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7-9 June 2024

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5th International Conference on Natural Products for Cancer Prevention and Therapy
7-9 JUNE 2024 CAPPADOCIA
SCIENTIFIC PROGRAM

Friday, June 7, 2024	
09:00-10:00	Opening ceremony
Session A:	Chair:
10:00-10:40	PL-1: Prof. Dr. M. Betül Yerer Aycan (Türkiye) "Preclinical & Clinical Research with Natural Products"
10:40-10:55	OP-1: Muriel Cuendet, "Withanolide analogs inhibit multiple myeloma cell proliferation through multiple signaling pathways"
10:55-11:25	Break
11:25-12:05	PL-2: Prof. Dr. Funda Nuray Yalçın (Türkiye) "Natural Products as New Approaches for urogenital cancers"
12:05-12:20	OP-2: Zakarya Al-Shaebi, Munevver Akdeniz, Pinar Sagiroglu, Mustafa Altay Atalay, Omer Aydın "Combating Antimicrobial Resistance: Leveraging Surface-Enhanced Raman Spectroscopy and Machine Learning for Classification of Staphylococcus aureus Isolates"
12:20-14:00	Lunch
14:30-19:00	Social Programme
Saturday, June 8, 2024	
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09:00-09:40	PL-3: Prof. Dr. Erdal Bedir (Türkiye) "Sapogenin-based Unique Nanoparticles as Immunotherapeutic Agents against Melanoma"
09:40-09:55	OP-3: Vahap Murat Kutluay, İclal Saraçoğlu "Digigrandifloroside; a cardioactive glycoside with potential cytotoxic activity and assessment of the role of apoptosis via caspase3/7 activity"
09:55-10:35	PL-4: Prof. Dr. Emine AKALIN, Yağız ÜRESİN, "The Use of Plants in Cancer Treatment: Clinical Research and Challenges"
10:35-11:05	Break
11:05-11:45	PL-5: Stefan Gafner, CSO of American Botanical Council Stefan Gafner (USA) "Quality assessment of botanical ingredients used in cancer chemoprevention and treatment of cancer therapy-related symptoms"
11:45-12:00	OP-4: Demet Saylan, Fatma Cebeci "Investigation of anti-inflammatory and anticancer properties of Trachystemon orientalis L. extract"
12:10-14:00	Lunch & Poster Presentations
Session D:	Chair:
14:00-14:40	PL-6: Prof. Dr. Corina Danciu (Romania) "4',5,7-trihydroxyflavone as a dietary phytochemical with anticancer potential. An in vitro-in ovo approach"
14:40-15:20	PL-7: Prof. Dr. Chin-Kun Wang (Taiwan) "Application of propolis on cancer intervention from cell to human"



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5th International Conference on Natural Products for Cancer Prevention and Therapy

7-9 June 2024

Plenary Lectures

PL-1

Preclinical and Clinical Research for Natural Products

Mükerrem Betül Yerer Aycan¹ ✉

¹ Erciyes University, Faculty of Pharmacy, Department of Pharmacology, Drug application and Research Center, Kayseri, Türkiye

Abstract

Natural sourced products have been widely used since ancient times for prevention and therapy of many diseases. However, to be able to use these products as drug candidates, we need to learn how we should design these R&D studies with this kind of products. Natural sourced products are usually plant based, however there many different kinds of natural sources such as marine, bacteria or fungi-based candidates those can be evaluated for their effectiveness in different conditions and diseases. Usually, the plant-based sources are being widely used for cancer studies. Among them sometimes the extracts, the fractions and pure compounds can be used for their efficacy and toxicity studies. If someone is working with a plant-based drug candidate all the quality assessment studies should start with (Good Agriculture Practice) GAP conditions and should be followed with other GxP facilities like Good Laboratory Practice (GLP), Good Manufacturing Practice (GMP) conditions in the preclinical studies. Furthermore, the standardized products should be used to be able to arrange the doses and calculate the kinetics of the pharmacological activity and the toxicity. After the preclinical studies under these quality assurance conditions, the drug candidates which are suitable for the clinical studies should also only can be tested under Good Clinical Pharmacy (GCP) conditions. The natural product-based drug candidates are also being widely used traditionally but their bioavailability is usually low and to enhance their efficacy in the last decades the nanoformulations of these drug candidates are being investigated. Even with the product itself or its nano formulation, the major things that we should always keep in mind to follow up the regulations such as OECD, FDA, EMA which always let us to follow us these quality assurance in preclinical and clinical studies



PL-2

Natural Products as New Approaches for Urogenital Cancers

Funda Nuray Yalçın¹ ✉

¹ Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, Ankara, Türkiye

Abstract

Urooncology investigates cancers occurring in urological organs such as the kidney, bladder, prostate, and testis, as well as treating and managing these cancers. In urogenital cancers, the inadequacy of the available treatment options, the high side effects and the high cost of treatment result in treatment failure. In this case, increasing survival, reducing treatment costs, providing optimum treatment options with maximum benefit to the patients with minimum side effects and providing a new perspective have directed people to natural products. For years, it has been observed that secondary metabolites of plants used for various purposes affect cancer. Phenolic compounds, flavonoids and terpenes are the significant molecules responsible for these effects. Secondary metabolites have exhibited antiproliferative/antitumoral, apoptotic, and antimetastatic effects on cancer cells within various mechanisms. There are many clinical trials on the treatment profile, side effects and properties of natural products that have the potential in urogenital cancers.

Keywords

Urooncology · Urogenital cancer · Natural product



PL-3

Sapogenin-based Unique Nanoparticles as Immunotherapeutic Agents against Melanoma

Göklem Üner¹, Cerem Ülker², Petek Ballar Kırmızıbayrak³ & Erdal Bedir¹ ✉

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³ Ege University, Faculty of Pharmacy, Department of Biochemistry, İzmir, Türkiye

Abstract

Saponin's antitumor potency is relatively weak, prompting natural product chemists to focus on modifying them to obtain compounds with higher potencies. With this goal in mind, we conducted studies on a rare group of sapogenin known as cycloastragenol. Our research revealed that one of the analogs (AG-08) primarily induced necrotic cell death and inhibited autophagy, setting itself apart from other derivatives. AG-08 also promoted a global proteolytic activation, leading to the cleavage of various key proteins. Additionally, AG-08 was also found as an inducer of lysosomal membrane permeabilization. Our further studies via Nile Red encapsulation assay and molecular dynamics simulations indicated that AG-08 formed circular supramolecular structures. Internalization studies also showed that AG-08 particles were taken inside cells via a cholesterol-dependent non-canonical endocytosis pathway. Additionally, affected signaling pathways were revealed by microarray assay. Moreover, by preparing 18 analogous derivatives, the role of residues in forming supramolecular structures and biological activities was established. The results demonstrated that unique structural features were required to form particulate structures and exceptional cell death mechanisms.

Intra-tumoral injection (ITI) is an immunotherapy approach designed to stimulate anti-cancer activity by inducing immunogenic cell death (ICD) through the release of damage-associated molecular patterns (DAMPs). Given the high potential of necrotic cell death inducers in ITI, we sought to investigate the anti-tumor effects of AG-08 and its derivatives in melanoma through ITI. After confirming that the compounds induced DAMP signals *in vitro*, we conducted *in vivo* experiments that demonstrated their anti-tumor activity in a syngeneic melanoma model. Together, the prepared sapogenin analogs form particles that trigger necrotic cell death through a novel mechanism. While small molecule-based supramolecular assemblies have often been considered a challenge in drug discovery, our findings suggest that these colloidal particles hold promise for the development of anti-cancer drugs, particularly as immunotherapy agents.

Keywords

Sapogenin · Cycloartane · Semi-synthesis · Necrotic cell death · Intratumoral injection Anti-tumor · Immunotherapeutic

Acknowledgment This study was supported by TÜBİTAK (Project Number: 118S709 and 121R086).



PL-4

The Use of Plants in Cancer Treatment: Clinical Research and Challenges

Emine Akalın¹ ✉ & Yağız Üresin²

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² İstanbul University, Faculty of Medicine, Department of Medical Pharmacology and Clinical Pharmacology, İstanbul, Türkiye

Abstract

It is clear that plants offer vast potential for the development of novel cancer therapies and supportive care interventions. The development of plant-derived drugs follows the established drug development and dissemination processes. In addition, plants are used as Medicinal Plant Products (MPPs) for cancer treatment and support in addition to serving as drug molecules. While the fundamental approach to MPPs development is similar to drug molecules, there are clear differences and considerations, such as product safety, standardisation and quality control, monitoring of side effects, or the regulatory framework.

