed for *Juniperus communis* fruit extracts [3] as well as for *Sedum roseum* [4]. In a recent study, essential oil as well as waste material from the hydrodistillation of *Lavandula angustifolia* had particular anti-biofilm effects. RNAseq data provided new insights into the influence of the essential oil on gene expression in *C. jejuni* [5].

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Keywords

Campylobacter jejuni, antibacterial, biofilm, quorum sensing, anti-adhesion, medicinal plants

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L20

NEW ANALYTICAL METHODS AND STRATEGIES FOR NATURAL PRODUCT RESEARCH – APPLICATIONS IN PHYTOPHARMACY, PHYTOCOSMETICS AND PHYTONUTRITION

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The success in natural product research is largely based on the continuous development of highly selective and sensitive technologies for analysis. Novel enrichment and purification methods based on advanced solid phase extraction techniques are used to reduce the complexity of plant extracts while modern HPLC allows the separation, pre-concentration and fractionation of active ingredients. A further hyphenation to high-resolution mass spectrometry facilitates the identification and quantification of active substances in natural substances. During the last years Ambient-MS systems such as Direct Analysis in Real Time (DART) or Atmospheric Solids Analysis Probe (ASAP) have become very popular in mass spectrometry. They both base on Penning ionization processes in the gas phase caused by electronically excited noble gas atoms. This leads to very clean mass spectra, which is one of the reasons why this ionization technique is used in many analytical fields including phytopharmacy, phytocosmetics and food analysis. In parallel, the combination of separation science with spectroscopic technologies such as near- or mid-infrared spectroscopy enables a quick qualitative and quantitative analysis of raw plants as well as liquid extracts without destruction. In this presentation, novel analysis techniques for various applications in the fields of phytopharmaceuticals, phytocosmetics and phytonutrients will be demonstrated and discussed. Many of these methods have already been successfully used by the recently established Phytovalley® Tirol Cluster. In this regard, the Austrian Drug Screening Institute (ADSI) acts as an interface between basic research and industrial applications and represents a center for science and the identification of natural substances.

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RECENT UPDATES ON THE PHYTOCHEMISTRY AND PHARMACOLOGY OF OXYPRENYLATED SECONDARY METABOLITES

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Oxyprenylated secondary metabolites are an emerging class of naturally occurring biologically active compounds. Great evidence to this concern has been accumulated across the last three years, especially for oxyprenylated coumarin and cinnamic acid derivatives. In particular, new natural sources of such phytochemicals have been discovered: these comprise edible, medicinal, and healthy plants like lettuce (Lactuca sativa L., Asteraceae), spinach (Spinacia oleracea L., Amaranthaceae), goji (Lycium barbarum L., Solanaceae), quinoa (Chenopodium quinoa Willd., Amaranthaceae), pomegranate (Punica granatum L., Lythraceae), and common wormwood (Artemisia vulgaris L., Asteraceae). In the mean time also powerful, versatile, and high yielding extraction methodologies have been set up, and these include subcritical butane extraction and solid phase adsorption. Studies on the in vitro and in vivo pharmacological properties and on the therapeutic potential of oxyprenylated phenylpropanoids also continued and led to the characterization of brand new effects like cholinesterase inhibition, modulation of melanogenesis and of nitric oxide biosynthesis, suppression of resistance to cancer chemotherapeutics, induction of glycoprotein P, suppression of colitis and inflammation related colorectal carcinogenesis, and finally inhibition of -a-amilase, a-glucosidase, and lipase. In this context we have also proposed how naturally occurring chemicals can be considered ad effective tools to inspire the semisynthesis of structurally related derivatives with enhanced properties. Considered as a whole, data acquired during recent years confirm and enforce the role and great potential of these phytochemicals to the point that the first clinical trial in humans of a oxyprentlated phenylpropanoids containing phytopreparation has been launched in the last months.

L22

ISOLATION AND NEUROPHARMACOLOGICAL ACTIVITY OF NATURAL PRODUCTS: DEFINING MEANINGFUL WORKFLOWS

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Natural products hold a great promise as potential drug leads to develop neuropharmacological therapies. However, few natural products have successfully inspired central nervous system drug development. One reason for this is a lack of critical insights into the translatability related to a knowledge about brain concentration in vivo. To assess the pharmacokinetic and pharmacodynamic behavior of neuropharmacologically active natural products, sufficient amounts in adequate purities are required. Given the complexity of central nervous system targets, sufficiently validated in vitro and in vivo assays play crucial factors in the evaluation of such compounds. Using state-of the art isolation techniques related to counter current chromatography and a battery of behavioral models in zebrafish and mice we define a workflow that allows to derive conclusions regarding the potential of CNS active natural products and their potential mechanisms of action. A major problem that is discussed, giving examples form coumarins, is the frequent lack of good brain exposure, rapid metabolism and multiple targets and U-shaped dose-response curves.

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DNA METABARCODING IN HERBAL PRODUCT AUTHENTICATION—WHERE ARE WE TODAY?

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Herbal products and other over-the-counter (OTC) drugs have limited medical oversight, frequent off-label use, and in-sufficient monitoring of adverse drug reactions. Many herbal products have a long history of use, but there are rising concerns over product efficacy, safety, and quality in the wake of recent cases exposing discrepancies between labelling and constituents. Quality and authentication assessment methods rely on morphology and analytical phytochemistry-based methods detailed in pharmacopoeias, but a variety of innovative methods have emerged. Herbal products, however, are often highly processed with numerous ingredients, and even if these analytical methods are accurate for quality control of specific lead or marker compounds, they are of limited suitability for the authentication of biological ingredients. Amplicon DNA metabarcoding is a high-throughput sequencing based method for molecular identification using DNA barcoding that has been shown to enable accurate species identification for products that contain mixtures of DNA from different species. Different methods of quality control and authentication have varying resolution and usefulness along the value chain of these products. DNA barcoding can be used for authenticating products based on single herbal ingredients and DNA metabarcoding for assessment of species diversity in processed products. DNA barcoding and metabarcoding have potential in the context of quality control of both well and poorly regulated supply systems. Innovations in DNA-based identification will further refine these approaches, and help consolidate the niche in which these methods augment current authentication.

STABILITY OF QUERCETIN IN CELL CULTURE

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Quercetin is evidently instable in Dulbecco's modified Eagle's medium (DMEM) at 37 °C. However, the underlying mechanism of this instability is not clear yet. The stability and new degradation products of quercetin in DMEM at 37 °C were investigated via in UPLC-MS-MS analysis. With increasing incubation time, quercetin formed various degradation products derived from its dimer and there were numerous isomers formed during this process. Ascorbic acid significantly improved the stability of quercetin by protecting quercetin from auto-oxidation in this medium. Ascorbic acid also significantly improved the stability of quercetin in the presence of A549 cells. Via enhancing the stability of quercetin in cell culture, ascorbic acid obviously enhanced the antiproliferative effect of quercetin towards A549 cells.

Keywords

Quercetin and Luteolin, A549 and Caco-2 Cells, Metabolites, Quinones

L25

ENGINEERED POLYSACCHARIDE NANOPARTICLES TO FIGHT AGAINST DRUG-RESISTANT PATHOGENS

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While the world is running into a global crisis of infectious diseases, including drug-resistant bacterial infections, the clinical pipelines for antibiotics are getting dried. Most antibiotics are small molecules targeting a crucial pathway for bacterial survival and proliferation, which has been readily overcome by bacteria. We aimed to develop a novel nanomaterial-based platform that utilizes the unique physico-chemical forces that bacteria cannot easily develop resistance against via mutations. Nanoantibiotics can also be merged with conventional antibiotics as well as emerging therapeutic modalities such as gene therapy. We molecularly engineered a natural polysaccharide, chitosan known for its antimicrobial property, to acid-transforming chitosan (ATC) with high solubility at a physiological pH and a capability of being activated by a biological stimulus. ATC demonstrated its substantial antimicrobial efficacy against gram-negative pathogens (E. coli, S. typhimurium, and P. aeruginosa), commonly resistant to clinically used antibiotics (beta-lactams, macrolides, tetracyclines, co-trimoxazole, and most fluoroquinolones). Particularly, when ATC was complexes with fragmented DNA, the resulting in ATC/fDNA polyplexes were readily internalized by RAW 264.7 macrophage cells co-infected with an intracellular pathogen, S. typhimurium, and efficient eradication in a dose-dependent manner was confirmed. The ATC's antimicrobial capability was found to be closely correlated with pH and it simultaneously tackles a broad range of key proteins for bacteria, which makes developing drug-resistance by bacteria very difficult. Overall, this presentation will introduce the demand, rationales synthesis, and evaluation of nanoantibiotics as a promising strategy to treating microbial infections.

L26

QUALITY ASSURANCE AND THE ROLE OF ACCREDITATION STANDARDS IN VIRTUAL PHARMACY EDUCATION

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COVID-19 has not only changed our daily routines, it also changed the traditional pharmacy education system into a distance learning or hybrid model with very little time to prepare for this change. In the United States, the US Department of Education has provided guidance to accreditors that allows schools and colleges to use distance education without the normal accreditor approval process for the duration of the national emergency declaration and 180 days following the date on which the COVID-19 national emergency declaration is rescinded. Normally, the Accreditation Council for Pharmacy Education (ACPE) requires one-year advance notice for the addition of a distance campus or the implementation of distance education for an existing accredited college or school (more than 25% of the curriculum) pharmacy degree program. Notification is required to allow ACPE sufficient time to conduct the monitoring needed to ensure readiness and continued compliance with the accreditation standards. This presentation will focus on the accreditor's role to assure quality as pharmacy degree programs transitioned to virtual or hybrid pharmacy education.

Keywords

Distance Education, Quality, Accreditation

L27

MENTOR-MENTEE RELATIONSHIP: A WIN-WIN CONTRACT IN MEDICAL EDUCATION

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Scholarly activities (i.e., the discovery of new knowledge; development of new technologies, methods, materials, or uses; integration of knowledge leading to new understanding) are intended to measure the quality and quantity of dissemination of knowledge. A successful mentorship program is necessary during postgraduate education to help students achieve the core competencies such as patient care, medical knowledge, practice-based learning and improvement, systems-based practice, professionalism, interpersonal and communication skills. The role of the mentor in this process is pivotal in the advancement of the students' knowledge about evidence-based medicine. With this process, while mentees become more self-regulated, exhibit confidence in their performance, and demonstrate more insight and aptitude in their jobs, mentors also achieve elevated higher self-esteem, enhanced leadership skills, and personal gratification. As such, we may conclude that mentoring is a two-sided relationship, i.e., a 'win-win' style of commitment between the mentor and mentee. Hence, both parties will eventually advance academically, as well as professionally.

L28

ONLINE LEARNING: A NEEDS-BASED PHARMACY EDUCATION IN THE 21ST CENTURY

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The COVID-19 pandemic has forced universities to rapidly transition to online teaching and learning. It is of paramount importance, that we remodel the way pharmacy education is delivered with particular attention to current societal needs and the competencies required to produce the desired pharmaceutical workforce of the 21st century. Many institutions continue to face challenges in delivering online teaching due to inadequate capacity, limited infrastructure or reduced access to teaching resources. Given the current situation, there is an urgent need to collaborate and re-imagine the way curricula are imparted to harmonise pharmacy graduate competencies that are aligned to minimum standards. This talk provides a concise incursion into the 21st century pharmacy education online classroom from an academic and student perspective. It shares a few strategies on contextualizing a supportive and interactive online learning environment. Intentionally designing online learning plans that provide opportunities for interpersonal interaction between students and faculty goes a long way in circumventing the many life circumstances that also present challenges to optimal online teaching in pharmacy.

L29

DEVELOPING FUNCTIONAL MEAT BASED FORMULATIONS FOR DYSPHAGIC INDIVIDUALS USING 3D FOOD PRINTING

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Three-Dimensional (3D) food printing is one of the foremost emerging manufacturing approaches for development of newly designed food products. This technique offers an exciting alternative to attain high quality products for specific needs of the consumers enabling preparation of foods customized with desirable texture, flavor, shape and size, and also assisted by remote commands for smart homes of the future [1, 2]. Swallowing difficulty, called dysphagia, is a common health problem among elderly and neurologic patients who need nutritious foods that are soft, moist, smooth, in other words, easy to swallow. High quality protein requirement for these individuals, in general, is supplied with meat-based products. However, texture modification is essential when these products are incorporated into the formulation because meats might not be suitable for direct consumption for these types of diets [2-4]. For this reason, the development of palatable and nutritious formulations to ensure safe swallowing is receiving particular attention these days. A study supported by Scientific and Technological Research Council of Turkey (TÜBİTAK-Project# 218O017) was performed for the purpose of developing functional chicken or beef based formulation for dysphagic individuals with a 3D food printer. Freeze-dried chicken meat or beef, hydrocolloids such as gelatin and κ-carrageenan as well as several functional plant based ingredients were used in successfully developing new functional meat-based 3D printed products with desired characteristics for dysphagic individuals. The results of this study would provide bases for the development of palatable, healthy and nutritious 3D printed functional meat based products for dysphagic individuals.

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L30

UNDERSTANDING AND SAFE GUARDING THE INTEGRITY OF HALAL FOOD FOR THE CONSUMER

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The worldwide Muslim population is increasing and is currently estimated to be around two billion. With education becoming more and more accessible to the world population over, the Muslim middle class has increased significantly. Due to their spending power, they have now become an important target market for the commercial enterprises. Halal food certification has become indispensable for Muslim consumers who want to live a lifestyle in-line with their faith. Halal simple means permissible according to the Islamic law (Quran). Halal certificate is the document that is given or should be given by ideally an accredited certification body (CB) as a proof and evidence that the food product is in compliance with the shariah law. An audit is normally conducted by qualified and trained personnel including a Muslim scholar who should be knowledgeable in the Islamic dietary laws. Even though there are still regulatory issues concerning most CBs in local markets (mostly in Europe), however, countries like Malaysia, United Arab Emirates, Indonesia, Turkey (SMIIC) and Saudi have all now developed their individual standard requirementss to monitor and control halal management activities in the market. The schemes developed by these countries are increasingly gaining credibility across the Muslim world. It is worth nothing that the production of halal food in the manufacturing companies are supervised constantly to ensure that, the halal integrity of the food product is intact from the farm to the fork for the final consumer.

Keywords

Halal Food, Muslim Consumer, Halal Certificate

O1

THE EFFECTS OF A NEW CYCLOSPORINE A NANOSUSPENSION ON NEPHROTOXICITY AFTER ORAL ADMINISTRATION: HK-2 CELL CULTURE AND IN VIVO HISTOPATHOLOGICAL EVALUATION

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Cyclosporine A (CsA) is one of the immunosuppressive agents and is widely used after transplantation, but nephrotoxicity is a side effect that limits the use of CsA [1]. The aim of this study was to examine the effect of CsA nanosuspension on CsA-related nephrotoxicity. CsA nanosuspension was prepared using the wet milling method with combined stabilizers [2]. CsA-induced nephrotoxicity of the developed CsA nanosuspension, physical mixture (PM), coarse powder (CsA), and commercial product (Sandimmun Neoral® - SI Neoral) was evaluated with cell culture and in vivo studies. HK-2 cell line, human kidney proximal tubular epithelial cells, were chosen since CsA treatment following transplantation was reported to cause mild to moderate nephrotoxicity [3]. The histopathological behavior on the kidneys was evaluated after oral administration at 10 mg/kg CsA to rats for 21 days. At the end of the 21st day, tubule degeneration scoring was performed in the right and left kidneys from all groups and histopathological examinations were conducted with hematoxylin eosin stain. The physical mixture cytotoxicity result was found to be significant at 200, 100, and 50 µg/mL concentrations ($P<0.0001$) (Figure). Nanosuspension was found increased cell viability compared to Sandimmun Neoral® at 50 and 25 µg/mL concentrations ($P<0.0001$). After the evaluations in the kidneys; there was no difference between the kidneys in all groups and it was found that nanosuspension caused less tubule degeneration compared to the Sandimmun Neoral®. These results demonstrated that CsA nanosuspension could be positive effects on nephrotoxicity.

Keywords

Cyclosporine A, Nanosuspension, Wet media milling, HK-2 cell culture, Nephrotoxicity

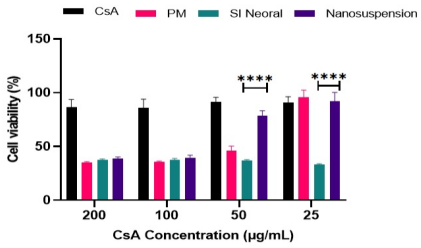

Figure. In-vitro cytotoxicity in HK-2 cells for 24 hour incubation periods (****P< 0.0001)

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O2

RVG-MODIFIED TARGETED GENE THERAPY FOR ALZHEIMER'S DISEASES

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The nano-sized delivery systems have been successfully applied for delivering various therapeutic molecules in the recent two decades. However, it remains challenging to develop therapeutic nanoparticles for neurodegenerative diseases such as Alzheimer's disease(AD). The 29-amino acid peptide derived from rabies virus glycoprotein (RVG) can bind to acetylcholine receptors that are highly expressed in neuronal cells and was chosen as the targeting agent in this study [1]. RNA interference shows great potential for treating AD by silencing the causative genes. Small interfering RNAs(siRNAs) against specific genes have been used to block Aβ production, thus decreasing neurodegenerative deficits of AD. This work aims to purpose a novel antisense gene therapy based targeting system for AD therapy. For this, liposome system was developed and the RVG peptide was bind to the outer surface by cooper-click chemistry to form RVG-modified liposomes(RVG-Lipo). The characterization studies showed that obtained system has a particle size under 100 nm with a PDI lower than 0.3 and positive charge over 25 mV. These characteristics are suitable for brain targeting [2]. Moreover, the RVG-Lipo is able to bind with siRNAs and protect them from RNase and serum nucleases. The cytotoxicity studies revealed that the developed system could be safely used on L929 and Neuro-2a cells up to 300 µg/mL doses. As a result, we developed a promising RVG29-modified liposome-based gene delivery system for AD therapy and this system could also be applied to other neurodegenerative diseases.

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Keywords

Alzheimer's disease, Rabies virus glycoprotein, siRNA

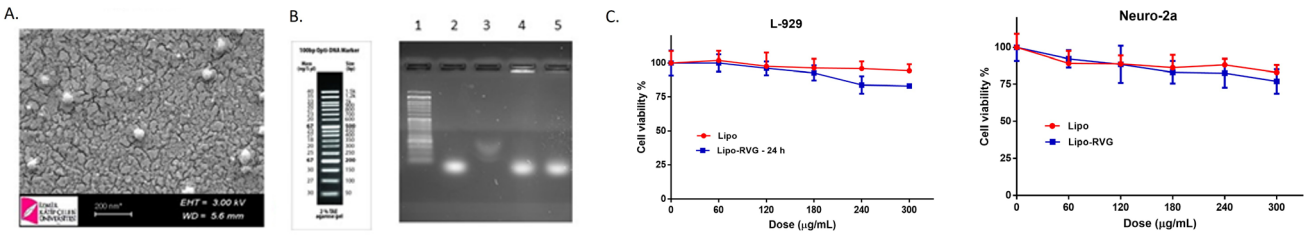

Figure. Evaluation of RVG-Lipo. A. SEM image. B. RNase protection C. Cytotoxicity study

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O3

NUCLEIC ACID LOADED EXTRACELLULAR VESICLES FOR TARGETING BRAIN DISEASES

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Extracellular vesicles (EVs) are nano-sized membrane vesicles, released by almost every cell type. They play crucial roles in many physiological events, as well as many pathological processes. Recent studies showed that EVs are promising systems for drug loading and nucleic acid delivery [1]. Nucleic acid based therapeutics have numerous advantages for gene-relevant diseases. Putting together the EVs and nucleic acids as a pharmaceutical therapy is an innovative strategy for non-curable diseases. EVs can be isolated from different types of bodily fluids such as blood, urine, and saliva. Based on the main principle employed in the isolation process, there are different types of isolation methods. The ultracentrifugation-based technique that we applied is one of the most common techniques. In brief, the cell-free conditioned media was first centrifuged to remove cells and debris. Subsequently, the supernatant was ultracentrifuged to obtain EV pellet. The EV pellets were resuspended and then filtered through 0.22 µm-filter and quantified using a BCA Protein Assay kit (Pierce, USA). The characterization studies were performed and the EVs loaded with disease specific siRNAs. According to the results, the obtained EVs are nanosized, spherical in shape, carrying EV markers on their surfaces, and show nucleic acid binding ability. The brain targeting ability was investigated and it was shown that radiation dramatically improved the targeting efficiency as we put forth in our previous study for nanoparticles [2]. The obtained results showed that EVs show a promising approach for brain diseases such as cerebral ischemia, glioblastoma, and Alzheimer's disease.

Keywords

Extracellular vesicles, Nucleic acid delivery, Brain diseases

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O4

EVALUATION AND CHARACTERIZATION OF FOLIC ACID MODIFIED SILICA NANOPARTICLES AS SIRNA CARRIERS

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Vascular endothelial growth factor (VEGF) releases from tumor cells to form new veins for better feeding [1]. VEGF blocking siRNAs can be carried by PEGylated and positively charged silica nanoparticles (SNPs) with appropriate surface modifications to achieve targeted delivery due to overexpression of folate receptor on tumor cells. In this study, silica-based siRNA delivery system was developed, characterized and in vitro evaluation were done. SNPs synthesis method was adopted from Quan et al [2]. PEGylation was performed and NPs were positively charged by (3-trimethoxysilylpropyl)diethylenetriamine (TMSPE) addition. Folic acid was conjugated on SNPs via carbodiimide chemistry. Two different formulations were obtained by higher or lower amounts of folic acid conjugation on SNPs. Gel electrophoresis was performed to evaluate the complexation efficiency. Cytotoxicity of the NPs were evaluated by MTS assay and cellular uptake was determined by flow cytometer and fluorescence microscopy. SNPs were synthesized with the size around 20 nm and zeta potential was -15 mV (Horiba nanoPartica SZ-100V2). After PEGylation, particle size was remained the same and NP surface was positively charged according to zeta potential results. Folic acid conjugation on NP surface was demonstrated by FTIR peaks at 1417, 1485 and 1605 cm^{-1}. Gel electrophoresis results showed that higher amount of folic acid conjugation leads better complexation. Blank NPs has no cytotoxicity and folic acid conjugation was increased the cellular uptake. Results show that positively charged and PEGylated SNPs might be promising approach for siRNA delivery.
Acknowledgements: This project was supported by TUBITAK project 118C470

Keywords

Silica nanoparticles, siRNA, Targeted drug delivery

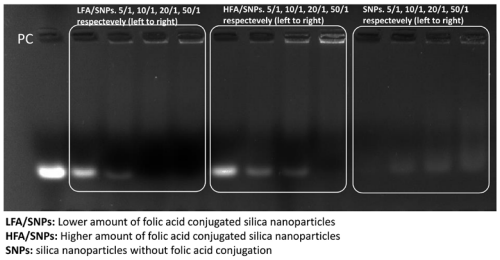

Figure 1. Gel electrophoresis results

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O5

EVALUATION OF NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEM AND MONOCLONAL ANTIBODY FOR SYNERGISTIC LYMPHOMA THERAPY

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Non-Hodgkin lymphoma is a class of hematologic cancer, that explains for 85% of all lymphoma and 4% of whole malignancies [1, 2]. Using standart rituximab and anthracycline treatment, relapse was occured. Therefore, improvement of treatment efficiency is an important requirement with novel drug combinations or new therapeutic approach. The aim of this study is to evaluate the activity of daratumumab in combination with polycaprolactone (PCL) nanoparticles for minimizing toxicity and increasing the anticancer efficacy of doxorubicin (Dox) for lymphoma. Nanoparticles were prepared with double emulsion method. Particle size, size distribution, zeta potential, encapsulation efficiency and stability were determined. Cell culture studies were carried out to show the safety of blank NPs and cytotoxicity of DOX-loaded NPs alone or combination with Daratumumab. For all nanoparticles; size changed within 235-250 nm with narrow distribution. Zeta potential values were -3.9 and -13.3 mV for blank and Dox-loaded PCL nanoparticles, respectively. High entrapment efficiency (%85) was obtained. There has been no significant change in characteristics of nanoparticles in 30 days. In cell culture study, blank nanoparticles have no toxicity in L929 cells. All formulations showed a time-dependent pattern; the cytotoxicity enhanced with the increase of incubation time. Dox-loaded nanoparticles showed more toxicity to A20 cells than Dox solution. Dox-loaded NPs in combination Daratumumab realized higher cell toxicity than Dox-loaded NPs and mAb solution, respectively ($P < 0.05$). In conclusion, nanotechnology in combination with antibody-targeted chemotherapy could be seen as promising synergistic strategy for controlling tumor growth by increasing anticancer efficacy while reducing toxicity.

Keywords

Doxorubicin, Daratumumab, Nanoparticle, Polycaprolactone, Monoclonal antibody, Lymphoma

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O6

NOVEL METHOD FOR DETECTION OF ESCHERICHIA COLI USING SMART DISPOSABLE ELECTRODE FROM DRINKING WATER

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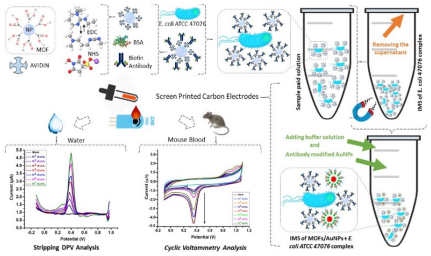
The climate change is significantly evolving novel microbes in the environment. There is a need to develop smart and efficient nano-biosensor to detect the pathogens, *Escherichia coli (ATCC 47076)*, in the drinking water to protect the public against the diseases like hemolytic uremic, gastroenteritis, and acute diarrheas. This study aims to construct an engineered dispersible electrode to enumerate *E. coli (ATCC 47076).* The immunomagnetic separation strategy enables detecting bacteria in water samples fast and efficiently. Functionalized magnetic MOFs serve as a capture probe and Spectro-electrochemical label. The stripping differential plus voltammetry (SDPV) and cyclic voltammetry (CV) techniques were used to quantify the different concentrations of the *E. coli*. Synthesized dispersible electrode was found competent to electrochemically detect the E. coli at 10^1 to 10^7 CFU/mL in water and blood with high accuracy r^2 = 0.992 and 0.921 respectively and a limit of detection (LOD) of 10 colony forming units CFU/mL. The selectivity of the method was tested with *Salmonella typhimurium, K. aerogenes, E. coli O157: H7*. The results suggest that the developed method is applicable for real-time detection of *E. coli ATCC 47076* in water and blood samples, and offers advantages such as large dynamic range, high sensitivity, high selectivity, and short analysis time (5 min). As for as we know, this is the first report to display the potential of the AuNPs and MOFs nanoparticles based dispersible electrode for the detection of targeted *E. coli* from water and blood.

Keywords

Disposable electrode, Blood, Water, Immunomagnetic Separation



Abstract Figure

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O7

A SIMPLE UV SPECTROPHOTOMETRIC APPROACH FOR MONITORING FAVIPIRAVIR-COVID19 BINDING

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As it is known, drug-protein binding is very important role to understand the pharmacokinetics (i.e., absorption, distribution, metabolism, and elimination) and pharmacodynamics (pharmacological effects) of a drug [1]. Many analytical methods have been applied to identify and quantify the binding constants of drug-protein. In these studies, UV spectrophotometric method is one of the most commonly used methodologies [2, 3]. In this study, a simple UV Spectroscopic monitoring was applied on Favipiravir (FAV)-Covid19 (COV2) binding. UV spectrophotometric measurements was performed using the interaction of FAV and COV2 in water. In our investigation, an isolated protein of COV2 was studied. Experiments are based on the conception of classical drug-protein binding. The following equation was used for the computation of the binding constant of FAV-COV2 interaction;

$$AA\text{-}A=\varepsilon A\varepsilon A\text{-}\varepsilon A+\varepsilon A\varepsilon A\text{-}\varepsilon Ax1K[D]$$

Where K denotes binding constant, [D] denotes the concentration of FAV, $_{A}$ and $_{A}$ are the absorbance of pure FAV and FAV-COV2 complex, respectively. $_{\varepsilon A}$ and $_{\varepsilon A}$ are molar absorption cofficients of the pure FAV and FAV-COV2 complex, respectively. In this study, the binding constant of FAV and COV2 complex was found to be $6.53x10^{3}$. The result showed that there was a weak interaction between FAV and COV2. For this reason, this research work may provide an opportunity to evidence the weak biological interaction of FAV-COV2.

Keywords

Favipiravir, Covid19, UV Spectrophotometry, Drug-protein binding

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O8

SERS BASED ON A DISPOSABLE GOLD-CELLULOSE NANOFIBRIL SUBSTRATE FOR DETECTION OF E.COLI

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A cheap and disposable paper-like gold nanoparticle-embedded cellulose nanofibril substrate was used in this research to develop a fast and cost-effective method for counting *Escherichia coli.* A simple disposable SERS substrate was built by combining CNF and gold chloride solution in a water bath, which is then heated to 120 °C. Enrichment and SERS detection of E. coli were used to apply the resultant substrate. As a way to rid the *E. coli* from contaminating the platform, the spherical gold nanoparticle-embedded cellulose nanofibril substrate was employed as a scavenger. After targeting the *E. coli* with specific antibodies, the mixture was transferred to a column where the bound bacteria were then separated. Next, the SERS substrate for mapping was added to the bottom of the column, where DTNB–coated Au nanorods acted as SERS probes. The distribution density of DTNB was seen using SERS mapping, and the test was finished in only one hour. Within the range of 15 cfu mL^{-1} to 1.5 × 105 cfu mL^{-1}, the correlation between the E. coli and SERS mapping signals was found to be linear. For the SERS mapping assay, the limit of detection was calculated to be 2 cfu mL^{-1}. To evaluate the selectivity of the proposed technique, *Micrococcus luteus*, *Bacillus subtilis*, and *Enterobacter aerogenes* were selected. These three microbes had no effect on the procedure, demonstrating its high selectivity. Moreover, the proposed technique was tested for identifying *E. coli* in intentionally contaminated samples, and the findings were compared with those of the plate-counting method.

Keywords

SERS, Nanoparticle, Nanofibril

O9

A MOLECULARLY IMPRINTED ELECTROCHEMICAL SENSOR FOR SELECTIVE DETECTION OF COVID-19 DRUG-FAVIPIRAVIR IN BIOLOGICAL SAMPLES

Çiğdem Kanbeş Dindar[1], Burcin Bozal-Palabiyik[1], Bengi Uslu[1]

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For the first time, the molecularly imprinted polymer (MIP) technique was applied for selective, fast, and sensitive electrochemical determination of Covid-19 drug favipiravir, in this study. Using cyclic voltammetry (CV), the novel MIP-based sensor (MIP@o-PD/GCE) was designed by electropolymerization of the functional monomer o-phenylenediamine (o-PD) in the presence of a template molecule favipiravir on a glassy carbon electrode (GCE). For the removal and rebinding procedures, as well as the optimization of conditions and performance measurement of MIP@o-PD/GCE, differential pulse voltammetry (DPV) was used. The ferrocyanide/ferricyanide redox marker was used to monitor each step of the experimental procedure using DPV. MIP@o-PD/GCE has a linear response to favipiravir in the range of $2x10^{-11}$ M to $1x10^{-10}$ M under optimal experimental conditions. The detection limit of MIP@o-PD/GCE was obtained to be $6.35x10^{-12}$ M, whereas the quantification limit was found to be $2.12x10^{-12}$ M. The designed sensor was successfully applied to a synthetic human serum sample to verify its applicability and validity. Electrochemical sensor selectivity was evaluated by comparing the binding of paracetamol and tenofovir, which are similar to favipiravir, and also oseltamivir and famciclovir, which are other drugs used in the treatment of Covid-19.

Keywords

Favipiravir, Molecularly imprinted polymer, Voltammetry, O-phenylenediamine

O10

DETERMINATION OF CULTIVATED BACTERIA IN INONU CAVE EXCAVATION SOIL SAMPLES: FIRST STEP

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Microorganisms in soil samples taken from İnönü Cave in Zonguldak, Karadeniz Ereğli, were determined by MALDITOF-MS method. The bacterial populations detected in the soil samples taken from the layers belonging to different ages are remarkable.
The archaeological excavation layers, which are the subject of our study, are classified as Early Iron Age - B.C. 1200- 980; Late Bronze Age- B.C. 1350-1200; Early Bronze Age- B.C. 2300-2100; Chalcolithic Age- B.C.4300-3900.
The data obtained from İnönü Cave, whose current excavations are continuing, will be able to present the microorganism profiles, lifestyles, disease agents and treatment options belonging to prehistoric periods. It can enable the discovery of new microorganisms that cannot be identified in existing databases (1,2).
Genetic analysis of different types of bacteria that naturally transform during human migration can be used as an indicator of human migration around the world (3).
The data obtained can provide an important basis for the traces of life that may be found in the surrounding regions by enabling the vital activities of the cultures that lived in the cave in question. It will also shed light on today's disease and treatment approaches.
In our study, blaCtxm and qnrS genes, which are antibiotic resistance genes, were also examined, but these genes were not found. For this reason, it is planned to perform a resistome study with whole genome sequence analysis.

Keywords

Soil microorganisms, microbiota, antibiotic resistance genes,archaeological excavation layers

Table 1: Bruker Daltonik Maldi Biotyper Classification Results

Age	Bacteria
Early Iron Age	*Chryseobacterium gleum, Glutamicibacter mysorens, Brevibacillus laterosporus*
Chalcolithic Age	*Pseudomonas oleovorans, Exiguobacterium aurantiacum, Citrobacter freundii, Acinetobacter johnsonii*
Late Bronz Age	*Pseudomonas corrugata, Bacillus mycoides, Pseudomonas oleovorans*
Early Bronz Age	*Pseudomonas putida*

Table1

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O11

STF-083010 MEDIATED TARGETING OF INOSITOL-REQUIRING ENZYME-1α/X-BOX BINDING PROTEIN-1 STRONGLY REDUCED THE TUMORIGENIC ABILITIES OF PROSTATE CANCER CELLS

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STF-083010 is a potent, cell-permeable inhibitor of ER-resident transmembrane protein IRE1α that directly inhibits IRE1α endonuclease activity and disturbs the IRE1α/XBP-1 signaling branch of unfolded protein response pathway [1]. Recent studies have pointed out that the UPR mechanism is an important key regulator in prostate carcinogenesis. Prostate cancer (PCa) is the second most frequent cause of cancer-related mortality among males in the United States. Although various treatment approaches have been developed for PCa, after androgen deprivation therapy, which is one of the most commonly used treatments, most parts of tumors eventually relapse to castration resistant PCa (CRPC). Although second-generation antiandrogens and chemotherapeutics have been developed that can effectively treat PCa, inherent or acquired drug resistance limits the success of treatment. Therefore, there is a continuing imperative to explore novel therapeutic approaches [2,3]. Here, we showed that modulation of the IRE1α/XBP-1 branch of UPR by STF-083010 efficiently limitate the tumorigenic ability of PCa cells. The limitation of the metastatic features associated with the aggressiveness of PCa cells is extremely important for treatment success. Our results demonstrate that STF-083010-mediated inhibition of IRE1α/XBP-1 strongly reduced colony formation, migrative and invasive capabilities of PCa cells. Moreover, STF-083010 significantly delayed anchorage-independent cell growth of PCa cells. Taken together, these results suggest that the IRE1α/XBP-1 inhibitor STF-080310 would be a candidate potent drug in PCa treatment.

