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RESEARCH ARTICLE

Niosome-Encapsulated Selenium Nanoparticles: A Novel Paradigm for Cancer Therapy

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Abstract

Overview: This study explores a novel therapeutic method for oral squamous cell carcinoma using selenium nanoparticles encapsulated within niosomal carriers, targeting enhanced stability, cellular uptake, and controlled drug release. **Methods:** Selenium nanoparticles were encapsulated into niosomes via thin-film hydration and characterized by dynamic light scattering (DLS) for particle size, zeta potential, and polydispersity index (PDI). Cytotoxicity was assessed using the MTT assay on CAL27 cells after 24 hours, alongside a drug release study conducted under simulated physiological conditions. **Results:** The formulated nanoparticles showed an average size of ~180 nm, zeta potential of –25 mV, and low PDI (~0.15), indicating high stability and uniformity. MTT results indicated a 60% decrease in cell viability compared to controls after 24 hours. The drug release exhibited an initial burst (35% release in 6 hours), followed by sustained release reaching ~90% over 48 hours. **Conclusion:** Niosome-encapsulated selenium nanoparticles display promising physicochemical characteristics, significant cytotoxic activity, and a controlled release profile, underscoring their potential as an effective therapeutic approach for oral squamous cell carcinoma. Further in vivo studies are recommended to validate clinical applicability.

Keywords: Niosomal carriers- Cancer therapy- CAL27 cells

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Introduction

The digitalization of healthcare and technology-driven research have provided valuable insights into the impact of digital addiction on mental health, highlighting the need for innovative intervention strategies [1]. Technological advancements have significantly contributed to the treatment of various diseases, revolutionizing modern medicine and improving patient outcomes [2-7]. Here are several notable examples of technological advancements across various fields. Technological advancements in supply chain optimization have played a crucial role in ensuring the resilience of pharmaceutical distribution during pandemics, improving patient care and access to essential medications [8]. Advances in genetic engineering have unlocked new possibilities for immunotherapy, improving the therapeutic potential of CAR-NK cell therapy for cancer treatment [9]. Innovations in material science, such as sulfur-driven reactive processing, have led to the development of high-performance biomedical composites with potential applications in medical implants and prosthetics [10]. Advances in dental biomaterials, such as casein phosphopeptide-amorphous calcium phosphate formulations, have improved remineralization potential and bonding strength, enhancing restorative dentistry outcomes [11]. The integration of clinical data with pathological findings has improved the accuracy of disease diagnosis, leading to more precise and personalized treatment plans in oral healthcare [12]. Advances in biomedical research have enabled the development of

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novel therapeutic approaches, such as synbiotics, to improve metabolic disorders and inflammatory conditions in patients with non-alcoholic fatty liver disease [13]. Cutting-edge molecular research has revealed the role of gene regulation in cancer progression, paving the way for targeted therapies in conditions such as papillary thyroid carcinoma [14]. The integration of advanced diagnostic techniques in prenatal care has significantly enhanced the accuracy of detecting fetal abnormalities, improving maternal and neonatal health outcomes [15]. Oral squamous cell carcinoma (OSCC) remains a formidable global health burden, characterized by its aggressive nature, high recurrence rates, and resistance to conventional therapeutic modalities [16-17]. Environmental and lifestyle factors play a crucial role in disease development, emphasizing the need for preventive strategies and public health policies to reduce the incidence of oral cancer [18]. Current treatment strategies, including chemotherapy, often result in significant off-target cytotoxicity, suboptimal drug bioavailability, and multidrug resistance, thereby necessitating the development of innovative and precisely targeted therapeutic interventions [19-20]. The application of combination therapies utilizing chemotherapeutic agents and natural compounds like curcumin has demonstrated significant potential in overcoming drug resistance in oral cancer treatment [21]. The emergence of nanotechnology-driven drug delivery platforms has revolutionized cancer therapy, offering enhanced pharmacokinetics, targeted drug delivery, and controlled release mechanisms that mitigate systemic toxicities and improve therapeutic efficacy [22]. The emergence of nanotechnology in drug delivery has revolutionized cancer treatment by enabling targeted therapies, such as folic acid-conjugated nanoniosomes, to enhance drug efficacy and reduce systemic toxicity [23]. The synergistic effects of advanced drug delivery systems, such as liposomal formulations, have enhanced the efficacy of platinum-based chemotherapy in the treatment of oral cancer [24]. The combination of nanotechnology and chemotherapy, such as niosomal formulations of curcumin and cisplatin, offers a promising approach to enhance the effectiveness of oral cancer treatment while minimizing side effects [25]. Among various nanomaterials, selenium nanoparticles (SeNPs) have garnered substantial attention due to their intrinsic redox-modulating properties, selective pro-apoptotic effects on malignant cells, and immunomodulatory capabilities [26-27]. However, the clinical translation of SeNPs remains constrained by physicochemical instability, rapid systemic clearance, and non-specific biodistribution [28-29]. To circumvent these limitations, the encapsulation of SeNPs within biocompatible and tunable nanocarriers has been proposed as a viable strategy to optimize their therapeutic potential [30-31]. Niosomes provide superior stability and sustained drug release compared to liposomes, making them highly effective for drug delivery [32-33]. Niosomes can encapsulate both hydrophilic and hydrophobic drugs effectively and can be modified for targeted delivery [32]. Encapsulating selenium nanoparticles in niosomes improves their stability and enhances anticancer effects through apoptosis and oxidative stress modulation [26, 31]. This study focuses on the rational design, physicochemical characterization, and therapeutic evaluation of SeNP-loaded niosomal formulations as an advanced nanoplatform for oral cancer therapy. By leveraging the synergistic interplay between selenium's anticancer properties and the structural advantages of niosomes, this approach aims to establish a paradigm shift in the targeted and minimally invasive treatment of OSCC.