It is crucial to consider that conducting clinical research with MPPs presents some special challenges. These can be grouped into several categories:

Variability in product quality (The inherent variability in the composition of plant materials can pose challenges in ensuring the consistency and reproducibility of research findings. This is why it is important to adhere to “good practices” in this regard) and Clinical trial design (the design of clinical trials for MPPs requires careful consideration of factors such as dosing, standardisation, and appropriate comparators to ensure valid and reliable results)

Ethical considerations are of the utmost importance. They must be addressed alongside data and clinical research ethics. The fair distribution of benefits arising from ethnobotanical research is also a key concern. Finally, we must consider the ecological impact of our actions. Sustainable practices for plant collection and cultivation are crucial to minimise environmental impact and preserve biodiversity.

Translational research plays a critical role in addressing the challenges associated with MPPs development and clinical research. By bringing together experts from different disciplines, translational research promotes a comprehensive approach.



PL-5

Quality Assessment of Botanical Ingredients Used in Cancer Chemoprevention and Treatment of Cancer Therapy-related Symptoms

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Abstract

Many epidemiological studies have reported that a diet rich in fruits and vegetables decreases cancer risk in humans. Among the most widely investigated botanicals for cancer preventative effects are turmeric (*Curcuma longa*), green tea (*Camellia sinensis*), pomegranate (*Punica granatum*), broccoli (*Brassica oleracea var. italica*) and other cruciferous vegetables, black cumin (*Nigella sativa*), and cranberry (*Vaccinium macrocarpon*). While data for some of the ingredients, especially the cruciferous vegetables, are quite compelling, the cancer preventative benefits of others, e.g., cranberry, have been studied only *in vitro* and in animals. For ease of consumer use and to overcome taste barriers, these botanicals are widely available as dietary or food supplements or as herbal medicines. However, many of the commercial products, especially in the food and dietary supplement category, are adulterated with lower-cost ingredients for financial gain. Adulteration has been reported for all botanicals above, although it is rare for green tea. Adulteration issues include spiking of extracts with marker compounds such as synthetic curcumin in turmeric or ellagic acid in pomegranate, and the undeclared addition of ingredients of similar chemical composition, i.e., the substitution of broccoli with other species of the family Brassicaceae, the dilution of black cumin oil with lower-cost vegetable oils, or the adulteration of cranberry extracts with proanthocyanin-rich materials from grape (*Vitis vinifera*) seed or peanut (*Arachis hypogaea*) skin.

Keywords

Adulteration · cancer prevention · dietary supplement · black cumin · broccoli · cranberry · pomegranate · turmeric



PL-6

4',5,7-trihydroxyflavone as a Dietary Phytocompound with Anti-cancer Potential. *An In vitro-in ovo* Approach

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Abstract

Background and Aims: The 4',5,7-trihydroxyflavone (apigenin), is a dietary phytocompound that can be found in significant amounts in *Matricaria chamomilla* L., *Petroselinum crispum* L., *Apium graveolens* L., *Rosmarinus officinalis* L., *Camelia sinensis* L., *Origanum vulgare* L. It is characterized by a variety of pharmacological properties, among which can be mentioned: anti-inflammatory, antioxidant, hypotensive, antiviral, antibacterial, antiproliferative, pro-apoptotic effects.

Methods: Using *in vitro* (MTT, flow cytometry for cell cycle assessment, scratch assay, caspase 3 detection, Annexin V-PI, LDH)-*in ovo* (angiogenesis-CAM) assays.

Results: The present study describes this compound as an active molecule against A375 human melanoma cell line in the selected dose range [0.3- 60 μM] with 30 μM and 60 μM being the doses with significant results. On the other hand apigenin did not play a significant role in stimulating the development and expansion of dendritic cells, not being involved in the activation of the immune system.

Conclusion: These correlations suggest that this dietary flavone represent a candidate for *in vivo* evaluations of anti-melanoma phytocompounds.

Keywords 4',5,7-trihydroxyflavone · apigenin · melanoma · *in vitro* · *in ovo* · dendritic cells



PL-7

Application of Propolis on Cancer Intervention from Cell to Human

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Abstract

Background and Aims: Inflammation is very critical for many diseases. Natural food resources and dietary intake can greatly improve the inflammation and terminate the advanced disease development. Phytochemicals from daily vegetables, fruits and foods are found to suppress the inflammation by specific pathway. Propolis is obtained from bees' nest and contains thousands of phytochemicals. Propolis extracts were used to evaluate the bioactivities and its effect on cancer intervention.

Methods: Cell models, animal model and human clinical trial were used to confirm its real application and effect.

Results: Results clearly show that, propolis extracts greatly inhibit the inflammation through NFκ-B in cell and animal models. Intervention in oral submucous fibrosis, leukoplakia and oral carcinoma patients strongly showed propolis extract improve the inflammation, syndrome and reduce tumor size. Caffeic acid phenethyl ester (CAPE) was the major contributor for antiinflammation. CAPE dose-dependently inhibited IFN-γ-induced Try701 and Ser 727 phosphorylation in STAT1. It was also observed that CAPE inhibited promoter activity of IP-10 gene and the secretion of IP-10 protein. CAPE has very poor bioavailability and stability, its modified similar compound K36 were also found positive effect on neurodegeneration.

Conclusion: Propolis shows great potential for different diseases and cancers.

Keywords

Propolis · NFκ-B · CAPE · STAT1 · K36



PL-8

Translating Precision Cancer Medicine: Integrating Phytochemicals and lncRNome Analysis for Targeted Therapies

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Abstract

Recent breakthroughs in genomics and cancer genome have revealed the pivotal role of long non-coding RNAs (lncRNAs) in oncogenesis and oncometabolism. lncRNAs, a diverse group of transcripts, are instrumental in dictating cell fate through a myriad of molecular pathways, making them an attractive subject in cancer biology. This talk aims to illuminate the modulation of lncRNAs by natural chemopreventive agents and elucidate the intertwined roles of lncRNAs in cancer progression and therapy. Utilizing ovarian cancer cells as a model system, our investigations have centered on the impact of several phytochemicals – Thymoquinone, Sulforaphane, Broccoli Sprout Extract, Resveratrol, and Curcumin – on the lncRNA landscape. We observed a consistent trend of upregulation of tumor-suppressive lncRNAs such as PTCSC3 and downregulation of oncogenic lncRNAs like PCAT1. These findings suggest a beneficial reshaping of the lncRNA profile in treated cancer cells, favoring the suppression of tumorigenic pathways. This talk will address the molecular targets of these lncRNAs and their interactions, highlighting the therapeutic potential of these natural agents. By integrating conventional and complementary medicine, this research opens new avenues for innovative cancer prevention and therapy strategies. Additionally, we will explore the broader implications of lncRNome analysis in precision cancer medicine, emphasizing its crucial role in targeted therapies.

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PL-9

Melanoma Therapy: Challenges and Options

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Abstract

Incidence of melanoma, a type of skin cancer is on the rise in Turkey requiring attention. Melanoma harboring BRAF mutations frequently develop resistance to BRAF inhibitors, limiting the impact of treatment. Our results established the mechanism of resistance and subsequently identified a suitable drug combination to overcome the resistance. Single treatment of BRAF mutant melanoma cell lines with vemurafenib or dabrafenib (BRAF inhibitors) alone or in combination with trametinib (MEK1/2 inhibitor) resulted in overexpression of Mcl-1. Overexpression of Mcl-1 in A375 and SK-MEL-28 by transfection completely blocked BRAF and MEK1/2 inhibitor-mediated inhibition of cell survival and apoptosis. Melanoma cells resistant to BRAF inhibitors showed massive expression of Mcl-1 as compared to respective sensitive cell lines. Silencing of Mcl-1 using siRNA completely sensitized resistant melanoma cells to growth suppression and induction of apoptosis by BRAF inhibitors. In vivo, vemurafenib resistant A375 xenografts implanted in athymic nude mice showed substantial tumor growth inhibition when treated with a combination of vemurafenib and Mcl-1 inhibitor or siRNA. Immunohistochemistry and western blot analyses demonstrated enhanced expression of Mcl-1 and activation of ERK1/2 in vemurafenib-resistant tumors whereas level of Mcl-1 or p-ERK1/2 was diminished in the tumors of mice treated with either of the combination. Biopsied tumors from the patients treated with or resistant to BRAF inhibitors revealed overexpression of Mcl-1. Interestingly, piperlongumine, a black pepper compound significantly inhibited the growth of BRAF-inhibitor resistant cell lines as well as tumor growth in vivo by inhibiting Mcl-1 and its upstream regulator STAT-3.