Keywords

STF-083010, Prostate cancer, UPR, IRE1α/XBP-1

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O12

EVALUATION THE EFFECTS OF PHENYLBUTYRIC ACID ON OBESITY INDUCED HYPOTHALAMIC VASCULAR INTEGRITY CHANGES

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Blood brain barrier (BBB) is a multi-cell vascular structure as a physiologically selective permeable barrier between the central nervous system and systemic blood circulation. The integrity of BBB is sustained mainly by tight junction (TJ) proteins and adherens junctions. In this study, we investigated the possible effects of chemical chaperone phenylbutyric acid (PBA) on obesity induced disruption of BBB at the hypothalamic region of the obese mice. Lean and ob/ob mice were divided into two groups (n=8) that received either vehicle or PBA (1g/kg/day) for thirty days. The expression of TJ proteins, zonula occludens-1 (ZO-1) and claudin-5, from the hypothalamus of all mice were analyzed by using western-blotting. Our initial results showed that there was a significant increase in ZO-1 protein level in PBA treated-ob/ob mice compared to ob/ob-controls. In addition, claudin-5 levels tended to increase in PBA treated-obese mice compared with obese controls, but statistically non-significant. Our results indicated that PBA might have beneficial effects on treatment of obesity induced hypothalamic BBB distruption as compensating ZO-1 protein levels. PBA has a neuroprotective effect and may be a new candidate as a therapeutic agent as providing and maintaining BBB integrity.

This study was supported by The Scientific and Technological Research Council of Turkey (TUBITAK) (project number: 118S656).

Keywords

Obesity, Phenylbutyric Acid, Blood Brain Barrier, Tight Junctions

O13

SELF-EMULSIFYING DRUG DELIVERY SYSTEMS FOR ANTIVIRAL THERAPY

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Molnupiravir is an oral antiviral drug, which is subjected to a number of clinical studies recently, and it is one of the promising candidates for the treatment of coronavirus disease [1]. Herein, self-emulsifying drug delivery systems (SEDDS) for the oral administration of this antiviral drug has been designed and in vitro characterization and cell culture studies have been performed. Preformulation studies were carried out using Gelucire® 44/14, Labrafil® M1944CS, Labrasol®, D-α-tocopheryl polyethylene glycol succinate (TPGS) and Tween80 as surfactant; Peceol™ and LabrafacTM lipophile WL1349 as oil phase and Transcutol®HP as cosolvent to determine the optimum formulation components. Suitable formulations were characterized for droplet size and zeta potential using Dynamic Light Scattering (DLS). Cytotoxicity studies were carried out using L929 cells. Stable SEDDS formulations with a droplet size under 300 nm were obtained using PeceolTM or Labrafac as oil phase, TPGS: Tween 80 (1:4), Labrafil: Tween 80 (1:2) or Gelucire® 44/14: Tween 80(1:2) mixture as surfactant, and Transcutol®HP as cosolvent. Zeta potential values were found to be close to zero due to the presence of nonionic surfactants. After 21 days of stability evaluation, no morphological change was observed, whereas droplet size was increased for all formulations except F2 ($p>0.05$). No difference in droplet size was observed for F1 and F2 when diluted in cell culture media. Blank F1, F2 and F7 showed biocompatibility with more than 80% cell viability, while cytotoxicity increased with addition of Molnupiravir. SEDDS formulations with droplet size under 300 nm were designed and optimized for antiviral therapy.

Keywords

Antiviral, Self emulsifying drug delivery systems, Cell culture, L929

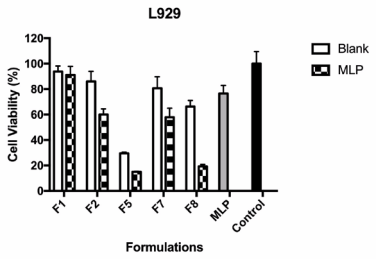

Figure 1. The amount of viable cells after treatment with SEDDS formulations on L929 cell line

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O14

FABRICATION AND CHARACTERIZATION OF METHYLPREDNISOLONE-LOADED COLON-SPECIFIC 3D-PRINTED DRUG DELIVERY SYSTEMS

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Methylprednisolone is a corticosteroid-derived, anti-inflammatory drug used for inflammatory bowel disease [1]. 3D printing technology can be defined basically as the process of obtaining a three-dimensional object layer-by-layer and it has advantages such as the possibility of precise and personal production, simplicity, controllable release profiles [2]. The aim of this study is to develop colon-specific 3D printed oral drug delivery systems of methylprednisolone. The formulations were printed layer by layer with 3D printing technolgy using an 18G needle and with 5 mm/s speed. The contents and codes of formulations are shown in Table 1. Methylprednisolone was dispersed in the polymer blend homogenously. The printed formulations were crosslinked with 4% $CaCl_2$ solution and dried at room temperature. Viscosity measurements of ink mixtures were carried out with Brookfield rheometer. Differential scanning calorimetry thermograms of formulations were obtained. Formulations were characterized in terms of diameter, thickness, hardness, friability, and in-vitro dissolution studies (n=3). Dissolution profiles were evaluated using USP Apparatus-1 at pH 1.2, 6.8 and 7.4 buffer solutions at 37°C. The highest viscosity among the ink mixtures was found in the F3 formulation. Differences were observed in the diameter, thickness and hardness of the formulations due to crosslinking and drying (Table 1). It was determined that the most suitable formulation for colon-targeting was F3, when the release profiles and tablet characterization studies were examined. Colon-targeted systems have been achieved successfully via 3D printing. The release profiles of the formulations varied with the ink mixture used in printing.

Keywords

3D printing, Eudragit, Pectin, Alginate, Controlled release, Colon-specific delivery

Formulation Codes	Content				Viscosity (cP)	Diameter (mm)	Thickness (mm)	Friability (%)	Hardness (N)	Drug Released (24 h, %)
	Drug (%)	Sodium Alginate (%)	Eudragit FS 30D (gram)	Pectin (%)						
F1	2	20	-	-	27038± 2606	11.5± 0.5	1.4±0.2	0	51.9±7.3	96.5± 3.3
F2	2	10	10	-	81044± 2190	15.3± 0.1	1.6±0.0	0	90.6±1.9	90.9± 8.0
F3	2	-	10	10	89261± 795	15.9± 0.2	1.1±0.1	0	80.5±7.4	100± 0
F4	2	-	-	20	55266± 1590	13± 0	1.1±0.1	0	14.9±0.9	101.3± 2.2

Table 1. The codes, component and characterization result of formulations (n=3; Mean±sd)

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O15

FABRICATION OF 3D PRINTABLE FILAMENTS USING PHARMACEUTICAL POLYMERS WITH HIGH GLASS TRANSITION TEMPERATURE

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FDM (Fused Deposition Modeling) is an extrusion-based 3DP technology depositing materials layer-by-layer. It requires thermoplastic filaments as feedstock materials. Fabrication of 3D printable filaments for polymers with a high glass transition temperature (Tg) is challenging since requiring high extrusion and printing temperatures causing degradation of polymers and thermo-labile drugs [1]. Thus, formulation and process parameters need to be modified using plasticizers, applying pre-plastification, pre-drying, and sieving steps to reduce the Tg of polymers [2,3]. This study aims to investigate printable filaments for pharmaceutical polymers with high Tg such as Eudragit-S100, Eudragit L100-55, HPMCAS, Ethyl cellulose (EC) and identifies the solutions to the challenges in filament production. By testing many formulations for each polymer, 3D printable filaments were successfully extruded for Eudragit-S100, HPMCAS, and EC using a single screw extruder (Noztek-Pro, UK). Eudragit L100-55 could not be extruded since highly aggregated in plastification. Intermediate steps included in the powder preparation process were shown to improve the mechanical and morphological properties of filaments. The diameters of the filaments were measured by a caliper. Mechanical and morphological properties of filaments were determined visually and manually Structural integrity and homogeneity of filaments were demonstrated by SEM. Printability of filaments was demonstrated by fabricating model tablets using an FDM-3D Printer (Craftboat-3, Hungary). In conclusion, by using process and formulation modifications, Eudragit-S100, HPMCAS, and EC filaments were successfully printed as tablets. Eudragit-S100, HPMCAS filaments obtained in this study can be used as coating layers for delayed-release tablets, and EC formulation can be used for extended-release tablets.

Keywords

Ethyl cellulose, Eudragit, Fused deposition modeling, Hot melt extrusion, 3D printing

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O16

DEVELOPMENT AND EVALUATION OF GINKGO BILOBA L. EXTRACT LOADED INTO SODIUM ALGINATE/POLYVINYLPYRROLIDONE FAST DISSOLVING SUBLINGUAL FILMS

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Fast dissolving Sublingual films (FDSFs) is novel approach to increase consumer acceptance by virtue of rapid dissolution, self administration. FDSFs provide the opportunity to administer medicine and avoid first-pass metabolism [1]. Nanofibers produced by electrospinning gained increasing importance because they present several advantages: burst control, stability, high surface area to volume ratio (which enhances drug release) and specific morphology which can be easily controlled during the process [2,3]. Oral bioavailability of flavonoids, including G. biloba extract, is limited due to their chemical complexity. The overall research objective was to compare the different techniques (electrospinning and solvent casting) used to prepare the FDSF containing freeze-dried G. Biloba extract(FDG) on the effect on their release profile of flavonoid glycosides, stability, disintegration time and morphological evaluation. Analysis of SEM micrographs showed that formulations considered uniform surface morphology with homogenous distribution of FDG and no crystalline structures visible on imagines (Figure 1). Dissolution rate tests showed that approximately 85% of loaded flavonoid glycosides had been released from FDSF-1 and 95% from FDSF-2. The disintegration time of the films was in ranged of 60 to 180 s. The quick in vitro disintegration was observed in FDSF 2 formulation. This study is of exceptional significance in the impact assessment of that the electrospinning process is more suitable to produce the FDSF formulations due to the obtained results. The preliminary results as a proof-of-concept demonstration reported here will shed new light on the future design and application of FDSFs by electrospinning method.

Keywords

Electrospinning, Solvent Casting Method, Flavonoid Glycosides

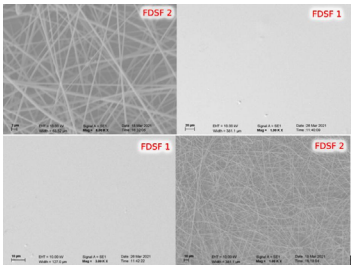

Figure 1. SEM images of FDSF formulations.

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O17

DESIGN AND INVESTIGATION OF CYTOTOXIC EFFECT OF CIPROFLOXACIN HCL-LOADED LIPID-POLYMER HYBRID NANOPARTICLE FORMULATIONS

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Ciprofloxacin HCL is a well-known broad-spectrum antibiotic. Besides, previous studies have demonstrated that ciprofloxacin in high doses induces apoptosis and inhibits the proliferation of cancer cells [1]. Nano-sized drug delivery systems promise to increase the therapeutic effect of conventional drugs in lower doses through their small size [2]. The objective of this study was to develop ciprofloxacin HCl-loaded lipid-polymer hybrid nanoparticles using poly(lactic-co-glycolic acid) as polymeric core, phosphatidylcholine and oleic acid as lipid shell and to investigate the anticancer activity of the optimized formulation on DU145 prostate cancer cells. Ciprofloxacin HCl-loaded hybrid nanoparticles were fabricated using double emulsion-solvent evaporation based single-step method. Developed formulations were characterized in terms of particle size and distribution, surface charge, encapsulation efficiency, in vitro drug release and thermal behavior, as well as anticancer activity. Negatively charged nanoparticles in the range of 200-400 nm were obtained. The lipid shell of the hybrid nanoparticles acted as a barrier and allowed to achieve an encapsulation efficiency approximately 4-times higher in lipid-coated hybrid nanoparticles compared to uncoated nanoparticles. Moreover, the effect of oleic acid added to the lipid layer on the particle characteristics was investigated. Adding oleic acid to the lipid layer increased the encapsulation of drug and positively affected the release of the drug. The anticancer activity of the drug-loaded and unloaded nanoparticles was evaluated on DU145 prostate cancer cell line by utilizing MTT assay. The unloaded nanoparticles showed no cytotoxicity whereas the ciprofloxacin HCl-loaded hybrid nanoparticles demonstrated a superior anticancer effect than pure drug on DU145 cells.

Keywords

Ciprofloxacin HCl, Cytotoxic effect, Lipid-polymer hybrid nanoparticle

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O18

EVALUATION OF CLINICAL PHARMACY SERVICES IN PEDIATRIC NEPHROLOGY SERVICE

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Although there have been some studies on drug-related problems (DRPs) in pediatric population, there has been no specialized research in pediatric nephrology patients[1,2]. The aim of this study is to provide clinical pharmacy services to hospitalized patients in the pediatric nephrology, to classify the detected DRPs and to determine the clinical pharmacist's contribution. The study was conducted between April 1st and October 31st, 2019 at a university hospital's pediatric nephrology service. In this process, 66 patients who were hospitalized in this service and using at least 1 drug were included in the study group and DRPs in their treatment protocol was prospectively evaluated according to the European Pharmaceutical Care Network (PCNE v.9). Patients were included in the control group, and their profiles were analyzed retrospectively using data obtained from medical reports for the first 66 patients collected immediately before April 1st. Both of the study group and control group were compared in terms of duration of hospital stay. In terms of overall demographic and clinical features, both groups were found to be similar ($p>0,05$). The most common causes of 134 DRPs in the study group were “patient-related” (36,2%). 96,3% of the clinical pharmacist’s interventions were accepted. Presence of polypharmacy and chronic kidney disease found as risk factors for DRPs. The intervention group median duration of stay was 7 (5-12,5) days, while the control group was 9,5 days (7-13) days ($p<0,05$). This study demonstrates that clinical pharmacists play an important role in the diagnosis and resolution of DRPs, and clinical pharmacy services can help reduce length of stay.

Keywords

Clinical pharmacy, Pediatric nephrology, Pediatrics, Drug related problem

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O19

THE ROLE OF THE CLINICAL PHARMACIST IN THE EVALUATION OF DRUG-RELATED PROBLEMS IN THE INTENSIVE CARE UNIT OF A UNIVERSITY HOSPITAL IN TURKEY

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Critically ill patients treated in the intensive care units (ICUs) often suffer from side effects and drug related problems (DRPs) that can be life-threatening [1]. One way to prevent DRPs and improve drug safety and efficacy is to include clinical pharmacists in the clinical team [2]. The aim of this study is to classify drug-related problems and determine risk factors by a clinical pharmacist in the ICU of a university hospital in Turkey. This prospective observational study was conducted between December 2020 and July 2021 in Gazi University Medical Faculty Hospital Internal Diseases Intensive Care Unit. During the study, the clinical pharmacist's recommendations and other clinical services for patients were recorded. DRPs were categorized according to the Pharmaceutical Care Network Europe methodology. Of the 151 patients, 108 patients had at least one DRP and the total number of DRPs was 206. Inappropriate combination of drugs (35.43%), high drug dose (24.27%), and low drug dose (14.56%) constituted most of the causes of DRPs, respectively. Dose change was the highest percentage of the planned interventions with a rate of 56.79 %. Intervention was accepted at a rate of 90.8% and it was fully implemented. In this study, the importance of the clinical pharmacist in the determination and analysis of DRPs was emphasized. Clinical pharmacist interventions were also effective in preventing DRPs and potential adverse effects.

Keywords

Clinical pharmacy, Drug related problems, Adverse drug events , PCNE DRP classification

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O20

EVALUATION OF SECONDARY METABOLITE PROFILING IN FIVE ULMUS SPECIES WITH UNTARGETED METABOLOMICS STUDY

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The genus *Ulmus* belonging to the Ulmaceae comprises four species (*U. glabra* Hudson, *U. minor* Miller., *U. canescens* Melville, *U. laevis* Pallas) in Turkey [1]. In India, China, and South Korea, and Turkey, different *Ulmus* species have been used as folk medicine. Additionally, *U. rubra*, known as slippery elm, takes part in the American Herbal Pharmacopoeia [2]. Although it has traditionally been used in treatment for several places in the world, there are very few biological and phytochemical studies on *Ulmus* species. The aim of this study was to dereplicate the secondary metabolites in *Ulmus* species and compare the metabolite profiles of the species to reveal the differences. 85% ethanol (maceration) and aqueous (decoction) extracts have been prepared from the inner bark of four *Ulmus* species grow in the flora of Turkey and from *U. rubra* as a reference plant in the pharmacopeia. Metabolic profiling of the extracts has been performed with LC-qTOF-MS system [3]. As a result of the analysis, especially 123 secondary metabolites that are common in all species, and totally 290 different metabolites have been determined in five *Ulmus* species. Multivariate analysis results showed that different metabolomic profiles between *Ulmus* species. In this study, the dereplication of the metabolites of the species was performed. At the same time, it is suggested that metabolomic profiles can be used in distinguishing of the extracts.

Keywords

Ulmus sp., Metabolomic, Dereplication

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O21

LC-MS/MS ANALYSIS AND BIOLOGICAL ACTIVITIES OF ENDEMIC ACHILLEA SIEHEANA STAPF FROM TURKEY

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The genus *Achillea* L. is described by 6 sections and 49 species (58 taxa), and 24 species of them are endemic with an endemism ratio of 49% in the Flora of Turkey [1]. In traditional medicine, *Achillea* species have been utilized for treating various diseases such as rheumatic complaints, cancer treatment, blood sugar and cholesterol problems, hemorrhoids, and respiratory diseases [2]. In this study, *in vitro* ABTS, DPPH, 5-lipoxygenase, and α-glucosidase inhibitory activities of *n*-hexane (ASH), dichloromethane (ASD), ethyl acetate (ASE), and methanol (ASM) extracts from the aerial parts of endemic *A. sieheana* were assayed for the first time. Also, the total amount of phenolic compounds of extracts were calculated, and the phytochemical content of ASE, the most active extract, has been determined by LC-MS/MS for the first time. ASE demonstrated significant antioxidant activity with IC_{50} values of 0.096 and 0.156 mg/mL for ABTS and DPPH, respectively. ASD and ASE with IC_{50} values of 0.045 and 0.089 mg/mL exhibited significant anti-inflammatory activity. ASE showed moderate α-glucosidase inhibitory activity with an IC_{50} value of 0.774 mg/mL. Also, the total phenolic content was found the highest in the ASE. Feruloylquinic acid, vitexin, luteolin glucoside, luteolin, 300MW methoxyflavonoid hexoside, 300MW methoxyflavonoid glucuronide, isorhamnetin and hispidulin 7-glucoside in the ASE were detected by LC-MS/MS. The results demonstrated that ASE had significant anti-inflammatory and antioxidant potential.

Keywords

Achillea sieheana, LC-MS/MS, Anti-inflammatory, Antioxidant

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ACETYLCHOLINESTERASE INHIBITORY POTENTIAL AND METABOLIC PROFILE OF BOLBOSCHOENUS MARITIMUS (L.) PALLA

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by loss of cognitive functions such as thinking, learning, and memory [1]. Acetylcholinesterase which degrades the neuromediator acetylcholine has been a key target to search for potential natural products for the treatment of AD [2]. In this current study the methanolic extract of *Bolboschoenus maritimus* (L.) Palla has been searched for its potential inhibitory effect on acetylcholinesterase enzyme by Ellman's method [3]. Gas chromatography-mass spectrometry (GC-MS) and liquid chromatography quadrupole time of flight mass spectrometry (LC-QTOF-MS) were used to identify the metabolites in the methanolic extract of *B. maritimus*. As a result of the activity studies, acetylcholinesterase inhibitory activity was defined as 70.8%. GC-MS and LC-QTOF-MS utilizations were resulted in determining 1747 and 19416 metabolites, respectively. 302 and 276 of them were annotated using retention index libraries and among these metabolites, flavonoid-3-*O*-glycosides and flavonoid-7-*O*-glycosides were the most abundant ones. According to our results, *B. maritimus* is a promising acetylcholinesterase inhibitory source and potential research target for AD. Since phenolic compounds have been reported to have acetylcholinesterase inhibitory activity [4] the phytochemical content of *B. maritimus* is compatible with its inhibitory activity.

Keywords

Alzheimer, Acetylcholinesterase inhibition, GC-MS, LC-QTOF-MS

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ISOLATION OF SILK PROTEIN AND SYNTHESIS/CHARACTERIZATION OF HYBRID NANOFLOWERS

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Silk protein obtained from silk cocoons have been used in the cosmetic, food, biotechnology and health sectors in recent years. Our aim in this study is to synthesize and characterize zinc (Zn) nanoflowers of biotechnologically important silk protein. In this study, firstly, certain amounts of *Bombyx mori* cocoons were taken and their gums were removed by the Na_2CO_3 method. The remaining mixture was colloidalized by the LiBr method. Dialysis was performed against deionized water for 72 hours. Obtained silk proteins were lyophilized [1]. Zn hybrid nanoflowers of the proteins was synthesized at different pH (6-7.4-8-9) and holding times (3 hours-6 hours-12 hours-24 hours). Zinc acetate solution was used as metal ion. After the synthesis, washing and drying processes were carried out [2]. Synthesized Zn hybrid nanoflowers were characterized from various aspects. SEM, FTIR, XRD, EDX analyzes were performed. Optimal conditions were determined. As a result of our studies, silk protein was isolated. Zn hybrid nanoflowers of isolated proteins were synthesized and characterized, pH 7.4 and 6 hours waiting time gave the most optimal results. Eco-friendly isolation of silk proteins and synthesis of organic-inorganic Zn hybrid nanoflowers by using proteins as an organic part with high surface/volume area will be presented in our study. Future studies will be continued with toxicity and biological activities.

Keywords

Silk protein, Zinc nanoflower, Biotechnology, Nanotechnology, Bombyx mori

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O24

THE PROBLEM OF PYRROLIZIDINE ALKALOID IN HERBAL TEA USED IN CHILDREN'S GAS PAIN

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Recently, the problem of pyrrolizidine alkaloid contamination has been observed in herbal teas [1]. Toxic effects related to the consumption of herbal products contaminated with pyrrolizidine alkaloids are frequently reported in the literature. The German Federal Institute for Risk Assessment concluded that there is a risk for children who consume large amounts of herbal teas [2]. This study, it was aimed to determine the pyrrolizidine alkaloid content in herbal products used in infant gas problems. Herbal tea samples were obtained from spice shops and the internet. After using 0.05 M sulfuric acid (H_2SO_4) extraction solution for the samples, solid phase extraction was performed in a vacuum chamber. Pyrrolizidine alkaloid contamination in herbal tea samples was analyzed qualitatively and quantitatively using the Liquid Chromatography Quadrupole Time of Flight Mass Spectrometry (LC-QTOF-MS) method. Interventions in different matrix types were controlled by adding pyrrolizidine alkaloid standards to the samples. Among the 12 pyrrolizidine alkaloid standards to be determined, up to 4 pyrrolizidine alkaloids were detected in a single sample. Pyrrolizidine alkaloid amounts were determined in a range from 20 ng/g (LOQ) to 540 ng/g levels. The N-oxide forms of the alkaloids which amounts were determined were also defined for confirmation purposes. The presence of pyrrolizidine alkaloid contamination has been detected in some tea samples sold for infant gas problems. In terms of public health, herbal teas sold on the internet should be inspected periodically by the health authority.

Keywords

Child, Pyrrolizidine alkaloids, Gas pain, Herbal tea

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O25

EVALUATION OF RADICAL SCAVENGING ACTIVITY AND TYROSINASE INHIBITION OF SOME CITRUS SPECIES CULTIVATED IN TURKEY VIA SPECTROPHOTOMETRIC METHODS AND HPTLC-EFFECT DIRECTED ANALYSIS

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Citrus species have an important place in the food, cosmetics, and fruit juice industries. However, parts such as the pericarp and seed emerge as waste at the end of production [1]. In the present study, the fresh fruit peels of some species of the genus *Citrus* L. (*Citrus aurantium* L. (sour orange), *C. reticulata* Blanco (Robinson mandarin), *C. unshiu* Marc. (Satsuma mandarin), *C. sinensis* L. (Washington navel orange), *C. limon* Brum. (lemon), *C. limetta* (sweet lime), *C. bergamia* (bergamot), *C. Medica* (citron), *C. paradisi* Macf. (Starruby grapefruit), *C. maxima* (pomelo) and *C. maxima x C. paradisi* (oroblanco)) cultivated in Turkey were extracted with 80 % methanol by accelerated solvent extraction (ASE). Total phenolic/flavonoid content, DPPH radical scavenging activity, and tyrosinase inhibition were evaluated with spectrophotometric methods. The fingerprint analyzes of the extracts were done by a High-Performance Thin Layer Chromatography system (HPTLC, Camag, Muttenz, Switzerland). HPTLC-effect directed analysis was employed to identify the compounds responsible for the radical scavenging/antityrosinase activities. Bioactive compounds were isolated with preparative-HPTLC and analyzed by Mass Spectroscopy system (Applied Biosystems, 3200 Q TRAP MS/MS). In the extracts, naringin (C3, *hRf* 42) which is responsible for the antityrosinase activity, hesperidin (C1, *hRf* 40), and neoeriocitrin (C2, *hRf* 37), which are associated with the radical scavenging activity were determined, tentatively.

Keywords

Citrus, HPTLC, Tyrosinase, Radical scavenging activity

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O26

COMPOSITION AND ANTIMICROBIAL ACTIVITY OF THE ESSENTIAL OILS OF FIVE DIFFERENT ARTEMISIA L. SPECIES

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The awarding of the 2015 Nobel Prize in Medicine for the discovery of artemisinin, a sesquiterpenoid lactone, in *Artemisia annua* L. and proving its effectiveness in the treatment of malaria sparked a huge interest in the chemistry and biological activity of other *Artemisia* species. The essential oils obtained by hydrodistillation from the aerial parts of five *Artemisia* species (*A. abrotanum* L., *A. annua* L., *A. absinthium* L., *A. incana (L.) Druce, A. tournefortiana* Rchb.) originated from Turkey were analyzed by GC-FID and GC-MS, simultaneously. We identified total number of compounds and their ratio within the essential oil for each species as *A. annua* (42, 92.31%), *A. absinthium* (26, 93.87%), *A. incana* (52, 94.65%), *A. abrotanum* (28, 81.40%), *A. tourfortiana* (22, 89.63%), respectively. The major components were identified as artemisia ketone in *A. annua* L. (%53.71), sabinyl acetate (%22.99) in *A. absinthium* L., camphor in *A. incana (L.) Druce* (%29.66), chrysanthenone in *A. abrotanum* L. (%55.88), and (*Z*)-beta-farnesene in *A. tournefortiana* Rchb. (%71.53). Investigating the antimicrobial activity of the essential oils on five bacteria (*Escherichia coli* NRRL B-3008, *Bacillus subtilis* NRRL B-4378, *Salmonella typhimurium* ATCC 13311, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 6538), the highest activity against all species was observed in *A. incana*. *Staphylococcus aureus* was observed to be the most sensitive bacteria to all essential oils.

Keywords

Artemisia, Essential oil, Antimicrobial activity

O27

NEUROPROTECTIVE EFFECTS OF SELECTED SALVIA SPECIES FROM TURKEY IN PARAQUAT-INDUCED PARKINSON'S DISEASE DROSOPHILA MODEL

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Parkinson's disease (PD) is the second most common neurodegenerative disorder caused by the progressive loss of dopaminergic neurons from the *substantia nigra* in the brain. Epidemiological data indicate that the herbicide paraquat (PQ) is an environmental risk factor for the development of PD [1, 2]. We used a *Drosophila* model of PD as an effective and inexpensive screening platform to identify potential therapeutics from natural products [3]. The genus *Salvia*, commonly known as sage, is the largest genus in the Lamiaceae family and includes several species that are protective against neurodegenerative diseases due to their wide range of phytochemical constituents [4]. In this study, we investigated the neuroprotective effects of 14 *Salvia* species (*S. absconditiflora*, *S. aethiopis*, *S. candidissima*, *S. cedronella*, *S. frigida*, *S. fruticosa*, *S. pisidica*, *S. potentillifolia, S. sclarea*, *S. syriaca*, *S. tomentosa, S. verticillata*, *S. viridis*, *S. wiedemannii*) growing in Turkey. The aerial parts of the plants were extracted with methanol and the partitioned aqueous fractions from the methanol extracts were tested on adult male wild-type flies, *Canton-S*. We employed survival, mobility and lipid peroxidation assays to assess protection against PQ-induced PD phenotypes. Interestingly, the aqueous fractions of *S. absconditiflora, S. aethiopis, S. cedronella, S. pisidica,* and *S. verticillata* at 2 mg/mL and *S. syriaca* at 1 mg/mL increased the survival percentages and rescued mobility defects against PQ toxicity. We have identified those 6 *Salvia* species as potential neuroprotective candidate extracts against PQ-induced neurotoxicity that can be further explored for therapeutic intervention to combat PD.

Keywords

Salvia, Lamiaceae, Parkinson's Disease, Drosophila, Neuroprotection

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O28

SCOPARONE – A COMPOUND OF LIQUORS CONTAINING ARTEMISIA SPECIES INFLUENCE ON EMOTIONAL STATE EVALUATED IN SWISS MICE

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Artemisia spp. has been used in Chinese medicine over centuries for the treatment of malaria, viral, bacterial, and microbial infections because of the contents of natural compounds such as coumarin derivatives, responsible for its medicinal properties. Also, the herb was found to be useful in preparing apéritifs and liquors consumed all over the world. The study aimed to evaluate if scoparone, a simple coumarin present in Artemisia spp. affects central nervous system function. To evaluate the influence of scoparone on depressive-like behaviors the forced swimming test (FST) was performed on both male and female Swiss mice. An elevated-plus maze (EPM) was applied to assess the level of anxiety in the male Swiss mice. The study showed that the single, i.p. injection of scoparone (5, 12.5, and 25 mg/kg) did not change the immobility time in the FST in male and female mice, thus we conclude that the compound did not influence depressive-like behaviors. Furthermore, the single dose of scoparone (2.5 and 5 mg/kg) decreased the time spent on the open arms and decreased the number of open arm entries in the EPM showing anxiogenic effects. Further study on the behavioral effects, mechanisms of action, and bioavailability of Artemisia spp. derived compounds are necessary to explain the central nervous system activity of this herb.

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Keywords

Artemisia spp., Scoparone, Mice, Anxiety, Depression

O29

IN VIVO AND IN VITRO ANTI-INFLAMMATORY POTENTIALS OF ABIES CILICICA (ANT. & KOTSCHY) CARR. SUBSP. ISAURICA COODE & CULLEN ESSENTIAL OIL: A POTENTIAL ACTIVE PHARMACEUTICAL INGREDIENT (API) FOR TOPICAL DRUG DELIVERY SYSTEMS

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Abies cilicica (Ant. & Kotschy) Carr. subsp. *isaurica* Coode & Cullen belonging to Pinaceae family, is endemic and native to Mediterranean region of Turkey [1]. The resin is known to have antiseptic, anti-inflammatory, antipyretic, antibacterial, and antiviral potentials [2]. In this study, we aimed to investigate the *in vivo* and *in vitro* anti-inflammatory potentials of *Abies cilicica* subsp. *isaurica* essential oil. The leaves were subjected to hydrodistillation to get essential oil for subsequent GC-FID/MS analysis. The *in vivo* and *in vitro* anti-inflammatory activities of the essential oil were evaluated by using *in vivo* HET-CAM method [3] and *in vitro* COX-1/COX-2 enzyme inhibitory assays [4]. *β*-Pinene(41.5%), *α*-pinene(12.9%) and intermedeol(10.6%) were found as the major compounds of the essential oil. At the concentration of 50 µg/pellet the oil showed strong *in vivo* anti-inflammatory activities with 75.8±0.3% inhibition value. The essential oil also exhibited significant *in vitro* COX-2 enzyme inhibitory potential with IC_{50} value of 83.3 µg/mL whereas no COX-1 inhibitory activity. Angiogenesis may become an effective therapeutic target in the discovery of more effective new bioactive plant derived natural angiogenesis inhibitors and anti-inflammatory agents including plant extracts, essential oils and their volatile compounds with less toxicity to treat angiogenesis originated pathologies such as cancer and inflammation. So, in the future stages of the study, different topical drug delivery systems will be designed and characterized by using the essential oil with anti-inflammatory potential as an API.

Acknowledgements: This study was financed by Anadolu University Scientific Research Project Foundation (No: 1906S121).

Keywords

Abies cilicica subsp. isaurica essential oil, Anti-inflammatory, Topical drug delivery

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O30

DIETARY FRUCTOSE AND KEFIR SUPPLEMENTATION CHANGE THE COMPOSITION OF FECAL MICROBIOTA IN THE RATS

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The fecal microbiota may be influenced by many factors including diet. High-fructose consumption might be a risk factor for several metabolic diseases. Kefir, which is known as a diary probiotic mixture, has several health improving effects, but its mechanism of action remains mostly unclear. This study aimed to evaluate the effects of fructose and kefir on the combination of fecal microbiota in rats. Fructose was given to the male Wistar rats as a 20% solution in drinking water for 15 weeks. Kefir supplementation (1ml/100 g body weight) was performed by gastric gavage once a day during final 6 weeks. Bacterial content of microbiota was determined with 16S rRNA sequencing and evaluated at the genus level. Dietary high-fructose significantly increased the relative abundance of Lactobacillus genus, but interestingly decreased the diversity of the Lactobacillus. Kefir treatment did not affect the Lactobacillus abundance, however markedly raised the variety of the Lactobacillus. Helicobacteracea abundance was also increased in fructose-fed rat, which responded to kefir supplementation with a significant decrease. Fructose rich diet also markedly increased the dybiosis apparent at genus level, including Blautia, Alistipes, Oscillibacter abundance, but kefir treatment decreased relative abundance of Blautia, Alistipes, but not Oscillibacter. In conclusion, dietary high-fructose may cause to unfavourable changes in the fecal microbiota; however kefir treatment exerted to improve the diversity of the microbiota. These findings could provide important information for understanding in dietary factor-induced alteration in composition of microbiota.