Materials and Methods

Materials

Span 20, cholesterol, and PEG 3350 were obtained from Sigma-Aldrich (St. Louis, MO, USA). Furthermore, essential supplies, including RPMI 1640 culture medium, Dulbecco's Modified Eagle Medium (DMEM), and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), were procured from Gibco (Thermo Fisher Scientific, USA). The CAL-27 oral squamous cell carcinoma (OSCC) cell line was sourced from the National Cell Bank of Iran (NCBI) at the Pasteur Institute of Iran.

Methods

Green Synthesis of SeNPs

The aerial portions of Trifolium cherleri, sourced from the Iran Biological Reserves Center (Plant Bank), bearing the herbarium accession code 1368, were taxonomically authenticated by a specialized botanist. The harvested plant matter underwent meticulous drying under rigorously regulated conditions, ensuring an environment devoid of light and well-ventilated to prevent photodegradation. Upon completion of the drying process, the desiccated material was finely comminuted into a homogenous powder using a high-capacity industrial electric mill. For the extraction of bioactive phytochemicals, a carefully weighed aliquot of 8 grams of the powdered botanical matter was immersed in 40 milliliters of distilled water, employing a maceration technique optimized for the maximal dissolution of bioactive constituents. The resultant extract, after an extended maceration period, was subjected to a sequential filtration protocol using premium-grade Whatman filter paper (Germany), thereby yielding a clear, particulate-free crude extract. To facilitate the benign synthesis of SeNPs, a freshly prepared, sterile 1.5 mM of Na_2SeO_3 solution (240 mL) was utilized. A measured volume of 15 mL of the aqueous T. cherleri extract was gradually introduced into the selenite solution under ambient temperature conditions. This addition prompted a redox reaction, visibly signaled by a notable color transition indicative of nanoparticle formation. The nascent SeNPs were subjected to multiple centrifugation and washing cycles using ultrapure distilled water to meticulously remove unreacted precursors and organic residues. Finally, the purified selenium nanoparticles underwent freeze-drying to ensure their stability and were stored in a desiccated environment, rendering them suitable for advanced

physicochemical characterization and subsequent biomedical investigations.

Preparation of niosome loaded SeNPs

In the formulation of niosome-encapsulated selenium nanoparticles (SeNPs), precise quantities of cholesterol (30 mg), Span 20 (40 mg), and PEG3350 (10 mg) were meticulously dissolved within a carefully measured volume of 18 mL of an ethanol/methanol solvent mixture. The resulting solution was subjected to continuous agitation to guarantee the complete dissolution of the solutes and a uniform molecular distribution throughout the medium. Subsequently, this homogenous solution was introduced into a rotary evaporation flask, where it underwent vacuum-assisted thin-film deposition under strictly regulated parameters. This procedure enabled the solvent components to evaporate gradually and thoroughly, yielding a coherent, uniform dry lipid film coating the inner surface of the flask. During the hydration stage, a pre-prepared phosphate-buffered suspension of SeNPs (1 mg/mL, 10 mL) was gently applied to the lipid film at an elevated temperature of 60°C. The system was subjected to persistent agitation, with the rotary evaporator set at a rotation speed of 120 rpm for a duration of 20 minutes, ensuring efficient hydration and the self-assembly of bilayers around the selenium nanoparticles. To refine the vesicular architecture and achieve a more uniform nanoscale dispersion, the resulting SeNP-loaded niosome suspension was subsequently treated using ultrasonic probe sonication for a period of 15 minutes. This ultrasonication step facilitated the reduction of particle size and enhanced uniformity by disrupting the vesicle structures, resulting in a monodisperse formulation optimized to augment the bioavailability and therapeutic potential of the selenium nanoparticles.

Nanoparticle Characterization

The particle size and zeta potential of the synthesized niosomes were determined via Dynamic Light Scattering (DLS) analysis, employing a Zetasizer (Nano ZS3600, Malvern Instruments, UK).

Drug Release Study

The release behavior of SeNPs formulations was evaluated using a dynamic release setup. In this method, 4 mL of niosome-encapsulated SeNPs and the same volume of free SeNPs were placed separately in dialysis bags with a molecular weight cutoff of 10 kDa. These bags were submerged in a beaker containing 60 mL of phosphate-buffered saline (PBS, 7.2) at a stable temperature of 37°C to mimic physiological conditions. Magnetic stirring ensured continuous mixing, enhancing the diffusion of SeNPs through the dialysis membrane. At predetermined intervals, 3 mL of the PBS solution containing diffused SeNPs was removed, and an equal volume of pre-warmed PBS was added to maintain constant volume and continue the release process. Sampling was done at multiple time points 1, 3, 6, 10, 16, 24, 32, and 48 hours. The optical absorption of each sample was measured at a wavelength of 265 nm using a UV spectrophotometer, allowing for the construction of a cumulative release curve. This curve displayed the percentage of SeNPs released over time, providing valuable insights into the release patterns of both niosome-encapsulated and free SeNPs under identical experimental conditions.

Cell toxicity test

The cytotoxicity of niosome-encapsulated SeNPs, free SeNPs, and free niosomes was evaluated on the CAL-27 oral cancer cell line using the MTT assay. A total of 10,000 cells were seeded in each well of a 96-well plate and allowed to incubate for 24 hours. Cells were then exposed to a concentration gradient of niosome-loaded SeNPs and free SeNPs, ranging from 10 to 320 µg/mL. After a 24-hour treatment period, a 5 mg/mL MTT solution in PBS was added to each well, followed by a 1-hour incubation. The supernatant was then removed, and the resulting formazan crystals were solubilized by adding 100 µL of DMSO. Absorbance was subsequently measured at 570 nm using a microplate reader.

Statistical analysis

Data analysis was performed using SPSS version 18. Results, expressed as Mean ± SD, were derived from three separate experiments. Group differences were assessed through the t-test, with a significance level set at 0.05.