Keywords

Melanoma · BRAF mutation · BRAF inhibitors · Mcl-1



PL-10

Marine Natural Products as an Immense Bioresource in the Search for New Anticancer Drugs

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Abstract

Marine natural products (MNPs) have emerged as a prolific source of bioactive compounds with significant potential in anticancer drug discovery. The unique and diverse marine environment offers a vast array of chemical entities with novel mechanisms of action, providing promising candidates for the development of new anticancer therapies. Recent research has highlighted a marked number of marine-derived compounds that exhibit potent anticancer activities through various mechanisms, including apoptosis induction, cell cycle arrest, angiogenesis inhibition, and disruption of cancer cell signaling pathways. Key examples include compounds such as trabectedin, a marine-derived alkaloid approved for the treatment of soft tissue sarcoma and ovarian cancer, and eribulin, a synthetic analog of a marine sponge natural product used in metastatic breast cancer therapy. The structural diversity and unique bioactivities of MNPs offer advantages over traditional chemotherapeutic agents, including reduced toxicity and the ability to overcome multidrug resistance in cancer cells. Additionally, advancements in marine biotechnology and synthesis techniques have facilitated the large-scale production and modification of these compounds, enhancing their clinical applicability. However, challenges remain in the sustainable extraction, supply, and comprehensive understanding of the pharmacokinetics and pharmacodynamics of MNPs. Further research and interdisciplinary collaboration are essential to fully harness the potential of MNPs in oncology. This talk will highlight anticancer drugs and highly promising molecules derived from marine organisms that have entered the clinic.

Keywords

marine natural products · anticancer · marine organisms



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Oral Presentations

OP-1

Withanolide Analogs Inhibit Multiple Myeloma Cell Proliferation Through Multiple Signaling Pathways

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Abstract

Background and Aims: Multiple myeloma is a hematological cancer originating from the bone marrow in which plasma cells abnormally proliferate, and it accounts for around 1% of cancer-related deaths worldwide. Despite the availability of a wide range of drugs, current multiple myeloma treatments display side effects, and drug resistance often appear.

Methods: Structure-activity relationship studies led to the identification of withanolides having an antiproliferative activity with IC₅₀ values around 20 nM against sensitive and bortezomib-resistant multiple myeloma cells, as well as other hematological cancer cell lines. Moreover, the selectivity index towards normal cells of one of the most active compounds was much more favorable than bortezomib, a proteasome inhibitor used in the clinics, and it displayed synergy when combined with dexamethasone and selinexor, two other drugs used in the clinics. Genomic and proteomic approaches were used to determine the genes and proteins involved in the mechanism of action of those compounds.

Results: Autophagy, a process that cells adopt to survive in unfavorable conditions by degrading and recycling non-essential proteins, as well as angiogenesis, were shown to be some of the involved pathway.

Conclusion: Therefore, these compounds should be further evaluated alone or in combination in preclinical multiple myeloma models.

Keywords angiogenesis · autophagy · hematological cancers · withanolides



OP-2

Combating Antimicrobial Resistance: Leveraging Surface-Enhanced Raman Spectroscopy and Machine Learning for Classification of *Staphylococcus aureus* Isolates

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Abstract

Background and Aims: The escalating threat of antimicrobial resistance (AMR) is a pressing concern in global health, with an estimated 700,000 deaths annually and projections of exceeding 10 million by 2050 if left unchecked. *Staphylococcus aureus*, a prevalent pathogen, exhibits concerning levels of AMR, particularly in multidrug-resistant strains. To tackle this issue, we employ Surface-Enhanced Raman Spectroscopy (SERS) in conjunction with machine learning techniques.

Methods: Our study focuses on four distinct *S. aureus* isolates, representing varying levels of antimicrobial resistance/susceptibility: Methicillin-resistant (MRSA), Clindamycin-resistant (CRSA), Erythromycin-resistant (ERSA), and susceptible (SSA) strains. SERS facilitates the identification of unique chemical profiles for each isolate.

Results: Through the utilization of diverse machine learning algorithms such as Random Forest, Support Vector Machine (SVM), k-Nearest Neighbors (kNN), Naive Bayes, Decision Tree, and Logistic Regression, we achieve an outstanding classification accuracy of 96.5%, notably with the kNN algorithm. Our research underscores the urgent necessity for innovative strategies like SERS and machine learning in combating AMR. Comprehensive understanding of resistance mechanisms is essential for optimizing treatment regimens and infection control measures.

Conclusion: This investigation provides valuable insights into addressing the multifaceted challenges posed by AMR and its profound implications for public health.

Keywords

Antimicrobial Resistance · Surface-enhanced Raman spectroscopy · Machine Learnings · *S. aureus* · Nanotechnology



OP-3

Digigrandifloroside: A Cardioactive Glycoside with Potential Cytotoxic Activity and Assessment of the Role of Apoptosis via Caspase3/7 Activity

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Abstract

Background and Aims: Cardioactive glycosides (CGs), compounds with similar chemical structures and pharmacological activity, have been used mainly for their positive inotropic effects. However, recent studies on CGs showed their antitumor potential in several cancers. Digigrandifloroside, a CG, was first reported from *Digitalis grandiflora* Miller.

Methods: In this study, cytotoxicity of digigrandifloroside was tested against MCF-7 (human breast carcinoma), HeLa (human cervix epithelial carcinoma) cancer cells and L929 (mouse fibroblast) non-cancerous cell by MTT method (concentrations of 0.1-10 μ M). Lanatoside A-C (CGs from *Digitalis*), and digitonin (a saponin from *Digitalis*) were also tested in the study for comparison with digigrandifloroside.

Results: IC₅₀ values for digigrandifloroside for MCF-7 and HeLa cells were found as <100 nM and 252.1 nM, respectively. To determine the role of apoptosis via caspase 3 and 7, Caspase-Glo 3/7 test was used. Digigrandifloroside at 100 nM increased enzyme levels, 1.29 and 2.35fold, compared to the control cells for MCF-7 and HeLa cells, respectively.

Conclusion: These findings suggest the role of apoptosis in cytotoxicity. Digitonin, a steroidal saponin, showed relatively lower cytotoxicity when compared to CGs on both cancer cells but showed higher cytotoxicity on L929 cells. The selectivity of CGs' cytotoxicity between cancer and non-cancerous cells is important for future studies on these compounds.

Keywords

cardioactive glycosides · *Digitalis* · cytotoxicity · MCF-7 · HeLa



OP-4

Investigation of Anti-inflammatory and Anticancer Properties of *Trachystemon orientalis* L. Extract

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Abstract

Background and Aims: Recently, there's a growing interest in exploring natural compounds, particularly phytochemicals sourced from commonly consumed plants, as promising candidates for cancer treatment. One such plant under scrutiny is *Trachystemon orientalis* (L.), a member of the Boraginaceae family. This plant, indigenous to damp areas along the northern coast of our country, harbors compounds of interest that have captured the attention of researchers.

Methods: This study focuses on investigating the anti-inflammatory properties of *Trachystemon orientalis*, as well as its potential impact on cell proliferation and survival in colon cancer cells. The anti-inflammatory efficacy of the extract was evaluated via a COX inhibition assay, while cell viability and proliferation in colon cancer cell lines were determined using MTT assays and trypan blue staining following exposure to varied concentrations of the extract.

Results: Remarkably, the extract exhibited notable *in vitro* antioxidant and anti-inflammatory properties (%35.5 COX-1 and %49,5 COX-2 inhibition for 10 mg/ml extract) with rosmarinic acid identified as the principal phenolic compound (10.3 mg/g extract) employing UHPLC analysis. Encouragingly, preliminary findings indicate the extract's statistically significant inhibitory effect on the HT29 cell line with the growth inhibitory effect (IC₅₀) values obtained for 10.42 mg/ml extract.

Conclusion: In conclusion, this study demonstrated the anti-inflammatory, antioxidant, and anti-proliferative properties of this extract, highlighting its significance in the pursuit of novel treatments for colon cancer.

Keywords

anticancer · antioxidant · *Trachystemon orientalis* · anti-inflammatory · colon cancer



OP-5

Antiproliferative Effect of Bitter Melon (*Momordica charantia*) Seed and Fruit Extract Through Non-Genomic Estrogen-Sensitive Endometrium Cancer Cells

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Abstract

Background and Aims: Due to its phytopharmaceutical content and anti-cancer qualities, *Momordica charantia* has attracted a lot of interest as a supplementary medicine in recent years.

Methods: The findings of this investigation demonstrate that *Momordica charantia* seed (McSE) and fruit (McFE) extracts block both the non-genomic estrogen receptor signaling pathway and the migration and proliferation of RL 95-2 cells.

Results: McSE and McFE blocked cell growth with an IC₅₀ value of 134,8 µg/mL and 165,9 µg/mL respectively. A short-term (15 min) administration of a small amount of 17-β-estradiol (1 nM) boosted the activation of the non-genomic signaling kinases P38MAPK, ERK1/2, and AKT, as well as caspase-9. Treatment with McSE (50 and 100 µg/mL) and McFE (75 and 150 µg/mL) significantly reduced the activation of P38MAPK, ERK1/2 and AKT and the phosphorylation of caspase-9. Further, treatment with McSE and McFE caused a significant reduction in relative closure of scratch in cell migration assay.