Keywords

High-fructose diet, Kefir, Fecal microbiota

O31

THE COMPARISON OF VASCULAR ENDOTHELIAL AND SMOOTH MUSCLE CELLS CO-CULTURING IN HYDROGEL-BASE AND BIO-PRINTING 3D-CELL-CULTURE SYSTEMS

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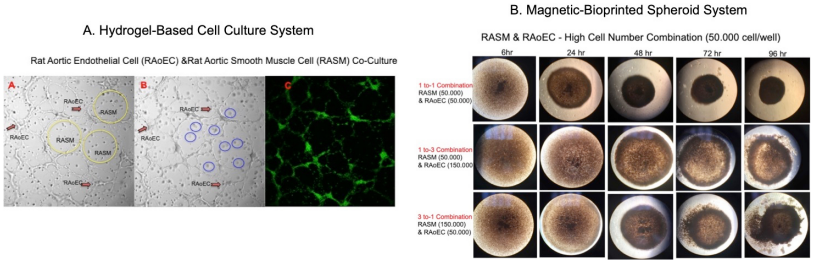
Two-dimensions (2D)-cell-culture systems have been largely used in conventional pre-clinical research and drug discovery; however, they have certain disadvantages to evaluate drug response. Recently, three-dimension (3D)-cell-culture systems have been developed to better characterize physiologic microenvironments of tissues, and they can be easily applied for high-throughput systems. They provide an opportunity for investigation mono- and multi-cell-to-cell interaction. In this study, we have attempted to develop co-cultured cells in two different 3D-cell-culture systems. First, we have optimized the co-culturing condition of primary rat aortic vascular smooth muscle cells (RASM) and endothelial cells (RAoEC) in terms of cell growth-rate, plating cell number combinations, media-composition. The optimized co-cultures have been applied to hydrogel-based and to magnetic-bio-printed systems. After applying protocols, the co-cultured cells were plated in glass-bottom 96-well-plates and evaluated for vessel development and spheroid formations, and cell-to-cell interaction by confocal-microscopy-Z-stack. Our findings showed that the vessel generation was detected only on the surface of the hydrogel, and not embedded. Longer time may be required for the vessel network to form 3D-structures by reaching from the surface to deeper inside of gel. In the bio-printed, spheroids were quickly formed, but high-cell number combinations tended to be easily dispersed over time. The cells in spheroid-forms were also found to be side-by-side and not interacting together in defined substructures. Each system has their advantages and disadvantages. Even though magnetic-bio-printing system cannot provide usable 3D-spheroids alone, optimization can be made by combining with hydrogel-based material to develop tissue-structure.

This study was supported by TUBITAK-2219 & Eleusis-PBC.

Keywords

Vascular cells, 3D co-culturing, Hydrogel System, Magnetic-Bioprinting System



Hydrogel-Based and Magnetic-Bioprinted spheroids co-culturing

THE EFFECT OF 4-PHENYLBUTYRIC ACID ON THE HYPERTENSION INDUCED CARDIAC STRESS RESPONSES

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4-phenylbutyric acid (4-PBA) is a low-molecular-weight chemical chaperone that attenuates the accumulation of misfolded proteins in the endoplasmic reticulum (ER) and inhibits the ER stress. ER stress pathway is considered as a therapeutic target for hypertension [1, 2]. In this study, the effects of 4-PBA on plasma total antioxidant capacity (TAC) and nitric oxide (NO) levels and cardiac expression of some functional proteins related to ER stress and apoptosis were investigated in hypertensive rats. Hypertension was induced by unilateral nephrectomy and then deoxycorticosterone acetate-salt administration in male Wistar rats for 12 weeks. ERS inhibitor 4-PBA (150mg/kg/day) was given by intraperitoneal injection last four weeks. Plasma TAC and nitrite levels, as an indicator of NO, were measured spectrophotometrically. Expression of proteins that are markers of ER stress and apoptosis were examined by Western Blotting in left ventricle. Plasma TAC levels were higher in hypertensive rats compared to the control group, 4-PBA administration did not affect TAC levels. Plasma NO levels were similar in all groups. In the hypertensive group, the increase in the expression of the ER stress marker GRP78 and p-PERK was prevented by 4-PBA treatment. While the expression of anti-apoptotic protein Bcl-2 was lower in the hypertensive heart, 4-PBA treatment reversed this decrease. Pro-apoptotic Bax expression did not differ between groups. These findings suggest that ER stress inhibition with 4-PBA may have a beneficial effect on some parameters related to cardiac stress and may be an important therapeutic target in treatment approaches for hypertension

Keywords

Hypertension, Oxidative stress, Endoplasmic reticulum stress, Apoptosis, 4-phenylbutyric acid, Heart

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O33

TRIMETAZIDINE ATTENUATES CYCLOPHOSHAMIDE-INDUCED CYSTITIS IN MICE BY INHIBITING TLR4/NFκB SIGNALING PATHWAY

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Cyclophosphamide (CP)-induced cystitis is a challenging clinical problem involving inflammation and dysfunction of bladder [1]. Trimetazidine (TMZ) is an anti-anginal drug with anti-oxidant and anti-inflammatory properties [2]. However, its effect on CP-induced cystitis is unknown. We aimed to investigate the potential protective effects of TMZ in CP-induced cystitis via inhibiting TLR4/NFκB pathway and its effect on the anti-tumor activity of CP. Cystitis was induced by a single injection of CP (300 mg/kg; i.p) in mice and TMZ was administered (10 and 20 mg/kg/day; i.p.) for 5 consecutive days before CP. 24 hours after cystitis induction, the bladders were removed for histopathological evaluation, functional contractility studies, biochemical analysis and western blotting. Effect of TMZ on the anti-tumor activity of CP was evaluated in MDA-MB-231 cells with MTT assay [3,4]. CP caused severe cystitis confirmed by histological alterations, which was partially ameliorated by TMZ. CP-induced cystitis caused a significant decrease in the carbachol-evoked contractions of bladder strips and TMZ (20 mg/kg) pretreatment restored the contractile response. SOD activity and GSH content –biomarkers of antioxidant status- were significantly increased and, TNF-α and IL-1β levels –proinflammatory cytokines- were markedly decreased in the bladders of TMZ-pretreated mice compared to CP. TMZ reduced the CP-induced increase in TLR4 expression and NFκB phosphorylation in the bladders. TMZ alone and CP co-treatment decreased the cell viability. Our study provides the first evidence that TMZ attenuates CP-induced urotoxicity due to its anti-oxidant and anti-inflammatory effects possibly via downregulating TLR4/NFκB signaling while not inerfering with the anti-tumor activity of CP.

Keywords

Bladder dysfunction, Cyclophosphamide, Cystitis, Inflammation, TLR4, Trimetazidine

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O34

PARAOXONASE 1 STATUS IN PSYCHIATRIC PATIENTS TREATED WITH PSYCHOTROPIC DRUGS

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Psychiatric patients showed a shorter life expectancy than the general population which is associated with side-effects of psychotropic drugs, such as dyslipidaemia and diabetes. Paraoxonase 1 (PON1) is a plasmatic enzyme with antioxidant, anti-inflammatory and antiatherogenic properties. PON1 activity is shown to be reduced in metabolic disorders such as obesity and type 2 diabetes. The most relevant polymorphism of PON1 is the Q192R, whose allele 192Q has higher protection than 192R against cardiovascular diseases. In the present study, associations between psychotropic drugs (active substances and their defined daily dose), biomarkers of the metabolic syndrome (with focus on cardiovascular diseases) and PON1 status will be evaluated in patients (n=74) of the Psychiatric Centre Dr. Esquerdo. Thus, the aims of the current work are to analyse the PON1 activity in serum samples using non-organophosphate substrates and to infer the Q192R functional genotype (QQ, QR and RR). Three PON1 activities were determined (n=28 as a pilot subset): 1) arylesterase without salt (PALSase) using phenyl acetate (PA), 2) arylesterase with salt (PAHSase) using PA and 3) CMPAase using 4-(chloromethyl)phenyl acetate (CMPA). The functional genotype was ascertained by plotting PAHSase vs CMPAase. Genotype frequency was 16 QQ (57%), 8 QR (29%) and 4 RR (14%). These results are in parallel with the frequencies in the Caucasian population determined in the scientific literature. Suggestive statistically significant associations between drugs, biomarkers and PON1 activities were already found in the preliminary subset, which will be corroborated when the sample size reaches an optimal size.

Keywords

Mental disorders, Metabolic diseases, Oxidative stress, Paraoxonase 1

O35

TARGETING ESTROGEN RELATED PATHWAYS AGAINST BREAST CANCER

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Breast cancer has the highest incidence rate among the cancers in women. Since,estrogens play a main role in estrogen receptor positive(ER+) breast cancer subtype,current study aimed to develop cost-effective therapy options with novel melatonin analogs via targeting the estrogen related pathways:ER mediated proliferation of cancer cells and the promotion of cancer cells via increased estrogen levels in breast tissue.The estrogen levels in the breast are associated with enzymes which are involved in estrogen synthesis and metabolism.Indole based melatonin analogs were synthesized and their cytotoxic, anti-proliferative, anti-migrative effects and estrogen receptor antagonist activity,have been screened in ER(+) breast cancer cell lines. The effects of molecules against estrogen synthesis inhibition were investigated via aromatase assay.Also,the actions of the molecules against estrogen metabolizing enzyme,CYP1B1 were evaluated. Among 24 molecules,M6 showed the most promising inhibitory actions against ER (+) breast cancer cell proliferation. Therefore,M6 was investigated further in *in vivo* syngeneic tumor model.In addition to tumor growth studies,the response of mononuclear cells in peripheral blood to treatment was monitored via extracellular flux analyses to screen effects of the molecule in intact animal.According to the results,the promising *in vitro* cytotoxic,anti-proliferative,anti-migrative, estrogen synthesis inhibitory effects of M6 was not confirmed in *in vivo* tumor model. However,the bioenergetic changes of peripheral blood mononuclear cells in tumor model have shown that M6 promotes mitochondrial coupling activity,which suggests a rewarding role for M6 as an adjuvant therapeutical agent.
This study was supported by Ege University Research Fund grant 18-ECZ-008,NIH NIGHMS P20GM109005 and UAMS FY19 Chancellor Award. A.T.A. was supported with TUBITAK2214/A scholarship.

Keywords

Breast cancer, Estrogen, Melatonin analog, Extracellular flux, Peripheral blood mononuclear cells

O36

CYTOTOXIC ACTIVITY AND PHYTOCHEMICAL ANALYSIS OF LECOKIA CRETICA (LAM.) DC.

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Medicinal plants and phytochemicals stand out in the search for new and effective compounds against cancer prevention and treatment. The Apiaceae family is one of the important families used in traditional medicine and has numerous biological activities including anticancer [1]. *Lecokia cretica* (Lam.) DC. (Apiaceae) is the only species belonging to *Lecokia* genus. In the literature, there is no cytotoxic activity study on *L. cretica*. This study aims to investigate the cytotoxic activity of *L. cretica* methanol extract and sub-extracts which are partitioned with water and extracted with *n*-hexane, dichloromethane, ethyl acetate, *n*-butanol, respectively, and to determine the phenolic profile. Cytotoxic activity was investigated by MTT assay on HeLa, HepG2, MCF-7, and A549 as well as BEAS-2B cell lines for determining selectivity. Phenolics and flavonoids in the methanol extract were identified and quantified by using HPLC. According to the results IC_{50} values of the methanol extract on MCF-7, HeLa, A549, HepG2, BEAS-2B were 13.5±1.54 µg/mL, 52.07±4.13 µg/mL, 29.75±2.71 µg/mL, 62.39±5.01 µg/mL, 12.58±1.26 µg/mL, respectively. Among the sub-extracts, *n*-hexane and dichloromethane extracts exhibited strong cytotoxic activity on cancer cell lines (IC_{50} ranges: 9.43-21.09 µg/mL), thus these extracts can be promising for cytotoxic activity-guided isolation studies. Luteolin-7-*O*-glucoside (1,53 g/100 g) was detected in the methanol extract. This is the first report on the cytotoxic activity of *L. cretica* and the presence of luteolin-7-*O*-glucoside in the plant.

Acknowledgments: This study was supported by the Scientific Research Projects Unit of Gazi University (02/2020-09).

Keywords

Anticancer, Cytotoxic activity, Lecokia cretica, Apiaceae, HPLC

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COMPARATIVE EVALUATION ON THE CHEMICAL COMPOSITIONS, ANTIOXIDANT, ANTI-INFLAMMATORY AND ANALGESIC ACTIVITIES OF CISTUS CRETICUS, C. SALVIIFOLIUS AND C. LAURIFOLIUS HYDROALCOHOLIC EXTRACTS

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Cistus species are frequently used as a folk remedy to relieve several ailments like rheumatism and renal inflammations [1]. This study aimed to comparatively characterize the phenolic composition and investigate the antioxidant, anti-inflammatory, and analgesic activities of the aerial parts of *C. creticus*, *C. salviifolius* and *C. laurifolius* hydroalcoholic extracts. In this study, phenolic compositions of the extracts were screened by HPTLC. Further, marker contents (rutin, hyperoside, isoquercitrin, astragalin, quercitrin, tiliroside, and quercetin) were quantified by a new validated HPLC method. HPTLC-direct bioautography is used to establish the compounds that exert antioxidant activity. Moreover, anti-inflammatory activity of the extracts was determined by nitrite and IL-6 levels in RAW264.7 cells. Besides, analgesic activity was assessed by the inhibition potential of PGE_2 level in LPS-activated murine macrophage cells. In conclusion, HPTLC fingerprinting helped to distinguish *Cistus* spp. from each other. The highest tiliroside content was found in *C. creticus* (2.42±0.01 mg/g), while the highest hyperoside content was detected in *C. salviifolius* (3.06±0.02 mg/g) and *C. laurifolius* (1.96±0.01 mg/g). HPTLC-DPPH revealed that rutin, hyperoside, isoquercitrin, quercitrin, and quercetin mainly contributed to the antioxidant activity of the extracts. Furthermore, *C. laurifolius* exerted the highest anti-inflammatory activity by reducing nitrite level at 0.5 mg/mL. In addition, IL-6 level was reduced dose-dependently by all *Cistus* spp. As a result of analgesic activity testing, *C. laurifolius* extract showed the most remarkable decline in PGE_2 level among the other *Cistus* species ($p<0.0001$). The results show that *Cistus* species are rich in flavonoids and have diverse pharmacological activities.

Keywords

Cistus L., HPTLC, HPLC, Antioxidant activity, Anti-inflammatory activity, Analgesic activity

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O38

EVALUATION OF DOSE-DEPENDENT EFFECTS OF SOME NATURAL COMPOUNDS ON BREAST CANCER CELL LINES

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Breast cancer, a global public health problem, is the most common female cancer and third most common cause of cancer-related deaths worldwide [1, 2]. This implies that there is a need for development of new effective method to kill cancer cells without affecting healthy cells [3, 4]. In our study, we have hypothesized that capsaicin, β-carotene, taurine and melatonin would have antiproliferative, antimigration and antioxidant activities on human breast cancer (MCF-7) cell lines. MCF-7 cell lines were treated with different concentrations of capsaicin, β-carotene, taurine and melatonin and its cytotoxicity effect was measured by MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4sulfophenyl)-2H-tetrazolium] assay. Dulbecco's Modified Eagles Medium (DMEM) and treated with different concentrations for two consecutive days. The effect of compounds on cell migration was evaluated using the wound-healing assay. Antioxidant and oxidant capacity were determined using Rel Assay kits. Capsaicin, β-carotene, taurine and melatonin showed cytotoxic activity on MCF-7 cell lines compared to healthy fibroblast (L929) cell lines. In the wound healing results, it was observed that the slits opened in the first 24 and 48 hours healed at the lowest level and the migration ability of the cells was restricted. Capsaicin at concentrations10 µM; β-carotene at concentrations 25 µM; melatonin at concentrations 10, 25 and 50 µM; taurine at concentrations 1, 50 and 100µM showed antioxidant activity in the MCF-7 cell line compared to the L929 cell line. According to these data capsaicin, β-carotene, taurine and melatonin may be a new candidate molecule in treatment of the breast cancer cell lines in future.

Keywords

MCF-7, Capsaicin, β-carotene, Taurine, Melatonin

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O39

COMPUTATIONAL DESIGN AND IN VITRO VALIDATION OF POTENT GLYCOGEN PHOSPHORYLASE INHIBITORS

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Regulation of the glycogen metabolism is an important therapeutic strategy for the development of new treatments for type 2 diabetes and, more recenty, different cancers such as glioblastoma. Glycogen phosphorylase (GP) is an allosteric enzyme with six different binding sites. It plays a key role in the glycogenolysis pathway and is an important target for compounds that prevent unwanted glycogen breakdown under high glucose conditions. *In silico* approaches are a useful tool towards the identification of new and better GP inhibitors [1]. Herein, we present recent computational studies on natural product analogues as inhibitors of GP supported by kinetics and X-ray crystallography in a multidisciplinary approach to drug design. Docking and post-docking strategies, combined with quantum mechanics methods have been successfully applied to predict the relative binding affinities of glucose and flavonoid analogues at different GP binding sites [2,3]. In the case of flavonoids, more accurate modeling of binding at the 'inhibitor site' required high-level quantum mechanics/molecular mechanics – Poisson Boltzmann Surface Area (QM/MM-PBSA) calculations to better account for the π-π stacking effects [3]. A number of the designed inhibitors have proved effective of reducing glycogenolysis at the cellular level in a further step towards translation.

Keywords

Cancer, Type 2 diabetes, Glycogen phosphorylase, Glucose analogues, Flavonoids

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O40

2(3H)-BENZOXAZOLONE DERIVATIVES AS POTENTIAL FATTY ACID AMIDE HYDROLASE (FAAH) INHIBITORS

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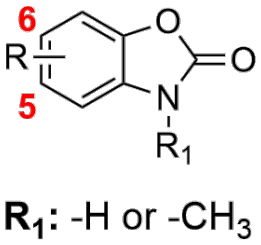
In vivo degradation of arachidonoylethanolamine (anandamide, AEA), an endogenous ligand of cannabinoid receptors, is carried out by fatty acid amide hydrolase (FAAH), an integral membrane-bound serine hydrolase. FAAH inhibitors have been considered to have promising therapeutic potential against pain manangement, inflammation, depression, and anxiety. Inhibition of both FAAH and MAGL (monoacylglycerol lipase), which is another serine hydrolase that activates cannabinoid receptors, thought to be advantageous to avoid the use of opioid analgesics in severe circumstances [1]. In the course of further studies to search for new chemotypes targeting FAAH, a small series of 6 benzoxazolone derivatives were prepared and evaluated as potential inhibitors of FAAH in order to define their potential utility. As a result, preliminary biological results of FAAH inhibition will be presented and discussed for their potential for further optimization as FAAH inhibitors.

This research was supported by Gazi University Scientific Research Projects Coordination Unit, Project Number: BAP 02/2020-24

Keywords

FAAH, MAGL, Benzoxazolone, Cannabinoid



R_1: -H or -CH_3

Figure 1.

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O41

COMPUTATIONAL INSIGHTS INTO THE BINDING PATTERN OF MICROSOMAL PROSTAGLANDIN E-2 SYNTHASE TYPE 1 INHIBITORS

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Prostaglandin E2 (PGE2) is an inflammatory lipid mediator which is produced from arachidonic acid (AA) and metabolized by cyclooxygenases (COX-1 and COX-2) and prostaglandin E2 synthases (microsomal PGE2 Synthase Type-1 and -2 (mPGES-1, mPGES-2) and cytosolic PGE2 Synthase (cPGES)). Nonsteroidal anti-inflammatory drugs (NSAID), which are frequently used in the market, inhibit COX activity and suppress PGE2 production. However, these drugs are causing gastrointestinal bleeding and several cardiovascular complications. Therefore, PGE2 production can be blocked at a lower step of the pathway via mPGES-1 inhibition, which is expected to result in a safer and promising treatment of inflammation, cancer, and cardiovascular diseases. There is no marketed mPGES-1 inhibitor, but there are ongoing efforts to evaluate novel compounds in preclinical and clinical stages. mPGES-1 has open and closed conformations, which affect the shape of the mPGES-1 inhibitor binding site [1]. The inhibitor binding site is located next to the GSH binding site. The active site is large and buried into the membrane and contains hydrophobic residues and flexible polar amino acids. mPGES-1 inhibitors mainly prefer three different binding patterns; we named them I, I-II and I-III regions. In this study, we analyzed binding patterns of cocrystallized inhibitors within those regions by visual inspection, cross-docking and molecular dynamics. The importance of ionic interactions, water bridges and hydrogen bonds with specific amino acids are identified by the conducted simulations. The findings of this study may help to design and discover novel mPGES-1 inhibitors.

Keywords

Inflammation, Crystal analysis, Molecular dynamics, Prostaglandin biosynthesis

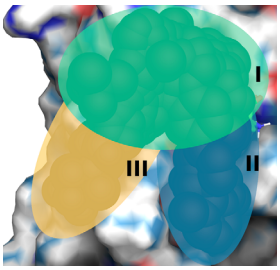

Figure 1: Binding regions within mPGES-1 active site.

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O42

SYNTHESIS OF NOVEL THIAZOLE DERIVATIVES AS 6-AMINOPENICILLANIC ACID MIMICS AND EVALUATION THEIR ANTIMICROBIAL ACTIVITY

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The rise of multi-resistant bacteria was noticeable in the final years of the twentieth century and the first decade of the twenty-first century. Many diseases become difficult to control if bacteria develop resistance to medications that are taken on a regular basis. As a result of this predicament, medicinal chemists are looking into new produced, more effective antibacterial medications. Thiazole is a five-membered heterocyclic ring that is a significant element of the naturally occurring chemical thiamine (vitamin B1), epothilones, carboxylase, thiamine pyrophosphate and the large family of macrocyclic thiopeptide antibiotics, thiostrepton and micrococcin P1. A wide range of biological and pharmacological activities have been documented for thiazole derivatives coupled with different heterocyclics such as anaesthetic, antitubercular, antibacterial, antifungal, analgesic, anticancer activity, and inhibition of acetylcholinesterase activity. The purpose of this study was to synthesize of novel 2,4,5-substituted thiazole derivatives as 6-APA mimics and screening for antimicrobial activity for eleven bacteria and sixteen fungi species. Compounds (4-methyl-2-(2-((5-methyl-1,3,4-thiadiazol-2-yl), (4-methyl-2-(2-((5-nitro-1*H*-benzimidazol-2-yl) and (4-methyl-2-(2-((5-methyl-4*H*-1,2,4-triazol-3-yl) bearing thiazole, 5-nitrobenzimidazole and triazole rings respectively exhibited high antimicrobial activity against most of the strains.

Keywords

Thiazole, 6-APA, Physicochemical property prediction, Antibacterial activity, Antifungal activity

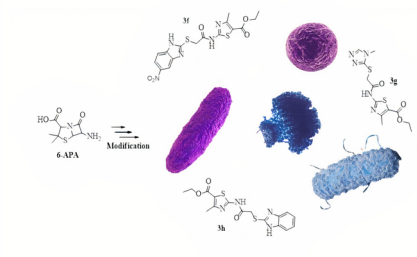

Figure 1. The core structure of penicillin derivatives (a) (6-APA), the core structure of the design

O43

SYNTHESIS OF NOVEL HYDRAZINECARBOTHIOAMIDE DERIVATIVES CONTAINING NAPHTHALENE RING AND ANTICANCER STUDIES

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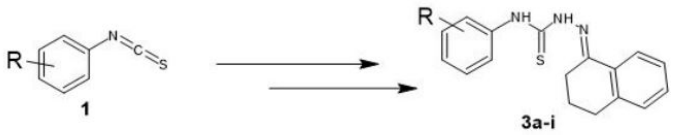
Since cancer is one of the most common diseases in the world, anticancer drug development studies attract the attention of medicinal chemists [1]. It is mentioned in the literature that naphthalene derivatives have anticancer activity [2]. In this study, 9 new 2-(3,4-dihydronaphthalene-1(*2H*)-ylidene)-*N*-(substitued phenyl)hydrazine-1-carbothioamide derivatives (Figure 1) were synthesized and characterized by ^{1}H NMR, ^{13}C NMR, IR and elemental analysis. These compounds were tested for their anticancer activity against A549 lung adenocarcinoma cell line and cytotoxicity against CCDLu19 lung fibroblast cell line. Among the tested compounds 3a and 3c displayed moderate activity against the A549 cell line and showed low cytotoxicity against the CCDLu19 fibroblast cell line with IC_{50} values of 4,53±0,35 and 11,5±0,71 µg/mL; 182,5±10,61 and 48,33±10,41 µg/mL respectively (Cisplatine IC_{50} for A549 cell line: 5,6±0,14 µg/mL).

This work was supported by TÜBİTAK Research Fund (Project Number: 119S010).

Keywords

Hydrazinecarbothioamide, Synthesis, A549 Lung adenocarcinoma



R: **3a**: 4-CN, **3b**: 4-NO_2, **3c**: 3-CF_3, **3d**: 3-Cl, **3e**: 4-OCF_3, **3f**: 4-Br, **3g**: 4-Cl , **3h**: 2-Br, **3i**: 4-CF_3

Figure 1: Synthesis of hydrazinecarbothioamide derivatives

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O44

SYNTHESIS AND ANTIMICROBIAL EVALUATION OF NEW NAPROXEN 1,2,4-TRIAZOLE-THIOSEMICARBAZIDE HYBRIDE DERIVATIVES

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Although naproxen is a nonsteroidal anti-inflammatory (NSAID) molecule, its chemotherapeutic effect is also being investigated due to its COX-2 inhibition effect [1]. The antimicrobial effects of thiosemicarbazides have already been proven [2]. In this study, novel naproxen derivatives were synthesized and evaluated their antimicrobial activity. Naproxen was used as the starting molecule to synthesize novel derivatives. In the first step, Naproxen Esther (1) was synthesized and it was converted to Naproxen hydrazide (2). After this reaction, a novel thiosemicarbazide derivative (3) was synthesized with Compound 2 and 4-fluoroisothiocyanate, furthermore, 1,2,4-triazole ring (4) was synthesized in 4N NaOH medium. To derive the new thiosemicarbazides, thioester (5) and thiohydrazide (6) molecules were synthesized from the 1,2,4-triazole ring [3]. In the last step, novel thiosemicarbazide molecules (7a-f) were synthesized with aromatic isothiocyanates and Compound 6 in the n-butanol at the reflux. All compounds were characterized using FT-IR, ^{1}H-NMR, ^{13}C-NMR, HR-MS, and melting points. The synthesized molecules evaluated antimicrobial activity against *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25922 (Gram-positive and Gram-negative bacteria, respectively), *Candida albicans* ATCC 10231 (fungus), and the clinical isolates of these microorganisms. The purpose of this study is to synthesize novel naproxen derivatives starting from naproxen molecules, evaluate their antimicrobial activity, and confirm their structures by spectroscopic data. All compounds showed antimicrobial activity to *E.coli* ATCC 25922 with a 128 MIC value. Among the compounds, compound 7f showed a 64 MIC value to *S.aureus* isolate.

Keywords

Naproxen, NSAID, Thiosemicarbazide, 1,2,4-triazole, Antimicrobial activity

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P1

PHARMACIST'S KNOWLEDGE AND BEHAVIORS TOWARD PHARMACOVIGILANCE AND ADVERSE DRUG REACTIONS REPORTING PROCESS IN TURKEY

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Adverse drug reactions (ADRs) increase patient-related morbidity, mortality and prolonged hospital stay, and increasing economic burden. Pharmacovigilance plays an important role in reducing ADRs and pharmacists have an important role in reporting ADRs. The aim of the study is to evaluate the knowledge and behavior of pharmacists towards pharmacovigilance and spontaneous ADR notifications in Turkey. The online questionnaire method was used with the pharmacists whose prior consent was obtained to participate in the study. The knowledge of pharmacovigilance practice, ADR reporting compliance rates, reasons for not reporting ADR and perceptions of the Turkish pharmacists on pharmacovigilance practice were evaluated. 406 pharmacists (45%) agreed to participate in the study. 81.8% of the pharmacists correctly defined the term pharmacovigilance. 91.6% knew the name of Turkish Pharmacovigilance Center. Pharmacists stated that they previously reported 18.7% of ADRs. Most of the pharmacists stated that the most important reason for not reporting ADRs was not knowing how and where spontaneous reporting should be done, a single spontaneous reporting would not make a difference and the report would generate extra work. These results showed that Turkish pharmacists had sufficient knowledge about the concept of pharmacovigilance and the spontaneous ADR reporting system. However, they had little experience in reporting. Training programs should continue to increase the knowledge and reporting experience of pharmacists about the reporting process and requirements.

Keywords

Adverse drug reactions, Pharmacovigilance, Pharmacist, Reporting system

DETERMINATION OF THE EFFECTS OF ENDOCRINE DISRUPTORS ON STEROIDOGENESIS BY HORMONE ANALYSIS

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Endocrine disruptors (ED) are defined as exogenous substances which cause adverse health effects and changes in endocrine functions in healthy organisms or in their future generations. In the present study the use of the OECD Steroidogenesis method, which is used for determination of ED, is evaluated to determine adverse drug reactions of two antioxidant drug candidates. In order to define the effects of possible drug candidates on steroidogenesis, a validated in vitro method, specified in the OECD TG-456 test guide, was applied in our laboratory and estradiol (E2) and testosterone (T) levels were determined by both ELISA and LC MS/MS methods as the endpoints of the assay. The effect of 2-Methyl-1-H-indole-3-carboxyaldehyde (4-chlorophenyl) hydrazone (M6) and phenyl hydrazone (M20), which are newly synthesized antioxidant drug active substance candidates, on the entire steroidogenesis pathway were investigated via the H295R steroidogenesis method, by performing hormone analyzes with both analytical methods. In vitro cytotoxic effects of the newly synthesized compounds were also investigated by MTT assay in H295R cells. Possible therapeutical role of the compounds, as well as their parent compound, melatonin, in estrogen receptor positive breast cancer were also discussed depending on their aromatase inhibitor activity. This work was supported by the EGE UNIVERSITY Scientific Research Projects Coordinatorship (BAP) 14-ECZ-018 Project number.

Keywords

Steroidogenesis, Endocrine disruptors, LC MS/MS, ELISA

P4

IN VITRO EVALUATION OF THERAPEUTICAL POTENTIAL OF 5-FLUORO INDOLE DERIVATIVES IN ESTROGEN- MEDIATED MECHANISMS OF BREAST CARCINOGENESIS

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Casual association between prolonged exposure to elevated levels of estrogen with breast cancer is well reported in many studies and estrogen is suggested to induce carcinogenesis via estrogen receptor (ER) and non-receptor pathways.Melatonin, an indolic hormon,is reported to have anticancer effects in breast cancer which is partly mediated by its preventive effects on estrogen-induced toxicity pathways.However,there are many limitations in therapeutic use of melatonin. Therefore novel melatonin analogues namely 5-fluoro indoles were sythesised in the light of molecular docking studies results.Their potential effects on known chemopreventive/therapeutic targets involved in breast cancer;aromatase(CYP19A1) -as resposible enzyme for local estrogen synthesis- , ER -since estrogen binds to its receptor and induces the proliferation of ER(+) breast cancer cells-, CYP1B1-as the enzyme responsible for convertion of estrogen to its reactive metabolites- and NAD(P)H oxidoreductase-1(NQO1)-as the enzyme catalyzes detoxification of reactive quione metabolites of estrogen- were investigated. Results indicate that among tested 23 compounds four of them were found to be effective more than one target.-*para* fluorinated derivative potently inhibited aromatase and human recombinant CYP1B1 enzyme while -*para* chlorinated derivative inhibited CYP1B1 and also increased NQO1 expression levels.Only difluoro halogenated compound inhibited estrogen induced cell proliferation and showed ER antagonist activity.Moreover several of the tested compounds inhibited CYP1 activity where halogen substitution at *para* position increased inhibitor activity.In conclusion, some of the tested compounds seem to be promising candidates for further studies on prevention/treatment of estrogen induced carcinogenesis via their dual benefits.
Acknowledgements: This work was supported by The Scientific and Technological Research Council of Turkey(TÜBİTAK) Grant117S065

Keywords

Estrogen, Breast cancer, Aromatase, Estrogen receptor, CYP1B1, NQO1

P5

INVESTIGATION OF SOME CONTAMINANTS IN BABY FOODS

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In this study, total number of samples analysed were 85 of baby foods which were collected from Ankara local markets, Turkey. Current study was conducted on different types of cereal based baby foods (cereal and cereal with milk) for multi-mycotoxins, total aerobic mesophilic bacteria (TAMB) and *Enterobacteriaceae* contamination. Baby foods were analysed for 12 toxicological important mycotoxins such as aflatoxin B_1, B_2, G_1, and G_2; fumonisin B_1, B_2; ochratoxin A; sterigmatocystin (STE); deoxynivalenol (DON); zearalenone (ZON); T-2 toxin and HT-2 toxin by LC-MS/MS multi-mycotoxin method. In addition to these mycotoxins, the presence of Aflatoxin M1 (AFM_1) was investigated in baby foods containing milk. Classical culture method was used for microbiological analysis. Consequently, at least one mycotoxin was detected in 69.41 % of the total samples. The most frequently detected mycotoxins were STE (34.12 %) and HT-2 (34.12 %). However, AFM_1 was not detected in any of the baby foods containing milk. Also, TAMB and *Enterobacteriaceae* were isolated from 30.59 % and 10.59 % of samples, respectively.

Keywords

Baby Foods, Food Safety, Mycotoxin, Microbiology

P6

EVALUATION OF CYTOTOXIC EFFECTS AND THERAPEUTICAL POTENTIAL OF NOVEL 3,3'-DIINDOLYLMETHANE DERIVATIVES ON BREAST CANCER CELLS

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Breast cancer is the leading cancer site in women and is the leading cause of death among female cancers. Indolic hormone melatonin (MLT) is reported to have anticancer effects in breast cancer via several mechanisms. Its short half life is a limitation in its therapeutic use and let scientists to synthesize MLT analogues with therapeutical benefits. In the present study, *in vitro* cytotoxicity of indol based MLT analogues were evaluated via MTT assay in non-malignant breast cells (MCF10A), estrogen receptor positive (ER+; MCF-7) and triple negative (MDA-MB-231) breast cancer cells. Compounds were further investigated for their aromatase (responsible for local estrogen synthesis) inhibitory and ER antagonist effects. Cytotoxicity of the compounds in three cell lines was evaluated by MTT. Aromatase inhibitory effect was evaluated by using a fluorescent substrate, 7-methoxy-4-trifluoromethylcoumarin. Potential ER antagonistic effects were evaluated by cell-based E-Screen assay. In total, five 3,3'-Diindolylmethane (DIM) derivatives were screened for their cytotoxic potential in three cell lines and X2 showed dose-dependent inhibition, with an IC_{50} value of 22.8µM in MCF-7 cells without having a significant cytotoxic effect on MCF10A and MDA-MB-231 cells. All derivatives strongly inhibited MCF7 cell proliferation even in the presence of estrogen and strongly inhibited aromatase activity. X2 was found to be the most potent aromatase inhibitor ($IC_{50}=7.9x10^{-7}$). In conclusion, DIM derivatives, specially X2, seem to be potent candidates for the treatment of ER+ breast cancer.