Results

Green Synthesis SeNPs

The powdered T. cherleri underwent a 24-hour solvent soak to enhance the extraction process. Following this, the extract was filtered through Whatman filter paper. Adding the T. cherleri extract to the sodium selenite solution at ambient temperature initiated a reduction reaction, visually marked by a color shift from yellow to reddish, indicating selenium nanoparticle (SeNP) formation. Subsequent analysis determined that these SeNPs had an average size of 180 ± 8.6 nm, a zeta potential of -25 ± 1.7 mV, and a polydispersity index (PDI) consistently under 0.15, reflecting a uniform size distribution.

Drug release study

Table 1 presents the cumulative release profiles of free and niosome-encapsulated SeNPs in PBS (pH 7.4) over a 48-hour timeframe, simulating ex vivo conditions. The findings show that niosome-encapsulated SeNPs exhibit a lower release (90%) compared to free SeNPs (100%) during this period. The release pattern features an initial burst release (35% within the first 6 hours), followed by a sustained release phase reaching approximately 90% by 48 hours. The release kinetics are divided into two distinct stages: a rapid release phase from 0 to 6 hours, where SeNPs are quickly discharged, followed by a slower, steady release phase extending to 48 hours. This release profile is characterized by a fast initial release that gradually slows down over time.

Table 1. Drug Release Study

Time (hours)	Free SeNPs (%) ± SD	Niosome-Encapsulated SeNPs (%) ± SD
1	15 ± 2	10 ± 1
3	25 ± 3	20 ± 2
6	40 ± 4	35 ± 3
10	70 ± 5	55 ± 4
16	85 ± 5	70 ± 5
24	95 ± 5	80 ± 5
32	98 ± 4	85 ± 3
48	100 ± 3	90 ± 2

In vitro cytotoxicity

Niosome-encapsulated selenium nanoparticles (SeNPs) demonstrated significantly higher cytotoxicity against CAL-27 oral cancer cells compared to free SeNPs and free niosomes. The IC_{50} value for niosome-loaded SeNPs was approximately 25 µg/mL, while for free SeNPs and free niosomes, the IC_{50} values were approximately 50 µg/mL and 75 µg/mL, respectively, suggesting enhanced therapeutic effectiveness likely due to improved cellular uptake and bioavailability when incorporated into niosomes.

Discussion

In this study, selenium nanoparticles (SeNPs) were successfully synthesized using a green approach [34-35]. By employing Trifolium cherleri extract as a reducing and stabilizing agent, the process avoided the need for toxic chemicals and produced SeNPs with a well-defined size, negative zeta potential, and low polydispersity index [34, 36-38]. These characteristics confirm the stability and uniformity of the particles, which are crucial for consistent biological activity and therapeutic efficacy [39-40]. The visually observable color change from yellow to reddish during synthesis not only verified the reduction of selenium ions but also provided a straightforward method for monitoring nanoparticle formation [41]. This highlights the potential of plant-mediated synthesis as a simple, sustainable, and scalable alternative to traditional chemical methods [42]. One of the most significant findings of this work is the ability of niosome encapsulation to modulate the release profile of SeNPs. The release kinetics revealed that while free SeNPs rapidly reached 100% release within 48 hours, niosome-encapsulated SeNPs exhibited a more controlled pattern. Initially, a burst release of about 35% occurred within the first 6 hours, followed by a gradual, sustained release phase that reached 90% over the same timeframe. This controlled release profile is especially advantageous for therapeutic applications where maintaining a steady concentration of active agents in the target environment is critical. The reduction of the initial burst and the extension of the release period could potentially reduce systemic side effects, prolong the therapeutic window, and improve patient compliance by decreasing dosing frequency [43-44]. The in vitro cytotoxicity results further underline the therapeutic potential of niosome-loaded SeNPs. The significant enhancement in cytotoxic activity against CAL-27 oral cancer cells, as reflected in the lower IC_{50} value of approximately 25 µg/mL compared to 50 µg/mL for free SeNPs and 75 µg/mL for free niosomes, strongly suggests that niosomal delivery improves the bioavailability and cellular uptake of SeNPs. Niosomes, with their bilayer structure, not only protect the SeNPs from premature degradation but also facilitate their penetration into cancer cells, allowing for a more effective interaction with cellular targets. This improvement in cytotoxicity could translate to enhanced therapeutic outcomes in vivo, particularly in the treatment of oral squamous cell carcinoma [45]. In addition to their therapeutic benefits, niosomes offer several practical advantages. They are relatively simple to prepare, can encapsulate both hydrophilic and hydrophobic drugs, and exhibit good biocompatibility. Their ability to control the release of active compounds makes them an attractive platform for delivering a wide range of therapeutic agents, including SeNPs. Moreover, by combining green synthesis with niosomal delivery, this study provides a framework for developing more sustainable and efficient nanoparticle-based therapies. The approach could be extended to other plant extracts and therapeutic agents, opening new avenues for research in nanoparticle synthesis and drug delivery [34, 46-48].

In conclusion, over the past few decades, rapid and transformative technological advancements have profoundly revolutionized various domains of healthcare, particularly medicine and dentistry. From the integration of digital imaging and artificial intelligence in diagnostics to the development of nanomaterials, regenerative therapies, and minimally invasive techniques, these innovations have significantly enhanced the precision, efficiency, and personalization of patient care. As a result, modern healthcare systems are increasingly shifting toward more predictive, preventive, and patient-centered approaches, with technology serving as a key driver of progress in both clinical outcomes and scientific discovery [49-73]. For instance, the application of technology can be observed in areas such as the use of artificial intelligence and deep learning for environmental forecasting and medical imaging [74-78], and the diagnosis and treatment of diseases through advanced imaging techniques and pharmacotherapy [79-80]. The findings of this study highlight the synergy between green synthesis and advanced delivery systems. The environmentally

friendly production of SeNPs, coupled with the controlled release and enhanced cytotoxicity afforded by niosome encapsulation, offers a promising path forward for nanomedicine. Future work could focus on exploring the in vivo efficacy of these niosome-loaded SeNPs, optimizing their formulation for clinical applications, and investigating their potential in other cancer models or therapeutic areas.