Conclusion: According to our research, *Momordica charantia* seeds and fruits contain a bioactive component or compounds that have the ability to kill endometrial carcinoma cells by inhibiting non-genomic estrogen receptor signaling pathway kinases. This suggests that the fruit and seeds could be a potential source of anticancer medications.

Keywords

endometrium cancer · non-genomic estrogen signaling pathway · caspase-9 · *Momordica charantia* · 17-β-estradiol.



OP-6

Cytotoxic Activity of *Cousinia birandiana* Hub.-Mor. Extract and Fractions Against Several Cancer Cell Lines

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Abstract

Background and Aims: *Cousinia birandiana* is one of the species of the *Cousinia* genus from the Asteraceae family. This species is endemic to Turkey and there are few studies on the pharmacological effects and phytochemical content.

Methods: In the current study, the 70% ethanol extract and n-hexane, ethyl acetate, n-butanol, and water fractions from this plant were investigated for their cytotoxic activity against DU-145 (human brain metastatic prostate cancer), HeLa (human cervix cancer) and MCF-7 (human estrogen positive breast cancer) cell lines by the MTT method after 24 h of treatment. In this study, cisplatin was used as a positive control, which has been widely used in the treatment of a range of cancers.

Results: According to the results, all the tested extracts showed cytotoxicity in a dose-dependent manner. However, the ethyl acetate fraction was found to be the most active with $78.86 \pm 1.896 \mu\text{g/mL}$, $78.02 \pm 2.173 \mu\text{g/mL}$, and $44.28 \pm 3.31 \mu\text{g/mL}$ IC_{50} values against DU-145, HeLa, and MCF-7 cell lines, respectively.

Conclusion: In conclusion, it is the first cytotoxic activity study with *C. birandiana* species, and our future studies will focus on cytotoxicity tests on other cancerous and healthy cell lines.

Keywords Asteraceae · DU-145 · HeLa · MCF-7



OP-7

Empagliflozin Demonstrates Cytotoxicity and Synergy with Tamoxifen in ER-Positive Breast Cancer Cells: Anti-proliferative and Anti-survival Effects

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Abstract

Background and Aims: Accumulating evidence suggest that the inhibitors of SGLT2 may have efficacy in eliminating tumor cells. While empagliflozin exhibits nearly the highest selectivity for SGLT2 over SGLT1, its specific impact alone and in combination with tamoxifen remains largely unexplored in ER α + breast cancer.

Methods: This study investigates the anticancer effects of empagliflozin and its potential synergy with tamoxifen in MCF-7 breast cancer cells. The individual and the combined cytotoxic effects of empagliflozin and tamoxifen were assessed using the xCELLigence system. The activities of AMPK α , p38 MAPK α , p70S6K1, and Akt were assessed using Western blotting. The gene expression levels of PGC-1 α and FOXO3a were assessed via qPCR.

Results: Our results reveal time and concentration-dependent cytotoxic effects of empagliflozin and tamoxifen whether administered separately or in combination. While tamoxifen exhibits potency with an IC₅₀ value of 17 μ M, approximately ten times higher than that of empagliflozin (IC₅₀ = 177 μ M), synergistic effects are observed when their concentrations approach their respective IC₅₀ values. Additionally, empagliflozin significantly increases AMPK α activity while concurrently inhibiting Akt, p70S6K1, and p38 MAPK α , and these effects are significantly enhanced when empagliflozin is combined with tamoxifen. Moreover, empagliflozin modulates gene expression, downregulating PGC-1 α while upregulating FOXO3a. In conclusion, empagliflozin exerts anti-proliferative and anti-survival effects by inhibiting mTOR, Akt, and PGC-1 α , and it exhibits synergy with tamoxifen in MCF-7 breast cancer cells.

Conclusion: This study sets the stage for further exploration of empagliflozin's anticancer potential in ER α + breast cancer.

Keywords

Empagliflozin · ER α + breast cancer · FOXO3a · PGC-1 α · Akt · p70S6K1



OP-8

Enhancing Ovarian Cancer Treatment: Advanced Drug Delivery Systems for Hydrophobic Drugs

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Abstract

Background and Aims: Ovarian cancer is a common, deadly cancer type among women globally. Chemotherapy is a primary treatment option, but its agents often suffer from low water solubility and eventual resistance and lack of target specificity. In our study, we synthesized various hydrophobic drugs with chemotherapeutic properties and assessed their anti-cancer effects on ovarian cancer cells using gold nanoparticles (GNPs) for delivery. The poor water solubility of these drug candidates complicates efficacy assessment and necessitates high dosages. We developed a drug delivery system to improve their bioavailability.

Methods: We synthesized GNPs and characterized them using SEM, UV-Vis, DLS. Hydrophobic drugs were bonded to GNPs covalently, and their stability and properties were analyzed. These complexes' cytotoxicity and anti-cancer efficacy were tested on ovarian cancer cells, including assessments of cell cycle and apoptosis.

Results: The complexes improved water solubility, distribution over free drugs, showed enhanced anti-cancer activity, and remained stable for three months. The solubility increase correlated with stronger cytotoxic effects and reduced dosage needs. A marked increase in apoptosis was noted in treated cells.

Conclusion: Hydrophobic drug-GNP complexes were more effective than free drugs, with covalent bonding to GNPs significantly enhancing drug bioavailability. This approach could potentially improve cancer treatment outcomes.

Keywords gold nanoparticles · ovarian cancer · hydrophobic drugs



OP-9

Characterization and Evaluation of *In-Vitro* Nanotoxicological Effect of Green Synthesized Gold Nanoparticles

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Abstract

Background and Aims: Since biosynthesis of nanoparticles using plant extract has become incredibly popular as a simple and environmentally friendly alternative to chemical and physical methods for synthesizing nanoparticles.

Methods: In this study, easy and green synthesis of gold nanoparticles (AuNP) using plant aqueous extract was achieved. Within the scope of this study, low-cost green synthesis of AuNPs was carried out by using the aqueous extract of ginger rhizome as a reducing and stabilizing agent, characterization studies of these synthesized nanoparticles were carried out, and in the last stage of the study, the cytotoxic effect of the nanoparticles was evaluated on both normal fibroblast and breast cancer cell lines by MTT assay.

Results: According to characterization studies, the hydrodynamic size of green synthesized gold nanoparticles (GS-AuNPs) was 83 nm, and the surface plasmon resonance absorption peak was 520 nm. The morphology of GS-AuNPs was identified by SEM. The cytotoxic effect of GS-AuNPs on cancer cells was also examined within the scope of this study.

Conclusion: It was concluded that nanoparticles had cytotoxic effects on both normal healthy and cancerous cell lines. As a result, it was concluded that GS-AuNPs have a high potential to be used especially in cancer therapy, in terms of their characteristics and functionality.

Keywords

Gold Nanoparticle · Green Synthesis · Breast Cancer



OP-10

Isolation of Actinobacteria from Coastal Ecosystems of İzmir and Their Cytotoxic Activities

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Abstract

Background and Aims: Microorganisms, with their distinct secondary metabolites exhibiting a variety of bioactivities, are valuable for new drug discovery. Around 45% of the bioactive compounds derived from microorganisms come from actinobacteria. While actinobacteria are predominantly found in terrestrial environments, the challenging conditions of marine environments—such as high salinity, and limited nutrients—could enhance the diversity of their secondary metabolites.

Methods: Driven by this possibility, we initiated a study to isolate actinobacteria from coastal sediments and explored the anticancer potential of their secondary metabolites. We collected sediment samples from seven different locations in Çeşme and Karaburun Peninsula in İzmir. In total, 975 actinobacteria were isolated and cultured, and their fermentation broths were extracted with ethyl acetate. Subsequently, these extracts were evaluated in MCF-7 and A549 cancer cell lines for their cytotoxicity.

Results: Extracts demonstrating IC₅₀ values below 32 µg/mL were categorized as bioactive. The screenings afforded 108 and 97 extracts with cytotoxicity against A549 and MCF-7 cell lines, respectively. The most active extracts were further analyzed for synergistic effects when combined with cisplatin in treating cisplatin-resistant A549 cancer cells.

Conclusion: In continuation, we will select two microbial isolates for bioassay-guided isolation studies based on dereplication data and synergism profiles in resistant cancers.

Keywords Actinobacteria · Cancer · Drug resistance



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Poster Presentations

PP-01

In Silico Studies Concerning Cytotoxic Potential of Some Bioactive Compounds Present in *Asphodeline lutea* Root Extracts

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Abstract

Background and Aims: Roots of *Asphodeline lutea* Rchb. (Asphodelaceae) are traditionally consumed in the Mediterranean diet. The methanol root extracts of *A. lutea* have been proved to possess cytotoxic activity against MCF-7 and MCF-10A cell lines. The present investigation aimed to determine the physicochemical, pharmacokinetic properties and probable cytotoxic effect of some bioactive components isolated from *A. lutea* roots using *in silico* methods.