Keywords

Breast cancer, Melatonin analogues, Aromatase inhibition, ER antagonist, Cytotoxicity

P7

DEVELOPMENT OF HPLC METHOD FOR THE DETERMINATION OF OPIOID ANTAGONIST USED IN THE TREATMENT OF OPIOID DISORDER

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Opioid use disorder becomes a major health problem worldwide. To prevent this addiction, opioid antagonists are used for treatment for almost 50 years. These types of compounds are approved for the treatment of both alcohol and opioid dependence. When administered orally, they are mostly metabolized in the liver to their primary metabolites. Due to this, an efficient extraction methodology and determination techniques are still essential for the analysis of opioid antagonists and their metabolites. This research aims to develop and optimize sensitive, fast, reproducible, and novel methodology by using liquid chromatography for the determination of XTZ-21 and one of its metabolites XTZO-21. To achieve this goal, various mobile phase systems, buffer types, and buffer concentrations were prepared to obtain the best separation. Different types of columns which have various chemistries such as Kinetex C18 (150 mm x 4.6 mm i.d., 2.6 µm and 5 µm), Kinetex F5 (150 mm x 4.6 mm i.d., 2.6 µm and 5 µm) and Kinetex EVO C18 (150 mm x 4.6 mm i.d., 2.6 µm) were tested to find the optimum and efficient resolution with the better peak shape for the studied compounds. Finally, the proposed method provided a simple procedure for simultaneous analysis by UV detection. The applicability of the method was demonstrated using synthetic plasma.

Acknowledgement: This work is partially produced from the MSc Thesis of Ceren H. Bozmaoglu (Ankara University, Health Science Institute).

Keywords

Addiction, Biological sample, Chromatography, Metabolite, Opioid

P8

DETERMINATION OF PHARMACEUTICAL CARE NEEDS OF COVID-19 PATIENTS IN THE 1ST WAVE OF PANDEMIC

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In 2020 COVID-19 pandemic spread all over the world. A multidisciplinary approach is necessary for the treatment. The aim of this study is to determine the pharmaceutical care need of COVID-19 patients in the 1st wave of the pandemic. A retrospective, observational study was conducted. After ethical approval was given with 13/274 number, prescription records were investigated by a clinical pharmacist (CP). drug-related problems (DRP) identified through prescription examination. Study was held in 2 branches *(i)* hospitalized patients (HP) where CP is present and *(ii)* ambulatory care patients (AP). In this study 183 HP and 182 AP patients prescriptions were examined. Half of the participants were female 89 (%48.6), 83 (%45.6) for HP and AP respectively. The mean±SD age for HPs and APs were 42±18, 42,5±16 respectively. Many participants had multiple comorbidities, in HPs 91 (%49.5) at least have 2 or more existing diseases. The median medication number of HPs and APs were 7, 5 respectively. CP identified DRP events for HPs and APs 144, 306 respectively. The most common DRP for HPs was using ondansetron instead of metoclopramide. On the other hand, the most prevalent DRP for APs was lack of any gastroprotective medication. DRPs are probable events. Our results demonstrated that HPs had a lower number of DRPs. This points out that CP is a valuable asset to prevent DRPs. In conclusion, every setting where a clinical pharmacist is present should be involved in the healthcare and take responsibility.

Keywords

Clinical pharmacist, COVID19, Pharmaceutical care need, Pandemic, Patient-oriented pharmacy practice

P9

EVALUATION OF A CLINICAL DECISION SUPPORT SYSTEM FOR THE DETERMINATION OF INAPPROPRIATE DRUG USE IN ELDERLY AT COMMUNITY PHARMACY SETTING – PRELIMINARY REPORT

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In this study, we aimed to produce a clinical decision support system (CDSS) to identify inappropriate drug use/prescribing (IDUP) in the elderly and to evaluate IDUP patterns identified by the CDSS. The study was planned to be carried out in 20 community pharmacies from March 1, 2021 to September 1, 2021 on patients >= 65 years who visited the study pharmacies for any reason. A CDSS was produced to identify and deliver solutions for IDUP; in elderly patients by using relevant guidelines and literature. The CDSS was composed of 78 criterion. Here we present the preliminary results of the first 2-months, which included 200 patients (mean [SD] age: 73.9 [7.4] years old; male/female 86/114). Only the current medications of the patient were taken into account; 70.0% (n=140/200) of the patients were identified to have been prescribed at least one inappropriate drug; the total number of IDUP was 315. The most frequently identified IDUPs were related with Proton Pumb Inhibitors (PPIs) 19.1% (n=60/315), beta blockers 11.7% (n=37/315) and non-steroidal anti-inflammatory drugs (NSAIDs) 8.3% (n=26/315). When faced with a pop-up offering to counsel with the prescriber about the IDUP, in 32.9% (n=46/140) of occasions, pharmacists accepted this offer, and in 67.1% (n=94/140) of occasions pharmacists did not accept this offer. It is anticipated that the widespread use of this product would prevent medication-related adverse events and related hospitalizations, morbidities and mortalities; thus would improve patients' health and quality of life, as well as lead to better economic outcomes.

Keywords

Clinical decision support system, CDSS, Elderly, Inappropriate drug use, Inappropriate prescribing

P11

INVESTIGATION OF THE ANXIETY AND KNOWLEDGE LEVELS OF INDIVIDUALS: THE ROLE OF PHARMACIST

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Generalized anxiety disorder (GAD) is characterized by constant and excessive worry about several different things in an individual's life. Prevention of this state can be achieved with proper treatment and pharmaceutical care. The main objective of this study is to investigate the contributions and role of the pharmacist in the early diagnosis and treatment of anxiety. A prospective, observational study was conducted. The online survey was created with google forms and disseminated through the mail, or WhatsApp message containing a link. Questionnaire consist of 3 sections, demographics, anxiety levels, and knowledge levels about GAD. Anxiety levels of individuals were determined by the Generalized Anxiety Disorder (GAD-7) Scale. The female/male ratio of 400 participants was 1.83. The median [IQR] age of the participants is 24[22-35] years. Most of the participants had moderate anxiety. According to our results, 22 participants had severe anxiety and 46 participants had moderate anxiety levels. Among participants with severe anxiety a seen in 55% of 22 female participants. Another important finding of our study is that youth (18-24 age), higher education, and single participants had more anxiety respectively. Pharmacists may contribute to the early diagnosis and treatment of GAD. As first-line healthcare workers pharmacists have the important mission of providing pharmaceutical care to patients with psychological disorders. In conclusion, implementation of anxiety screening questionnaires such as GAD-7 by pharmacists would contribute to early detection of and appropriate referral of anxious individuals.

Keywords

Generalized Anxiety Disorder (GAD-7), Pharmaceutical care, Clinical pharmacist, Anxiety knowledge

DETERMINATION OF THE KNOWLEDGE LEVEL OF PHARMACISTS ABOUT ALZHEIMER DISEASE

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Alzheimer's Disease(AD) is a progressive and neurodegenerative disease. There are 42.3 million AD patients and increasing. Pharmacotherapy is essential part of AD treatment which is complex and multidiciplinary approach is required. Pharmacists are important component of multidiciplinary AD healthcare team. This duty of requires sufficient knowledge level of AD. The aim of this study is to investigate the knowledge level of pharmacists on AD. A descriptive, cross sectional study held to evaluate the knowledge level of pharmacist. An online survey was conducted with participation pharmacists. Strucutred survey consisted of 10 questions which was based on the Alzheimer's Disease Knowledge Scale(ADKS). The first section of survey was about the AD and the second was about the drugs used in AD. 186 pharmacists participated for the survey. 73% of them were female. Age of participants was 33[27-44.8] (median[IQR]) years. Majority of participants had work experience less than 20 years (%72). One third of the parpticipant (n=43,%31) were from Marmara region. The mean score of the participant were %71.7. The AD knowledge score was %73.25±15.90(mean±SD), and knowledge level about AD drugs was %76.24±16.69(mean±SD). According to our results, it was seen that Turkish pharmacists had sufficient knowledge about AD. Pharmacists play a key role in early diagnosis and prognosis of AD by providing pharmacutical care to patients with AD. Pharmacist with adequete knowledge about AD had additional benefits to therapy such as preventing drug related problems, patient or care giver education or increasing adherence.

Keywords

Alzheimer's disease, Pharmacist, Clinical pharmacist, Pharmaceutical care, Knowledge level

P13

KNOWLEDGE AND ATTITUDES OF COMMUNITY PHARMACISTS ABOUT DRUG USE IN PREGNANCY

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The aim of the study is to assess the level of knowledge of community pharmacists about drug use during pregnancy. This study was a descriptive cross-sectional study and was conducted between January-June 2020 in Istanbul at Turkey. Profile record form and a structured questionnaire were applied to pharmacists online. The questionnaire was prepared by the researchers and consisted of 12 questions. Of 56 pharmacists 46 (82%) were female and 39% were served for 0-15 years. A total of 20% of the pharmacists had at least one education about this issue. Drug information leaflets were found to be the most used source for drug use during pregnancy (39%). Eighty-seven of the pharmacists stated that the drugs used in the treatment of chronic diseases during pregnancy may be harmful to the baby, and 74% stated that drug use at any time during pregnancy would be harmful. It was determined that 93% of the pharmacists thought that one of the possible teratogenic side effects of drugs was fetal growth retardation. While 39% of the pharmacists thought that pharmacist/physician advice was needed in the use of over-the-counter drugs/food supplements/herbal products during pregnancy, 55% were stated that it may be potentially harmful. Considering the possible teratogenic effects of drug use before and during pregnancy, we think that health professionals, especially pharmacists, will contribute significantly to increasing the knowledge of the public about drug use in pregnancy.

Keywords

Pregnancy, Drug use, Knowledge, Community pharmacists

P14

EVALUATION OF DRUG-DRUG INTERACTIONS IN ELDERLY PATIENTS WITH CHRONIC DISEASE

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Polypharmacy can be seen in elderly patients with chronic diseases. The aim of our study is to determine the frequency of possible drug-drug interactions in the prescriptions of elderly patients. Our study is a retrospective study and was conducted in one community pharmacy in Istanbul between 01.01.2021 and 01.04.2021. A total of 161 prescriptions of elderly patients aged 65 and over were examined. Possible drug-drug interactions were evaluated using the Medscape database. Sociodemographic characteristics of the patients and possible drug-drug interactions were expressed as %. Thirty patients were included in our study, and 50% were male patients. The mean age was 73 years and 35% of the patients had coronary artery disease and 32% had hypertension. The total number of drugs in the 161 prescriptions reviewed was 414, and the total number of interactions was 1692, according to the Medscape database. The most common degree of interaction was found to be moderate with a rate of 91%. A total of eleven interactions were detected per prescription. According to the data of our study, we think that the drug interactions may have arisen as a result of comorbidities and therefore polypharmacy, especially in the elderly population. We think that pharmacists will make positive contributions to the identification and management of drug-drug interactions.

Keywords

Elderly patient, Drug-drug interactions, Community pharmacy

P15

INVESTIGATION OF BIOFILM FORMING ABILITY IN ESCHERICHIA COLI ISOLATES ISOLATED FROM CHILDREN'S PARK

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Biofilm-producing bacteria has become a major public health problem worldwide. The biofilm structure makes the bacteria resistant to the host defense mechanism. Biofilm plaques detected in many medical devices used in the health sector cause infections arising from these devices. The biofilm formed by *Escherichia coli* consists of a bacterial colony composed of extracellular exopolysaccharide. Colonies from pure bacterial cultures will be transferred to 100µl TSB and incubated for 18 hours.The 0.5 McFarland standard will be diluted to obtain turbidity. 100µl will be added to the microplate wells by diluting with TSB medium. 100µl of 1:100 dilution of the prepared bacterial suspension will be added to these wells and incubated for 24 hours at 35°C. The wells will be washed 3 times with 200µl sterile distilled water and dried at 60°C. 200µl of 0.1% crystal violet will be added to dried microplates and stained for 15 minutes at room temperature. After staining, the wells will be washed with sterile distilled water and 200µl of 33% glacial acetic acid will be added after washing and the results will be measured in terms of optical density at 620nm in the spectrophotometer. Sterile TSB medium will be used for sterility control and wells that do contain *Staphylococcus epidermidis* and its formulations will be used for growth control. For *E. coli* strains, biofilm formation was interpreted according to the determined control groups. In conclusion; Low biofilm formation was observed in 10%, moderate in 70% and high in 20% of the strains.

Keywords

Biofilm, Escherichia coli, Microbiology

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P16

THE EFFECTS OF NEW SUBSTITUTED HEXAHYDROQUINOLINE DERIVATIVES ON CYTOTOXICITY, INTRACELLULAR OXIDATION AND INFLAMMATION MEDIATORS IN HUMAN HEPATOMA CELL LINE

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Calcium channel blockers that have 1,4-dihydropyridine (1,4-DHP) ring are an important group of drugs in the treatment of hypertension and coronary artery diseases [1]. In recent years, 1,4-DHPs, which have calcium channel blocking activity, are discovered to inhibit transforming growth factor-beta (TGF-β) and inflammation mediators [2, 3]. In this study, 24 compounds having alkyl 2-methyl-4-(substituted phenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate structure, in which the 1,4-DHP structure is condensed with the cyclohexanone ring, were obtained with the modified Hantzsch synthesis. Structural elucidation was carried out by spectral methods. MTT assay was performed to determine the cytotoxic effects of compounds on HepG2 cells. Cells were treated with various concentrations of compounds (5-200 µM). After MTT assay, 12 compounds with the lowest cytotoxic properties were selected. The effects of selected compounds on intracellular reactive oxygen species (ROS), TGF-β1 and TGF-β2 levels in HepG2 cell line were investigated. When the intracellular ROS levels were evaluated, RG105 significantly decreased ROS levels (%14,7, $p<0,05$) while four compounds increased ROS levels (%20,4, %12,3, %10,9, %9,1 respectively, $p<0,05$). Other compounds did not cause any significant changes. None of the compounds caused a statistically significant change on TGF-β1 and TGF-β2 levels. However, RG105 decreased both TGF-β1 and TGF-β2 levels (%14 and %29,5, respectively; $p>0,05$). We can suggest that RG105 may be a drug precursor molecule. Further studies are required to better understand the mechanism of action of RG105 on inflammation biomarkers.

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Keywords

Hexahydroquinoline, TGF-β, MTT, ROS, Inflammation

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P17

THE ASSOCIATION BETWEEN ANGPTL8 AND PI3K-MTOR-PPAR EXPRESSIONS IN ADIPOSE TISSUE OF HIGH-FRUCTOSE-FED RATS: THE MODULATORY EFFECT OF KEFIR

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High consumption of fructose, particularly in the form of soft drinks, may contribute to the high prevalence of metabolic disorder. Fructose-induced metabolic disturbance is more likely to abdominal fat accumulation, but independent of general obesity. Kefir, a fermented milk product, consumption was reported to have beneficial effects in several disease models. The aim of the present study was to investigate the influence of kefir supplementation on lipogenesis-related factors in adipose tissue of high-fructose-fed rats. Fructose was given to the rats as a 20% solution in drinking water for 15 weeks. Kefir was administrated by gastric gavage once a day during the final six weeks. Gene expressions were determined by real-time PCR. There was an upregulation of ANGPTL8 mRNA expression in adipose tissue of rats given fructose. However, expressions of PI3K, mTOR, and $PPAR_y$ mRNAs were impaired in the adipose tissue. Kefir supplementation suppressed expression of ANGPTL8, but increased PI3K and mTOR in adipose tissue of high-fructose-fed rats. Kefir supplementation has modulatory effects on fructose-induced changes except for $PPAR_y$ expression. These findings showed that dietary fructose and kefir might reciprocally affect the lipogenesis-related genes in the adipose tissue.

Keywords

Dietary fructose, Kefir, ANGPTL8, PI3K-mTOR-PPAR

P18

INVESTIGATION OF ANTIDEPRESSANT-LIKE EFFICIENCY OF TANGERETIN AND RELATED MECHANISMS

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In this preclinical study, the antidepressant-like efficacy of tangeretin, a phytochemical found in citrus peels, was investigated for the first time by reliable and validated in vivo methods and some mechanisms underlying this effect have been elucidated by antagonism studies. The antidepressant-like efficacy of tangeretin (10, 20 ve 40 mg/kg, p.o.) was examined by tail suspension (TST) and modified forced swimming tests (MFST), while its effect on the motor coordination of experimental animals was evaluated using the Rota-rod method. The data obtained revealed that doses of 10 and 20 mg/kg tangeretin decreased the immobility time of mice in TST and immobility number of mice in MFST compared to control animals not receiving tangeretin. These findings indicated that tangeretin showed an antidepressant-like efficacy comparable to the reference drug fluoxetine (30 mg/kg) when administered at doses of 10 and 20 mg/kg. Tangeretin, at the same doses, did not alter the climbing number of mice in MFST, but significantly increased their swimming number. The 40 mg/kg dose of this flavonoid did not cause a statistically significant effect in either test. While α-methyl-para-tyrosine methyl ester pretreatment, which was carried out to elucidate the mechanism of action of tangeretin, did not change the antidepressant-like efficacy induced by 20 mg/kg dose of this flavonoid; pretreatment of p-chlorophenylalanine methyl ester, NAN-190 and ketanserin reversed this activity. These findings indicated that tangeretin has an antidepressant-like activity mediated by the serotonergic system and pointed out that 5-HT1A and 5-HT2A/5- HT2C serotonergic receptor subtypes play roles in this effect.

Keywords

Tangeretin, Antidepressant-like effect, Tail suspension test, Modified forced swimming test,Rota-rod

jpeg

P19

THE EFFECT OF RESVERATROL AND REGULAR EXERCISE ON THE CARDIAC OXIDATIVE STRESS AND ADRENERGIC RESPONSES IN THE HYPERTENSION

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Resveratrol and regular exercise, which are non-pharmacological approaches, have protective effects in various pathological conditions [1,2]. In this study, the effects of resveratrol consumption and regular exercise training on the parameters related to oxidative stress and cardiac functions were examined in hypertensive rats. Hypertension was induced by deoxycorticosterone-acetate injection and adding salt to drinking water in male rats for 12 weeks. Resveratrol (in the drinking water) and exercise training (for 40 minutes, five days per week) were applied for last six weeks. Blood pressure was measured weekly. Right atrium (RA) and left papillary muscle (LPM) were isolated and isoprenaline and phenylephrine-induced rhythmic activity and contractions of tissues were recorded. Plasma and cardiac tissue total antioxidant capacity (TAC) and tissue malondialdehyde (MDA) levels were measured. Resveratrol and regular exercise significantly reduced systolic blood pressure in hypertensive rats. The increased TAC levels as a defensive mechanism in the hypertensive group were reversed by resveratrol and regular exercise. However, these applications unchanged the elevated MDA levels in hypertensive rats. The reduction in phenylephrine-mediated LPM contraction of the hypertensive group was improved by resveratrol and regular exercise. High isoprenaline concentrations-stimulated contractions of tissues were lower in the hypertensive rats. Isoprenaline-mediated contractions of the RA and LPM were improved by resveratrol and regular exercise, respectively. The elevation in isoprenaline-mediated sinus rate in the hypertensive group was reversed by resveratrol and exercise training. These findings suggest that resveratrol and regular exercise may have beneficial effects on cardiac oxidative stress and impaired adrenergic responses induced by hypertension.

Keywords

Hypertension, Resveratrol, Exercise, Oxidative stress, Cardiac function

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P20

A POTENTIAL SENOTHERAPEUTIC DRUG: THEOPHYLLINE RESTORES THE DOXORUBICIN-INDUCED SENESCENT CELL MORPHOLOGY IN A549 CELLS

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Cellular senescence is induced in cancer cells in response to chemotherapeutics at low concentrations that do not stimulate cell death. Although senescent cancer cells are not able to proliferate, they cause various negative pro-tumorigenic paracrine effects on the cells in the cancer microenvironment with the various factors they secrete called senescence-associated secretory phenotype (SASP). Thus developing senotherapeutic drugs that kill senescent cells and inhibit the secretory activity of senescent cancer cells is a new approach in cancer therapy. The current work evaluated the possible role of theophylline in doxorubicin-induced senescence and senescent cell morphology in A549 cells. We demostrated that while incubation of doxorubicin significantly induced SA-β-gal-positive cancer cells, the proportion of cells positive for SA-β-gal increased after the pre-incubation of theophylline. In addition, a significant reduction in senescent cell area was observed after theophylline pre-incubation. Changes in cell shape and morphology modulate cell function in biological organisms. Senescent cell form and secretory function are also closely related. In the current study, the decrease in cell morphology caused by theophylline may result in a decrease in the secretory activity of the senescent cell. Therefore, with the potential senotherapeutic activity of theophylline, undesirable effects caused by the secreted factors of senescent cancer cells can be eliminated. Our ongoing studies investigating the effect of theophylline on the secretory activity of the senescent cancer cell will provide additional evidence for the senotherapeutic efficacy of this compound.

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Keywords

Senescence, SASP, Cancer, Theophylline, Senotherapeutic

P21

CHLOROGENIC ACID ALTERS POTASSIUM CONDUCTANCE IN DORSAL ROOT GANGLION NEURONS

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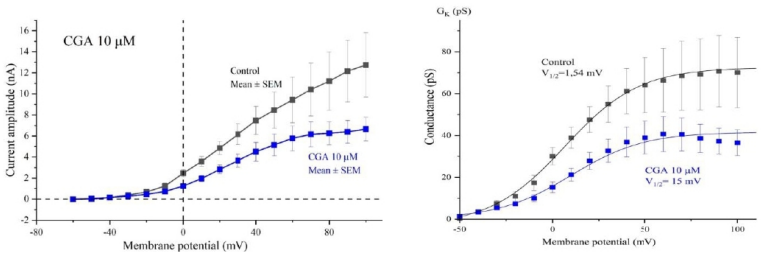
This study presents preclinical data on the peripheral aspect of pain under chlorogenic acid (CGA) treatment, a bioflavonoid displaying several pharmacological effects including analgesic and antihyperalgesic actions [1]. Dorsal root ganglion (DRG) neurons were dissected from male Sprague Dawley rats. The primary cell culture was prepared via enzymatic and mechanical digestions. Electrophysiological recordings were performed on DRG neurons via voltage clamp technic. Depolarizing pulses up to 0 mV for 300 ms each were used after clamping the membrane potential to -60 mV. The current–voltage (IV) curve was obtained using depolarizing steps of 10 mV increments from −60 mV to +80 mV. Conductance of K^+ channels in relation to membrane potential from control cells and after application of 10 µM CGA were evaluated and the value of potential of half activation ($V_{1/2}$) was calculated using Boltzmann equation and nonlinear curve fitting function in OriginPro. Control recordings of K^+ current densities, and after application of 10 µM of CGA are represented as mean values ± S.E.M. [2]. Application of 10 µM of CGA significantly reduced maximum conductance and K^+ current densities (n=5). CGA does not affect voltage dependence but reduce the conductance. This reduction might be originated from a reduction in the number of active channels, or from a modification in the open state probability or from the amplitude of signal of the channel. The inhibitory effect observed on K^+ conductance has been accepted as an indicator of analgesic effects [3]. Herewith, data represented in this study emphasize the possible analgesic effects of CGA.

Keywords

Chlorogenic acid, Electrophysiology, Voltage-clamp technique, Dorsal root ganglion



Effects of 10 µM CGA treatment on K+ current amplitude and conductance

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APPLICATION OF DESIGN OF EXPERIMENT APPROACH FOR OPTIMIZATION OF PIROXICAM LOADED POLYMERIC BASED NANOCARRIERS

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Hepatocellular carcinoma is the cause of third most common cancer-related death in the world after lung and prostate cancer. However, the clinical diagnosis and treatment modalities are still relatively limited, which urgently require the development of new effective technologies [1]. A number of prior experimental studies have suggested that non-steroidal anti-inflammatory drugs (NSAIDs), including piroxicam, may potentially protect against liver cancer [2]. The aim of this research is to design and optimize polymeric based nanocarriers of piroxicam via design of experiment (DoE) approach. Two-factor, three-level full factorial design was used to optimize the process parameters like amount of PLGA (X1) and Poloxamer 188 percentage ratio (X2). Two dependent variable's particle size and surface charge were specified as responses. Entrapment efficiency, surface morphology, in-vitro drug release performance and DSC studies were performed for the characterization of nanocarriers of piroxicam. The nano-sized formulation at the lower level of the design was chosen as the optimized formulation due to its lowest particle size as 184.6 ± 0.92 nm and highest zeta potential value as -31.8 ± 0.81 mV. Entrapment efficiency of the optimized formulation was determined as 98.88 ± 0.87 %. In conclusion, the DoE approach was successfully applied to optimize the process parameters, namely the polymer amount and surfactant concentration, and evaluate the effectiveness on the particle size and surface charge of the polymeric carriers.
This work was supported by Ankara University Scientific Research Projects Coordination (21L0237008).

Keywords

Hepatocellular carcinoma, Piroxicam, DoE, Polymeric based nanocarriers

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PREPARATION AND EVALUATION ONDANSETRON HCL LOADED POLYMERIC NANOPARTICLES

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Ondansetron HCl (OND) is a water soluble antiemetic drug [1]. The encapsulation of hydrophilic drug is problematic due to their short half life and poor bioavailability [2]. In this study, we aimed to improve the encapsulation of OND, by loading it into polymeric nanoparticles. Formulations were prepared by modified double emulsion solvent evaporation method [3] using polycaprolactone (PCL) and poly(lactic-co-glycolic acid (PLGA) as polymer. The prepared formulations were evaluated in terms of particle size (PB), polydispersity index (PDI), zeta potential (ZP)and encapsulation efficiency (EE). In order to determine the amount of OND, HPLC method [4] was developed and validated according to the ICH guideline in different media including ultrapure water, pH7.4 phosphate buffer and acetonitrile. It was observed that prepared formulations with PCL had larger PB, a wider particle size distribution and lower EE values compared than prepared formulations with PLGA. ZP values were measured negatively for all formulations. Compared to our previous study [5] results, better results were obtained in terms of EE% in the acid terminal groups of PLGA as to the ester. In conclusion, an accurate, precise, linear and repeatable HPLC method has been developed and validated. The method has been efficiently applied in the formulation development studies for OND. It has been found that PLGA is a more suitable polymer than PCL to achieve better PB, PDI and EE%.

This work has been supported by Gazi University Scientific Research Projects Coordination Unit under grant number TCD-2021-6957. OND was a kind gift of Adeka Pharmaceutical (İstanbul, Turkey).

Keywords

Ondansetron HCl, Polymeric nanoparticle, Drug delivery systems

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EVALUATION OF THE ANALGESIC ACTIVITY OF BERBERINE PHYTOSOME

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Berberine (BER) is a quaternary benzylisoquinoline alkaloid that can be obtained from many different plants. BER has wide ranging pharmacological and biological activities, which include anti-inflammatory, anti-microbial, anti-amnesic, anti-malarial, hypolipidemic and anxiolytic-like effects. In addition, BER is commercially used medically to treat diarrhea and is considered to be an effective and non-noxious agent in this context [1]. The therapeutic utility of BER was significantly compromised due to its poor absorption and low bioavailability. Due to hydrophobicity and poor aqueous solubility of BER, it results in decreased effective concentration and minimal absorption in the gastrointestinal tract, which seriously limits its development and application as a pharmaceutical preparation [2]. For these reasons, innovative dosage forms were needed in the application of BER. Phytosomes for the successful delivery plant bioactives which nowadays are very popular. Molecules with low oral bioavailability can be better targeted to enhance their bioavailability by phospholipid complexation [3]. BER was therefore considered to be a suitable candidate for preparing phytosomes [4]. In this study BER phytosomes were prepared by a reverse phase evaporation method. The objective of the present study is to evaluate the analgesic activity of the BER phytosome formulation in comparison with BER by using *in vivo* methods. Pain caused by p-benzoquinone and hot plate tests were used for the determination of analgesic activity of BER phytosomes.

Keywords

Berberine, Phytosomes, Analgesic activity, In vivo tests

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DEVELOPMENT OF RISK ANALYSIS BASED FORMULATION IN THE DEVELOPMENT OF GENERIC ONCOLOGY DRUG MITOMYCIN 20 MG POWDER FOR SOLUTION FOR INJECTION/INFUSION

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Generic drugs, which have an important place in our country, have gained critical importance especially with the increase in cancer diseases. Generic drugs are expected to be equivalent the original product in terms of quality, efficacy and safety. In this context, from the antineoplastic drug groups that have a high degree of importance in terms of patient health and have strategic importance in our country; Mitomycin 20 mg Powder For Solutıon For Injection/Infusion, the first generic of the product was developed by Onko İlaç. Mitomycin is a sterile, lyophilized powder used in the treatment of bladder (urinary bladder) cancer, breast cancer, head and neck cancer, stomach and pancreatic cancers, prostate cancer and cervical cancer. In the pharmaceutical industry, it has been observed that innovative approaches used in the pharmaceutical product development process recently. With one of these approaches, Qualİty by Design(QbD); as specified in the ICH Q8 guide; appropriate formulation development studies are carried out by foreseeing the risks in before [1]. In the study, risk analyzes were carried out during the formulation development process with the QbD approach and the number of formulation trials was determined according to this risk assessment. In the results, better quality formulation have been obtained with less trials.

Keywords

Pharmaceutical Development, Pharmacology, Cancer drug, CQA

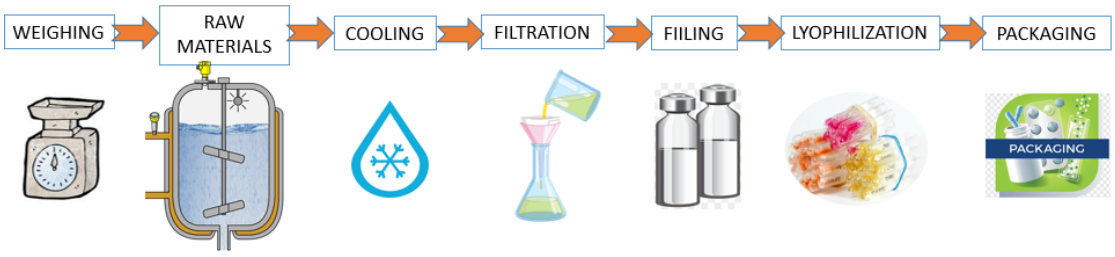

Figure 1-Manufacturing Steps for Mitomycin 20 mg Drug

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IN-VITRO RELEASE STUDY OF POLYPHENOLIC COMPOUND FOR DERMAL DRUG DELIVERY

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The in vitro release of resveratrol within microemulsion (ME), macroemulsion, and control solution was investigated and compared in this study. For evaluating in vitro release through the membrane, a microemulsion was prepared by using a magnetic stirrer. Additionally, macro emulsion and control solutions were utilized for comparison. To identify the area where the microemulsions formed a triangle phase diagram was utilized. Simultaneously, the macroemulsion area was determined within the same triangle phase diagram. Some formulations were chosen from the microemulsion region to elicit optimal formulation. Chosen formulations were exposed to some pre-stability and characterization tests. The formulation that droplet size, zeta potential, and polydispersity index (PDI) was 12.42 ± 0.16 nm, -10.6 mV, 0.145 ± 0.001, respectively, was chosen as optimal The optimal microemulsion, and optimal macroemulsion, and control solution containing same quantity resveratrol (%0.05 w/w) were applied to cellulose acetate membrane mounted in Franz diffusion cells. The amount of resveratrol released into the receptor medium was measured by HPLC. The most released resveratrol for 6 hours was determined within the microemulsion, control solution, and macroemulsion, respectively. Release profiles were evaluated according to zeroth order kinetic, first-order kinetic, and Higuchi kinetic model. It was determined that the release profiles of the formulations were more suitable to the higuchi kinetic model. The amounts of resveratrol passing through the cellulose acetate membrane were evaluated statistically by one-way analysis of variance (ANOVA). In the in vitro study, the amount of active substance released by all formulations after 6 h showed a significant difference ($p<0.05$).

Keywords

Dermal Drug Delivery, In-vitro Release, Microemulsion, Resveratrol

P27

OPTIMIZATION OF LC METHOD FOR THE DETERMINATION OF FLUTICASONE PROPIONATE FROM DRUG DELIVERY SYSTEMS

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Fluticasone propionate is a steroid medication. In a topical form can be used to treat skin conditions such as eczema, psoriasis, and rashes. Solid lipid nanoparticles (SLNs) are colloidal drug delivery systems prepared by non-irritant and nontoxic lipids that attract great interest because of their unique features. Semisolid SLNs are a novel approach for the dermal application of SLNs. The aim of this study was to show the development, validation, and application of a simple, selective, and reliable HPLC-UV method that was fully validated for its specificity and stability-indicating properties from its forced hydrolytic, oxidative, photolytic, and thermal degradation products. In addition, the proposed method presented to the application of FP from rat skin extract according to the United States Pharmacopeia and International Council on Harmonization Guidelines. For this reason, Kinetex C18 (150x4.6 mm;ID:5µm) column was chosen for the best resolution. The mobile phase consisted of 25 mM acetate buffer (pH 4.0) and acetonitrile (40:60,v/v). The detector was set up at 236 nm. The developed stability-indicating method presented low limit of detection, low limit of quantitation, and good resolution between any of interferences from both commercial formulation and developed SLN formulation from rat skin, with symmetric, pure, and enough peak homogeneity. High percentage of recovery results shows that the proposed method is free from the interferences of the commonly used excipients and additives in the formulations of the commercial product or semisolid SLN formulations and also biological derivatives.
This study was supported by The Scientific and Technological Research Council of Turkey (117S967).

Keywords

Fluticasone propionate, HPLC, Drug delivery, Method development, Validation

PHASE SOLUBILITY STUDIES, PREPARATION AND CHARACTERIZATION OF INCLUSION COMPLEXES OF BUTOCONAZOLE NITRATE WITH α-CD AND HP-α-CD.

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Imidazole derivatives such as butoconazole nitrate (BUT) with lower aqueous solubility have been used as the drug of choice for vaginal fungal infections. BUT was found more effective against Candida species than econazole, miconazole or ketoconazole [1]. The aim of this study was to prepare an inclusion complex of BUT and α-CD/HP-α-CD to improve the physicochemical and biopharmaceutical properties of BUT. The effect of on the solubility of BUT was investigated according to the phase solubility technique [2]. The solubility phase diagram of BUT in the presence of α-CD and HP-α-CD were determined as A_L type. According to the A_L type phase diagram, inclusion complexes of BUT and α-CD/HP-α-CD were prepared at a molar ratio of 1:1 using lyophilization. Inclusion complexes were evaluated for morphology, thermal behavior, aqueous solubility, solid state characteristics to assess the efficiency of the polymers as solubility enhancers. While the BUT solubility was 0.242 $mg.ml^{-1}$, it was found to be 0.870 $mg.ml^{-1}$ (3.5-fold) and 1.720 $mg.ml^{-1}$ (7-fold) for the inclusion complexes prepared with α-CD and HP-α-CD, respectively. An increase in saturated solubility with complex formation is a common and expected finding in the literature [3]. SEM, DSC, FT-IR and NMR results confirmed the formation of inclusion complexes and provides the information about the state of the active agent in the polymeric network.