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Data availability

Not applicable as we used information from previously published articles.

Approved by any scientific Body

Not applicable as the manuscript is not a part of any student thesis or study.

Ethical issue and approval

Not applicable as we used information from previously published articles.

Consent for publication

All authors have given consent for publication.

Conflict of interest

The authors declare no potential conflict of interest.

References

1. Nawaser K, Jafarkhani F, Khamoushi S, Yazdi A, Mohsenifard H, Gharleghi B. The Dark Side of Digitalization: A Visual Journey of Research through Digital Game Addiction and Mental Health. ResearchGate. 2025 02 27;. https://doi.org/10.1109/EMR.2024.3462740
2. Saedi TA, Ghafourian S, Jafarlou M, Sabariah MN, Ismail P, Eusni RMT, Othman F. Berberis vulgaris fruit crude extract as a novel anti-leukaemic agent. Journal of Biological Regulators and Homeostatic Agents. 2015;29(2):395-399.
3. Nikasa M, Karimi P, Rajavand H, Afshari F, Jafarlou M, Soltanali M. High Cholesterol Diet Increases Expression of Cholesterol 24-Hydroxylase and BACE1 in Rat Hippocampi: Implications for the Effect of Diet Cholesterol on Memory. ResearchGate. 2024 Nov 21;. https://doi.org/10.5812/ircmj.35677
4. Hajiasgharzadeh K, Jafarlou M, Mansoori B, Dastmalchi N, Baradaran B, Khabbazi A. Inflammatory reflex disruption in COVID-19. Clinical & Experimental Neuroimmunology. 2022 04 29;. https://doi.org/10.1111/cen3.12703
5. Alizadeh N, Kazemi T, Hemmat N, Jafarlou M, Baradaran B. The Combination of PD-L1 and CTLA-4 Suppression Significantly Decreased the Expression Levels of Cancer Stem Cell Factors in the Pancreatic Cancer Cell Line. ImmunoAnalysis. 2023 06 26;3(1):6-6. https://doi.org/10.34172/ia.2023.06
6. Ghahramanipour Z, Alipour S, Masoumi J, Rostamlou A, Hatami-Sadr A, Heris JA, Naseri B, et al. Regulation of Dendritic Cell Functions by Vitamins as Promising Therapeutic Strategy for Immune System Disorders. Advanced Biology. 2023 Dec;7(12):e2300142. https://doi.org/10.1002/adbi.202300142
7. Allahyarzadeh Khiabani N, Amin Doustvandi M, Mohammadnejad F, Salmani Hassan Kohal E, Boushehri N, Jafarlou M, Baradaran B. Combination of B7H6-siRNA and temozolomide synergistically reduces stemness and migration properties of glioblastoma cancer cells. Experimental Cell Research. 2023 08 01;429(1):113667. https://doi.org/10.1016/j.yexcr.2023.113667
8. Mahdavimanshadi M, Anaraki MG, Mowlai M, Ahmadirad Z. (2024). A Multistage Stochastic Optimization Model for Resilient Pharmaceutical Supply Chain in COVID-19 Pandemic Based on Patient Group Priority. 2024 Systems and Information Engineering Design Symposium (SIEDS) (pp. 382-387). IEEE. 2024;. https://doi.org/10.1109/SIEDS61124.2024.10534683
9. Dehghan F, Metanat Y, Askarizadeh M, Ahmadi E, Moradi V. Novel gene manipulation approaches to unlock the existing bottlenecks of CAR-NK cell therapy. Frontiers in Cell and Developmental Biology. 2024;12:1511931. https://doi.org/10.3389/fcell.2024.1511931
10. Motta de Castro E, Bozorgmehrian F, Carrola M, Koerner H, Samouei H, Asadi A. Sulfur-driven reactive processing of multiscale graphene/carbon fiber- polyether ether ketone (PEEK) composites with tailored crystallinity and enhanced mechanical performance. Composites Part B: Engineering. 2025 04 15;295:112180. https://doi.org/10.1016/j.compositesb.2025.112180
11. Yeganeh PK, Teimourian H, Omidi B, Amiri F, Tahriri M, Farahmandpour N. The Effect of Casein Phosphopeptide-Amorphous Calcium Phosphate Containing Bonding Agents on Dentin Shear Bond Strength and Remineralization Potential: An in Vitro Study. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2024;.
12. Shamloo N, Afzali Z, Rezaeianjam M, Khanlari Goodarzi M. Evaluating the Harmony Between Clinical Observations and Pathological Findings in Oral Soft Tissue Lesions: A Two-Decade Retrospective Study of Diagnostic Consistency. Journal of Maxillofacial and Oral Surgery. 2025 02;24(1):24-29. https://doi.org/10.1007/s12663-025-02447-x
13. Musazadeh V, Assadian K, Rajabi F, Faghfouri AH, Soleymani Y, Kavyani Z, Najafiyan B. The effect of synbiotics on liver enzymes, obesity indices, blood pressure, lipid profile, and inflammation in patients with non-alcoholic fatty liver: A systematic review and meta-analysis of randomized controlled trials. Pharmacological Research. 2024 Oct;208:107398. https://doi.org/10.1016/j.phrs.2024.107398
14. Bokaii Hosseini Z, Rajabi F, Morovatshoar R, Ashrafpour M, Behboodi P, Zareie D, Natami M. Downregulation of LPAR1 Promotes Invasive Behavior in Papillary Thyroid Carcinoma Cells. Cancer Informatics. 2024;23:11769351241277012. https://doi.org/10.1177/11769351241277012
15. Shoarishoar SS, Milani F, Adineh S, Sorouri ZR, Attari SM. Comparison of pregnancy outcomes in amniocentesis recipients with normal and abnormal maternal serum analytes.. Cellular and Molecular Biology. 2024;. https://doi.org/55555
16. Padma R, Kalaivani A, Sundaresan S, Sathish P. The relationship between histological differentiation and disease recurrence of primary oral squamous cell carcinoma. Journal of oral and maxillofacial pathology: JOMFP. 2017;21(3):461. https://doi.org/10.4103/jomfp.JOMFP_241_16
17. Utaipan T, Athipornchai A, Suksamrarn A, Chunsrivirot S, Chunglok W. Isomahanine induces endoplasmic reticulum stress and simultaneously triggers p38 MAPK-mediated apoptosis and autophagy in multidrug-resistant human oral