Methods: The ADMET profiles were determined via freely available SwissADME server. The anti-cancer activities were predicted by online server CLC-Pred.

Results: Chrysophanol, helminthosporin, asphodelin and 10, 7'-bichrysophanol expected to manifest a strong cytotoxic effect against cisplatin-resistant ovarian carcinoma (A2780cisR) cell line with probability for being an active compound (Pa) = 0.912, 0.911, 0.888, 0.885 respectively. They exerted a strong to modest cytotoxic effect against non-small cell lung carcinoma (HOP-18), clear cell renal cell carcinoma (RCC4) and melanoma (M19-MEL) with Pa = 0.726, 0.724, 0.649 and 0.678 for HOP-18 cell line; Pa = 0.58, 0.594, 0.475 and 0.426 for RCC4 cell line; 0.581, 0.592, 0.564 and 0.598 for M19-MEL cell line. 1,5,8-Trihydroxy-3-methylantraquinone exhibited modest action against gastrointestinal stromal tumor (GIST430) cell line, while 10, 7'-bichrysophanol had moderate activity against ovarian carcinoma (A2780) and pancreatic adenocarcinoma (SW1990) cell lines.

Conclusion: Our findings justify further studies of *A. lutea* plant extracts and their main compounds *in vitro* and *in vivo* and highlighted them as a potential anticancer agent

Keywords Asphodeline lutea · cytotoxicity · *in silico*

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PP-02

Evaluation of Antiproliferative Effect of Bitter Melon (*Momordica charantia*) Seed Extract Through Non-Genomic Estrogen Receptor Pathway In Breast Cancer

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Abstract

Background and Aims: Because of its high nutritional value and anti-cancer features, *Momordica charantia* has gained a lot of interest as a supplementary medicine in recent years.

Methods: *Momordica charantia* seed extract (McSE) blocked cell growth and 17- β -Estradiol (E2)-induced cell migration with an Half-maximal inhibitory concentration (IC₅₀) value of 242.2 μ g/mL. The non-genomic signaling kinases ERK1/2 and PI3K/AKT were increased by a short time (15 min) administration of low concentration E2 (1nM), which led to the activation of caspase-9. Treatment with McSE significantly reduced the activation of ERK1/2 and PI3K/AKT and the phosphorylation of caspase-9.

Results: The results of this study demonstrate that (McSE) inhibits the migration and proliferation of MCF-7 cells, as well as potential mechanisms of action. Further, treatment with McSE caused a significant reduction in relative closure of scratch in cell migration assay.

Conclusion: The study's findings suggest that McSE would be a good place to look for recently identified compounds for use in cancer therapy.

Keywords

Breast cancer · non-genomic estrogen signaling pathway · caspase-9 phosphorilation · *Momordica charantia* · 17- β -estradiol · estrogen receptor.



PP-03

Assessment of Cytotoxic Potential of *Aronia melanocarpa* L. and *Populi gemmae* Extract on A549 and MCF-7 Cell Lines

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Abstract

Background and Aims: Breast and lung cancers are among the most common types of cancer. According to the latest data produced by the International Agency for Research on Cancer, lung cancer is the most commonly diagnosed type of cancer with 12.4% of all cancers worldwide, female breast cancer with 11.6% followed up. *Aronia melanocarpa* L. is a plant belonging to the Rosaceae family and rich in bioactive compounds. *Populus nigra* L., popularly known as the black poplar tree, is a member of the Salicaceae family.

Methods: The aim of this study is to evaluate the antiproliferative effect of extracts obtained from the fruits, respectively from the buds of the above mentioned species, on breast cancer and non-small cell lung cancer cell lines. Frozen and dried methanol (+0.3% HCl) extracts were prepared from *Aronia Melanocarpa* L. fruits, ethanol extracts were prepared from *Populi nigra* L. gemmae in accordance with the extraction methodology. To investigate the cytotoxic potential of these extracts real time xCELLigence system (RTCA) was used. A549 (12500 cells/well) and MCF-7 (5000 cells/well) cells were seeded in E-plate then approximately 24 h postseeding, the cells were treated with the samples at 50, 100 and 200 µM concentrations. Cell viability was observed during 72 h after treatment.

Results: According to the observed results, extracts showed no significant cytotoxic effects for the selected concentrations on both screened cell lines.

Conclusion: Further studies are needed that involve the test of a greater range of concentrations as well as physico-chemical modulations of the selected extracts.

Keywords

Cancer · cytotoxicity · xCELLigence · *Aronia melanocarpa* L. · *Populi gemmae*



PP-04

Exploring Nor-Sapogenins as Potential Androgen Receptor Antagonists in Prostate Cancer Treatment

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Abstract

Background and Aims: Androgen receptor (AR) antagonists play an essential role in the treatment of prostate cancer (PC) as the majority of patients, after hormone deprivation therapy, eventually develop castration-resistant PC (CRPC), which relies on AR activity at low androgen levels. Based on structural similarities to androgens, sapogenins are projected as potential AR modulators. However, there is a limited number of studies focusing on saponin skeletons as AR antagonists.

Methods: Therefore, we aimed to virtually screen our chemical library containing triterpenic sapogenins (Cycloastagenol; CG, Astragenol; AG, 20,27-octanor cycloastragenol; SCG and Cyclocanthogenol; CCG) and their derivatives obtained via semi-synthesis and biotransformation to identify possible AR antagonists.

Results: Our results showed that the side chain extending from the C-17 position of AG, CA, and CCG, abolished the interaction with the ligand binding domain (LBD) of AR, while SCG and its 15 derivatives had stronger binding affinity scores ranging from -100.323 to -112.702 kcal/mol compared to testosterone (-98.048 kcal/mol). Western blotting and qRT-PCR studies proved that the selected seven SCG derivatives significantly decreased PSA protein and mRNA levels between 0.23 and 0.72 fold.

Conclusion: Our data prove that this unique nor-sapogenin framework has the potential to be a lead compound.

Keywords

Androgen Receptor · Sapogenin, Prostate Cancer · Docking



PP-05

Investigation on the Cytotoxic Activity of *Pulicaria dysenterica* (L.) Bernh. Extracts and Fractions Against Triple-negative Breast Cancer

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Abstract

Background and Aims: *Pulicaria* is a genus in the Inulae tribe of Asteraceae family. There are approximately 100 species in the genus which have a distribution from Europe to North Africa and Asia, particularly around the Mediterranean. Many species of the genus have long been used traditionally for their tonic, expectorant, antipyretic, antidiareic, and painkiller effects around the World. Phytochemical studies on *Pulicaria* species have yielded some phenolic acids, flavonoids, and terpenoids, especially sesquiterpenoids and diterpenoids.

Methods: In the current study, the methanol extract and its petroleum ether, chloroform, ethyl acetate and n-butanol fractions and water extract of *Pulicaria dysenterica* (L.) Bernh were investigated for their cytotoxic activity against triple-negative breast cancer cell line, MDA-MB-231 by the MTT method after 24 h of treatment (6.25 -200 µg/mL). In this study, cisplatin was used as a positive control, which has been widely used in the treatment of a range of cancers.

Results: According to the results, all the tested extracts showed cytotoxicity in a dose-dependent manner. However, the chloroform fraction was found to be the most active, with 20.96±0.507 µg/mL IC₅₀ value against MDA-MB-231.

Conclusion: It is the first cytotoxic activity study of *Pulicaria dysenterica* against MDA-MB-231 cell line. Our future studies will be focus on isolation and structure elucidation in order to determine the compounds responsible for the activity.

Keywords Pulicaria · cytotoxicity · MDA-MB-231



PP-06

Investigation of the Effect of Sildenafil, a Phosphodiesterase 5 Inhibitor, Against Penicillin-induced Neurotoxicity in SH-SY5Y Cells

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Abstract

Background and Aims: Phosphodiesterase 5 (PDE5) is a critical component of the cyclic guanosine monophosphate/protein kinase G signaling pathway in neurons. It is thought that PDE5 inhibition may have neuroprotective effects and may soon be potential therapeutic agents.

Methods: In this study, we aimed to investigate the effect of sildenafil, a PDE5 inhibitor, against penicillin-induced neurotoxicity in the SH-SY5Y cell line. After seeding SH-SY5Y cells, various concentrations of penicillin and sildenafil were applied, and at the end of 24 hours, neuronal viability test (MTT) was performed to decide the concentrations of penicillin and sildenafil for the study. The effect of sildenafil (50, 100, 200 μ M) against penicillin (800 μ M)-induced neurotoxicity in SH-SY5Y cells was tested with three different experimental designs (pre-treatment, co-treatment, post-treatment).