Keywords

Butaconazole nitrate, α-CD, HP-α-CD, Enhanced solubility, Characterization, Inclusion complex

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PREPARATION AND CHARACTERIZATION OF INCLUSION COMPLEXES OF ANTIFUNGAL DRUG ISOCONAZOLE NITRATE WITH β-CD OBTAINED BY FREEZE-DRYING AND SPRAY DRYING METHODS

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Cyclodextrins (CDs) are the cyclic oligomers of glucose which has a lattice-like super molecular structure with lipophilic inner cavity and hydrophilic exterior surfaces. CDs can form inclusion complexes easily with many of the drug molecules. Inclusion with CDs protect the drug from physical, chemical and enzymatic degradation and also increase the membrane permeability and bioavailability of active molecule [1,2]. Isoconazole nitrate (ISN) is belong to the azole category with superior antifungal and antibacterial (gram-positive) features. ISN is an active substance with low water solubility and has light-sensitive properties. For these reasons, the scope of this research was aimed to prepare ISN/β-CD inclusion complexes with different methods and characterize these structures for enhancing physicochemical properties, photostability and antifungal efficacy of ISN [3]. Phase solubility studies were performed according to the Higuchi and Connors method [4]. Establishment of the equilibrium was verified by the comparison of β-CD phase solubility after 24, 48 and 72h. The results demonstrated no significant difference; hence the equilibrium time was set to 24h. Phase solubility diagram obtained with β-CD showed a linear relationship between the amount of ISN solubilized and the concentration of CD in solution. According to Higuchi and Connors, the curve obtained was fitted to type A_L and this may be attributed to the formation of soluble 1:1 ISN/β-CD inclusion complexes. Inclusion complexes of ISN and β-CD were prepared by freeze drying and spray drying techniques. Inclusion complexes were characterized for morphological, thermal, solid-state and solubility characteristics to highlight interactions of host-guest system.

Keywords

Isoconazole nitrate, β-CD, Inclusion complex, Enhanced solubility, Freeze drying, Spray drying

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P30

DEVELOPMENT AND IN VITRO CHARACTERIZATION OF PEGYLATED PLGA NANOPARTICLES ENCAPSULATING OSELTAMIVIR PHOSPHATE AS AN ANTICANCER DRUG CARRIER SYSTEM

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The polymeric nanoparticles (NPs), have demonstrated remarkable potential to come through cancer treatment difficulties by demonstrating sustained and/or controlled release of anticancer active substances. Higher cellular uptake, improved encapsulation ability, better pharmacokinetics and biodistribution, as well as superior specificity for cancerous cells owing to surface decorations and charge, are all benefits of NPs used as anticancer drug carriers [1,2]. Both for its biodegradable and biocompatible nature, poly (lactic-co-glycolic acid) (PLGA), which is composed of lactic and glycolic acid, is a frequently utilized polymer for drug delivery. The most commonly used polymer for developing stealth particles is polyethylene glycol (PEG). Stealth NPs have improved shelf stability and the capability to monitor control the release of encapsulated drugs than other long-circulating drug dosage forms [3,4]. The aim of the research was the development of OSE containing stealth pegylated PLGA NPs for delivery of OSE into the lung adenocarcinoma cells. For this target, OSE encapsulated pegylated PLGA NPs were formulated with spray drying method. After spray drying process, OSE loaded PLGA NPs were coated with PEG. NPs were investigated for zeta potential, particle size, encapsulation efficiency, DSC, FT-IR, ^{1}H-NMR and SEM analyses. *In vitro* release patterns of OSE were examined in freshly prepared phosphate buffer saline with dialysis membrane.

Keywords

Oseltamivir phosphate, PLGA, Nanoparticles, PEG, Release pattern, Lung cancer

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P31

PREPARATION OF CHITOSAN TRIPOLYPHOSPHATE AND CHITOSAN SULFOBUTYL-ETHER-β-CYCLODEXTRIN NANOPARTICLES FOR ORAL INSULIN DELIVERY

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Diabetes Mellitus (DM) is a chronic metabolic disease that affects more than 400 million people worldwide. Although various types of insulin is being used in DM treatment via subcutaneous route, oral insulin was reported to be superior at mimicking the physiological insulin pathway after its endogenous secretion. Oral delivery of peptides/proteins, as well as insulin is challenging due to the poor physical and chemical stability which usually results in inadequate therapeutic efficacy [1]. In this study, it was aimed to develop insulin-loaded nanoparticles through ionic gelation of cationic chitosan (CS), which has the ability to increase absorption, with an anionic linker tripolyphosphate (TPP) or sulfobutyl ether-β-cyclodextrin (SBE-β-CD). It was decided to find out if SBE-β-CD an oligosaccharide that has been established to increase oral bioavailability can be used as an alternative to TPP, which is widely used for preparation of CS nanoparticles [2]. Insulin quantification was evaluated at 272 nm and spectrophotometric quantification method was validated. While preparing nanoparticles; the effects of pH, CS/TPP and CS/SBE-β-CD ratio and stirring time were compared and optimized by particle size, polidispersity index, zeta potential and encapsulation efficacy measurements. CS-SBE-β-CD nanoparticles were obtained with a particle size of 291.2±14.5 nm, a PDI of 0.165±0.104, a zeta potential of 22.6±2.6 mV and a encapsulation efficiency of 41.7%±6.7. Our studies are going on with optimisation of enteric coating process using Kollicoat® MAE 30 DP. Studies to date showed that CS/SBE-β-CD nanoparticles would be promising for oral insulin delivery.

Keywords

Oral insulin delivery, Chitosan nanoparticles, Ionic gelation, Sulfobutyl ether-β-cyclodextrin

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P32

DEVELOPMENT OF IN VITRO LIPOLYSIS-PERMEATION METHOD TO ESTIMATE ORAL ABSORPTION OF EXEMESTANE-LOADED LIPID-BASED FORMULATION

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In vitro lipolysis study is used to evaluate the performance of lipid-based formulations (LBFs) as the amount of drug in aqueous phase of lipolysis medium is suitable for absorption. However, in vitro lipolysis is a closed system and lacks an absorption step. It may not reflect the dynamics such as drug solubilization, precipitation, permeation, and sink condition present in gastrointestinal tract [1]. Therefore, development of lipolysis-permeation method can improve the prediction of absorption of LBFs and the estimation of the effect of lipid hydrolysis on absorption of drug [2]. In this study, in vitro lipolysis-permeation model with sink condition ensured was developed and the effect of lipolysis on exemestane permeation was investigated using the lipolysis-permeation system. In model, pH-stat auto-titrator (Titrando 902, Metrohm) was combined with Franz diffusion cells equipped with dialysis membrane (cut-off 14 kDa). HPLC method was developed and validated for lipolysis-permeation samples in pH 7.4 phosphate buffered saline containing 0.5% SLS. The permeation of exemestane was determined for lipolysis samples taken at three time points (0, 15, 60 min of lipolysis in fasted and fed state). The cumulative amounts of permeated exemestane for 0, 15, and 60. min lipolysis samples were 55.1%, 59.1%, 48.6% in fasted state, 62.1%, 66.7%, 65.1% in fed state, respectively. The obtained results demonstrate that the lipolysis did not affect the amount of exemestane permeation ($p>0.05$). The in vitro lipolysis-permeation method could be promising to estimate the absorption of exemestane-loaded formulation, but it needs to be supported with in vivo studies.

Keywords

Exemestane, In vitro lipolysis-permeation method, Lipid-based formulation, HPLC

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A NEW PERSPECTIVE FOR DEXPANTHENOL ORALLY DISINTEGRATING FILMS THROUGH DESIGN OF EXPERIMENT APPROACH

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Dexpanthenol is a topical agent that has unique properties such as emollient and wound healing efficiency, and thus has been investigated against sore throat in post-intubation. However, a commercial Dexpanthenol orally disintegrating film is not available in the market. Film formulations applied to mouth have some requirements for mechanical properties, disintegration, viscosity and adhesion. Mechanical properties of films have importance on packaging, handling and shelf life stability whereas a suitable disintegration, viscosity and adhesion is needed for an optimum formulation (1). In this study, the effect of independent variables Dexpanthenol and Kollicoat IR (kindly provided from BASF) on HPMC 100 LV films were evaluated using DoE approach by means of 3^2 factorial design as shown in Figure 1a (2,3). Thirteen films (between 95-130 µm) by repetition of a center point of design were produced by solvent casting technique for investigating the efficacy on five responses: elongation at break, elastic modulus, disintegration time, viscosity and adhesion properties. The results of DoE experiments showed that Dexpanthenol affected the mechanical properties of the films by reducing the elastic modulus and tensile strength (0,107 mm^2/kg/% and 3,2 mPa, respectively) and decreased the contact angle up to 59 degrees, while the increasing amount of Kollicoat decreased the gel viscosity thus provided a faster disintegrating film due to the porous structure proven by SEM micrograph. Therefore, the film containing the highest amounts of Kollicoat and Dexpanthenol was chosen as optimum formulation based on the desirability function methodology in context of the DoE approach (Figure 1b).

Keywords

32 factorial design, Dexpanthenol, Kollicoat IR, Mechanical properties, Orally disintegrating films

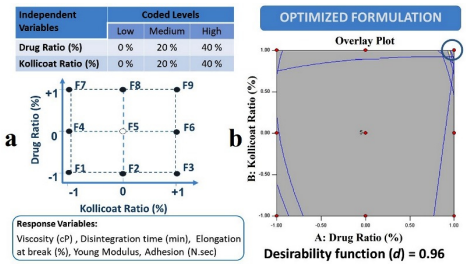

Figure 1: a.Variables for DoE , b. Overlay plot for optimized formulation

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COMPARISON OF TABLET SPLITTING TECHNIQUES FOR DOSING ACCURACY OF NEBIVOLOL TABLETS: HAND SPLITTING VERSUS TABLET CUTTER AND KNIFE

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Tablet splitting is a common practice in clinical settings to lower doses, facilitate swallowing or save costs [1]. However, data on the accuracy of tablet splitting are limited and it presents a number of patient or formulation-related problems. The purpose of this study was to compare the accuracy and precision of three splitting techniques (hand, knife, cutter) for 5 mg-scored nebivolol tablets. Nebivolol is a selective beta1-blocker with vasodilatory properties used for the treatment of hypertension and heart failure. Dose titration is required in the range of 1.25-10 mg. However, only 5 and 10 mg nebivolol tablets are commercially available. Thirty tablets were split by hand, a tablet cutter (Rabır®) or a knife, and tested for weight variation, loss of mass, disintegration, and friability. The accuracy of split tablets was in the range of 77.0-123, 82.5-115, and 85.5-113% when split by hand, the cutter, and knife, respectively. No significant difference in accuracy was determined between left and right sides split by the cutter($p=0.222$). The differences were significant for hand and knife splittings($p<0.005$). The precision was 9.02, 7.87, and 6.11% (CV%) for hand, the cutter, and knife, respectively. Only hand splitting failed to comply with the subdivision test of European Pharmacopoeia. The split portions met USP standards for friability(< 1%). Splitting decreased the disintegration time(4.5 vs. 2.2 min). Overall, the accuracy of the tablet cutter was more favorable than hand splitting and knife. The study demonstrated that the splitting technique may result in inaccurate dosing and significant drug fluctuations for nebivolol tablets.

Keywords

Tablet splitting, Dose accuracy, Nebivolol, Antihypertensive treatment

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DEVELOPMENT AND VALIDATED OF UV SPECTROPHOTOMETRIC AND HPLC METHOD OF BOSENTAN MONOHYDRATE FOR IN VITRO AND EX-VIVO SAMPLES

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Bosentan monohydrate (BOS) is an endothelin antagonist which is classified as a Biopharmaceutic Classification System Class II drug because it is insoluble in water and a highly permeable compound [1]. This study aimed to develop a validated UV spectrophotometric and HPLC method for BOS and assess its application for the *in vitro* and *ex-vivo* studies on BOS formulations. UV analysis was conducted on Agilent Cary 60 UV-Vis for oil solubility studies at 267 nm. HPLC system was operated using buffer solution: acetonitrile (45:55) with a flow rate of 1.5 mL/min. The injection volume was 100 µL. The detection wavelength was 220 nm. Separations were carried out using Waters XSelect® HSS C18 column at 25°C. Both methods were validated according to ICH guidelines. Different solutions (methanol for UV spectrophotometry and 1% SLS in distilled water and biorelevant media (FaSSIF, FeSSIF, FaSSIF-V2, and FeSSIF-V2) for HPLC) were used. The validated analytical methods have been successfully applied in solubility, dissolution, and permeability studies of BOS formulations. The methods were linear in the range of 0.0195-40 µg/mL for all media ($r^2 \geq 0.999$). The retention time of BOS was 4.7-5.5 min in all media for HPLC. For both methods, the limit of quantification ranged from 0.245 to 1.43 µg/mL and recovery ranged from 92% to 100%. The UV spectrophotometric and HPLC methods proved to be sensitive, simple, reproducible, rapid, and precise for *in vitro* and *ex-vivo* samples.

This study was supported by a grant (217S602) from The Scientific and Technological Research Council of Turkey (TUBITAK).

Keywords

Bosentan monohydrate, UV spectrophotometry, HPLC, method validation, Biorelevant media

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STRUCTURE-GUIDED SELECTION OF SUITABLE NANOEMULSION FORMULATION COMPONENTS FOR A RECOMBINANT FORM OF HUMAN INTERLEUKIN-2 (ALDESLEUKIN)

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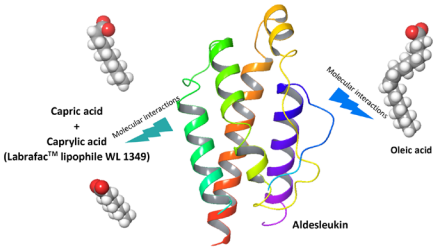
Interleukin-2 (IL-2) is an immunostimulatory cytokine and interacts with IL-2 receptors (IL-2Rs); IL-2Rα, IL-2Rβ, and γ_c receptor. IL-2 binds to β, γ receptors for fighting cancer or α, β, γ receptors for autoimmune diseases [1]. Aldesleukin was the therapeutic version of IL-2 and developed with minor modifications to the sequence of IL-2. There are ongoing efforts to develop better IL-2 treatment options and to eliminate toxicity by using lower doses of the drug. The studies focused on developing novel modified IL-2s, new small molecules, and antibodies that block interaction with IL-2Rα or using different formulation components to slow down the interaction with the same receptor. In this study, we simulated with primary emulsion components (with water and oil phases) to examine the effects of aldesleukin with different nanoemulsion formulations that we developed in previous studies [2]. Molecular dynamic simulations were conducted using Desmond [3] to see time-dependent interactions with the excipients and the protein [4], to select the most suitable formulation components in terms of solubility, intestinal permeability, and stability. The preliminary results indicate that medium-chain triglycerides can reversibly mask polar side chains of the protein with longer residence time. Masking polar side chains can help to increase the lipid solubility of the protein. Additionally, these residues are found to be related to the ones that interact with IL-2Rα, which might let using lower doses in cancer therapy.

Seval OLGAC was supported by scholarships from The CoHE 100/2000 PhD Scholarship Program and TÜBİTAK 2211-C National PhD Scholarship Program.

Keywords

Interleukin-2, Molecular dynamics, Nanoemulsion



The molecular interaction between aldesleukin and components of different nanoemulsion formulations.

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MODELING AND COMPARISON OF IN VITRO DISSOLUTION PROFILES OF BOSENTAN MONOHYDRATE: COMMERCIAL TABLET VS S-SNEDDS TABLET

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Bosentan (BOS) is an endothelin receptor antagonist in the treatment of pulmonary arterial hypertension. BOS is a weak acid BCS Class 2 drug; it is poorly soluble in an aqueous solution, especially at low pH [1]. The aim of this study was to modeling and compare *in vitro* dissolution performance of BOS using reference (Tracleer®) *versus* test [2] (solid self-nanoemulsifying drug delivery system (S-SNEDDS) tablet). The *in vitro* dissolution studies were performed using USP Apparatus-II at 50 rpm at 37±0.5°C in 900 mL of 1% SLS in distilled water, FaSSIF, FeSSIF, FaSSIF-V2, and FeSSIF-V2. The samples were analyzed by HPLC at 220 nm. The dissolution data analysis was performed model-dependent using DDSolver®. The adjusted coefficient of determination (R^2adj), Akaike information criterion (AIC), and model selection criterion (MSC) were used to determine the most appropriate release model, which is with a lower AIC, highest MSC, and R^2adj. The model-dependent results differed for reference and S-SNEDDS tablets for all media. However, when the model parameters were examined in the adapted models, it was seen that the scale (α) and the shape (β) factors were effective on almost all results. The difference between the models for different media is thought to be due to the low pH-dependent solubility for the reference tablet, and the desorption mechanism of SNEDDS for the S-SNEDDS tablet from the adsorbent substance depending on the different pH of the media.

This study was supported by a grant from The Scientific and Technological Research Council of Turkey (TUBITAK), Project No:217S602.

Keywords

Bosentan, Biorelevant dissolution, Model-dependent method

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SOLID-STATE CHARACTERIZATION STUDIES OF BOSENTAN-LOADED SOLID SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEM (S-SNEDDS) COMPRISING OF NEUSILIN® US2

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Bosentan (BOS) is the first non-peptidic endothelin receptor antagonist administered orally in the specific treatment of pulmonary arterial hypertension (PAH) [1]. BOS is a BCS Class II drug with low solubility and high permeability. The aim of this study was to evaluate the solid-state characterization of bosentan-loaded S-SNEDDS adsorbed Neusilin® US2. The SNEDDS were prepared according to our previous studies [2]. The SNEDDS formulation was converted into S-SNEDDS using Neusilin® US2 by the physical adsorption method. The SNEDDS was added at 1:1, 1.25:1, 1.5:1 liquid SNEDDS: carrier ratios by weight on Neusilin® US2. Adsorption was carried out by triturating the liquid formulations with the adsorbents in a mortar until they formed a homogenous mixture. The powder samples were evaluated for the physical, molecular state, thermal properties, the assessment of crystallinity, the possible interactions between the drug and excipients, morphological properties, and surface area of the porous carrier. For this purpose, differential scanning calorimetry (DSC), X-ray powder diffraction (X-RPD), Fourier transforms infrared spectroscopy (FT-IR), scanning electron microscopy (SEM), and The Brunauer-Emmett-Teller (BET) analyses were performed. Neusilin® US2 S-SNEDDS formulations containing a 1.25:1 ratio of BOS-loaded SNEDDS: Neusilin® US2 was selected for further studies. The solid-state characterization studies of the BOS-loaded solid SNEDDS (1.25:1) showed acceptable physical characteristics in *in vitro* evaluations.

This study was supported by a grant from The Scientific and Technological Research Council of Turkey (TUBITAK), Project No: 217S602.

Keywords

Bosentan, S-SNEDDS, Solid-state characterization, Neusilin® US2

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IN VITRO CHARACTERIZATION OF EXEMESTANE-LOADED SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEM CONTAINING MEDIUM CHAIN MONO AND DIGLYCERIDES

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Exemestane, which is an aromatase inhibitor used for the treatment of breast cancer in postmenopausal women, has a poor oral bioavailability which is due to its low water solubility (80 µg/mL) [1,2]. To improve oral bioavailability of exemestane, self-nanoemulsifying drug delivery system (SNEDDS) was develop and optimized using the Box-Behnken design in previous study [3]. This study aims to evaluate in vitro characterization studies of optimum SNEDDS. For this purpose, droplet size and polydispersity index (PDI) analysis, thermodynamic stability studies, dispersibility test, self-emulsification time measurement, viscosity determination, transmittance % measurement, dilution and pH effect analysis, drug loading, lipolysis studies were carried out. The droplet size ve PDI were found less than 100 nm and 0.2, respectively. SNEDDS passed dispersibility test in Grade A and the thermodynamic stability which is determined using heating-cooling cycle, centrifugation and freeze-thaw cycle stress tests. SNEDDS showed Newtonian flow behavior and high transmittance which is considered optically clear. The formulation exhibited robustness against dilution and pH effect. According to the equilibrium solubility of exemestane in the formulation, the drug amount to be loaded into SNEDDS was found to be 15 mg. The fate of the drug loaded on SNEDDS (solubilized or precipitated) can be determined by lipolysis study. In this study, lipolysis data showed that SNEDDS formulation presented high amount of drug in aqueous phase both fasted (86.5%) and fed state (86.9%) after 90 min digestion. According to the results, the SNEDDS formulation was successfully developed and characterized.

Keywords

Exemestane, SNEDDS, In vitro characterization, In vitro lipolysis

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EVALUATION AND FABRICATION OF DISSOLVING PVA-DICLOFENAC SODIUM MICRONEEDLES

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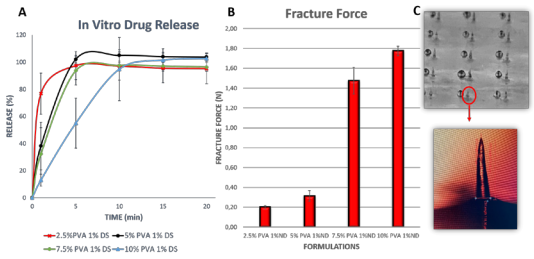
Microneedles are revolutionary novel dosage forms for transdermal drug delivery. They are able to increase transdermal absorption of conventional drugs as well as macromolecules or proteins [1]. In this study, diclofenac sodium (DS), a commonly used NSAID, as a hydrophilic drug was loaded to polyvinyl alcohol (PVA) microneedles [2]. PVA (Polyviol G04/140) was supplied from Wacker Chemie AG (Germany). DS was donated by Vem Pharmaceuticals (Turkey). Aqueous solutions of PVA (2.5%, 5%, 7.5% and 10%(w/w)) were prepared. DS (1% w/w) was added to the PVA solutions. Viscosity, surface tension and contact angles of aqueous mixtures were investigated. After pouring the mixtures into PDMS microneedle molds, air bubbles were removed by centrifugation and molds kept under laminar flow for at least 48 hours for drying. Obtained microneedles (≈500 um) were examined in terms of morphology, mechanical properties and in vitro drug release. It was determined that the viscosity increased as the PVA concentration increased, and accordingly, defects in film formation occurred. Viscosity and contact angle were thought to be effective in needle formation, in contrast to surface tension. However, with the increasing amount of PVA, the mechanical strength promoted and the release extended. Since all formulations reached complete release within 20 min, 10% PVA(w/w) and 1% DS(w/w) formulation with the highest mechanical strength was found to be most suitable formulation. This study showed that PVA dissolving microneedles are easily prepared formulations for transdermal application of hydrophilic drugs with low skin permeability.

Keywords

Microneedle, Diclofenac Sodium, Polyvinyl Alcohol, Transdermal Drug Delivery



A) In vitro drug release profiles B) Fracture force measurements C) Morphological analyzes

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PREFORMULATION STUDIES OF TOFACITINIB CITRATE LOADED MICROSPHERES INTENDED FOR INTRA-ARTICULAR ADMINISTRATION

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Rheumatoid arthritis (RA), a chronic and systemic autoimmune disease, involves many joints at the same time with unknown etiology [1]. Although, tofacitinib citrate (TOFA), an orally used JAK inhibitor, was approved by the FDA in the treatment of RA in 2012, it may cause many systemic serious side effects [2,3]. The aim of this study is to develop tofacitinib citrate loaded microspheres for intraarticular administration to reduce side effects and provide effective local treatment of RA. Microsphere formulations were prepared by emulsion chemical cross-linking method [4]. Chitosan in acetic acid solution and Tween 80 was used as water phase, while the oil phase was liquid paraffin and Span 85 mixture in water/oil emulsion. TOFA was added to the water phase of emulsion at 10 $mg.mL^{-1}$ concentration. Following the obtaining of homogeneous distribution, glutaraldehyde was added to crosslink chitosan in the inner phase of the emulsion. After the preparation, the formulations were characterized in terms of their particle size, morphological characteristics, encapsulation efficiency and in vitro release behaviour. Characterization properties of different microsphere formulations and particle size were given in Table 1. The encapsulation efficiency of TOFA in optimum microsphere formulations (Microsphere-9) was calculated as ~41%, and the release profile of TOFA from was found compatible with Korsmeyer-Peppas kinetic. As a result, TOFA loaded microspheres were found to be promising for future in vitro and in vivo experiments due to its characterization properties and controlled drug release ability.

Acknowledgements: This study was supported by TUBITAK Scientific Research Project [Project number: 119S639].

Keywords

Microsphere, Tofacitinib citrate, Rheumatoid arthritis

FORMULATION CODE	CHITOSAN (%)	TWEEN 80 (%)	PARAFFIN	SPAN 85	GLUTARAL	STIRRER RATE (rpm)	PARTICLE SIZE (μm, ± S.D.)
MICROSPHERE 1	3	-	20 mL	1 mL	1 mL	15 min 1400 rpm; 3 h 500 rpm	644±10.79
TOFA-MICROSPHERE 1	3	-	20 mL	1 mL	1 mL	15 min 1400 rpm; 3 h 500 rpm	636±16.92
MICROSPHERE 2	3	%10	20 mL	1 mL	1 mL	15 min 1400 rpm; 3 h 500 rpm	635±7.55
TOFA-MICROSPHERE 2	3	%10	20 mL	1 mL	1 mL	15 min 1400 rpm; 3 h 500 rpm	643±6.56
MICROSPHERE 3	3	%10	20 mL	1 mL	1 mL	15 min1400 rpm; 3 h 1400 rpm	531±15.69
MICROSPHERE 4	3	%30	20 mL	1 mL	1 mL	15 min1400 rpm; 3 h 1400 rpm	245±3.79
MICROSPHERE 5	3	%10	20 mL	2 mL	1 mL	15 min1400 rpm; 3 h 1400 rpm	193±1
MICROSPHERE 6	3	%30	20 mL	2 mL	1 mL	15 min1400 rpm; 3 h 1400 rpm	214±0.58
MICROSPHERE 7	3	%10	20 mL	2 mL	1.5 mL	15 min1400 rpm; 3 h 1400 rpm	67.4±0.15
MICROSPHERE 8	3	%10	20 mL	1 mL	0.5 mL	15 min1400 rpm; 3 h 1400 rpm	49.4±0.92
MICROSPHERE 9	3	%20	20 mL	1 mL	1 mL	15 min1400 rpm; 3 h 1400 rpm	60.2±0.12
TOFA-MICROSPHERE 9	3	%20	20 mL	1 mL	1 mL	15 min1400 rpm; 3 h 1400 rpm	168.333±2.082

Table 1. Preparation parameters of microsphere formulations

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DETERMINATION OF PYRROLIZIDINE ALKALOIDS IN GALACTAGOGUE HERBAL TEAS

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Herbal teas may contain hepatotoxic, carcinogenic and genotoxic compounds such as pyrrolizidine alkaloids (PA). Toxic effects can be seen with chronic consumption of teas prepared from plants contaminated with plants containing these compounds during harvest. This study aimed to evaluate whether this group of products pose a risk for breastfeeding mothers and babies by determining PA in galactagogue herbal teas purchased from the internet site and herbalists. In this study, we investigated the PA contents of 19 herbal tea samples obtained from the internet site and herbalists which were sold for promoting milk production in lactating women. Herbal tea samples were analyzed for quantification of 12 PA by LC-MS/MS method which includes solid-phase extraction (SPE). Analyzes were performed on LC-MS Q-TOF system. Interventions in different matrix types were controlled by adding standards to the sample types. Up to 4 PA were detected in some herbal tea samples among the 12 PA compounds to be determined. Results ranged from 20 ng/g (LOQ) to 540 ng/g. The N-oxide forms of the quantified pyrrolizidine alkaloids were also defined for confirmation purposes. As a result of the analyzes made, it was determined that 10 of the 19 samples had PA contamination (Europine and Seneciphylline). These results showed us that, since PA is toxic compounds, herbal teas that are easily obtained from the market should be analyzed in terms of these compounds and then the teas containing PA in appropriate limits should be sold in pharmacies for maternal and child health.

Acknowledgements: Gazi University Scientific Research Projects Unit (02/2020-05)

Keywords

Pyrrolizidine alkaloids (PA), Herbal tea, Lactation, Hepatotoxic, LC-MS/MS.

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PHYTOCHEMICAL AND BIOLOGICAL ACTIVITY INVESTIGATIONS ON HYPERICUM SECHMENII OCAK & O. KOYUNCU

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The genus *Hypericum* L. (Hypericaceae) comprises nearly 500 species which spread all the world. *Hypericum sechmenii* Ocak&O.Koyuncu, has been described by Ocak et. al. as an endemic species that grows naturally around Eskişehir. In this work, *H. sechmenii* was subjected to phytochemical and biological tests for the first time [1-3]. The essential oil of the aerial parts was obtained by hydrodistillation method. The extracts of roots and leaves were obtained by maceration with *n*-hexane (HHR/HHL, resp.), methanol (HMR/HML), and water (HWR/HWL). The total phenol and flavonoid content determined with spectrophotometric method. The antioxidant activity investigated by DPPH and TEAC assays and antidiabetic potency were determined by α-amylase inhibition assay. The essential oil was characterized with germacrene D (14.5%), bicyclogermacrene (12.8%), b-elemene (7.0%).The yields of extracts were found to be as 1.34%/12.03% (HHR/HHL), 4.09%/23.59% (HMR/HML) and 1.43%/6.74% (HWR/HWL). The highest phenol content was found in HML (219,33 GAEmg/$g_{extract}$) and HMR (205,53 GAEmg/$g_{extract}$) and highest flavonoid content was found in HML (122,00 REmg/$g_{extract}$) and HMR (117,76 REmg/$g_{extract}$). The highest TEAC values were obtained in HML (2,25 mM) and HMR (1,74 mM). The highest DPPH values was found in HMR (IC_{50}, 6,0 ug/mL) and HML (IC_{50}, 46,0 ug/mL). The highest α-amylase inhibition effect was detected in HHL ($IC_{50,}$ 0,25 mg/mL). The study revealed that methanolic root and leaf extracts have significant antioxidant activity and the hexane leaf extract have remarkable anti diabetic activity.

Acknowledgement: Thanks to the Scientific Research Department of Anadolu University for financial supporting (BAP №2105S092).

Keywords

Hypericum sechmenii, Extract, Essential oil, Activity

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P45

PHENOLIC PROFILE, MINERALS AND ANTIOXIDANT CAPACITY DETERMINATION OF OLIVE LEAF AND SEEDS ACCORDING TO DIFFERENT EXTRACTION TECHNIQUES

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In the scope of the research, the by-products in the olive oil industry olive seeds and leaves were subjected to different extraction techniques and determination of the phenolic and mineral profiles and antioxidant potential. *Olea europaea* L. seeds and leaves were extracted by Continuous Solvent, Accelerated Solvent, Microwave-Assisted and Ultrasonic extraction techniques with water and 60% methanol-water. The total phenolic content of the extracts was determined with FC-reagent [1]. Phenolics in the extracts were quantified with HPLC-PDA [2]. The antioxidant potential of the extracts was determined with DPPH and ORAC tests [3,4]. The minerals in the seeds and leaves were identified with ICP-OES [5]. The highest TPC values were determined in the leaf extracts obtained with aqueous methanol. The methanolic Sx_{Leaf}, MW_{leaf} and US_{Leaf} extracts were rich in oleuropein and luteolin-7-glucoside, however caffeic acid was not detected in any extract, dicaffeoylquinic acid was minor and *p*-coumaric acid was trace in different extracts. The ICP-OES analysis revealed high abundance of Zn and Cd in the leaves, and Zn and Na in the seeds. The leaf extracts demonstrated higher results than seed extracts, similar domination was seen in the methanolic extracts. This study revealed that industrial by-products olive seed and leaf can be used as a source of many compounds that are valuable in the research field of food and phytochemistry.

Acknowledgement: Authors thanks to the Scientific Research Department of Anadolu University for financial supporting of the research project (BAP № 2005S069).

Keywords

Olive, Phenolics, Minerals, Antioxidant

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P46

PHYTOCHEMICAL AND BIOLOGICAL ACTIVITY INVESTIGATIONS ON HEPTAPTERA TRIQUETRA

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The genus *Heptaptera* (Apiaceae) is represented in Turkey with 4 species. Chemical studies of *Heptaptera* species showed the widespread occurrence of a variety seconder metabolites: alkanes, sesquiterpenes [1, 2], and coumarins [3]. A previous biological activity screening on *Heptaptera* species resulted with wide range of activities: cytotoxic [4], anticholinesterase [5]. In the present work, the fruit and inflorescence essential oils as well as methanolic extracts of *H. triquetra* have been subjected to phytochemical and biological activity investigations. The fruits and aerial parts with inflorescence of *H. triquetra* were hydrodistlled to get essential oils. The extracts were obtained by maceration of fruit, leaf and stem parts of *H. triquetra* in methanol (HTE1, HTE2, HTE3, respectively). The oils and extracts were subjected to investigation for free radical scavenging (DPPH, TEAC) and antidiabetic (a-amylase inhibition) activities. The fruit lipids were extracted and subjected to transesterification. The essential oils and fatty acids were investigated with GC-FID/MS techniques. Heptacosane (22.6%), pentacosane (7.1%), epoxy-*trans*-pseudoisoeugenyl angelate (7.3%), myristicin (7.3%), phytol (5.2%), and dill apiole (5.1%) were detected as main constituents in the inflorescence oil. Heptacosane (23.6%), pentacosane (17.2%), heneicosane (8.4%), (*E*)-geranylacetone (4.5%), hexahydro-farnesylacetone (4.4%), and acorenone B (3.5%) were detected in the fruit oil. The fruit extract demonstrated significant antioxidant activity (Inh. 87%). All the tested extracts showed a moderate anti-a-amylase activity (Inh. <30%). In scope of the study, antioxidant and antidiabetic potential of *Heptaptera triquetra* were evaluated. *H. triquetra* methanol extract demonstrated strong antioxidant activity.

Keywords

Heptaptera triquetra, Essential oil, Extract, Antioxidant, Antidiabetic, Activity

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P47

TIME DEPENDENT MICROBIAL TRANSFORMATION OF HESPERIDIN BY ASPERGILLUS NIGER

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Microbial transformations are environmentally friendly biotechnological procedures that employ diverse fungi, bacteria, yeast or their enzymes to create new metabolites from the defined substrates. This is a common technique utilized in various disciplines including pharmacognosy for the derivatisation of natural products [1]. Hesperidin (hesperetin-7-O-rutinoside) belongs to the flavanone group of flavonoids and can be isolated from the bark of several *Citrus* species. Hesperidin and its aglycone hesperetin have been shown to have therapeutic benefits in a variety of diseases in preclinical investigations and clinical trials [2, 3]. Within the scope of the study, the hesperidin was subjected to microbial transformation studies by *Aspergillus niger* and conversion took place. The compounds were analyzed by LC-MS. The time-dependent abundances of the metabolites were analyzed 4, 8 and 12 days and the highest yields of metabolites were obtained on 8 days. In this way, hesperetin and naringenin, which are less than hesperidin in nature, were obtained by this method. Microbial transformation of hesperidin with *Aspergillus niger* occurred for the first time. In previous studies, while hesperetin was obtained by *Aspergillus terreus* and *A. ochraceus;* the conversion of naringenin by *A. niger* was performed for the first time [4].