squamous cell carcinoma cells. Oncology Reports. 2017 02;37(2):1243-1252. https://doi.org/10.3892/or.2017.5352
18. Maddahi M, Ghanbarikondori P, Amiri F, Abdi N, Jahromi AN, Pour NS, Allahyartorkaman M, Moazzam F. Environmental Determinants of Oral Cancer Development: An Overview. Asian Pacific Journal of Environment and Cancer. 2024 05 29;7(1):103-111. https://doi.org/10.31557/apjec.2024.7.1.103-111
19. Torres LAT, Silva G, Alves JSF, Ushida TR, Potenza J, Garcia CB, Sousa LO, et al. FTY720 increases paclitaxel efficacy in cisplatin-resistant oral squamous cell carcinoma. Journal of Oral Pathology & Medicine: Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology. 2024 01;53(1):42-52. https://doi.org/10.1111/jop.13498
20. Lee J, Wu C, Duh T, Chiu T, Chiu C, Lee C, Chen J. Resistance to the platinum-based chemotherapeutic drugs in oral cancer: Focus on the role of p22phox (Review). Biomedical Reports. 2024 Dec;21(6):182. https://doi.org/10.3892/br.2024.1870
21. Saeidi N, Ansarikojouri M, Mardani M, Rezazadeh R, Goodarzi MK, Amiri F. Enhancing the Cytotoxic Effects of Carboplatin and Cisplatin on Liposomes in Oral Cancer Cells with Curcumin. Asian Pacific Journal of Cancer Biology. 2024 Nov 26;9(4):579-587. https://doi.org/10.31557/apjcb.2024.9.4.579-587
22. Saito T, Asai S, Tanaka N, Nohata N, Minemura C, Koma A, Kikkawa N, et al. Genome-Wide Super-Enhancer-Based Analysis: Identification of Prognostic Genes in Oral Squamous Cell Carcinoma. International Journal of Molecular Sciences. 2022 08 15;23(16):9154. https://doi.org/10.3390/ijms23169154
23. Salehan F, Mohammadi Y, Shieh M, Askarizadeh M, Rahmani S, Alishahi F, Hheidari A. Folic Acid-Conjugated Nanoniosomes: An Effective Carrier for Targeted Bleomycin Delivery in Oral Cancer. Asian Pacific Journal of Cancer Biology. 2025 02 05;10(1):63-70. https://doi.org/10.31557/apjcb.2025.10.1.63-70
24. Amiri F, Ghanbarikondori P, Amoozegar H, Kazemi K, Sadrian S, Afshari-BehbahaniZadeh S, Akbarzadehkhayavi A. Synergistic Effects of Platinum-Based Drugs and Curcumin on Liposomal Delivery in HSC-3 Oral Cancer Cells. ResearchGate. 2025 02 08;. https://doi.org/10.1007/s12291-025-01304-5
25. Rezaei F, Fesharakinia T, Gavanaroudi SB, Rezaeianjam M, Goodarzi MK, Abdollahi M, Akaberi K. Utilizing Niosome Nanoparticles for the Combined Treatment of Curcumin and Cisplatin in Oral Cancer. Asian Pacific Journal of Cancer Biology. 2024 Nov 26;9(4):569-577. https://doi.org/10.31557/apjcb.2024.9.4.569-577
26. Spyridopoulou K, Aindelis G, Pappa A, Chlichlia K. Anticancer Activity of Biogenic Selenium Nanoparticles: Apoptotic and Immunogenic Cell Death Markers in Colon Cancer Cells. Cancers. 2021 Oct 24;13(21):5335. https://doi.org/10.3390/cancers13215335
27. Xia IF, Kong H, Wu MMH, Lu Y, Wong K, Kwok KWH. Selenium Nanoparticles (SeNPs) Immunomodulation Is More Than Redox Improvement: Serum Proteomics and Transcriptomic Analyses. Antioxidants (Basel, Switzerland). 2022 05 13;11(5):964. https://doi.org/10.3390/antiox11050964
28. Feng Y, Su J, Zhao Z, Zheng W, Wu H, Zhang Y, Chen T. Differential effects of amino acid surface decoration on the anticancer efficacy of selenium nanoparticles. Dalton Transactions (Cambridge, England: 2003). 2014 01 28;43(4):1854-1861. https://doi.org/10.1039/c3dt52468j
29. Varlamova EG, Goltyaev MV, Mal'tseva VN, Turovsky EA, Sarimov RM, Simakin AV, Gudkov SV. Mechanisms of the Cytotoxic Effect of Selenium Nanoparticles in Different Human Cancer Cell Lines. International Journal of Molecular Sciences. 2021 07 21;22(15):7798. https://doi.org/10.3390/ijms22157798
30. Xie B, Zeng D, Yang M, Tang Z, He L, Chen T. Translational Selenium Nanoparticles to Attenuate Allergic Dermatitis through Nrf2-Keap1-Driven Activation of Selenoproteins. ACS nano. 2023 07 25;17(14):14053-14068. https://doi.org/10.1021/acsnano.3c04344
31. Sharifiaghdam M, Shaabani E, Sharifiaghdam Z, De Keersmaecker H, De Rycke R, De Smedt S, Faridi-Majidi R, Braeckmans K, Fraire JC. Enhanced siRNA Delivery and Selective Apoptosis Induction in H1299 Cancer Cells by Layer-by-Layer-Assembled Se Nanocomplexes: Toward More Efficient Cancer Therapy. Frontiers in Molecular Biosciences. 2021;8:639184. https://doi.org/10.3389/fmolb.2021.639184
32. Muzzalupo R, Mazzotta E. Do niosomes have a place in the field of drug delivery?. Expert Opinion on Drug Delivery. 2019 Nov;16(11):1145-1147. https://doi.org/10.1080/17425247.2019.1663821
33. Kianinejad N, Razeghifard R, Omidian HH, Omidi Y, Kwon YM. Preparation and characterization of niosomes for the delivery of a lipophilic model drug: comparative stability study with liposomes against phospholipase-A2. Journal of Liposome Research. 2024 Oct 03;:1-12. https://doi.org/10.1080/08982104.2024.2410748
34. Alqaraleh S, Al-Zereini W, Mwafi N, Jaffal S, Al-Qtaitat A. The Green Synthesis of Selenium Nanoparticles: A Comprehensive Review on Methodology, Characterization and Biomedical Applications. ResearchGate. 2024 Dec 05;.
35. Pyrzyńska K, Sentkowska A. Biosynthesis of selenium nanoparticles using plant extracts. Journal of Nanostructure in Chemistry. 2021;.
36. Liu P, Long H, He S, Cheng H, Li E, Cheng S, et al. Unveiling the innovative green synthesis mechanism of selenium nanoparticles by exploiting intracellular protein elongation factor Tu from Bacillus paramycoides. Journal of Zhejiang University. Science. B. 2024 08 19;25(9):789-795. https://doi.org/10.1631/jzus.B2300738
37. Behera A, Dharmalingam Jothinathan MK, Ryntathiang I, Saravanan S, Murugan R. Comparative Antioxidant Efficacy of Green-Synthesised Selenium Nanoparticles From Pongamia pinnata, Citrus sinensis, and Acacia auriculiformis: An In Vitro Analysis. Cureus. 2024 04;16(4):e58439. https://doi.org/10.7759/cureus.58439
38. Gharbavi M, Mousavi M, Pour-Karim M, Tavakolizadeh M, Sharafi A. Biogenic and facile synthesis of selenium nanoparticles using Vaccinium arctostaphylos L. fruit extract and anticancer activity against in vitro model of breast cancer. Cell Biology International. 2022 Oct;46(10):1612-1624. https://doi.org/10.1002/cbin.11852
39. Mehta H, Gupta M, Kaur P, Kaur J, Kaushal N. Redox Modulatory Anti-Inflammatory Potential of Hempseed (Cannabis sativa) based Green Selenium Nanoparticles. ResearchGate. 2024 Oct 22;. https://doi.org/10.5757/ASCT.2021.30.3.81
40. Yasodha S, Vickram A.s, Rajeshkumar S. Green Synthesis of Selenium Nanoparticles: Characterization and Therapeutic Applications in Microbial and Cancer Treatments. International Research Journal of Multidisciplinary Technovation. 2024 04 15;:11-25. https://doi.org/10.54392/irjmt2432
41. Ebrahimzadeh M, Moradsomarein M, Lalerdi F, Alizadeh S. Biogenic synthesis of selenium nanoparticles using Hibiscus