Results: Sildenafil showed a neuroprotective effect in the pre-treatment and co-treatment experimental designs, especially in the pre-treatment experimental design.

Conclusion: With this study, we predict that sildenafil may have a neuroprotective effect and can be used in neurodegenerative diseases due to this effect. However, we need further studies to elucidate the mechanisms underlying the neuroprotective effect of sildenafil, and from now on, we will focus on this in our studies.

Keywords

Sildenafil · SH-SY5Y · Phosphodiesterase 5 · Neuroprotective effect



PP-07

Isolation and Structure Determination of Secondary Metabolites from the Fungus *Trichaptum biforme*

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Abstract

Background and Aims: *Trichaptum biforme* is reported as the only cosmopolitan *Trichaptum* species, which is common in the eastern USA, Europe, and Asia. This wood-destroying mushroom was explored more in terms of its chemical profile, however, most of the studies were performed on liquid cultures of *T. biforme*, and little is known about the chemistry and pharmacology of the wild growing fruiting bodies of this species.

Methods: This study aimed to investigate the chloroform fraction of the fruiting body of *T. biforme*. Comprehensive set of isolation and purification was conducted using a normal- and reversed-phase flash chromatography and reversed-phase HPLC. The structure of the isolated compounds was elucidated by spectroscopic methods including LC-MS and NMR.

Results: The mycochemical investigation led to the isolation of six compounds for the first time from this species: hydroxydihydrobovolide, schumannione, sterepinic acid A, 2-furannonanoic acid (2,5-dihydro-2-methoxy-3,4-dimethyl-5-oxo-), trans-4-hydroxy-2-nonenic acid and betulin.

Conclusion: Pharmacological assays, including antiproliferative tests, are planned to explore the potential beneficial bioactivities of the isolated compounds.

Keywords medicinal mushroom · secondary metabolite · isolation · *Trichaptum biforme*



PP-08

Hybrid Membrane Camouflaged Gold Nanoparticles: Golden Arrow for Cancer Treatment

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Abstract

Background and Aims: Cancer ranks as the second leading cause of mortality, following cardiovascular diseases and an estimated 18 million new cases of cancer emerge annually in the world. The surgery is the first action of the solid tumor, but tumor metastasis and recurrence are new problems. In this stage, nanotechnology-based approaches will be a promising solution in cancer treatment.

Methods: For this, we are providing a promising method by coating gold nanoparticles with bacterial cell membrane, outer membrane vesicle, and cancer cell membrane. Bacterial cell membranes can be exploited to enhance specific antitumor reactions by promoting adaptive immune response and cancer cell membranes contain a high proportion of antigenic motifs and are proposed for targeting cancer cells. We aimed to develop hybrid nanoparticles mimic the cancer and bacteria cells for drug delivery or vaccine development in this study. We isolated OMV from *E. Coli DH5 α* , *E. Coli* membrane from *E. Coli BL21*, and CC membrane (B16F10 cell) from melanoma cells by ultracentrifuge. Then we coated gold nanoparticles with membranes by two different methods: sonication and extruder. Characterization of these particles was done by NTA, DLS, and FESEM.

Results: The coating ratios of hybrid nanoparticles were calculated and EM-CM-AuNP was %57 and OMV-CC-AuNP was %47.

Conclusion: As a conclusion, we isolated membranes successfully and coated them on gold nanoparticles. Hybrid membrane-coated gold nanoparticles could be used in cancer drug delivery.

Keywords

Bacteria membrane · Cancer cell membrane · Hybrid Coated Nanoparticles · Cancer Therapy



PP-09

Engineering Smart Nanoparticles for Enhanced CRISPR-Cas9 Gene Delivery and Therapeutic Efficacy in Cancer

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Abstract

Background and Aims: Breast cancer and chordoma, though distinct malignancies, both exhibit MUC1 protein expression, highlighting a potential therapeutic target. Gene therapy, leveraging CRISPR-Cas9 technology via plasmid delivery, offers potential for treating diseases like cancer. This study aims to develop a novel gene therapy approach utilizing CRISPR-Cas9 technology to target MUC1 in both malignancies.

Methods: We designed polymeric nanoparticles incorporating FDA approved β -CD (Hydroxypropyl- β -Cyclodextrin) to facilitate precise gene editing and address delivery challenges. Experimental validation was conducted on cancer cell lines to assess toxicity, complex formation, nuclear entry, and therapeutic efficacy.

Results: Our system demonstrated nontoxic profile, successful complex formation, efficient nuclear entry, and higher apoptosis rates compared to commercial carriers. Therapeutic efficacy against MUC1 protein was confirmed, with synergistic effects observed with imatinib.

Conclusion: This study presents a promising breakthrough in targeted cancer therapy, providing a platform for effective treatment of rare chordoma and triple-negative breast cancer through precise gene editing of MUC1. In vivo studies further support the potential clinical application of this approach.

Keywords chordoma · rare disease · breast cancer · nanobiotechnology · CRISPR/Cas9 · smart nanoparticle

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PP-10

Silene behen L. Methanol and Ethyl Acetate Extract: Investigation of Cytotoxic Effect on MCF7 Cells

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Abstract

Background and Aims: Cancer is a highly lethal and widespread disease worldwide, with over 100 known types affecting the human body. Among these, breast cancer is one of the most diagnosed cancers globally. In the treatment of breast cancer, options such as surgery, radiotherapy, chemotherapy, and hormonal therapy are utilized, either individually or in combination. Chemotherapeutic agents often comprise synthetic and natural substances, with a particular emphasis on herbal materials. Various active groups in herbal materials can exhibit cytotoxic effects, potentially benefiting. In Turkey's flora, there are 10,754 plant species, of which 3,708 are endemic.

Methods: This study investigated the potential cytotoxic effect of *Silene behen* L., a member of the Caryophyllaceae family found in the Turkish flora, on MCF7 human breast cancer cells. The cytotoxic effect of methanol and ethyl acetate extracts of *S. behen* L. on MCF7 cells was assessed using the colorimetric MTT assay.

Results: *S. behen* methanol IC₅₀ value is 181.89 µg/mL whereas *S. behen* ethyl acetate IC₅₀ value is 433.95 µg/mL.

Conclusion: Our results indicated that the cytotoxic activity of the extracts increased with rising concentrations, suggesting that *Silene behen* could be a potential agent in human breast cancer treatment.

Keywords

S. behen L. • MTT • breast cancer • MCF7 • cytotoxic effect



PP-11

Investigation of the Anti-inflammatory Effect of Eggshell Membrane with a Real-time Cell Analyzer

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Abstract

Background and Aims: In this study, the anti-inflammatory effects of eggshell membrane were investigated. Eggshell membrane is used in inflammatory disorders such as hordeolum, popularly known as “dog elbow”, and paronychia. Therefore, it was thought that this natural compound may be effective in diseases in which inflammatory processes are involved.

Methods: Firstly, HEK293 cells were grown in an incubator with 5% CO₂ at 37°C. After reaching the appropriate number of cells, they were seeded with 10,000 cells/well in each well in the special plates of the xCELLigence system, where the impedance difference generated during the adhesion of the cells to the plates is measured in real time via gold-coated circuits. Eggshell membrane was applied at various concentrations (50, 100 and 200 µg/mL) 6 hours after cells were stimulated with LPS (1µg/mL). In addition, the same experiment was repeated in normal cell culture plates and anti-inflammatory activities were evaluated using an ELISA kit on TNF-alpha and IL-1beta.

Results: The results showed that eggshell membrane significantly reduced the levels of TNF-alpha in particular compared to the LPS group.

Conclusion: This is the first study to demonstrate the anti-inflammatory potential of eggshell membrane.

Keywords

Eggshell Membrane · HEK293 · LPS · TNF-alpha · IL-1Beta · xCeLLigence · ELISA



PP-12

Design and Development of siRNA-Loaded Liposomes for Glioblastoma Therapy

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Abstract

Background and Aims: Glioblastoma multiforme (GBM) is an aggressive brain cancer that significantly impacts patient survival and quality of life. Despite medical advances, GBM's rapid progression and poor prognosis remain major challenges. Temozolomide (TMZ), the standard chemotherapy for GBM, has limited efficacy. While apoptosis is a key therapeutic target, recent research suggests autophagy could be a viable alternative. Autophagy's role in cancer is complex; it can promote tumor growth and drug resistance, including resistance to TMZ. This study aimed to enhance TMZ sensitivity in GBM cells by using liposomes to deliver LC3 siRNA to suppress autophagy.

Methods: DOTAP liposomes were prepared via thin-film hydration, with evaluations of siRNA loading, size, shape, and surface charge. Cellular uptake, cytotoxicity, LC3 suppression, and combined efficacy with TMZ were assessed in U87 MG and CT2A cell lines.