Acknowledgments: This study was financially supported as a Scientific Research Project (BAP 1901S001) by Anadolu University.

Keywords

Microbial transformation, Hesperidin, Aspergillus niger, Flavanoids

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P48

DEVELOPMENT OF PLANT-BASED DERMOCOSMETIC PRODUCTS USING EFFICACY AND SAFETY TESTS WITH 2D/3D CELL CULTURE METHODS

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Skin aging is a complex biological process affected by different internal and external factors that disrupt the skin structure, especially in sun-exposed areas. Elastin and collagen in the dermis layer, responsible for the skin's resistance and elasticity, have also been the main subject of researches. Since tyrosinase is an enzyme found in different organisms and plays an important role in melanogenesis, inhibitors of this enzyme have been the target mechanism for skin bleaching product researches. In the light of this information, within the scope of our ongoing studies, we have screened the inhibitory effect of approximately 100 plant extracts against elastase, collagenase, and tyrosinase enzymes, as well as their antioxidant activities by *in vitro* methods. We selected plant species/propolis which were effective against at least two of these enzymes and prepared fresh extracts for further studies. The extracts were also tested with cell-free enzyme assay using validated anti-elastase, anti-collagenase, and anti-tyrosinase assay kits in the Austrian Drug Screening Institute (ADSI). The European Union banned animal testing in cosmetic products or cosmetic raw materials in March 2013. For this reason, studies on alternative methods have been carried out, and in recent years, three-dimensional (3D) skin models consisting of fibroblast and keratinocyte cell cultures have been successfully applied. Our data revealed propolis among the tested extracts, which displayed remarkable antiinflammatory activity in our 2D and 3D assays. Additionally, *Cotinus coggygria* leaf extract and mangosteen have anti-inflammatory activity in the 2D luciferase reporter assay via TNFα addition.

Keywords

Dermocosmetic, Propolis, Cotinus coggygria, 3D cell culture

P49

MICROBIAL TRANSFORMATION OF QUERCETIN BY 25 DIFFERENT MICROORGANISMS

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Quercetin is a plant pigment that is mostly found in onions, grapes, berries, cherries, broccoli, and citrus fruits. It is a powerful antioxidant flavonoid and more particularly a flavonol. Quercetin has linked to a variety of health advantages, including anti-inflammatory, antiviral, and anticancer properties, as well as the ability to relieve several cardiovascular disorders. Also, It is a multifunctional antioxidant that has been shown to protect against tissue injury due to a variety of drug toxicity [1,2]. So, the biological derivatization of quercetin with the goal of producing new bioactive metabolites is an important field for cosmetic, medicine and pharmacology. In this research, it was aimed to produce quercetin derivatives using microorganisms as biotechnological methods. Pre-biotransformation of quercetin was carried out with 25 different microorganisms for 12 days at 25°C in an α-medium. Thin-layer chromatography (TLC) was used to detect the metabolites. It was found that extracts obtained from biotransformation of quercetin with *Penicillium claviforme* (MR 376) (M1), *Aspergillus nidulans* (Abraham) (M2), *Alternaria alternata* (NRRL 20593) (M3) and *Aspergillus flavus (*ATCC 9807) (M4). While M1 and M2 compounds are more polar than quercetin; M3 and M4 are more nonpolar than quercetin.

Keywords

Microbial transformation, Quercetin, Flavonoids, Microorganisms

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P50

LC-Q-TOF-MS QUANTIFICATION OF GINKGOTOXIN IN GINGKO BILOBA L.-CONTAINING DIETARY SUPPLEMENTS SOLD IN TURKEY AND IN THE PLANT SAMPLE NATURALIZED IN TURKEY

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Ginkgo biloba L. is one of the well-known medicinal plants used against serebrovascular disorders including Alzheimer's disease, tinnitus,etc.The plant is known to contain mainly flavonoids and diterpene trilactones,which are associated with standardization of its officinal leaf extract (EGb761). *G. biloba* preparations are among the best-selling dietary supplements all over the world. In addition to flavonoids and lactones, the plant has rich in phytochemistry such as ginkgolic acids, phenolic acids, coumarins, lipids, tannins. One of those phytochemicals is ginkgotoxin, a neurotoxin naturally occurring in *G. biloba* L. The compound occurs in the seeds and has been also detected in some species *e.g. Albizzia* sp. Some poisoning cases resembling to epileptic seizures have been reported on in livestock with *Albizzia* sp. called "albizziosis" due to existence of ginkgotoxin. Therefore, it is important to search presence of ginkgotoxin in dietary supplements prepared with leaf extracts of *G. biloba*. For this goal, we carried out analyses in 13 commercial products containing *G. biloba* leaf extracts sold in dietary supplement category in Turkey. For comparative purposes, the seed and leaf extracts prepared from *G. biloba* tree naturalized in Turkey (Ankara province) were also analyzed in terms of ginkgotoxin presence. According to our preliminary findings, ginkgotoxin was found to be present between 1.24-48.39 mg/g in the commercial products, whereas its quantity was determined 255.25 mg/g in the seed extract as well as 9.99 mg/g in the leaf extract of *G. biloba.* Our findings indicated that ginkgotoxin presence must be analyzed in the dietary supplements containing *G. biloba* leaf extracts.

Keywords

Ginkgotoxin, Epileptic seizures, Serebrovascular disorders, Ginkgo biloba

P51

INVESTIGATION OF ANTIOXIDANT ACTIVITY OF DIFFERENT EXTRACTS FROM ACHILLEA GONIOCEPHALA

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The goal of this research is to examine at the biological activity of 19 different extracts from *A. goniocephala* (endemic) using three different extraction techniques (Maceration, Soxhlet and Supercritical fluid extraction method). The antioxidant capabilities of different plant extracts were tested using the DPPH, CUPRAC, and TEAC techniques. The FCR technique was also used to determine the total phenolic content of the extracts [1,2]. In comparison to other extracts, 50% methanol extracts of the plant produced using the Soxhlet technique exhibited significant DPPH radical scavenging (IC_{50}: 0.031 mg/mL) and copper(II) ion reducer activity (4.2615±1.2859 mMTE/mg extract), according to the findings. It was determined that the maceration 70% ethanol (1.1919 mM trolox equivalent/g extract) and Soxhlet 70% methanol (1.0992 mM trolox equivalent/ g extract) extracts of plant had higher TEAC values than the other extracts. In the total phenolic experiment, it was determined that Soxhlet 50% methanol extract contained the highest phenolic contents (9.4875±0.840 mg GAE/g extract) compared to other extracts. The biological activity of the plant is affected by different consuming techniques and solvents, according to the experimental results.

Keywords

Achillea goniocephala , Antioxidant activity

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SIRT2 INHIBITORY ACTIVITIES OF N-ARYLOXYPHENYL-2-(ARYLTHIO)ACETAMIDE DERIVATIVES

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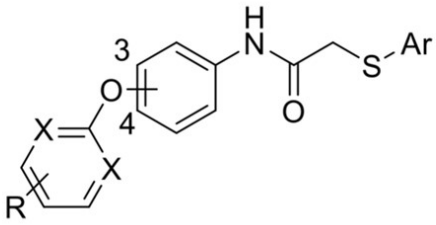
Sirtuins (SIRTs) are a enzyme family belonging to NAD^+ dependent histone deacetylases, which is responsible for reversibly deacetylating lysine residues in histone or non-histone substrates. SIRTs consist of seven isoforms (SIRT1-7), which differ in cellular localization, enzymatic function, and substrate proteins. Among these isoforms, SIRT2 predominantly resides in the cytoplasm but can also function in the nucleus [1]. Due to taking part in various biological processes such as gene expression, energy metabolism and regulation of the cell cycle, SIRT2 inhibition has emerged as a strategy to combat cancer, neurodegeneration and inflammation [2]. Herein, we represent the synthesis and SIRT2 inhibition profile of a series of *N*-aryloxyphenyl-2-(arylthio)acetamides.

This study was supported financially by the Scientific and Technological Research Council of Turkey (TÜBİTAK; 118S673).

Keywords

SIRT2, Enzyme inhibition, Arylthioacetamide



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P53

N-(5-ARYLMETHYL-1,3,4-OXADIAZOLE-2-YL)-2-(ARYLTHIO) ACETAMIDE AS A NEW SCAFFOLD FOR DEVELOPING SMALL-MOLECULE SIRT INHIBITORS

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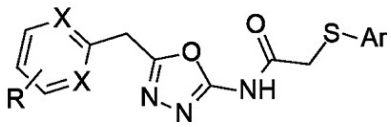
Epigenetics is a term used to refer to changes in gene expression that occur except the structure or base sequence of DNA. One of the most well-known epigenetic abnormalities in the literature is ''histone acetylation''. Histone deacetylase deregulation causes silencing of tumor suppressor genes and overexpression of oncogenes. The SIRT family is known as NAD^+-dependent Class III histone deacetylase enzymes. There are seven sirtuin isoforms (SIRT 1-7) that diverge in cellular localization, regulation, and substrate selectivity in mammals [1]. Inhibition of SIRT activity has been associated with diabetes, cancer [2], inflammation, and neurodegeneration pathogenesis [3]. Therefore, SIRT has become a promising epigenetic drug target [4]. In this study, we demonstrate the synthesis and SIRT inhibition profile of a series *N*-(5-arylmethyl-1,3,4-oxadiazole-2-yl)-2-(arylthio)acetamides.

This study was supported financially by the Scientific and Technological Research Council of Turkey (TÜBİTAK; 118S673).

Keywords

SIRT, Epigenetic, Enzyme inhibition, 1,3,4-Oxadiazole



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DISCOVERY OF 5-BENZYL-1,3,4-OXADIAZOLE/ THIADIAZOLE-2-CARBOXAMIDES AS POTENTIAL LEADS FOR SELECTIVE SIRT2 INHIBITION

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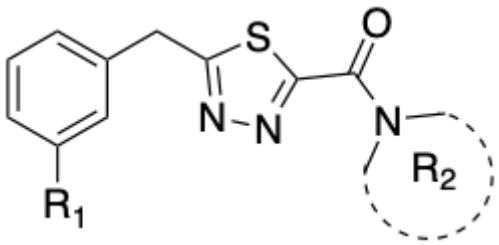
SIRT2 plays a significant role in cancer development since it affects several biological processes, including aging, gene transcription, inflammation, apoptosis, and metabolism [1]. A number of scientific studies have revealed that SIRT2 has a dual role in cancer development, acting as a tumor suppressor or a tumor promoter [2]. Therefore, SIRT2 has been a target in drug discovery for cancer treatment. For this purpose, we designed and synthesized novel 5-benzyl-1,3,4-oxadiazole-2-carboxamide and 5-benzyl-1,3,4-thiadiazole-2-carboxamide derivatives. Further, SIRT inhibitor activities of the compounds were investigated. The results indicated that 5-benzyl-1,3,4-thiadiazole-2-carboxamides are promising lead compounds for selective SIRT2 inhibition.

This study was financially supported by the Scientific and Technological Research Council of Turkey (TUBITAK SBAG 118S673).

Keywords

SIRT2, Thiadiazole, Oxadiazole



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SOME NEW 2,5-DISUBSTITUTED 1,3,4-OXADIAZOLE AND 3,6-DISUBSTITUTED-7H-1,2,4-TRIAZOLO[3,4-B][1,3,4]THIADIAZINE DERIVATIVES WITH IN VITRO ANTI-INFLAMMATORY ACTIVITY

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Inflammation means body's defense system response to the stimulation of many factors. Changing in vascular permeability, disruption of the membrane structure and protein denaturation are leading reasons that initiate the inflammation process. As protein denaturation is a well-documented reason of inflammation, the compounds that can inhibit heat induced protein denaturation, are considered as potential anti-inflammatory agents. Non-steroidal anti-inflammatory drugs (NSAIDs) are also effective by inhibiting albumin denaturation. To obtain new anti-inflammatory agents, recent studies have aimed to replace the carboxylate functionality of NSAIDs with less acidic heterocyclic bioisosters like 1,3,4-oxadiazole and 1,2,4-triazole to protect gastric mucosa from free carboxylate. In this study, novel 2,5-disubstiuted-1,3,4-oxadiazoles and 3,6-disubstituted-7*H*-1,2,4-triazolo[3,4-b][1,2,4]thiadiazines were synthesized and evaluated for their anti-inflammatory activities. 2,5-Disubstituted-1,3,4-oxadiazoles were obtained by reaction of previously synthesized 5-(3,5-dimethylphenyl)-1,3,4-oxadiazole-2(*3H*)-thione with phenacyl bromides in basic medium. This compounds were cyclized with hydrazine hydrate to yield 3,6-disubstituted-7*H*-1,2,4-triazolo[3,4-b][1,2,4]thiadiazines. The anti-inflammatory activity of the synthesized compounds was investigated using *in vitro* albumin denaturation assay. The structures of the newly synthesized compounds were verified by IR and ^{1}H NMR spectral methods. The activity test results demonstrated that while indomethacin showed 86.92% activity, compounds 3a and 3b showed inhibition activity with 82.20% and 73.73% at 100 µg/mL, respectively. In addition, the compounds 3a-c, 3f and 4a showed more than 50% inhibition activity (Table 1). Compounds which showed more than 50% inhibition in the albumin denaturation test, 3a-c, 3f and 4a, were selected for further investigation to elucidate the anti-inflammation mechanism.

Keywords

1,3,4-Oxadiazole, 1,2,4-Triazole, Anti-inflammatory agent, Albumin denaturation assay

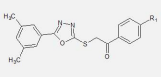
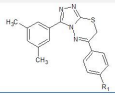
Structure of the compounds	Compound	R_1	Activity (%) (100 µg/mL)
	Indomethacin		87.15
	**3a**	H	82.20
	3b	F	73.59
	3c	Cl	71.89
	3d	Br	17.80
	3e	CH_3	14.27
	3f	NO_2	73.59
	**4a**	H	51.13
	4b	F	40.25
	4c	Cl	49.15
	4d	Br	38.84
	4e	CH_3	36.86

Table 1. Albumin denaturation test results of synthesized compounds

P56

SYNTHESIS AND IN VITRO ANTI-INFLAMMATORY ACTIVITY OF SOME NEW 1,3,4-OXADIAZOLE DERIVATIVES

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Inflammation occurs as an immediate body response to tissue and cellular damage. It is related to many chronic conditions. Since denaturation of proteins is one of the causes of inflammation, compounds inhibiting heat-induced protein denaturation are considered to have potential therapeutic properties as anti-inflammatory agents. NSAIDs (non-steroidal anti-inflammatory drugs) a group of drugs that inhibit albumin denaturation. Previous studies were undertaken with an aim to convert the free carboxylic group of compound into biologically active, five membered heterocyclic rings like 1,3,4-oxadiazole, in an attempt to obtain potential and safer NSAIDs. Previously synthesized 2-[(Substitutedphenyl)amino]acetohydrazide and substituted aromatic aldehyde in ethanol-water system (1:2, v/v) solvent was refluxed for 10–12 h with addition of 20 % solution of $NaHSO_3$ to obtain targeted products. The anti-inflammatory activity of the synthesized compounds was investigated using *in vitro* albumin denaturation assay. The structures of the synthesized compounds were identified by IR, ^{1}H NMR, ^{13}C NMR, LC-MS spectral methods. The activity test results demonstrated that while indomethacin showed 87.15 % activity at 100 µg/mL, compounds 4b showed inhibition activity with 82.06 % at 100 µg/mL, respectively. In addition, at the same concentration, compounds 4a, 4c and 4e showed more than 70 % inhibition activity (Table 1). Synthesized compounds which showed more than 70 % inhibition in the albumin denaturation test, were selected for further investigation to elucidate the anti-inflammation mechanism.

Keywords

Oxadiazole, Anti-inflammatory, Albumin protein denaturation

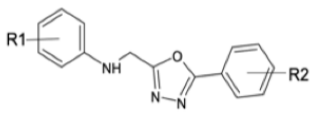
Structure of the compounds	Compound	-R1	-R2	Activity(%)
	Indomethacin			87,15
	4a	2,6-DiCH3	2,5-DiCH3	78,62
	4b	2,6-DiCH3	4-OCH2CH3	82,06
	4c	2,6-DiCH3	2-NO2	74,15
	4d	2,6-DiCH3	3-OCH2CH3-4-OCH3	12,71
	4e	2,3-DiCH3	2-NO2	69,63

Table 1. In vitro serum albumin inhibitory activity of synthesized compounds

P57

MICROWAVE SYNTHESIS OF BENZOTHIAZOLONE-2(3H)-3-ACETYL-2-(SUBSTITUE/NONSUBSTITUEINDOL OR PYRIDINE)HYDRAZONE DERIVATIVES

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Schiff bases are compounds formed by the nucleophilic addition reaction of primary amines with the activated carbonyl group of aldehydes or ketones and contain carbon-nitrogen double bonds (-C=N-) [1]. Some studies have shown that the presence of an electron pair in an sp2 hybridized orbital of the nitrogen atom of Schiff bases is of great chemical and biological importance. In addition, these compounds are excellent metal chelators, especially when bound to functional groups such as - OH or - SH [2]. Schiff bases are not only easy to synthesize, but also find wide application in medicinal chemistry and the pharmaceutical industry, which has increased importance of these compounds [3]. In addition, Schiff bases showed antimicrobial [4], antiviral [4], antinociceptive [5], antiplatelet [5], antiproliferative [4,5], anticancer [4,5], and anticonvulsant [4,5] activities. Benzothiazolone is bicylic ring system of pharmaceutical importance due to its strong and important biological effects. In this study, new schiff base of Benzothiazolone-2(3H)-3-il-acetohyrazid derivates with substitue/nonsubstitueindol or substituepyridine aldehydes have been microwave synthesized. Structures of the synthesized compounds were verified by ^{1}H-NMR and LC-MS spectrospy methods.

Keywords

Schiff base, Benzothiazolone, Hydrazone, Indole, Pyridine

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P58

THE FIRST PREPARATION OF BIOENGINEERED LOW MOLECULAR WEIGHT HEPARIN FROM A REMODELED BOVINE INTESTINAL HEPARIN

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Heparin, a member of the sulfated glycosaminoglycan (GAG) family, is derived from animal tissues and has been widely used clinically as an anticoagulant. Currently, porcine intestinal heparin is the only approved UFH in the USA and Europe, although bovine lung was the primary source of heparin until 1960 and bovine intestinal heparin was approved by the US Food and Drug Administration (FDA) in the USA until the mid-1990s. Bovine intestinal heparins are structurally distinct from porcine intestinal heparins and exhibit lower specific anticoagulant activity (units/mg). The reduced content of *N*-sulfo, 3-*O*-sulfo glucosamine, the central and critical residu in heparin's reduced activity. Previous studies demonstrated that treatment of bovine intestinal heparin with 3-O-sulfotransferase in the presence of 3'-phosphoadenosine-5'-phosphosulfate afforded remodeled bovine heparin with an enhanced activity reaching the United States Pharmacopeia's requirements. Starting from this remodeled bovine intestinal heparin, we report the preparation of a bovine intestinal low molecular weight heparin having the same structural properties and anti-factor IIa and anti-factor Xa activities of Enoxaparin. Moreover, this bovine intestinal heparin-derived enoxaparin analog showed comparable platelet factor-4 binding affinity, suggesting that it should exhibit similarly low levels of heparin induced thrombocytopenia, HIT.

Keywords

Bovine heparin, Enoxaparin, 3-OST-1

P59

NOVEL PIPERAZINYL UREA DERIVATIVES AS POTENTIAL FATTY ACID AMIDE HYDROLASE (FAAH) INHIBITORS

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Fatty acid amid hydrolase (FAAH), a member of endocannabinoid system (ECS), is an enzyme responsible of hydrolyzing fatty acid amides. The dysfunction of the regulation of ECS causes disorders such as immunogenic disorders, epilepsy, Parkinson and Alzheimer's diseases. Inhibition of FAAH, results in the elevation of N-arachidonylethanol amine (AEA), which is a partial agonist of CB1, thus causing a neuroprotective effect [1]. In the recent literature, urea, carbamate and amide bearing aryl/heteroaryl groups have been widely studied as FAAH inhibitors [2]. In this presentation, we prepared a series of piperazinyl urea bearing thiadiazol core that target FAAH inhibition (Figure 1). Our first preliminary results have revealed that benzyl-substituted piperazine derivatives more preferably inhibited FAAH activity as compared to phenyl-substituted piperazine derivatives based on the results of a fluorometric-based enzyme assay, which was used for the evaluation of biological activities. The most potent derivative in the series inhibited FAAH with an IC_{50} of 0.14 µM. Herein, we will share and discuss our synthetic approach, biological data and SAR results.

This research was supported by Gazi University Scientific Research Projects Coordination Unit, Project Number: BAP 02/2020-24

Keywords

Urea, Piperazine, FAAH, Endocannabinoid

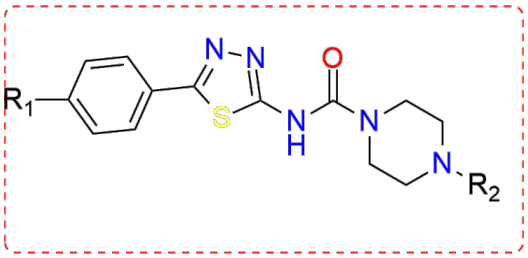

Figure 1

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P61

SYNTHESIS, CHARACTERIZATION, CRYSTAL STRUCTURE AND DFT ANALYSIS OF BENZYL 4-[2-FLUORO-4-(TRIFLUOROMETHYL)PHENYL]-2,6,6-TRIMETHYL-1,4,5,6,7,8-HEXAHYDROQUINOLINE-3-CARBOXYLATE

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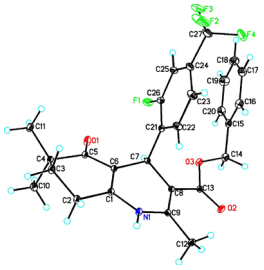
Inflammation is the underlying cause of many diseases such as cancer, cardiovascular and autoimmune diseases. Recently 1,4-dihydropyridine (1,4-DHP) compounds and their condensed analogs such as hexahydroquinoline (HHQ) have been found effective to reduce inflammation which contributes to development of mentioned diseases. Based on these data we synthesized annulated 1,4-DHP molecule and proved the structure of this molecule by spectral methods. The biological activity of the synthesized compound tested in vitro. The compound crystallizes in the triclinic space group, P`1, with the following unit-cell dimensions a = 7.0889(11) Å, b = 12.4861(18) Å, c = 14.338(2) Å, α = 66.899(4)°, β = 89.025(4)°, γ = 85.101(4)° and V = 1162.9(3) Å^3, Z=2. The data collection for, ($C_{27}H_{25}F_4NO_3$), was performed with an Xcalibur, Ruby, Gemini (Diffractometer) at low temperature of 100(2) K. The structures were solved by direct method using the program SHELXT, and refined by full-matrix least-square techniques against F^2 using SHELXL2016/6. The final refinement with 323 parameters converged at R_1 = 0.0426 and Goodness of fit was 1.033. The largest and the lowest peak for electron density were 0.643 and -0.581 eÅ^{-3}, respectively. In the crystal structure stabilized by the intra- and intermolecular N—H···O, C—H···O and C—H···F interactions. The molecule has been optimized by DFT method. QTAIM, molecular surface, partial charge analysis have been performed based on the optimized molecule. Bonding properties and intramolecular nonbonding interactions have been anaylzed by using quantities obtained from QTAIM analysis. The extent of intermolecular interactions and mass density have been predicted based on the molecular surface analysis.

Keywords

1,4-DHP, Hexahydroquinoline, Inflammation, X-ray structural analysis, Spectra, DFT, QTAIM



Ortep-3 diagram of the title compound.

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P62

THE ANTIMICROBIAL EFFECT OF R-LIMONENE NANOEMULSION ON ENTEROCOCCUS FAECALIS

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R-limonene is a terpene derivative, which has antimicrobial activity [1]. The aim of this study is to evaluate the antibacterial efficacy of R-limonene nanoemulsions against *Enterococcus faecalis*, which is highly resistant to repetitive applications of calcium hydroxide used in the chemomechanical preparation of root canal treatment [2]. Oil/water R-limonene nanoemulsions were prepared by phase inversion method [3]. Formulation factors are listed in the table below (Table 1). The particle size (PS), polydispersity index (PDI) and zeta potential (ZP) values were evaluated and were given in the table below (Table 2). It was observed that the ZP values decreased as the Tween 80 ratio increased. Therefore, F3, F4 and F6 formulations were eliminated. F1, F2 and F5 formulations were subjected to a one-week stability test at 4, 25 and 40 °C and it was observed that the ZP of the F1 formulation decreased at all temperatures. There were not significant changes in the F2 and F5 formulations. The MIC values of F2 and F5 formulations were determined compared to pure R-limonene on *Enterococcus faecalis*. The MIC values of pure R limonene, F2 and F5 were 210.3 mg/mL, 49.80 mg/mL and 48.82 mg/mL, respectively. These results show that emulsion formulations of R-limonene are approximately 4.5 times more effective than pure R-limonene.

Acknowledgments: This study was supported by the Gazi University, BAP Council (Project Number: 03/2020-09). A. YILMAZ and I.D. SEKER were supported by scholarships from the CoHE 100/2000 PhD Scholarship Program. A. YILMAZ was supported by TÜBİTAK 2211/A Domestic PhD Scholarship Program.

Keywords

Nanoemulsions, R-limonene, Enterococcus faecalis

Table 1

	Water phase	Oil phase	
	Sterile distilled water / Propylene glycol (w/w)	R-limonene (w/w)	Tween 80 (w/w)
F1	2:1	10 %	5 %
F2	2:1	10 %	7.5 %
F3	2:1	10 %	10 %
F4	2:1	10 %	15 %
F5	2:1	20 %	7.5 %
F6	2:1	20 %	10 %

Table 2

	PS (nm)	PDI	ZP (mV)
F1	166 ± 1	0,169 ± 0,03	28,7 ± 0,9
F2	146 ± 3	0,213 ± 0,02	28,7 ± 1,6
F3	133 ± 4	0,213 ± 0,02	26,5 ± 0,8
F4	130 ± 1	0,336 ± 0,05	25,2 ± 1,7
F5	182 ± 1	0,244 ± 0,05	28,0 ± 1,7
F6	155 ± 1	0,182 ± 0,02	26,6 ± 0,9

Table 1 and Table 2

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P63

EVALUATION OF THE EFFECT OF INFILL DENSITY AND TABLET GEOMETRY ON DISINTEGRATION OF 3D PRINTED TABLETS

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FDM (Fused Deposition Modeling) is the most recently researched 3DP method for solid dosage forms. It has a huge potential in producing tablets with different release properties by changing the formulation components or printing parameters[1-3]. This study aims to investigate the effect of infill density and tablet geometry on the disintegration of the fluticasone propionate (FLT) loaded 3D printed sustained-release tablets containing ethyl cellulose (EC) as the main polymer. FLT-loaded filaments were extruded using a single-screw extruder (Noztek-Pro, UK). Mechanical and morphological properties of filaments were determined visually and manually. The drug loading amount were calculated with HPLC. Structural integrity and homogeneity were demonstrated by SEM. Filaments were printed to form tablets with two different infill percentages (25%, 50%) and geometries (round-shaped, donut-shaped) using an FDM-3D Printer (Craftboat 3, Hungary). Tablet quality tests were performed in the round-shaped with %50 infill density. 3D Printed tablets were compared with the disintegration times in pH 6.8 (n=3, Pharmatest, Germany). Neither the round-shaped nor donut-shaped tablets with 50% infill percentage did not completely disintegrate in 24 hours. The round-shaped tablets with a 25% infill percentage started to delaminate after six hours and largely disintegrated in 24 hours. Consequently, the donut-shaped tablets having hollows in the middle did not accelerate the disintegration, while the infill density was significantly affected the disintegration rate. Accordingly, 50% infill density was not found appropriate for a sustained-release since not disintegrating in a daylong, while the 25% infill may be suitable. The results must be supported by dissolution tests.

Keywords

Ethyl cellulose, Fluticasone propionate, Fused deposition modeling, 3D printing, Sustained release

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OPTIMIZATION AND VALIDATION OF SILK FIBROIN PRODUCTION PROCESS

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Silk fibroin is a natural, protein-based biopolymer produced by silkworm (Bombyx mori). Silk fibroin is obtained with various processes and the basis of these processes is the removing of sericin in the cocoon, and then obtaining silk fibroin using different agents, such as LiBr and Ajisawa's reagent (Figure 1). The aim of this study was to evaluate the various process steps for optimization of silk fibroin production and validatation of these processes. Distilled water was boiled and sodium carbonate was added to the boiling water. Silkworm cocoons were weighed, cut into small pieces, added to the boiling water and stirred for 30 minutes. It was mixed with distilled water for 2 hours, and then kept in the fume hood overnight to dry. This step was kept the same in all the process. Next, dried fibroin was completely dissolved in LiBr solution or Ajisawa's reagent, and dialyzed against distilled water with a 12,000 or 3,500 Da dialysis membrane for 24, 48 and 72 hours. After dialysis, the solution was centrifuged or not centrifuged, and the obtained materials were lyophilized for 48 hours [1, 2]. According to the modifications on silk fibroin production methods, it was concluded that the cut-off value of dialysis membrane used for the dialysis process, dialysis time, centrifugation process and extraction agent type (LiBr/Ajisawa) were effective factors on the impurity and the obtained form of silk fibroin.

Keywords

Silk fibroin, Bombyx mori cocoons, Production process, Optimization

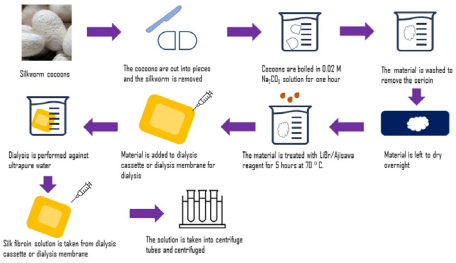

Figure 1. Production process of silk fibroin from Bombyx mori cocoons

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P65

NASAL PERMEABILITY STUDIES OF RASAGILINE MESYLATE LOADED SOLID LIPID NANOPARTICLES IN A THERMOREVERSIBLE MUCOADHESIVE GEL

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Parkinson's disease is a neurodegenerative disorder, characterized by contraction, rigidity, tremor [1]. Rasagiline mesylate (RM) is an irreversible MAO-B inhibitor used in the treatment of Parkinson's disease. The brain is separated from the bloodstream by a unique barrier called the blood-brain barrier (BBB) [2]. BBB prevents the passage of many molecules to the brain. Thanks to the nasal administration, drug molecules can be passed from olfactory region to the brain [3]. However, the residence time of the drug molecules in the nose is the biggest difficulty in reaching the desired area. One of the approaches to increase the residence time in the mucosa is the use of thermoreversible and mucoadhesive gels [4]. Solid lipid nanoparticles (SLN) and their lipid structures provide a great advantage in targeting drug molecules to the brain [5]. The aim of this study was to determine permeability properties of RM-SLN-GEL through the nasal mucosa. SLNs were prepared with Gelucire 50/13, Labrasol, Cremophor RH40. Microemulsion method was used. Thermoreversible mucoadhesive gels (GEL) were prepared with Poloxamer 407 and HPMC E5. Optimal formulation (RM-SLN-GEL) had a suitable gelation temperature at 31°C ± 0,2°C. With the Franz diffusion cells, permeability (P) and flux (J) values of the formulations (RM loaded GEL, RM loaded SLN, RM-SLN-GEL) were calculated. Permeability and flux values of RM-SLN-GEL were $93{,}6 \times 10^{-3}$ cm/h and 1,872 mg/cm^2/h respectively. Consequently, permeability and flux values of RM in RM-SLN-GEL through nasal mucosa is better. However, results should be supported by in-vivo experiments.

Keywords

Rasagiline mesylate, Solid lipid nanoparticle, Thermosensitive mucoadhesive gel, Ex-vivo permeation

References

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P66

OPTIMIZING CRYOPROTECTANT TYPE AND RATIO FOR LYOPHILIZATION OF NANOSUSPENSIONS

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Nanosuspensions are defined as colloidal dispersions of nano-sized pure drug particles prepared using an appropriate stabilizer[1]. Lyophilization is one of the methods to improve the physical and chemical stability of nanosuspensions[2]. The aim of this study was to determine the appropriate cryoprotectant type and ratio to prepare lyophilized Lidocaine (LID) nanosuspensions. To prepare LID-nanosuspensions, firstly drug and 0.5% poloxamer solution were stirred with Ultraturrax at 15.000rpm-10min. It was then prepared by wet milling using 0.5 bead size for 2 hours milling time at 300rpm milling rate. Freshly nanosuspensions were lyophilized with different types (trehalose, mannitol, glucose) and different concentrations (0%;2.5%;5%;7.5%;10%) of cryoprotective agent using with experimental design (DoE). Briefly, 1.5ml of nanosuspensions were taken and cryoprotectant agent was added, frozen at -80°C, followed by drying at -55°C 0.021 mbar for 48h[1]. The lyophilized powders were again dispersed in distilled water and the particle size(PS), polydispersity index(PDI), zeta potential(ZP) values of nanosuspension were measured using a Malvern Zeta Sizer. In addition, FTIR (Perkin-Elmer-Spectrum400 FT-IR) and DSC (Shimadzu-DSC60) studies were carried out on the optimum lyophilized nanosuspensions. The most suitable cryoprotectant agent was determined as trehalose with a concentration of 2.5%. In this way, the PS, PDI and ZP were found as 176.83±0.85nm, 0.225±0.004 and -30.3±0.7mV, respectively. In the FTIR and DSC studies conducted, no incompatibility was detected between the drug and excipients. It was concluded that the effect of cryoprotectant type and concentration in the lyophilization of nanosuspensions is important and can be determined more practically by designing an experiment.