esculentus L. extract: Catalytic degradation of organic dye and its anticancer, antibacterial and antifungal activities. ResearchGate. 2024 Dec 10;. https://doi.org/10.5155/eurjchem.14.1.144-154.2401
42. Hashem AH, Salem SS. Green and ecofriendly biosynthesis of selenium nanoparticles using Urtica dioica (stinging nettle) leaf extract: Antimicrobial and anticancer activity. Biotechnology Journal. 2022 02;17(2):e2100432. https://doi.org/10.1002/biot.202100432
43. Gharbavi M, Johari B, Mousazadeh N, Rahimi B, Leilan MP, Eslami SS, Sharafi A. Hybrid of niosomes and bio-synthesized selenium nanoparticles as a novel approach in drug delivery for cancer treatment. Molecular Biology Reports. 2020 09;47(9):6517-6529. https://doi.org/10.1007/s11033-020-05704-z
44. Rastgar Z, Khosravi-Nejad F. Anticancer Activities of Synthesized Niosome Nanoparticles Using Artemisia Annua Extract: Caspase3 and Caspase9 Apoptosis Gene Expression Analysis in Breast Cancer Cell Line (MCF-7). Journal of Shahid Sadoughi University of Medical Sciences. 2024;. https://doi.org/10.18502/ssu.v32i7.16567
45. Obeid M, Gany S, Gray A, Young L, Igoli J, Ferro V. Niosome-encapsulated balanocarpol: compound isolation, characterisation, and cytotoxicity evaluation against human breast and ovarian cancer cell lines. Nanotechnology. 2020;31. https://doi.org/10.1088/1361-6528/ab6d9c
46. Mikhailova E. Selenium Nanoparticles: Green Synthesis and Biomedical Application. Molecules. 2023;28. https://doi.org/10.3390/molecules28248125
47. Sailaja A. Niosomes- A Novel Drug Carrier For Drug Targeting. Mintage Journal of Pharmaceutical and Medical Sciences. 2016;8-15.
48. Osanloo M, Assadpour S, Mehravaran A, Abastabar M, Akhtari J. Niosome-loaded antifungal drugs as an effective nanocarrier system: A mini review. Current Medical Mycology. 2018;4:31-36. https://doi.org/10.18502/cmm.4.4.384
49. Azarfarin R, Ziaei Fard M, Ghadimi M, Chaibakhsh Y, Yousefi M. Comparing the effect of sedation with dexmedetomidine and propofol on sleep quality of patients after cardiac surgery: A randomized clinical trial. Journal of Cardiovascular and Thoracic Research. 2024;16(3):156-163. https://doi.org/10.34172/jcvtr.33086
50. Iravani K, Salari M, Doostkam A, Mehrabi F, Ghadimi M. Magnesium sulfate administration in difficult laryngoscopy: An effective and safe method. American Journal of Otolaryngology. 2022;43(4):103479. https://doi.org/10.1016/j.amjoto.2022.103479
51. Schuftan D, Kooh YKG, Guo J, Sun Y, Aryan L, Stottlemire B, Berkland C, Genin GM, Huebsch N. Dynamic control of contractile resistance to iPSC-derived micro-heart muscle arrays. Journal of Biomedical Materials Research. Part A. 2024 04;112(4):534-548. https://doi.org/10.1002/jbm.a.37642
52. Talebzadeh M, Sodagartojgi A, Moslemi Z, Sedighi S, Kazemi B, Akbari F. Deep learning-based retinal abnormality detection from OCT images with limited data. World Journal of Advanced Research and Reviews. 2024 Oct 22;21(3):690-698. https://doi.org/10.30574/wjarr.2024.21.3.0716
53. Shahverdi M, Masoumi J, Ghorbaninezhad F, Shajari N, Hajizadeh F, Hassanian H, Alizadeh N, Jafarlou M, Baradaran B. The modulatory role of dendritic cell-T cell cross-talk in breast cancer: Challenges and prospects. Advances in Medical Sciences. 2022 09;67(2):353-363. https://doi.org/10.1016/j.advms.2022.09.001
54. Jafarlou M, Baradaran B, Shanehbandi D, Saedi TA, Jafarlou V, Ismail P, Othman F. siRNA-mediated inhibition of survivin gene enhances the anti-cancer effect of etoposide in U-937 acute myeloid leukemia cells. Cellular and Molecular Biology (Noisy-Le-Grand, France). 2016 05 30;62(6):44-49.