Results: The DOTAP liposomes, approximately 155 nm in diameter, had zeta potentials of 30 mV (empty) and 15 mV (loaded). Results showed that LC3 siRNA-loaded liposomes improved therapeutic efficacy compared to free TMZ.

Conclusion: In conclusion, the liposomes effectively delivered siRNA into GBM cells, protected it from degradation, and inhibited LC3 protein, enhancing the effect of TMZ. Further in vivo studies are underway to validate these findings.

Keywords Lipozom • GBM • LC3 si RNA



PP-13

Label-free Exosome Analysis via SERS and Machine Learning for the Detection of Acute Leukemia

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Abstract

Background and Aims: Liquid biopsy is a revolutionary non-invasive technique for early cancer diagnosis and monitoring through the analysis of biomarkers in bodily fluids such as blood, urine, and saliva. Exosomes, small extracellular vesicles secreted by various cell types, carry diverse nucleic acids, proteins, and lipids that reflect their parent cells' molecular properties. These exosomes are present in bodily fluids and hold promise for early cancer detection, disease monitoring, and therapeutic response assessment. Surface-enhanced Raman spectroscopy (SERS) enhances Raman signals via plasmonic nanostructures, offering improved sensitivity and specificity in exosome analysis.

Methods: In this study, exosomes were isolated from the serum of patients with acute leukemia (AL) and healthy individuals and collected SERS spectra using an AuNPs-based SERS substrate.

Results: Unique spectral profiles of exosomes were defined to discriminate between groups, and machine learning algorithms were employed for classification. In the peaks around 682, 887, 1001, 1075, 1157, and 1531 cm⁻¹ assigned to proteins, lipids, and nucleic acids were observed slight differences in spectra of AL and healthy exosomes. Furthermore, the groups were classified by machine learning algorithms including RF, kNN, and SVM.

Conclusion: Consequently, SERS and machine learning provide a rapid, low-cost, and promising tool for the detection of exosomes related to acute leukemia.

Keywords exosomes • acute leukemia • Surface-enhanced Raman Spectroscopy • artificial intelligence



PP-14

Utilizing 'Smart' Nanoparticles for miRNA Delivery in Breast Cancer Therapy

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Abstract

Background and Aims: Breast cancer is an important health problem worldwide, accounting for 30% of all female cancer cases and 15% of cancer-related deaths in women. MicroRNAs (miRNAs) have emerged as potential therapeutic agents for cancer treatment due to their ability to regulate gene expression. MiRNA has been implicated in breast cancer progression and metastasis. However, efficient delivery of miRNA to breast cancer cells remains a challenge

Methods: We develop β -CD-based nanocarriers to encapsulate and deliver miRNA to breast cancer cells. The nanocarriers are designed to protect miRNA from degradation and facilitate its efficient cellular uptake. Experimental validation was performed on cancer cell lines to evaluate toxicity, formation of complexes, entry into the cytoplasm, and therapeutic effectiveness.

Results: Our system showed non-toxicity, successful complex formation, and efficient endosomal escape.

Conclusion: This study offers a platform for the successful treatment of triple negative breast cancer and represents a promising development in targeted cancer therapy.

Keywords

Breast cancer · miRNA · Gene delivery · Gene therapy · Nanomedicine · Nanoparticles



PP-15

Apitherapy Offers a Novel Strategy for Treating TNBC: Enhanced Delivery and Efficacy of Melittin in Triple-negative Breast Cancer Cells Through Polymeric Micelles

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Abstract

Background and Aims: Current treatments for triple-negative breast cancer (TNBC) present significant challenges due to their high toxicity, potential for drug resistance, and risk of metastasis. Apitherapy, utilizing honeybee venom's melittin, has potential for treating TNBC, but its effectiveness is hindered by toxicity and bioavailability issues. To improve the therapeutic effect of melittin, we have developed polymeric micelles that are specifically designed to carry the drug to cancer cells.

Methods: In this study, we utilized RAFT polymerization to synthesize a negatively charged copolymer SPMA-co-PMMA, which was then employed to create micelles for delivering melittin. The study evaluated the binding efficiency of these complexes and their impact on cell viability.

Results: According to our Dynamic Light Scattering (DLS) and ζ -potential measurements, the size of our nanoparticles increased slightly from 164.6 \pm 9.7 nm to 172.5 \pm 13.9 nm. Additionally, the charge of the particles increased from -43.3 \pm 2 mV to -23.2 \pm 1.7 mV. The binding efficiency of melittin was found 64.1 \pm 3%. When using MLT@NPs, cell viability in TNBC cells remained above 95% even at concentrations (15 μ g/mL) exceeding melittin's IC50 value (5.2 μ g/mL) after 48 hours.

Conclusion: Micelles' size and surface charge changes after melittin binding indicate successful melittin integration and cell viability data confirm effective delivery of melittin to cells.

Keywords TNBC · Melittin · Drug resistance · Micelles.



PP-16

Drug Delivery to Breast Cancer Cells Using Dopamine-Conjugated Polymeric Micelles

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Abstract

Background and Aims: Breast cancer poses a widespread and aggressive health challenge, necessitating innovative therapeutic approaches. Polymeric micelles offer a promising avenue to enhance drug delivery efficiency while minimizing undesired systemic effects

Methods: To achieve precise targeting of breast cancer cells, we synthesized dopamine-conjugated polymeric micelles (DCPMs) through reversible addition-fragmentation chain transfer (RAFT) polymerization. These DCPMs feature a hydrophobic core consisting of the biocompatible poly (methyl methacrylate) (PMMA) and a hydrophilic shell composed of a statistical copolymer of biocompatible oligo(ethylene glycol)-methacrylate (OEGMA) and a dichloromaleimide functional monomer (DCMMA). Furthermore, the well-established breast cancer chemotherapy drug, doxorubicin, was efficiently loaded into the DCPMs using the nanoprecipitation method. The loading efficiency was precisely assessed and confirmed through UV absorption spectroscopy (UV abs).

Results: These DCPMs demonstrated excellent stability and monodispersity, positioning them as promising candidates for effective drug delivery. Notably, their significant cellular uptake efficiency emphasizes their potential as a platform for targeted doxorubicin delivery, aiming to enhance breast cancer treatment effectiveness.

Conclusion: This study underscores the role of dopamine-conjugated polymeric micelles as a potential strategy for targeted doxorubicin delivery, offering a solution to the challenge of non-specific drug release and contributing to the advancement of more efficient breast cancer therapies.

Keywords

Reversible Addition-Fragmentation Chain Transfer Polymerization (RAFT) · Polymeric Nanoparticles · Active Targeting · Dopamine · Doxorubicin · Breast Cancer



PP-17

Easyvolt: Cost-effective Piezoelectric-Driven Electroporation Device for Enhanced Accessibility and Efficiency

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Abstract

Background and Aims: Biomedical engineering is witnessing a surge in the need for novel technology that can enhance accessibility and efficiency in various medical procedures. One such technology is the innovative piezoelectric-driven electroporation device, which has demonstrated remarkable promise in increasing the delivery of therapeutic substances into cells for diverse biomedical purposes.

Methods: In response to the limitations of existing electroporation devices, we describe a new alternative utilising piezoelectric-based technology. Our product solves issues of cost, size, and accessibility by adopting a compact design and straightforward operation, offering clear advantages over existing devices. The device is designed to be user-friendly, with a single push button to complete all operations, instilling confidence in its practicality. Utilising piezoelectric material as a high-voltage pulse generator, we have constructed a 3D model capable of incorporating both commercial electroporation cuvettes and the piezoelectric system.

Results: Through experiments, our system reliably creates high-voltage pulses, as evidenced by oscilloscope readings of roughly 5 kV for exponential decaying pulses. Application of these pulses to *E.coli* bacteria for MUC1 plasmid transfection resulted in successful colony growth on antibiotic agar.

Conclusion: This innovative approach shows promising developments in electroporation technology, providing a user-friendly, cost-effective, and efficient tool for genetic transformation experiments, with the aim to function similarly to existing devices.

Keywords Electroporation · piezoelectric · *E.coli*



PP-18

One pot fabrication of Size / Shape-Controlled Mesoporous Silica Nano-Spheres for Drug Release Systems

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Abstract

Background and Aims: Silica nanospheres have a wide range of applications due to their easy synthesis and unique properties such as high surface/volume ratio, tunable pore size, high stability, adsorption capacity, and biocompatibility. In materials science, it is used as a surface coating template with its water-repellent properties, in energy to increase the efficiency of solar cells, and in cosmetics to provide dullness to the skin in skin products. In pharmacy, it is used as a controlled drug delivery system. Nanoparticle-based materials offer several advantages over free and unformulated drugs. Mesoporous silica nanoparticles (MSNs) as nanosized porous silica carriers provide more sustained and controlled drug release or enhanced oral bioavailability.