Keywords

Nanosuspension, Lyophilization, Lidocaine, Cryoprotectant, Experimental design

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P67

DESIGN AND IN VITRO CHARACTERIZATION OF IN SITU FORMING CONTROLLED RELEASE IMPLANTS OF A NARCOTIC ANTAGONIST DRUG

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Opioid and alcohol addiction are one of the major health problems. Opioids account for 76% of deaths involving drug use disorders, while alcohol is responsible for about 3.6% of global deaths. Opioid antagonists block the effects of psychoactive substances and alcohol acting on μ, κ, and δ opioid receptor sites by binding competitively to these receptors. Because of the extensive first-pass metabolism, the bioavailability of this group of active pharmaceutical substances is low and fluctuations in plasma concentrations occur when used orally. In addition, oral tablets have been associated with high rates of early withdrawal from treatment. For all these reasons, it would be advantageous to develop a dosage form in which the liver is bypassed, a constant plasma concentration can be achieved, and patients are not burdened with taking medication. In this study, in situ forming gel systems containing XTZ-21 have been investigated to meet all the requirements based on a gelling mechanism by solvent exchange. Resomer R 203 S as a biodegradable polymer and dimethyl sulfoxide, N-methyl pyrrolidone, poly(ethylene glycol) dimethyl ether (M_n = 250), poly(ethylene glycol) 400, benzyl alcohol, and ethyl heptanoate as solvents, were used for the preparation of formulations. The optimized formulation was determined by low burst drug release and controlled release of the drug for one month.

Keywords

Addiction, Implant, In situ gel, Solvent exchange, Controlled release

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DEVELOPMENT, CHARACTERIZATION AND IN VITRO EVALUATION OF NANOEMULSION CONTAINING MEGESTROL ACETATE

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Megestrol acetate (MGA) is a synthetic derivative of progesterone. It is widely used for endometriosis, menstrual disorders, contraception and hormone replacement therapy in post-menopausal women. In addition, it is used as an antineoplastic agent to treat advanced breast cancer and appetite enhancer in patients with AIDS [1, 2]. For appetite stimulation in patients with HIV/AIDS, cancer, and other chronic diseases, the recommended dose of MGA is 800 mg per day and the high dose of MGA could be a problematic issue [3]. Thus, new platform of MGA is essential to enhance the bioavailability and decrease the dosing size. In recent years, nanoemulsions (NEs) have drawn great attention, as it can improve the oral absorption and reduces the food-effect. The aim of this study was to develop, characterize and evaluate MGA-loaded NEs in order to determine critical formulation parameters. In this research, the effect of ethanol volume, medium chain triglyceride (MCT) amount , lecithin-Tween 80 ratio and MGA amount on NEs characteristic properties has been investigated. The higher amount of ethanol and MCT increase the droplet size. Increasing the amount of lecithin from 0 up to 400 mg led to a decrease in mean droplet size from 308.1 nm to 176.3 nm. Based on the optimization of formulation, the average droplet size and zeta potential of MGA-loaded NEs were found to be 166.9 ± 3.0 nm and -12.2 ± 1.1 mV, respectively.

Keywords

Megestrol acetate, Nanoemulsion, Characterization, Stability

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P69

STUDIES ON FORMULATION OPTIMISATION OF HYALURONIC ACID COATED CHITOSAN NANOPARTICLES LOADED WITH HYDROCORTISONE ACETATE

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Rheumatoid arthritis (RA) is the most common chronic, inflammatory, autoimmune disease of the joints affecting 0.5–1.0% of the general population worldwide. RA patients are compelled to use glucocorticoids during certain periods of their life time for relieving persistent inflammation resulting in joint swelling, deformity and degradation of daily functional capacity. Despite their benefits, glucocorticoids lead to several side effects at high doses which limits their role in treatment. It reported that activated macrophages which overexpress CD44 receptors is crucial in RA pathophysiology as a potential target site for RA treatment. In the past decade, nanoparticles as drug carriers gained significant attention for effective RA treatment to change the pharmacokinetics of traditional anti-arthritis drugs and enhance their accumulation in joint tissues and hence to reduce the side effects [1]. In this study, hydrocortisone acetate (HCA) was chosen as a model glucocorticoid drug for development of chitosan (CS) nanoparticles by ionic gelation technique using TPP as an anionic linker [2,3]. In the second step, CS nanoparticles loaded with HCA were coated with hyaluronic acid (HA), which is a natural ligand of CD44 receptors. For the optimization of the preparing process of nanoparticles, pH of chitosan solution, CS/TPP ratio, stirring rate, stirring time and CS/HA ratio were evaluated by measuring particle size, polidispersity index, zeta potential and encapsulation efficiency. CS solution pH, CS/TPP ratio, stirring rate, stirring time and CS/HA ratio was determined as 3, 2:1, 1000 rpm, 35 minutes, 0.5:1 ratio was chosen as the optimum conditions.

Keywords

Chitosan nanoparticles, Ionic gelation, Glucocorticoids, Rheumatoid arthritis

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P70

VALIDATION OF AN HPLC METHOD FOR THE DETERMINATION OF TALAZOPARIB FROM NANOPARTICLE FORMULATIONS

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Talazoparib, which is a PARP inhibitor, is a molecule that is frequently used in cancer treatment [1]. In this study, it was aimed to develop and validate an HPLC method for the determination of talazoparib poly(lactic-co-glycolic acid) (PLGA) nanoparticle formulations. A method was developed for the validation of talazoparib's assay and the chromatographic conditions were optimized. Agilent 1200 Separations Module equipped with DAD detector (227 nm) and C18 column were used. The mobile phase consists of acetonitrile and pH 6.25 phosphate buffer and the flow rate was 1 mL/min. A mixture of methanol and acetonitrile was used as solvent for talazoparib. Method was validated with triple replicates of standard solution of talazoparib for each validation parameter. In order to evaluate the suitability of the developed HPLC method, the parameters specified in the ICH Q2A guideline were tested [2]. For this purpose, parameters of selectivity, linearity, accuracy, and precision were assessed. The retention time for talazoparib standard solution was 6.888 minutes. For linearity, R^2=0.9999 was calculated from the calibration curve with a range of 0.1-10 µg.mL^{-1}. The average recovery was 100.65±0.48%. The developed HPLC method was successfully validated to quantitate talazoparib in PLGA nanoparticles.

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Keywords

Nanoparticle, Talazoparib, Validation, Cancer therapy, HPLC

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P71

DEVELOPMENT AND CHARACTERIZATION OF ELECTROSPUN NANOFIBERS CONTAINING RUTIN AND COPPER NANOPARTICLES

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Rutin is a flavonoid derived from the *Ruta graveolens* plant [1]. Copper, an important mineral, is known to have antimicrobial properties. In this study, it was aimed to prepare and characterize rutin containing nanofibers and both rutin and copper nanoparticles containing nanofibers to investigate for use in wound healing. The cytotoxic effects of the prepared nanofibers were investigated by MTT experiments on L-929 mouse fibroblast cells [2]. Polymer solutions were prepared with 7.5% of polyvinylpyrrolidone (PVP) in 20 ml of ethanol and five different nanofiber formulations were prepared with rutin ratios of 0.25, 0.5, 0.75, 1 and 1.5%. The characterization studies of the prepared polymer solutions and mechanical properties of the nanofibers were investigated [3]. According to the results, copper nanoparticles were incorporated to nanofibers containing 1% rutin. Copper nanoparticles were used at 0.5 and 1% concentrations. In addition, in vitro release studies were performed on Franz diffusion cells. As a results of the characterization studies of polymer solution, they were found to be suitable for the electrospinning process. According to the SEM images, it was observed that the nanofibers had a regular nanofiber structure. According to the results of the cytotoxicity study, rutin-copper loaded nanofiber should be considered as a safe drug delivery system. In this study, electrospun nanofibers containing only rutin and both rutin and copper nanoparticles were successfully obtained. The results showed that rutin and copper nanoparticle-containing nanofibers may have potential for use as antimicrobial wound dressings.

Keywords

Nanofiber, Rutin, Copper nanoparticle

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DEVELOPMENT AND CHARACTERIZATION OF VORICONAZOLE LOADED ORGANOGEL FORMULATIONS FOR VAGINAL DELIVERY

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Voriconazole (VRC) is an antifungal agent that is poorly soluble in water and has low stability in aqueous solutions, used in the treatment of vaginal candidiasis[1]. Vaginal drug delivery provides advantages such as high drug concentration in the vagina, rich vascularity, high permeability, and side effects [2]. The aim of this study is to develop and evaluate organogel formulations for vaginal administration of VRC. VRC was dissolved in different oils for the preparation of the oil phase. To prepare the water phase, HPMC(2%) was mixed in water at 800 rpm for an hour. Formulations were prepared in ratio 1:4 as the oil phase/water phase. For oleic acid, lavender, and clove essential oils, the blank organogels were codded as O1, O2, and O3, and VRC-loaded organogels were coded as O4, O5, and O6, respectively. Viscosity of organogel was characterized by viscometer. Mechanical properties of formulations were carried out with Texture Analyzer. The in-vitro permeation of organogel was studied using Franz diffusion cell. Viscosity and mechanical properties of formulations are shown in Table 1. VRC in-vitro permeation of O4, O5, and O6 from dialysis membrane was 38.6±2.8%, 82.7±2.7%, and 77.7±12.9%, respectively. While a decrease was observed in the mechanical and viscosity values of the oleic acid formulation with VRC loading, an increase was observed in the clove essential oil formulation. VRC-loaded organogels have potential use for the vaginal treatment of candida infections. According to viscosity, mechanical, and in vitro permeation studies of organogels, O5 formulation was found suitable for vaginal application compared to other formulations.

Keywords

Organogel, Vaginal drug delivery, Voriconazole

Properties		Codes O1	O2	O3	O4	O5	O6
Mechanical Properties	Hardness(N) ± SD	121.71±2.45	83.69±4.79	56.23±2.68	91.62±5.90	88.21±0.89	89.55±4.85
	Adhesiveness (g.sec) ± SD	-162.1±1.7	-120.3±3.4	-68.03±2.82	-121.75± 2.96	-108.40±10.18	-117.67±8.07
	Cohesiveness ± SD	1.49±0.02	-0.24±0.39	0.56±0.52	0.93±0.66	0.84±0.58	0.61±0.80
	Elasticity ± SD	0.77±0.01	0.64±0.02	0.60±0.02	0.66±0.03	0.75±0.05	0.75±0.05
Viscosity (%)		15.3±19.9	6.1±11.5	1.0±2.8	14.3±2.3	10.2±1.2	1.4±4.9

Table 1. The mechanical properties of VRC loaded organogel formulations

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INVESTIGATION OF VARIOUS CRITICAL PROCESS AND FORMULATION PARAMETERS OF NANOSUSPENSIONS INCLUDING INDOMETHACIN

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Nanosuspension are nano-sized (<1000 nm) colloidal dispersions of pure active substance particles stabilized with suitable surfactants and/or polymers. Nanosuspensions can be successfully prepared using a variety of techniques. The aim of this study is to evaluate the preparation process of nanosuspensions to identify and predict various critical processes and formulation parameters. In the study, nanosuspensions were prepared with the bottom-up approach. The solvent/anti-solvent method was chosen among various adaptations of this approach and nanosuspensions were prepared using the bath sonicator [1,2]. Particle size and polydispersity index were evaluated by changing surfactant type and ratio, solvent and antisolvent ratio. Indomethacin (IND) was chosen as a model drug because it is known to be a Class II drug with poor solubility and high permeability and soluble in organic solvents such as ethanol and DMSO. Nanosuspensions were prepared to increase the solubility of IND in water and reduce the particle size and side effect profile. Both molecular weight and concentration of polyvinyl alcohol (PVA) were found to affect the particle size and polydispersity of the nanosuspensions ($p<0.05$). The optimum parameters were found to be 0.2% PVA (mol.wt. 31.000) with a solvent-antisolvent ratio of 3:50 (particle size: 301.5 ± 31.1 nm, polydispersity index: 0.159 ± 0.035). As a result, nanosuspension formulations were successfully prepared using the solvent/anti-solvent method. Therefore, it can be concluded that the type or concentration of stabilizer is important to obtain stable nanosuspensions.

Keywords

Nanosuspension, Indomethacin, Bath sonicator

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VITAMIN D-LOADED POLY(L-LACTIC ACID) NANOPARTICULAR IMPLANTS IMPROVES OSSEOINTEGRATION

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Dental implants are widely used as a treatment choice for edentulous patients. To ensure long-term use of the implants, a connection between the bone and the implant surface, osseointegration, is expected in the absence of fibrous tissue formation. With the deterioration of osseointegration, early implant losses are observed, and the failure of this procedure depends not only on the material used or the surgical protocol, but also on the quality and amount of bone [1]. Vitamin D is known as playing an important role in homeostasis of calcium and phosphorus and its deficiency has negative effects on bone regeneration, and osseointegration of implants [2]. Polylactic acid (PLA) is a non-toxic biodegradable polymer with high mechanical properties. It is widely used especially in bone implants [3]. In our study, vitamin D-loaded PLA nanoparticles were prepared and their physicochemical properties such as production yield, particle size, size distribution (PDI), surface charge, scanning electron microscopy, and in vitro drug release characteristics were evaluated. Nanoparticles with the particle size of 146.8 ± 0.4 nm, PDI value of 0.103 ± 0.005, surface charge of -31.8 ± 2.5 mV, production yield of 80.30 ± 2.14% and encapsulation efficiency of 73.0 ± 2.2 % were obtained. In vitro drug release study showed that more than 50% of drug was released at the end of 7th week. Finally, bone implant contact and new bone formation value were evaluated in in vivo experiments. The prepared formulation can be accepted as promising way of improving osseointegration in patients.

Keywords

Vitamin D, Poly lactic acid, Nanoparticle, Osseointegration, Implant,

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IN VITRO RELEASE AND EX VIVO PENETRATION STUDIES OF BIGEL SYSTEMS CONTAINING CICLOPIROX

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Onychomycosis is an infection of dermatophytes, non-dermatophytic molds and yeasts. It causes discoloration, onycholysis, and thickening of nail plate [1]. Onychomycosis is the most common nail disease, accounting for approximately 50% of all nail diseases [2]. Treatment generally are oral and topical antifungal. Oral treatment has many side effects, especially hepatotoxicity, drug interactions. Topical treatment has no side effects. But penetrate to the infected area is limited due to hard keratin structure of the nail. In addition, topical formulations are easily removed from nail plate. Many techniques have been developed to facilitate topical application to nail [3]. Bigels with outer phase water and urea to increase penetration, inner phase oil and containing ciclopirox are promising for topical treatment. In the optimum formulations selected in previous studies, release from dialysis membrane, Strat-M membrane, and penetration from rat skin were performed. In addition, amount of active substance that penetrated through skin and remained on the skin after the study was completed was determined by HPLC. The dialysis membrane release results are 58.7, 36.01, 60.65 ug/ml. When rat skin and Strat-M membrane were used, ciclopirox and urea could not be determined in the receptor phase. The results were found to be similar to other studies. The maximum amount of ciclopirox remaining in the skin is 317.76±37.21 ug/ml. The amount of ciclopirox was higher than the minimum inhibition value. It shows that the bigel system can be used successfully in the treatment of onychomycosis.

Keywords

Onychomycosis, Topical treatment,Bigels, Ciclopirox

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P76

PREPARATION, OPTIMIZATION, AND IN-VITRO EVALUATION OF NARINGENIN LOADED MICROEMULSION FORMULATIONS FOR ANTI-AGING PURPOSES

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Flavanones such as Naringenin are known as antioxidant, anti-inflammatory agents due to their free radical scavenging properties [1]. Topical *in vivo* applications of rose oil improve skin barrier function, support keratinocyte differentiation, and have antioxidant effects [2]. Microemulsions are isotropic, thermodynamically stable, transparent dispersions of oil and water, surfactant and a co-surfactant [3]. The aim of the current study was to prepare and evaluate the potential use of naringenin and rose oil loaded microemulsion formulations for anti-aging purposes. The Pseudo-ternary phase diagrams were constructed at a specific surfactant/cosurfactant weight ratio of oleic acid as oil phase, Tween 80, Cremophor RH40 and Labrasol, Transcutol as surfactants, ethanol, and propylene glycol as co-surfactants and rose water as aqueous phase. 1% rose oil and 5%(w/w) naringenin were added to ideal formulations and when stabilization was completed, the mixtures were evaluated by visual characterization. The physicochemical properties of microemulsions such as droplet size, polydispersity index (PDI), zeta potential, conductivity, pH, viscosity, refractive index, and turbidity were measured. In addition, mechanical properties such as hardness, compressibility, adhesiveness, and cohesiveness were measured. Furthermore, spreadability and bioadhesion studies were performed. The results of the measurements of droplet size, PDI, zeta potential, conductivity, pH, viscosity, refractive index and turbidity were found in between 0.9147±0.0316 and 101.500±2.576 nm, 0.271±0.057 and 0.449±0.012, -0.0361±0.0001 and -0.0990±0.01100 mV, 0.0257±0.00652 and 0.0688±0.00210 mS/cm, 5.080±0.010 and 5.527±0.006, 163.333±5.773 and 7893.333±20.816 cP, 1.424±0.0001 and 1.438±0.0001, 5.723±0.068 and >1100 ntu, respectively. The results of the studies showed that prepared formulations were promising for further anti-aging applications.

Keywords

Naringenin, Microemulsion, Anti-aging, Topical, Flavanones

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DEVELOPMENT AND OPTIMIZATION OF ELECTROSPUN PVA NANOFIBERS FOR VAGINAL DRUG DELIVERY USING DESIGN OF EXPERIMENT METHOD

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Polyvinyl alcohol (PVA) is widely used polymer in the pharmaceutical field with its hydrophilic, biodegradable, non-toxicity, mucoadhesive, and easy process properties [1]. Nanofibers provide many advantages for vaginal application, such as production in desired geometries, softness, flexibility and less leakage [2]. The aim of this study was to develop PVA nanofiber formulations using an experimental design approach for vaginal applications. PVA was dissolved in distilled water (DW) at 90°C to prepare polymer solutions, then N, N-Dimethylformamide (DMF) or ethanol was added. The surface tension, viscosity, and conductivity of the polymer solutions were evaluated. For the production of nanofibers via electrospinning method, different parameters were selected as 7.5 and 15% PVA concentration, 100 and 1000 rpm rotating speed, and two types of solvent system (DMF:DW and Ethanol:DW). Mechanical, mucoadhesion and wettability properties of nanofibers were measured. Viscosity and surface tension values were increased with increasing polymer concentration. The contact angles were found to be 0° in all formulations. Mucoadhesion, tensile strength, and elongation at break values increased with increasing polymer concentration. Differences in mechanical and mucoadhesive properties were observed, since the solvent system and rotational speed may affect the morphological structure of the fibers. P6 formulation was found to be more suitable compared to other formulations with its mechanical and mucoadhesive properties (Table 1). It was concluded that in the production of PVA nanofibers, the rotating speed of the collector, the polymer concentration, the solvent system directly affect the mechanical and mucoadhesive properties of the nanofibers.

Keywords

Polyvinyl alcohol, Vaginal drug delivery, Nanofiber, Electrospinning

Formulation Code	Content of Formulation			Characterization of Nanofiber Formulations		
	Polymer Concentration (%)	Solvent System	Rotating Speed (rpm)	Tensile Strength (MPa)	Elongation at break (%)	Work of mucoadhesion (mJ/cm²)
P1	7.5	DW:Ethanol	100	1.66±0.04	56.2±5.2	0.014±0.010
P2	7.5	DW:DMF	100	1.56±0.07	26.9±8.0	0.037±0.009
P3	7.5	DW:Ethanol	1000	1.40±0.02	96.2±21.5	0.037±0.006
P4	15	DW:DMF	1000	3.92±0.38	94.8±2.7	0.029±0.010
P5	15	DW:Ethanol	1000	3.36±0.18	65.7±19.3	0.054±0.016
P6	15	DW:DMF	100	3.47±0.40	125±9	0.086±0.003
P7	7.5	DW:DMF	1000	0.20±0.02	8.12±4.41	0.052±0.019
P8	15	DW:Ethanol	100	3.80±0.16	103±13	0.027±0.002

Table 1. Mucoadhesive and mechanical properties of PVA nanofiber formulations

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DEVELOPMENT OF CONTROLLED RELEASED QUERCETIN MICROEMULSION BASED GEL SYSTEM FOR TOPICAL APPLICATION: AN IN VITRO EVALUATION

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Naturally occurring compounds, especially Quercetin flavonoids, gains considerable attention in skin protection due to their anti-oxidant activity. But the poor solubility of quercetin is the main challenge that restricts its applications [1] The aim of this study was to develop a new microemulsion based gel formulation for topical application of quercetin. Microemulsion based gel systems has several advantages during application such as consistency, easily spreadable-removable, water soluble, and emollient [2]. In order to develop a convenient microemulsion system, the pseudo-ternary phase diagrams of microemulsion systems were constructed at different surfactant/co-surfactant ratios using; Kolliphor EL as surfactant, Transcutol® P as a co-surfactant and oleic acid as an oil phase. Some physicochemical properties such as droplet size, polydispersity index, electrical conductivity, pH and viscosity of the microemulsion systems were measured. Microemulsions were dispersed in carbopol gel 1:1 (w/w) for aplication and to obtain a controlled release profile for quercetin. After dispersion in the gel, physicochemical properties were evaluated. Solubility studies performed to determine suitable dissolution media and maintaining sink condition during release studies. According to results release studies were conducted at pH 5.5 Phosphate Buffer Saline : Ethanol (60:40) mixture. The results obtained from release studies, microemulsion based gel formulation showed controlled release while there was an increase in the cumulative amount of quercetin, compared to microemulsion formulation.

Keywords

Quercetin, Microemulsion, Topical delivery

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PREPARATION OF CARBAMAZEPINE SOLID DISPERSIONS AND DETERMINATION OF SOLUBILITY

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Carbamazepine (CBZ) is an anti-epileptic drug with oral bioavailability problems due to its low aqueous solubility and slow dissolution rate [1]. The aim of this study was to prepare CBZ solid dispersions using different carriers in different ratios to improve its low aqueous solubility. CBZ solid dispersions were prepared by solvent-evaporation method. Polyethylene glycol 4000 (PEG 4000), polyethylene glycol 6000 (PEG 6000), SoluPlus®, polyvinylpyrrolidone K30 (PVP K30) and, poloxamer 188 were used as carriers at different ratios (1%, 2%, 4%). Shake-flask solubility study (37±1°C, 80 rpm, 24 h) was conducted according to the World Health Organization (WHO) guideline [2]. Statistical analysis of solubility data was performed using two way ANOVA followed by post-hoc Tukey's multiple-comparisons test. Aqueous solubility of CBZ solid dispersions (222.1-355.4 µg /mL) was higher than CBZ (218.1 µg /mL). The highest solubility was achieved in the presence of 1% SoluPlus®. In solid dispersions prepared with PEG 4000 and SoluPlus®, the aquoeus solubility decreased as the percentage of carrier increased, while solubility increased in solid dispersions prepared with PEG 6000, PVP K30 and, poloxamer 188. A statistically significant difference was found between the solubility results obtained for all carriers and carrier ratios compare to the raw drug. The solubility of CBZ was increased significantly by using different carriers in the formulation of solid dispersions.

Keywords

Carbamazepine, Solid dispersions, Solubility

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P80

DEVELOPMENT AND CHARACTERIZATION STUDIES OF HYDROCORTISONE LOADED EUDRAGIT-BASED COLON TARGETED NANOFIBERS

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Nanofibers are suitable drug delivery systems for colon targeting due to the large surface area, superior mechanical properties and one-step production techniques [1]. Eudragits are polymer which provide pH-dependent drug release. Hydrocortisone (HC) is an immunosuppressant and anti-inflammatory drug used in the treatment of inflammatory bowel disease [2]. The aim of the our study was developed hydrocortisone loaded eudragit derivatives based nanofibers for colon targeting. All polymer solutions were prepared at room temperature using ethanol and N,N dimethylformamide (7:3) and were stirred. Contents of formulations are shown in Table 1. Viscosity, surface tension and conductivity properties of polymer solutions were determined. Electrospun nanofibers were examined in terms of mechanical properties, contact angles and mucoadhesion properties. Mucoadhesion studies were carried out using cow colon tissue. The conductivity and viscosity values decreased with the addition of HC. Addition of HC in nanofiber formulations showed a decrease in contact angle values. Differences were observed in the mechanical and mucoadhesive properties of nanofiber formulations with the addition of HC (Table 1). The mechanical properties of the M and L formulations are suitable for colon targeting, and L formulation showed superior mucoadhesive properties. Eudragit-based nanofibers, especially “L” formulations, demonstrated suitable mechanical and mucoadhesive properties for colon targeting in the treatment of intestinal diseases.

Keywords

Hydrocortisone, Nanofibers, Colon targeting

Formulation Code	Content of Formulations			Characterization of Polymer Solutions			Characterization of Nanofiber Formulations			
	HC (%)	Eudragit S100 (%)	Eudragit L-100-55 (%)	Viscosity (cPa)	Surface Tension (mN.m^{-1})	Conductivity (µS.cm^{-1})	Tensile Strength (mPa)	Elongation at break (%)	Contact Angle (°)	Work of mucoadhesion (mJ/cm^2)
S+	1	15		3418±205	27,56±0,08	36,54±0,28	0,718±0,079	27,2±1,9	95,9±2,4	0,1079±0,008
S-		15		3504±555	27,67±0,08	27,67±0,08	0,614±0,05	18,98±1,82	108,13±3,21	0,027±0,08
L+	1		15	3790±53	29,93±0,37	40,43±0,05	1,4836±0,1191	2,81±0,11	86,23±4,62	0,1017±0,0200
L-			15	2538±286	27,93±0,09	26,54±0,12	1,2±0,1	9,35±1,06	96.27±1,46	0,243±0,063
M+	1	7.5	7.5	3035±92	26,36±0,09	39,36±0,13	1,7196±0,1410	4,21±0,45	93,45±0,45	0,1368±0,0499
M-		7.5	7.5	3115±76	27,89±0,15	27,64±0,21	4,27±0,17	8,14±0,97	95,71±0,75	0,075±0,01

Table 1. Content, codes and characterization result of polymer mixtures and nanofiber formulations

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DETERMINATION OF THE EFFECTS OF DIFFERENT CARRIERS ON IN-VITRO CYTOTOXICITY OF CARBAMAZEPINE SOLID DISPERSIONS

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Carbamazepine (CBZ) is an anti-epileptic drug with different crystalline forms, all of which are responsible for its low and irregular oral bioavailability [1]. In this study, we aimed to investigate the effects of different carriers and ratios of carriers on the in-vitro cytotoxicity of CBZ solid dispersions. Polyethylene glycol 4000 (PEG 4000), polyethylene glycol 6000 (PEG 6000), SoluPlus®, polyvinylpyrrolidone K30 (PVP K30) and, poloxamer 188 were used as carriers at different ratios (1%, 2%, 4%) in CBZ solid dispersions. L929 cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) and seeded at a density of 50,000 cells / mL in a 96-well plate. Three different concentrations (0.625 , 5 and, 20 µg/mL) of CBZ and solid dispersions were applied to the cells. Cell viability was evaluated by MTT assay after 24 h incubation. The detection of cell viability of CBZ below 80% at all doses indicated that the drug was cytotoxic. Solid dispersions prepared with SoluPlus®, PVP K30 and poloxamer 188 at low doses provide a significant decrease in the cytotoxicity of the drug at high carrier ratios (2% and 4%), while only SoluPlus® provided this effect at the highest dose. It was generally found that the cytotoxicity of CBZ increased depending on the dose and solid dispersions prepared with all carriers except PEG 6000 caused a decrease in the cytotoxicity of the drug.

Keywords

Carbamazepine, Solid dispersions, Cell culture study

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ANTIMICROBIAL ACTIVITY OF DIFFERENT PARTS OF COLCHICUM SPECIOSUM STEVEN (COLCHICACEAE)

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The species of *Colchicum* L. genus (Colchicaceae) are perennial flowering plants containing amount 160 species and they grow from bulb-such as corms. The bulbs and seeds of *Colchicum* L. genus have colchicine and its derivatives and is utilised for the therapy of gout and thalassemia. *C. speciosum* is known as "Vargit, Güz Çiğdemi, Acı Çiğdem" in Turkey [1,2]. The compounds has been utilised since ancientry to decreaes urea in the blood [3]. The aim of this study to assess antimicrobial, activity of corm, leaf and flower methanol extracts of *C. speciosum. Colchicum speciosum* was collected from Erzurum and dried corms, leaves and flowers were macerated with methanol. Antimicrobial activities were evaluated by microdilution method with some modifications [4,5]. The corm and leaf extracts showed best antimicrobial activity against *C. tropicalis* ATCC 750 with MIC =160> µg/mL and the leaf extract was also found effective against *Candida krusei* ATCC 14243 (MIC= 320 µg/mL). The leaf and flower extracts showed same antimicrobial activity against *Staphylococcus aureus* ATCC 6538 (MIC =1280 µg/mL) and *Candida albicans* ATCC 10231 (MIC =640 µg/mL). All of the extracts showed same antimicrobial activity against *Escherichia coli* ATCC 8739 and *Bacillus subtilis* ATCC 19659 with MIC=2560 µg/mL. These findings should be useful in future investigations about this genus.

Keywords

Antimicrobial activity, Colchicum speciosum

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CHYMOTRYPSIN AND UREASE INHIBITORY ACTIVITIES OF SOME PLANTS USED AS FOLK MEDICINE IN DUZCE (TURKEY)

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In this research, investigation of chymotrypsin and urease inhibitory activities, along with antioxidant activity, total phenol and flavonoid content, of five species [*Mentha longifolia* (L.) L. subsp. *thyphoides* (Briq.) Harley, *Origanum onites* L., *Rubus ulmifolius* Schott, *Thymus longicaulis* C.Presl, *Trachystemon orientalis* (L.) D. Don] that used as folk medicine in Düzce were aimed [1]. For these purpose methanol and water extracts were prepared from shoot of *R. ulmifolius*, aerial parts of *M. longifolia* subsp. *thyphoides*, *O. onites*, *T. longicaulis* and *T. orientalis.* Then, their *in vitro* urease and chymotrypsin inhibitory activities were determined [2-3]. In addition, their total phenol, flavonoid contents and antioxidant activities by different methods (ABTS, CUPRAC, DPPH) were also evaluated. The methanol extracts of *O. onites* and *T. longicaulis* exhibited moderate urease inhibitory activity (34% inhibition), while the others exhibited low urease inhibitory effect. The strongest chymotrypsin inhibitory activity was observed with *R. ulmifolius* methanol extract with an IC_{50} value of 65.32 µg/ml. *M. longifolia* subsp. *thyphoides* methanol extract, *T. orientalis* and *T. longicaulis* water extracts have strong chymotrypsin inhibitory effect, as well. Generally, studied extracts showed high antioxidant activity, in accordance with their high phenol and flavonoid contents. As a result, *R. ulmifolius, M. longifolia* subsp. *thyphoides, T. orientalis* and *T. longicaulis* draw attention with their important chymotrypsin inhibitory activity. But, the urease inhibitory activity of the studied extracts was low or moderate. The results suggest further investigations into the chymotrypsin inhibitory activity of *R. ulmifolius, M. longifolia* subsp. *thyphoides, T. orientalis* and *T. longicaulis*.

Keywords

Chymotrypsin, Urease, Antioxidant, Folk medicine, Medicinal plant

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SCOPARONE BLOOD-BRAIN-BARRIER PENETRATION AND ENDOCANNABINOIDS RELATED MECHANISM UNDERLYING ITS ACTIVITY

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Coumarins, both synthetic and natural, show effects on the central nervous system (CNS) in preclinical *in vivo* experiments, suggesting their penetration to the brain. Scoparone (6,7-dimethoxycoumarin), a simple coumarin derivative, enhanced the cognitive properties and exerted anxiogenic-like effects in male Swiss mice. Here, we studied the influence of scoparone on the endocannabinoids system (ECS) which is a major modulatory system of synaptic transmission and plasticity. We evaluated the brain exposure of scoparone and its major metabolites and concomitantly assessed the impact on brain lipids related to the ECS at different doses of scoparone (12.5 mg/kg and 5 mg/kg). A quantitative LC-MS/MS method was established for scoparone and its metabolites. The monoterpene borneol, a p-glycoprotein inhibitor, was co-administered with scoparone and it was found to increase the brain penetration of this coumarin. No metabolites of scoparone were detected in the brain. Targeted lipidomics in mouse brain homogenates revealed distinct acute versus chronic effects of scoparone on arachidonic acid, endocannabinoids, *N*-acylethanolamines and prostaglandins. The unexpected lipid remodeling and impact on the ECS were independent of serine hydrolase inhibition. This is a new finding in coumarin pharmacology and demonstrates that scoparone exerts effects directly in the CNS. Future studies will show whether the ECS modulation could be causative for the behavioral changes.

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Keywords

Scoparone, Coumarins, Endocannabinoid system, Lipidomics

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ANTIOXIDANT CAPACITY AND PHENOLIC COMPOSITION OF COLCHICUM SPECIOSUM STEVEN (COLCHICACEAE)

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The genus *Colchicum* belongs to the Colchicaceae family and represented with 35 species and 15 of these species are endemic to Turkey [1]. *C. speciosum* is a perennial stemless plant, purplish pink flowers, underground organ is corm, which known as "Vargit, Güz Çiğdemi, Acı Çiğdem" in Turkey [2]. *Colchicum* species are the source of colchicine. Colchicine is used in the treatment of gout, Behçet's disease, familial Mediterranean fever, pericarditis, coronary artery disease [3]. The aim of this study was to evaluate the antioxidant capacity and phenolic composition of *Colchicum speciosum*. *Colchicum speciosum* was collected from Erzurum and dried corms, leaves and flowers extracted with methanol. This extracts were evaluated for their antioxidant capacities by DPPH and ABTS methods and phenolic content using Folin-Ciocalteu's reagent [4]. In the $ABTS^{\bullet+}$ scavenging activity alpha-tocopherol (TK) was used as standard, the leaf extract (L) showed highest activity compared to corm (C) and flower (F) extract [(TK)90.1>(L)73.1>(C)48.1>(F)39.1%; 40 µg/ml]. In the $DPPH^{\bullet}$ scavenging activity trolox (TR) was used as standard. The results of this test were similar to those of the $ABTS^{\bullet+}$ test [(TR)90.4>(L)14>(C)7.4>(F)4.4%; 40 µg/ml]. Leaf extract was the highest phenolic composition (µg GAE/ mg extract). Our results should be useful in future studies about this genus.