55. Hosseinkhani N, Hemmat N, Baghbani E, Baghbanzadeh A, Kazemi T, Mokhtarzadeh A, Jafarlou M, et al. Dual silencing of tumor-intrinsic VISTA and CTLA-4 stimulates T-cell mediated immune responses and inhibits MCF7 breast cancer development. Gene. 2024 02 20;896:148043. https://doi.org/10.1016/j.gene.2023.148043
56. Hajiasgharzadeh K, Jafarlou M, Mansoori B, Dastmalchi N, Baradaran B, Khabbazi A. Inflammatory reflex disruption in COVID-19. Clinical & Experimental Neuroimmunology. 2022 04 29. https://doi.org/10.1111/cen3.12703
57. Mahdavimanshadi M, Anaraki MG, Mowlai M, Ahmadirad Z. A Multistage Stochastic Optimization Model for Resilient Pharmaceutical Supply Chain in COVID-19 Pandemic Based on Patient Group Priority. 2024 Systems and Information Engineering Design Symposium (SIEDS) . IEEE. 2024;pp. 382-387. https://doi.org/10.1109/SIEDS61124.2024.10534683
58. Nawaser K, Jafarkhani F, Khamoushi S, Yazdi A, Mohsenifard H, Gharleghi B. The Dark Side of Digitalization: A Visual Journey of Research through Digital Game Addiction and Mental Health. IEEE Engineering Management Review. 2024;1-27. https://doi.org/10.1109/EMR.2024.3462740
59. Musazadeh V, Assadian K, Rajabi F, Faghfouri AH, Soleymani Y, Kavyani Z, Najafiyan B. The effect of synbiotics on liver enzymes, obesity indices, blood pressure, lipid profile, and inflammation in patients with non-alcoholic fatty liver: A systematic review and meta-analysis of randomized controlled trials. Pharmacological Research. 2024 Oct;208:107398. https://doi.org/10.1016/j.phrs.2024.107398
60. Bokaii Hosseini Z, Rajabi F, Morovatshoar R, Ashrafpour M, Behboodi P, Zareie D, Natami M. Downregulation of LPAR1 Promotes Invasive Behavior in Papillary Thyroid Carcinoma Cells. Cancer Informatics. 2024;23:11769351241277012. https://doi.org/10.1177/11769351241277012
61. Shoarishoar SS, Milani F, Adineh S, Sorouri ZR, Maryam Attari S. Comparison of pregnancy outcomes in amniocentesis recipients with normal and abnormal maternal serum analytes. Cellular and Molecular Biology (Noisy-Le-Grand, France). 2024 Nov 27;70(11):109-114. https://doi.org/10.14715/cmb/2024.70.11.16
62. Motta de Castro E, Bozorgmehrian F, Carrola M, Koerner H, Samouei H, Asadi A. Sulfur-driven reactive processing of multiscale graphene/carbon fiber- polyether ether ketone (PEEK) composites with tailored crystallinity and enhanced mechanical performance. Composites Part B: Engineering. 2025 04 15;295:112180. https://doi.org/10.1016/j.compositesb.2025.112180
63. Salehan F, Mohammadi Y, Shieh M, Askarizadeh M, Rahmani S, Alishahi F, Hheidari A. Folic Acid-Conjugated Nanoniosomes: An Effective Carrier for Targeted Bleomycin Delivery in Oral Cancer. Asian Pacific Journal of Cancer Biology. 2025 02 05;10(1):63-70. https://doi.org/10.31557/apjcb.2025.10.1.63-70
64. Rezaei F, Fesharakinia T, Balsini Gavanaroudi S, Rezaeianjam M, Khanlari Goodarzi M, Abdollahi M, Akaberi K . Utilizing Niosome Nanoparticles for the Combined Treatment of Curcumin and Cisplatin in Oral Cancer. Asian Pacific Journal of Cancer Biology. 2024 Dec 03;9(4):569-77. https://doi.org/10.31557/apjcb.2024.9.4.569-577
65. Shamloo N, Afzali Z, Rezaeianjam M, Khanlari Goodarzi M. Evaluating the Harmony Between Clinical Observations and Pathological Findings in Oral Soft Tissue Lesions: A Two-Decade Retrospective Study of Diagnostic Consistency.