Methods: The study is based on the synthesis and characterization of mesoporous silica nanospheres (MSNs) for drug delivery. Highly porous nanospheres with a high surface/volume ratio were obtained using the method of Preparation of Seed Particles and Seed Particle Growth. The comprehensive characterization of our nanospheres was carried out using the following methods: SEM, STEM, EDX, XRD, DLS, and FT-IR.

Results: Our analysis highlights the potential of MSNs in providing sustained and controlled drug release, enhancing bioavailability.

Conclusion: In conclusion, the synthesis and characterization of mesoporous silica nanospheres demonstrate their significant potential in drug delivery systems by offering sustained and controlled release, as well as enhanced bioavailability.

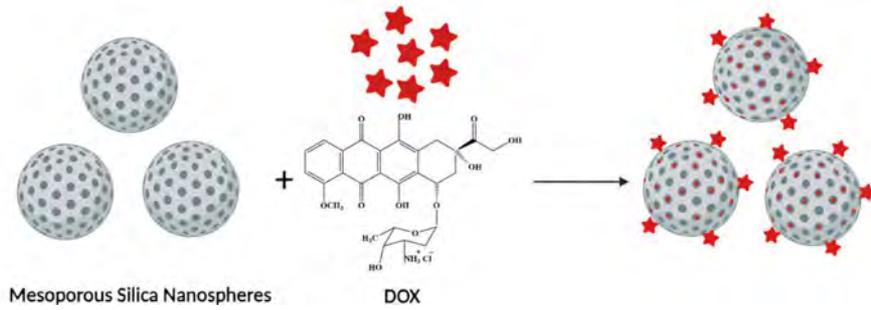


Figure 1: The covalent bonding of DOX molecules with MSNs

Keywords

Meso-porous Silica Nano-Spheres • Doxorubicin • Drug release



PP-19

Innovative Approach: The Controlled Drug Release of Cu Metal-Phosphate Organic Frameworks

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Abstract

Background and Aims: The porous structure, biocompatibility, biodegradability, and high drug-loading capacity of metal-organic frameworks (MOFs) have made them suitable potential candidates for drug delivery systems. In drug delivery systems, the implementation of drug release is often important to prevent the explosive release effect or to improve the efficacy and safety of the product by maintaining the drug concentration at a desired level for a long period of time. Methotrexate (MTX) is an anticancer agent that acts as an antimetabolite of folic acid and is used in the treatment of many malignancies.

Methods: The aim of this study was to determine the drug release profile of MTX by immobilizing it on Cu-MPOF. For this purpose, the Cu metal-phosphate organic frameworks (Cu-MPOFs) were synthesized under different pH conditions and characterized using FT-IR, XRD, FESEM, EDX, and elemental mapping techniques. MTX was then immobilized on Cu-MPOFs and the drug release profile was evaluated at 30, 120, 240, 1440, and 2880 min using UV-Vis spectroscopy.

Results: The analysis revealed a controlled drug release profile indicating an increase in drug release over time.

Conclusion: In summary, this study successfully demonstrated that Cu-MPOFs can provide a controlled release profile for Methotrexate (MTX), highlighting their potential as effective drug delivery systems by ensuring a sustained and gradual release of the drug.

Keywords

Metal-Phosphate Organic Framework · Methotrexate · Drug release



PP-20

Cytotoxic Activities of the Fabricated Ca-MPOF and Zn-MPOF Nanoparticles

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Abstract

Background and Aims: Nanotechnological applications are used in many sectors today. Among adaptive nanomaterials, nanoparticles stand out for their extraordinary properties such as size, morphology, versatility, and biocompatibility. Metal-organic frameworks (MOFs), which consist of a metal ion and an organic ligand, are the newest class of these structures and have applications in many fields such as optics, gas storage, catalysis, and biomedicine. Determining the cytotoxic effects of various physical or biological agents is of therapeutic importance.

Methods: In this study, we aimed to investigate the cytotoxic effect of metal-phosphate organic framework (MPOF) structures *in vitro* to assess their biological activity. For this purpose, Ca-MPOF and Zn-MPOF were synthesized by combining blueberry extract with calcium and zinc metals. The synthesized products underwent characterization using various spectroscopic techniques, including Fourier Transform Infrared Spectrophotometer (FT-IR), Field Emission Scanning Electron Microscopy (FESEM), X-ray Diffraction (XRD), Energy Dispersive X-ray Analysis (EDX), and elemental mapping analysis. Subsequently, Methotrexate (MTX), used in the treatment of cancer and autoimmune diseases, was encapsulated into the nanoparticles, and a drug release study was conducted. A cell culture study was performed using an MTT assay to determine the anticancer activity of the nanoparticles on the human lung carcinoma cell line (A549) and the human breast cancer cell line (MCF-7).

Results: The results were evaluated using a microplate reader device. The data obtained indicate that MPOF constructs are a therapeutically promising candidate.

Discussion: The findings of this study suggest that Ca-MPOF and Zn-MPOF constructs, particularly those synthesized with blueberry extract, hold significant therapeutic potential due to their promising anticancer activity observed *in vitro*.

Keywords

Metal-phosphate organic frameworks • anti-cancer • cytotoxicity



PP-21

Synthesis and Characterization of Novel Crystalline Covalent Organic Frameworks (COFs)

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Abstract

Background and Aims: Covalent organic frameworks (COFs) are crystalline porous polymeric materials with a repeating pattern, usually formed from light elements such as H, B, C, N, and O with strong covalent bonds. Photocatalysis is the process by which reactive oxidizing species (ROS) are formed, leading to the photoactivation of photocatalysts by photons emitted from an ultraviolet (UV) light source. The search for materials with ideal properties for photocatalysis offers significant potential for environmental and energy applications such as the degradation of organic pollutants and hydrogen production. Some studies show that COFs in photocatalysis have significant potential for energy conversion and environmental applications. A new porous crystalline covalent organic framework was synthesized by the reduction of nitrobenzaldehyde to aminobenzaldehyde.

Methods: The characterization of the synthesized covalent organic frameworks was carried out using field emission scanning electron microscopy (FE-SEM), elemental mapping, energy dispersive X-ray analysis (EDX), Fourier transform infrared spectroscopy (FT-IR), and single crystal X-ray diffraction.

Results: These comprehensive analyses were used to elucidate the structural and chemical properties of the synthesized nanomaterials.

Conclusion: In conclusion, the synthesis and comprehensive characterization of the new covalent organic framework highlights its significant potential in photocatalysis, particularly for environmental and energy applications, such as the degradation of organic pollutants and hydrogen production.

Keywords

Covalent organic framework · photocatalysis · crystal.



PP-22

Cytotoxic Activity of *Arbutus unedo* L. Flower Extract on MCF-7 Breast Cancer Cells *In Vitro*

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Abstract

Background and Aims: *Arbutus unedo* L. is a species that belongs to the *Ericaceae* family and has long been used as an astringent, diuretic and urinary antiseptic in traditional medicine. Cancer is a disorder that results in abnormal and irregular proliferation of cells in the organ or tissue of the body.

Methods: In this study, the cytotoxic activity of methanol extract prepared from the flowers of *A. unedo* by maceration method was investigated in breast cancer (MCF-7 and MDA.MB.231) and lung cancer (A549) cell lines.

Results: In the MTT assay, the methanol extract of *A. unedo* showed a moderate cytotoxic effect against MCF-7 with 225.6 µg/mL IC₅₀ values, however same extract was inactive against MDA.MB.231 and A549 cells.

Conclusion: The above can support the potential use of *A. unedo* flower extract in neoadjuvant therapy to reduce the progression of breast cancer tumors.

Keywords

Arbutus unedo · cancer · cytotoxicity and MTT assay.



PP-23

Cytotoxic effects of the *Momordica charantia* seed extract in the MTT assay on Lung cancer cells (A549)

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Abstract

Background and Aims: *M. charantia* is a medicinal plant often used in folk medicine for its rich phytochemical content.

Methods: The aim of this study was to investigate the cytotoxic effect of *M. charantia* fruit and seed extract on the human lung cancer cells and non-malignant lung cells. The cytotoxic effect of fruit and seed ethanol extract on A549 (lung cancer cell) and BEAS-2B (non-malignant lung cell) were determined using an MTT reduction assay. After 48 hours of incubation, the fruit extract was inactive on cell viability.

Results: At the same incubation time, the seed extract showed a moderate cytotoxic effect in cancer cells with an IC50 value of 285,2 µg/mL, while its cytotoxic effect was strong (IC50<75 µg/mL) in non-malignant cells.

Conclusion: Our experimental results show that *M. charantia* seed effect can be used to reduce the progression of lung cancers in neoadjuvant cancer treatment.

Keywords MTT · *M.charantia* · cytotoxic