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Keywords

Colchicum speciosum, Antioxidant, Total Phenolic Compound, ABTS, DPPH

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EVALUATION OF ACETYLCHOLINESTERASE INHIBITORY AND DPPH RADICAL SCAVENGING ACTIVITY OF GERANIUM AND ERODIUM TAXA FROM TURKEY

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The genera *Geranium* and *Erodium* belonging to the Geraniaceae family have been reported to have various ethnopharmacological uses worldwide. In this study, the ethanol extracts obtained from *Geranium* and *Erodium* species were screened for their DPPH radical scavenging and acetylcholinesterase enzyme inhibitory activity, which are associated with the pathophysiology of Alzheimer's disease.*Geranium and Erodium* species were collected throughout Turkey. The antioxidant activity of the extracts prepared with 96% ethanol was investigated by DPPH radical scavenging method and their *in vitro* inhibitory effect on AChE were determined using ELISA microtiter assays. 24 extracts out of 47 extracts showed concentration-dependent inhibitory effect towards AChE over 50% inhibition. The highest AChE inhibitory activity at 2000 µg/mL was found in *G.macrostylum* Boiss. collected from Antalya 87.90 ± 2.15% (IC_{50}= 4.73± 2.96 µg/mL). The inhibitory activity of galanthamine at 1000 µg/mL, used as the reference drug, was found 97.11±1.26% (IC_{50}= 0.68 ± 0.05 µg/mL). All of extracts exhibited excellent antioxidant activity. The highest antioxidant activity at 2000 µg/mL was found in *G.purpureum* Vill. collected from Antalya (85.80 ± 0.26%). The radical scavenging activity of quercetin used as reference to compare in the antioxidant activity was found 85.51 ± 0.17 at 1000 µg/mL.Our findings revealed that *Geranium and Erodium* species screened in this study display high radical scavenging activity against DPPH and remarkable inhibitory activity against AChE.The phytochemical analysis of the active extracts to elucidate the compounds responsible for the mentioned activities is in progress in our laboratory.

Keywords

Geranium macrostylum, Geranium purpureum, Antioxidant activity, Acetylcholinesterase inhibition

EVALUATION OF RESVERATROL CONTENT OF SOME POLYGONUM L. SPECIES GROWING IN TURKEY

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Resveratrol is a phytoalexin with a phenolic structure and has various pharmacological effects such as anti-inflammatory, cardioprotective, anticancer, antioxidant, and anti-aging activities. Resveratrol can be found in almost 100 plant species such as *Vitis vinifera* L., *Polygonum cuspidatum* Sieb. et Zucc., *Arachis hypogea* L., and wine [1]. There are 43 taxa in the *Polygonum* L. (Polygonaceae) genus, 8 of which are endemic in Turkey [2]. This study aimed to determine the contents of resveratrol and other bioactive compounds in some *Polygonum* species, which are widely grown in our country. The plant materials of *P. aviculare* L., *P. cognatum* Meissn., *P. patulum* Bieb. subsp. *patulum* and *P. setosum* Jacq. subsp. *setosum* were collected from Konya in May 2020. The ethanol extracts were prepared from the aerial parts and roots of the *Polygonum* species. Analysis of resveratrol and other bioactive components in extracts was performed on the Agilent 1260 series HPLC system and the Agilent 6550 iFunnel High Resolution Mass Spectrometer instrument connected to this system (Agilent Technologies, Inc., CA, USA). Resveratrol was not detected by LC-MS QTOF in *Polygonum* extracts. Catechin and quercetin glucosides were determined as major components by LC-MS QTOF analysis on the extracts. As a result, although *Polygonum* species do not contain resveratrol, it is predicted that they may have important biological activities due to the other bioactive compounds they contain.

Keywords

Polygonum, LC-MS QTOF, Resveratrol

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PHYTOCHEMICAL INVESTIGATION OF EREMOSTACHYS MOLUCCELLOIDES BUNGE

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The genus *Eremostachys* (Lamiaceae) is widely distributed in Western and Central Asia and comprises 60 species. A comprehensive phytochemical investigation of *E. mollucelloides* leaves+flowers and roots was carried out for the first time. *E. moluccelloides* volatiles were extracted using MSD-SPME technique. Lipids in the aerial and root parts of the plant were extracted using the Fatty Acids Extraction Kit. The leaves+flowers (LF) and roots (R) of E. moluccelloides were macerated with n-hexane (HE) and methanol (ME). The total phenol and the flavonoids content were spectrophotometrically determined. The chemical composition of the fatty acids and volatiles were investigated with GC-FID/MS method. Heptanal (15.3%), carvacrol (11.9%), and linalool (10.9%) were the major constituents of the leaf and flower volatiles of E. molucelloides. Carvacrol (6.3%), 1-octen-3-ol (6.2%), and linalool (5.7%) were determined in the root volatiles. Palmitic, nonadecanoic, octadecanoic and nonanedioic fatty acids were found in high percentages. The highest total phenol content was found in ME LF (39.25 mgGAE/gextr). The highest total amount of flavonoids was found to be 20.38 mgQE/gextr. The volatiles profile of LF and R was predominated with a high abundance of oxygenated monoterpenes. The fatty acid composition was predominated with saturated fatty acids for both LF and R.

Acknowledgement: Authors thanks to Scientific Research Department of Anadolu University for financial supporting of the research project (BAP No: 2105S091).

Keywords

Eremostachys moluccelloides, Volatiles, Fatty acid, MSD-SPME, Phenolics

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BIOLOGICAL ACTIVITIES OF THE EXTRACTS AND ESSENTIAL OILS OF SCABIOSA PSEUDOGRAMINIFOLIA HUB.- MOR.

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Scabiosa genus belongs to the subfamily Dipsacaceae, which is a subfamily of the Caprifoliaceae family [1]. In general *Scabiosa* species contain flavonoids, coumarins, irridoids, saponins and terpenes [2]. The plant material was collected in Sivas. The aerial parts have been subjected to hydrodistillation in Clevenger type apparatus to get the essential oil. The extracts were obtained by maceration of leaves (L) with *n*-hexane (HE_L), methanol (ME_L), and water (WE_L). The essential oil and extracts were tested for antioxidant activities and inhibition of porcine pancreatic α-amylase enzyme. The total phenol content was spectrophotometrically determined with Folin-Ciocalteau Reagent, the flavonoids content was determined with $AlCl_3$ reagent. The yields of hexane, methanol, water extracts and essential oil obtained from leaves were calculated as 0.43% (HE_L), 13.44% (ME_L), 7.26% (WE_L) and %0.02 essential oil respectively. The highest antioxidant activity TEAC values were detected for WE_L (IC_{50} 0.16±0.004 mg/mL) and (2.33±0.2 mM), respectively. The highest total phenol content was found in ME_L (0.52±0.01 mgGAE/g). The highest total amount of flavonoids was found to be 0.081±0.009 mgRE/g in the WE_L. In this study, biological activities of *S. pseudograminifolia* plant was investigated for the first time.

Keywords

Scabiosa pseudograminifolia, Extract, Essential oil, DPPH, TEAC

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P91

STUDIES ON ANTICHOLINESTERASE AND ANTIOXIDANT EFFECTS OF TURKISH PISTACHIO

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Pistachio (*Pistacia vera* L.) is a plant from the Anacardiaceae family known as “Antepfıstığı” in Turkish. The pistachio nut is mainly cultivated in Turkey, Iran, Syria, Greece, Sicily and the USA. Pistachio seeds are usually used as ingredients in the food industry or roasted and consumed as snack food. Also, seeds are a rich source of phenolic compounds and have very high antioxidant potential amoung food products. In the present study, the extracts prepared from the leaves, seeds and its soft outer shells (pericarp) of crude alongwith mature of *P. vera* collected from Gaziantep, Turkey. These extracts have been investigated for their cholinesterase inhibitory activity against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) linked to Alzheimer’s disease, using ELISA microplate reader. In addition, antioxidant capacity of the extracts was measured by radical scavenging activity test against 2,2-diphenyl-1-picrylhydrazyl (DPPH) as well as metal-chelation capacity and ferric-reducing antioxidant power (FRAP) tests. From the tested samples, the hexane, dichloromethane and ethyl acetate extracts prepared from the pericarps of both crude and mature *P. vera* strongly inhibited AChE (92.04±0.60% - 98.11±0.07%) and BChE (91.69±1.65% - 99.13±0.54%) at 200 mg/mL. The extracts, displayed scavenging activity above 50% against DPPH, showed significant ferric-reducing antioxidant power (FRAP) (1.298±0.04 - 1.602±0.19) at 2000 mg/mL. However they exhibited very low metal-chelation capacity. As conclusion, our findings reveal that *P. vera* pericarps possess potent anticholinesterase activity *in vitro* by enzyme inhibition associated with neurodegeneration. Our studies are continuing for the determination of bioactive compounds from the active fractions.

Keywords

Anticholinesterase, Antioxidant, Activity, Alzheimer’s Disease, In vitro

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PHYTOCHEMICAL AND BIOACTIVITY STUDIES ON NEPETA CONGESTA FISCH. & MEY. VAR. CONGESTA FISCH. & MEY.

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In this study, we investigated the acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) enzyme inhibitory activity of the extracts with different polarity (hexane, chloroform, ethyl acetate, methanol) and infusion prepared from *Nepeta congesta* Fisch. & Mey. var. *congesta* Fisch. & Mey. (Lamiaceae), an endemic species collected from Eskişehir. The analyses were carried out using the spectrophotometric method of Ellman in ELISA microplate reader at 100-200 µg/mL. Since Alzheimer's disease is associated with oxidative degeneration of cells, several methods of antioxidant activity were applied to the studied extracts such as 2,2 diphenyl-1-picrylhydrazyl radical scavenging activity, metal-chelation capacity, ferric-reducing antioxidant power and ABTS radical cation decolorization assays. Total phenolic contents of the extracts ranged from 71.93 to 205.38 mg GAE/g extract. Rosmarinic acid was the dominant phenolic acid found in infusion and methanol extract and ranged from 1.04 to 2.15 mg/g extract. While DPPH, ABTS and metal chelating capacities of the same extracts were higher, AChE and BuChE inhibitory activities of the hexane and ethyl acetate extracts were found to be higher. In conclusion, the polar extracts (infüsion and methanol) possessed the highest antiradical and antioxidant activities and highest totatl phenol content. A positive linear correlation was observed between phenolic content and antioxidant activity of the extracts. In anti-AChE assay, the most active one was extract having 32.41 (AChE) - 51.46 (BuChE) % of inhibition. The phenolic acid compositions and anti-alzheimer activities of the extracts from *N. congesta* var. *congesta* were presented for the first time in this study.

Keywords

Nepeta congesta var. congesta, Lamiaceae, Antioxidant, Anti-Alzheimer's, Rosmarinic acid

HISTORY OF MEDICINE

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Human treatment has been able to evolve throughout the history of man beginning in prehistoric times to the modern era in which we live [1]. Humans have suffered and continue to suffer from many diseases and health conditions that need medical attention. Traditional medicine and modern medicine have been used for human treatment. This study aims to determine the integration of traditional and modern medicine in human treatment. Specifically, it investigates how well traditional medicine can be incorporated in modern times to complement modern medicine use in human treatment. In this context traditional medicine are medicines derived from medicinal plants that grow naturally and are not industrially produced. In addition, they have been used since the existence of man and mostly in their natural form. Research study was done by use of qualitative and quantitative methods to collect research data and analyze the data collected. Secondary review of existing information was carried to determine the existing research gap that has been addressed and also gather relevant information for this research study. Primary research was done to collect information from respondents who were randomly and also systematically selected to provide responses to formulated questionnaires and interviews conducted. The responses showed that traditional medicines have contributed to human treatment for ages and also been used as resources to develop modern medicines [2]. In addition, traditional medicines have been effective when used appropriately. It was however noted that there usage need to be monitored for effective treatment and patient stability.

Keywords

Development, Ancient, Traditional medicine, Natural form, Modern medicine

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DETERMINATION OF ARTEMISININ IN FIVE ARTEMISIA L. SPECIES (ASTERACEAE) THAT GROWN IN TURKEY

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Artemisinin is a compound of current interest in the treatment of drug-resistant malaria. Analysis of artemisinin is challenging due to the unstable nature of the compound, its low content in the plants, and other constituents in plants with its detection [1]. Various methods were proposed for the detection and quantification of artemisinin [2]. The aim of this study was to find novel artemisinin sources. Five different *Artemisia* L. species (*A. annua* L., *A. absinthium* L., *A. incana* Druce, *A. abrotanum* L. and *A. tournefortiana* Rchb.) were collected from different locations throughout Turkey were analyzed by HPLC. Artemisinin standard solutions and crude extracts of five species were treated with first 0.2% (by weight) NaOH solution and then 0.08 M acetic acid. HPLC analyses of artemisinin were achieved on a *Ultisil* ™ *XB-C18* column (250 mm x 4.6 mm, 5 µm) by using formic acid (% 0.2 v/v): acetonitrile [50:50 v/v] mixture as a mobile phase. The standard calibration curve was linear within the range of 0.5 – 100 µg/mL (R^2 = 0.9998). Artemisinin content in crude hexane extract and dried aerial parts of *A. annua* L. was 2.14% and 0.122%, respectively. The recovery was calculated as 92.4%. However, artemisinin was not detected in the other four species. To the best of our knowledge, this is the first analysis of *A. tourneforitana* and *A. incana* species. Qualitative and quantitative studies on other *Artemisia* L. species grown in Turkey should be carried out on the component of artemisinin.

Keywords

Artemisinin, HPLC, Artemisia species

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ENZYME INHIBITORY EFFECTS AND PHYTOCHEMICAL STUDIES OF SOME MEDICINAL PLANTS CULTIVATED IN TURKEY

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In this study, it was aimed to evaluate the antioxidant, antidiabetic, antihyperlipidemic and antiobesity activities of 10 plants cultivated in Turkey. These species are *Artemisia absinthium* L., *Calendula officinalis* L., *Achillea millefolium* L., *Alchemilla vulgaris* L., *Urtica dioica* L., *Salvia officinalis* L., *Salvia triloba* L., *Fumaria officinalis* L., *Mentha piperita* L., *Origanum onites* L. The effects on α-glucosidase, α-amylase, pancreatic lipase and cholesterol esterase enzymes on the extracts were investigated by *in vitro* methods. In the evaluation of antioxidant activity; metal chelating activity, ferric reducing power, DPPH radical scavenging activity and ABTS radical scavenging activity methods were used. These species are used as herbal tea among the people. Therefore, the infusion method was used while preparing the extract. The highest activity was detected in α-glucosidase enzyme. Species with the highest α-glucosidase enzyme inhibitor: *M. piperita* (91.43±0.90), *O. onites* (70.18±2.02), *S. officinalis* (64.69±0.23), *A. vulgaris* (61.95±1.57). Chemical content illumination studies on these 4 species were carried out by HPLC method. In future studies, it is aimed to evaluate these extracts *in-vivo* in terms of antidiabetic activity.

Keywords

Enzyme inhibitory, Antidiabetic, Phytochemistry, HPLC

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CHEMICAL CONSTITUENTS OF PULICARIA ARMENA BOISS. & KOTSCHY EX BOISS. (ASTERACEAE); AN ENDEMIC TURKISH SPECIES*

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The genus *Pulicaria* which belongs to the family Asteraceae, includes more than 100 species with a distribution from Europe to North Africa and Asia, particularly around the Mediterranean. *Pulicaria* species are represented by 9 taxa belonging to 6 species in Flora of Turkey. Some plants within the genus are used as traditional herbal medicines in different countries and cultures. Up to date, various phenolic compounds especially flavonoids together with sesquiterpenes, diterpenes, triterpenes have been reported from different *Pulicaria* species [1]. Phytochemical investigation of *P. armena* led to the isolation of one simple phenolic glucoside; Citrusin C (1), together with 8 flavonoids quercetagetin 5,7,3' trimethyl ether (2), quercetin 3-*O*-glucronide (3), quercetin 3-*O*-glucronide-6"-methyl ester (4), quercetin 3-*O*-rutinoside (5), luteolin (6), quercetin (7), 6-hydroxy apigenin, 7-methyl ether (8), and 6-hydroxy luteolin 7,4'-dimethyl ether (9). The chemical structures of the compounds were elucidated based on 1D and 2D NMR and MS spectra, as well as comparison with the relevant literature data. To the best of our knowledge, this is the first detailed phytochemical study about *P. armena* and the first report on the isolation of all the compounds from *Pulicaria armena*. The chemotaxonomic significance of the isolated compounds was also discussed.

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Keywords

Pulicaria armena, Asteraceae, NMR, Flavonoid, Chemotaxonomy

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LAVANDULA X INTERMEDIA EMERIC EX LOISEL ESSENTIAL OIL-LOADED TOPICAL CREAM SUITABLE FOR DERMACOSMETIC USE: PREPARATION, CHARACTERIZATION, IN VITRO BIOLOGICAL ACTIVITY

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Lavandula x *intermedia* (lavandin or lavandulil), known to be a natural sterile hybrid obtained by crossing *L. angustifolia* x *L. latifolia* [1]. The essential oil of *L. angustifolia* has been used medically for its sedative, antidepressive, antimicrobial, cytotoxic and anti-inflammatory properties. Also, the oil is used in perfume and soap production due to its high content of camphor [2]. In the present study, the cream containing *L.* x *intermedia* essential oil was characterized and screened for *in vitro* antioxidant and antimicrobial activities. The essential oil obtained from the leaves was screened for its composition by using GC-FID/MS method. *In vitro* antioxidant and antimicrobial activities of the cream were screened by using ABTS, DPPH scavenging, metal chelating potential, reducing power and agar microdilution tests, respectively. Linalool (20.2%), *trans*-linalool oxide (10.9%) and camphor (10.7%) were found as the major compounds of the essential oil. Inhibiton values of DPPH scavenging, metal chelating and TEAC value of ABTS decolorization potentials of the cream were found as 20.43% at 2.5 mg/mL, 47.2% at 5 mg/mL and 0.42±0.01 mM respectively. EC_{50} value for reducing power were found as 7.28±0.52 mg/mL. Antimicrobial potentials were determined against *E. coli*, *S. aureus* and *L. reuteri* as ˂250 µg/mL, 250 µg/mL, >250 µg/mL for cream when compared with Chloramphenicol, respectively. This study reports that topical cream containing *L.* x *intermedia* essential oil with good *in vitro* antioxidant and antimicrobial potentials may represent a promising and affordable topical agent for dermacosmetic use.

Keywords

L. x intermedia essential oil, Cream, Dermacosmetic, Antioxidant, Antimicrobial

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THE POSITION OF HERBAL DRUGS IN COMPOUNDING

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Herbal medicine has been used for human and animal treatment. It has provided treatment option for manufactured drugs that are expensive and with given side effects for patients with health conditions. The Phyto constituents present in herbal medicines have less negative effect to human system. This study aims to determine the position of herbal drugs in compounding. Further, it investigates how herbal medicine compounding has contributed to progress in health care and concerns that have arisen as a result of it use in human treatment. Herbal drugs compounding refers to the preparation, mixing, assembling, packaging and labelling of herbal drug in accordance with a licensed practitioners prescription [1]. Research study was done by use of qualitative and quantitative methods to collect and analyse the collected data. Secondary review of existing information was carried to determine the existing research gap that has been addressed and also gather relevant information for this research study. Primary research involved the use of interviews and questionnaires to gather information. The responses showed that herbal drugs have been used for compounding and provide alternative medical options in health care, though further research on contamination and modern processing need to be looked at [2]. These results suggest that herbal drugs have a crucial role, and provide affordable effective medical treatment to mankind. The use of herbal drugs in modern era in health care will therefore promote human welfare and medicine progress and compliment manufactured drugs in treatment.

Keywords

Herbal, Compounding, Phyto

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TOPICAL CREAM CONTAINING RUTA MONTANA L. ESSENTIAL OIL: PREPARATION, CHARACTERIZATION, IN VITRO AND IN VIVO BIOLOGICAL ACTIVITY

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Ruta montana L. (Rutaceae) which is native to the Mediterranean region and Southwest Asia [1] is used traditionally for its antifungal, antioxidant and anti-inflammatory activities [2]. A topical cream containing *R. montana* essential oil was designed, characterized and screened for its *in vitro* antioxidant, antimicrobial and *in vivo* anti-inflammatory activities. The essential oil obtained from the leaves was screened for its composition by using GC-FID/MS method. *In vitro* antioxidant and antimicrobial activities of the essential oil and cream were screened by using ABTS decolorization, DPPH scavenging, metal chelating potential, reducing power and agar microdilution tests, respectively. *In vivo* anti-inflammatory activity was screened by using HET-CAM assay. 2-Undecanone (90.5%), 2-nonanone (2.2%) and 2-decanone (1.3%) were found as the major compounds of the essential oil. Inhibition values of DPPH scavenging, metal chelating activities and TEAC value of ABTS decolorization potentials of the cream were found as 8.12%, 6.7% and 0.31±0.02 mM respectively. EC_{50} value for reducing power was found as 8.26±0.35 mg/mL. Antimicrobial potentials were determined against *E. coli*, *S. aureus* and *L. reuteri* as 500 µg/mL, >500 µg/mL, 250 µg/mL for cream when compared with Chloramphenicol, respectively. The cream also exhibited strong *in vivo* anti-inflammatory activities with 78.13±0.48% value whereas the essential oil showed weak potential (62.5±0.71%) compared with Hydrocortisone (80.30 ± 6.75%). This study reports a promising topical cream containing *Ruta montana* L. essential oil with good *in vitro* antimicrobial and *in vivo* anti-inflammatory potentials.

Keywords

Ruta montana L. Essential oil, Cream, Antioxidant, Antimicrobial, Anti-inflammatory

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ENZYMES INHIBITORY OF VARIOUS METABOLISM DISEASES AND PHYTOCHEMICAL STUDIES ON PISTACIA EURYCARPA YALT.

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Pistacia eurycarpa Yalt., known as Bendek, is a species belonging to the Anacardiaceae family that grows in Turkey. Various traditional uses and ethnobotanical reports of various species of the genus *Pistacia* are available in the literature [1]. In this study, the enzyme inhibition potential of *P. eurycarpa* leaves in various metabolic diseases was evaluated. The phytochemical content of the tested extract was examined by HPLC technique [2, 3]. *P. eurycarpa* samples were collected from Van province in 2019. The inhibitory effects of α-glucosidase, α-amylase, pancreatic cholesterol esterase and pancreatic lipase of extracts with 80% ethanol from leaf parts of the plant were evaluated. Qualitative analysis of phenolic acids and flavonoids in *P. eurycarpa* leaves was performed using HPLC method. In addition, quantitative analysis was conducted on gallic acid and ellagic acid. *P. eurycarpa* leaves showed excellent and dose-dependent inhibitory effect on the α-glucosidase enzyme. The highest α-amylase inhibitor activity was found at 2 mg/ml dose (88.23±0.63%). While the extract provided inhibition on pancreatic lipase enzyme (30.00±3.95%) at dose of 2mg/ml, it had inhibition on pancreatic cholesterol esterase enzyme (12.02±5.84%). Results of HPLC analysis, *P. eurycarpa* leaf ethanol extract was determined to have a content of 4.115±0.100 gallic acid and 0.333±0.011 ellagic acid g/100 g. The findings from the experiments revealed the potent antihyperglycemic and potential antiobesity activity of *P. eurycarpa* leaves. Antihyperglycemic activity guided isolation studies should be carried on *P. eurycarpa* leaves.

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Keywords

Enzyme inhibition, Phytochemistry, HPLC

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P103

DETERMINATION OF ALCOHOLS IN BEVERAGES BASED ON DIRECT EXTRACTION BY HEAD SPACE GAS CHROMATOGRAPHY-FLAME IONISATION DETECTION

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Detection and quantitation of ethanol (EtOH) in matrices is a common practice although sample preparation is inevitable and time-consuming. The matrix becomes a challenging process, makes the methods inefficient, or more extraction methods have to be implanted. Direct extraction by the headspace chromatographic method has been developed for the determination of the EtOH content of wine in our method. Isopropanol (IPA) was preferred as an internal standard, and TritonX-100 (TX-100) was used as a diluting solution. The amount of TX-100 and the total volume of solution were optimized. 2.5%TX-100 and 2 ml of total volume were used as an optimum condition. The stationary phase was the fused silica, Agilent J&W DB-624 column (30 m x 320 mm x 1.8 mm) and helium was used as a mobile phase. The oven temperature program was 40 °C (5 min), 5 °C/min ramp to 60 °C (0 min) and 30 °C/min to 150 °C (1 min) [1]. Calibration curve was drawn between the concentration of 2.5% to 15.0% EtOH (y= 1.572x – 0.702, R^2 = 0.9960, y; the ratio of peak area of EtOH to IPA, x; EtOH%). The slopes of the standard addition and external calibration curve were statistically the same. Recovery of the method was 97.5±3.5 for three different concentrations and the precision was %5.8 (n= 11). LOD and LOQ were 0.80% and 2.5%, respectively. The amount of EtOH was found as 13.1±0.9% and 11.8±0.7% in two different wines. The proposed method has the potential to check the quality and analysis of residual alcohol without the matrix effect.

Keywords

Headspace, Gas chromatography, Ethanol

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P104

METHOD DEVELOPMENT FOR SELENIUM NANOPARTICLE DETERMINATION AND CHARACTERIZATION USING SINGLE PARTICLE INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY

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Selenium (Se) is essential for human health, but has a narrow therapeutic window and the toxicity margins and the bioavailability of selenium varies according to its chemical form. Selenium nanoparticles (SeNPs) when compared with several extensively studied Se compounds such as sodium selenite, selenomethionine, and methyl selenocysteine, were reported to exhibit markedly lower acute toxicity and significantly lower short-term and subchronic toxicities. SeNPs show better bioavailability, biological activity compared with inorganic and organic selenium compounds [1, 2]. There is a need for reliable analytical methods that can rapidly determine the particle number concentration, size distribution of SeNPs as well as dissolved selenium concentration in various samples. Single particle inductively coupled plasma mass spectrometry (SP-ICP-MS) is a technique that attracts attention for the nanoparticle determination with high sensitivity and short analysis time. In this study, a method with SP- ICP-MS was developed for simultaneous determination of the size distribution, particle and dissolved selenium concentrations in a SeNP solution. A quadrupole Agilent 7800 ICP-MS (Agilent Technologies, USA) was used throughout the experiments. Commercial Nanocs SeNP used as standard and SeNPs synthesized in different protective agents in our laboratory were characterized under optimum conditions and the results were compared with transmission electron microscopy (TEM). The particle size for Nanocs SeNP was experimentally found as 133±43 nm and 95±5 nm by TEM and SP-ICP-MS, respectively.The size detection limit was calculated as 44 nm by SP-ICP-MS. SP-ICP-MS is an easy and fast technique for the characterization of nanoparticles at low concentrations.

Keywords

Selenium nanoparticles, Single particle ICP-MS, Nanoparticle characterization

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P105

DETERMINATION OF RIVASTIGMINE BY USING MOLECULARLY IMPRINTED SOLID-PHASE EXTRACTION

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Molecular imprinted solid phase extraction (MISPE) is a method that uses molecularly imprinted polymer (MIP) as a sorbent during solid phase extraction process. MISPE is useful and efficient technique for extraction and cleaning process as compared with traditional solid phase extraction (SPE) procedure. Rivastigmine, (RIV) is an acetylcholine esterase inhibitor of the carbamate type approved for the treatment of Alzheimer's disease, which is a continuous, degenerative brain disorder that affects reason, knowledge and memory. It is thus necessary to develop a fast, sensitive, and cost-effective method to determine RIV in various media. This work presents to development of a simple, reliable and sensitive method based on MIPs as selective SPE sorbents for the removal of rivastigmin in aqueous and organic media. MIP was synthesized using RIV as a template molecule, methacrylic acid (MAA) as a functional monomer, ethylene glycol dimethacrylate (EGDMA) as a crosslinker, and N, N-asobisisobutyronitrile (AIBN) as an initiator, and dimethyl sulfoxide (DMSO) as a porogen. A non-imprinted polymer (NIP) was prepared using the procedure aforementioned above, but in the absence of template. The bulk polymer (MIP/NIP) was crushed, ground, and sieved through 20 µm -140 µm sieve and then RIV was removed from MIP using Water:Acetic Acid (8:2, v/v) till no more signal of RIV could be detected by spectrophotometer. Synthesis parameter optimization was performed after bulk polymer synthesis, which are the effect of monomer amount, RIV amount and crosslinker amount on binding was determined. All experiments were carried out in aqueous and organic media.

Keywords

Spectroscopy, Molecularly Imprinted Polymers, Molecularly Imprinted Solid-Phase Extraction

P106

ANALYTICAL METHOD VALIDATION OF HPLC ASSAY METHOD FOR DEVELOPING OF A PEPTIDOMIMETIC GENERIC DRUG CONTAINING ICATIBANT 30 MG

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By completing the research it is aimed to develop a peptidomimetic generic medication, a 30mg/3ml icatibant acetate injector containing the drug ingredient icatibant acetate for the treatment of acute bouts of hereditary angioedema (HAE), and make it available inside Onko İlaç. Validation is done in this context to demonstrate that the assay analytical technique established for injector containing 30mg/3ml icatibant acetate produces accurate and reliable findings in accordance with ICH recommendations and pharmacopoeas, and that the method is applicable. It is a critical criteria to ensure that the developed technique produces findings that are consistent with the assay specification and to evaluate the method's applicability in routine usage with parameters. The linearity, precision, and accuracy characteristics, as well as the validation of the HPLC technique established, were investigated in this study. The acquired findings demonstrated the analytical method's accuracy and dependability.

Keywords

Icatibant, HPLC

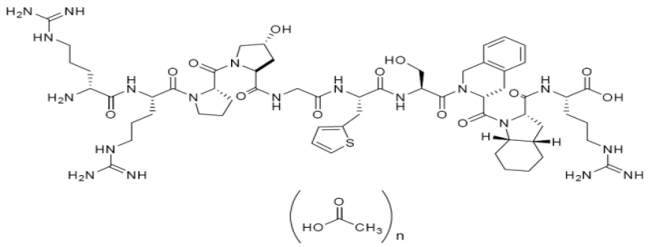

Figure 1- Icatibant Chemical Structure

SYNTHESIS OF L-CYSTEINE MEDIATED COPPER NANOCLUSTERS AS A TURN-OFF FLUORESCENT PROBE FOR THE DETECTION OF INDIGOTINE

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Indigotine (Indigo carmine, E132) as an artificial food color has significant adverse effect on the human health such as hyperactivity, brain tumor, and abnormal cell growth [1]. For this reason, it is needed to develop the sensitive, selective, fast, and cost effective methods. The copper nanoclusters (CuNCs) were synthesized based on the reaction of copper and L-cysteine as a stabilizing agent by the one-pot hydrothermal process and characterized with different methods such as transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR), X-ray photoelectron spectroscopy (XPS), UV-vis and fluorescence spectrometry, dynamic light scattering (DLS), fluorescence life time, and zeta potential measurements. The experimental parameters such as pH value, reaction temperature, and incubating time were optimized. The addition of indigotine into nanocluster solution caused the quenching of fluorescence. In order to identify the quenching mechanism, fluorescence data were used for Stern-Volmer equation, and quenching constant was calculated. Under the optimum conditions, the linear range was achieved in the range from 0.25 to 10.02 µg mL^{-1} with the low LOD value at 0.06 µg mL^{-1} . Proposed fluorescence sensor had good sensitivity and selectivity for Indigotine determination and was applied for different candy samples. High recovery values for Candy I 98.06-104.46%, Candy II 101.92-104.32%, and Candy III 99.21- 99.97% with low RSD% values for Candy I 5.68%, Candy II 2.92%, and Candy III 4.26% were achieved. Indigotine concentrations were found for Candy I 0.06 mg g^{-1} , Candy II 0.36 mg g^{-1} , Candy III 0.09 mg g^{-1} .

Keywords

Copper nanocluster, Indigotine, Fluorescence sensor

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VALIDATION OF HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC METHOD FOR THE ANALYSIS OF DRY POWDER INHALER CONTAINING FLUTICASONE PROPIONATE

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Pulmonary delivery is the preferred route of drug administration in the treatment of many respiratory diseases, such as asthma and chronic obstructive pulmonary disease. Fluticasone propionate, chemically S-(fluoromethyl)-6α,9-difluoro-11β,17-dihydroxy-16α-methyl-3-oxoandrosta-1,4-diene-17β-carbothioate-17-propionate (Figure 1), is a synthetic steroid with glucocorticoid receptor activity. It is used to treat asthma and allergic rhinitis [1]. A high-performance liquid chromatographic (HPLC) method was developed for the determination of fluticasone propionate in dry powder inhaler formulation. The separation was achieved on C_{18} (250 mm x 4.6 mm with 5 µm particles) column. The mobile phase consists of ultrapure water: acetonitrile (35:65 v/v) used at a flow rate 1.5 ml/min. The column temperature was maintained at 30 °C and the detector was monitored at a wavelength of 236 nm [2]. The injection volume was 10 µl and the retention time was found to be 4.95±0.01 min. The linearity was found for concentration range 10 – 100 µg/mL of fluticasone propionate. The correlation coefficient of linearity was found to be 0.9992. The percentage recoveries were found to be 99.29-99.66%. The limit of detection (LOD) was found to be 0.185 µg/ml and the limit of quantitation (LOQ) was found to be 0.416 µg/ml. The developed method was validated for system suitability, specificity, accuracy, precision, linearity, limit of detection, limit of quantitation and robustness according to International Conference on Harmonization (ICH) guidelines [3]. The proposed method was successfully used for the estimation of fluticasone propionate in dry powder inhaler dosage form.

Keywords

Fluticasone propionate, HPLC method, Validation

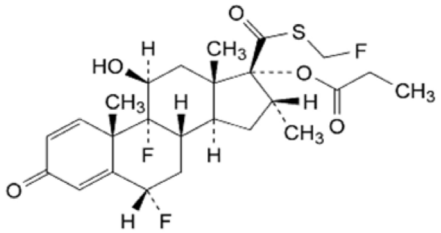

Figure 1. Chemical structure of fluticasone propionate molecule

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P109

DEVELOPMENT AND VALIDATION OF A NEW HPLC-PDA METHOD FOR DETERMINATION OF PEPTIDE DAPTA (D-ALA-PEPTIDE T-AMIDE)

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d-Ala-Peptide T-amide (DAPTA), the first viral entry inhibitor, was derived from the envelope protein of HIV in 1986, blocks two major chemokine receptors, CCR5 and CXCR4. The selective chemokine receptor antagonism activity makes peptide DAPTA a promising candidate for the anti-inflammatory research field [1]. In this study, we aimed to develop a rapid and simple method for the determination of peptide DAPTA, by high-performance liquid chromatography–photodiode array (HPLC-PDA) detection. The analyses were performed on a C18 column (150 x 4.6 mm, 5 µm particle size) at room temperature with UV detection at 275 nm, and the retention time was 6.72 minutes. The mobile phase consisted of 2 mM aq. o-phosphoric acid solution/acetonitrile/methanol (75:15:10, v/v) at a flow rate of 1 mL/min. The method was validated according to the International Committee of Harmonization (ICH) Q2 (R1) validation guidelines. Specificity, linearity, range, accuracy, precision, detection limit, stability, quantitation limit, robustness, and system suitability testing were evaluated during the method validation process. The method was linear in the range of 2-50 µg/mL with excellent determination coefficients (R2 >0.99). The intra-assay and inter-assay accuracy and precision were found within acceptable limits of the ICH guideline. The developed method was successfully applied for in vitro determination of peptide DAPTA in chitosan nanoparticles.

Keywords

Peptide DAPTA, HPLC

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