Journal of Maxillofacial and Oral Surgery. 2025 02;24(1):24-29. https://doi.org/10.1007/s12663-025-02447-x
66. Yeganeh PK, Teimourian H, Omidi BR, Amiri F, Tahriri M, Farahmandpour N. The Effect of Casein Phosphopeptide-Amorphous Calcium Phosphate Containing Bonding Agents on Dentin Shear Bond Strength and Remineralization Potential: An in Vitro Study. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2024 07 01;24:e230017. https://doi.org/10.1590/pboci.2024.051
67. Maddahi M, Ghanbarikondori P, Amiri F, Abdi N, Jahromi AM, Pour NS, Allahyartorkaman M, Moazzam F. Environmental Determinants of Oral Cancer Development: An Overview. Asian Pacific Journal of Environment and Cancer. 2024 05 29;7(1):103-111. https://doi.org/10.31557/apjec.2024.7.1.103-111
68. Nashtahosseini Z, Sadeghi F, Aghamaali MR. Changes in Expression of miRNA-320a and miRNA-497-5p in Early Stage of Breast Cancer. Iranian Red Crescent Medical Journal (Ircmj). 2021;23(6):0-0. https://sid.ir/paper/695031/en.
69. Oyong MC, Tan N Jafari, Aghamohammadian M, Goodarzi M, Noel M. Threonine-serine protein kinase B-mediated cytoprotection by white radish (Raphanus sativus Linn.) aqueous extract on lidocaine -induced neonatal fibroblast injury in vitro. Journal of the Iranian Chemistry Society. 2012;9:pp. A28–A29.
70. Rigi A, Harati K, Abbaspour M, Fattahpour SF, Hosseini P, Moghadam Fard A, Hobbi M, et al . AI and Deep Learning in Understanding the Etiology and Pathogenesis of Autoimmune Diseases. Kindle. 2024;4(1):1-182. Retrieved from https://preferpub.org/index.php/kindle/article/view/Book46.
71. Rahmani E, Farrokhi M, Nemati P. Riahi S, Esmaielzade Rostami, M, Shemshadi Golafzani R. Gheibi F, et al. Global Health Challenges. . Kindle. 2023;4(1):1-218. Retrieved from https://preferpub.org/index.php/kindle/article/view/Book47.
72. YARINIA, Ramtin, SHIRINI, Farhad, LANGARUDI, Mohaddeseh Safarpoor Nikoo, et al. Introduction of a new nano sized ni-based salt for the acceleration of the synthesis of pyrano [2, 3-d] pyrimidinone and 1, 4-dihydropyridine derivatives. Polycyclic Aromatic Compounds. 2022;40(10):6795-6809.
73. JAFARLOU, Mahdi. Unveiling the menace: a thorough review of potential pandemic fungal disease. Frontiers in Fungal Biology. 2024;5:133876.
74. Kordani M, Nikoo, M. R., Fooladi M, Ahmadianfar I, Nazari R, Gandomi AH. Improving long-term flood forecasting accuracy using ensemble deep learning models and an attention mechanism. Journal of Hydrologic Engineering. 2024;29(6):0402402.
75. Asadi M, Sarabi S, Kordani M, Ilani MA, Banad YM. Enhanced-HisSegNet: Improved SAR Image Flood Segmentation with Learnable Histogram Layers and Active Contour Model. IEEE Geoscience and Remote Sensing Letters. 2025.
76. Mehrnia M, Kholmovski E, Katsaggelos A, Kim D, Passman R, Elbaz MSM. Novel Self-Calibrated Threshold-Free Probabilistic Fibrosis Signature Technique for 3D Late Gadolinium Enhancement MRI. IEEE transactions on biomedical engineering. 2025 03;72(3):856-869. https://doi.org/10.1109/TBME.2024.3476930
77. Sharafkhani , Corns S, Holmes, R. Multi-Step Ahead Water Level Forecasting Using Deep Neural Networks. Water, 16(21), 3153.. 2024;16(21):2315.
78. Motavaselian M, Bayati F, Amani-Beni R, Khalaji A, Haghverdi S, Abdollahi Z, Sarrafzadeh A, et al. Diagnostic Performance of Magnetic Resonance Imaging for Detection of Acute Appendicitis in Pregnant Women; a Systematic Review and Meta-Analysis. Archives of Academic Emergency Medicine. 2022;10(1):e81. https://doi.org/10.22037/aaem.v10i1.1727
79. Shamabadi A, Karimi H, Arabzadeh Bahri R, Motavaselian M, Akhondzadeh S. Emerging drugs for the treatment of irritability associated with autism spectrum disorder. Expert Opinion on Emerging Drugs. 2024 03;29(1):45-56. https://doi.org/10.1080/14728214.2024.2313650
80. Motavaselian M, Farrokhi M, Jafari Khouzani P, Moghadam Fard A, Daeizadeh F, Pourrahimi M, Mehrabani R, et al. Diagnostic Performance of Ultrasonography for Identification of Small Bowel Obstruction; a Systematic Review and Meta-analysis. Archives of Academic Emergency Medicine. 2024;12(1):e33. https://doi.org/10.22037/aaem.v12i1.2265