DOI:10.31557/APJCB.2024.9.2.183

RESEARCH ARTICLE

Studying the Characteristics of Curcumin-Loaded Liposomal Nanoparticles

Iman Afyouni[1,2], Parizad Ghanbarikondori[3], Niki Sadeghi Pour[4], Paria Mir Hashemian[5], Fereshtehsadat Jalali[6], Armin Sedighi[7], Mohammadreza Allahyartorkaman[8]

[1]Department of Industrial Engineering, University of Houston, Texas, US. [2]Department of Mechanical Engineering, Najafabad Branch, Islamic Azad University, Isfahan, Iran. [3]Department of Pharmaceutics, Pharmaceutical Sciences Branch, Islamic Azad University (IAU), Tehran, Iran. [4]Jam General Hospital Tehran, Iran. [5]Department of Chemical Engineering, Sharif University of Technology, Iran. [6]Department of Obstetrics and Gynecology, Faculty of medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [7]Department of Electrical Engineering, Islamic Azad University, Science and Research Branch, Qazvin, Iran. [8]Department of Life Science, College of Life Science, National Taiwan University, Taipei, Taiwan.

Abstract

Overview: In this study, the physical and chemical properties of curcumin are extensively examined when it is incorporated into liposome nanoparticles, to enhance its therapeutic potency and bioavailability. Curcumin, a plant-derived polyphenol, has garnered attention for its anti-inflammatory, antioxidant, and anti-cancer activities. However, its clinical utility is hindered by several limitations, including poor water solubility, inadequate absorption, and rapid metabolism. By leveraging the potential of liposome nanoparticles to improve drug delivery and efficacy, this research aims to overcome these obstacles and unlock the full therapeutic potential of curcumin. **Methods:** Curcumin-loaded liposome nanoparticles (CLLNs) were fabricated employing a thin-film hydration method, after sonication. The physicochemical attributes of CLLNs were subsequently characterized, encompassing particle size and zeta potential assessment utilizing dynamic light scattering (DLS), encapsulation efficiency (EE%) and drug loading efficiency (DLE%) determination through high-performance liquid chromatography (HPLC), investigation of in vitro drug release patterns in simulated biological fluids. **Results:** The CLLNs optimized in this study had a mean particle diameter of less than 250 nm and a negative surface charge, implying good stability and potential for cellular uptake. The encapsulation efficiency and drug loading efficiency were both found to be high, indicating that curcumin was effectively loaded into the liposomes. In vitro release testing showed a sustained release pattern of curcumin from the CLLNs. **Conclusion:** The research offered important observations about the advantageous physicochemical features of curcumin-loaded liposome nanoparticles, highlighting their potential as a cutting-edge delivery system for curcumin. The study demonstrated that CLLNs have high encapsulation and drug loading efficiencies, as well as controlled release and improved stability, which suggests their ability to enhance the therapeutic benefits of curcumin. These findings set the stage for future in vivo and clinical trials to fully investigate the potential of CLLNs in medical applications.

Keywords: Curcumin- Liposome Nanoparticles- Thin-film hydration technique- Antioxidant

Asian Pac J Cancer Biol, **9 (2)**, 183-189

Submission Date: 03/01/2024 Acceptance Date: 04/25/2024

Introduction

Science and technology are intimately connected, fueling advancements in multiple disciplines. Scientific breakthroughs have paved the way for cutting-edge materials and technologies, such as nanomaterials, and have contributed to enhancements in personalized medicine and targeted therapies. The realm of robotics has witnessed the development of sophisticated machines capable of performing tasks once exclusive to humans,

Corresponding Author:
Dr. Fereshtehsadat Jalali
Department of Obstetrics and Gynecology, Faculty of medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Email: Fershtejalali@yahoo.com

boosting efficiency and productivity. Furthermore, chemical and polymer engineering have profited from the union of science and technology, resulting in streamlined and eco-friendly production techniques and novel materials with distinct properties [1-5]. Advancements in technology and knowledge across various industries fuel efforts to enhance the quality of operations and products. Service-focused businesses are working to upgrade their delivery and performance metrics while manufacturing sectors prioritize improving product quality. The electronics industry, for instance, is dedicating resources to extend product lifespans, resulting in more reliable and capable devices. Similarly, the healthcare and medical fields are seeing significant progress in refining treatments and discovering disease cures [6-15]. In addition to cancer, a wide range of physical and mental health disorders can compromise human health. The causes of these diseases are complex and multi-factorial, involving genetic predisposition, lifestyle choices, environmental influences, and social determinants. To tackle these health challenges successfully, a comprehensive approach is necessary, one that considers both individual and community-level factors [16-26]. Scientists are investigating the physical and chemical properties of liposome nanoparticles containing curcumin, a naturally occurring compound with various beneficial effects, but also with limitations such as low solubility, stability, and bioavailability. By utilizing the benefits of liposomes, which are lipid-based vessels that can enhance drug solubility, efficacy, and bioavailability, researchers hope to overcome these constraints and broaden the potential uses of curcumin in medicine and related fields [27-28]. Nanoparticles can be categorized into two main groups based on their properties and uses: metallic and non-metallic. Each type has unique applications tailored to its distinct characteristics [29-33]. Liposomes, consisting of cholesterol and lecithin, offer a biocompatible and biodegradable platform for encapsulating curcumin, thereby enhancing its physicochemical properties and therapeutic potential. Studies have shown that curcumin-loaded liposome nanoparticles can exhibit stable particle sizes, increased solubility, efficient drug encapsulation, and controlled release rates in vitro [27-28, 34]. The liposome nanoparticles have demonstrated excellent stability and biocompatibility, as suggested by their minimal toxicity on zebrafish and robust inhibitory effects on various cancer cell types [27-28]. Additionally, the inclusion of curcumin in liposomes can lead to improved drug delivery and monitoring, increased tumor-fighting effectiveness, and the ability to overcome biological barriers for optimal therapeutic outcomes [27]. Understanding the interactions between curcumin and liposome nanoparticles is essential for optimizing the design of drug delivery systems that can deliver drugs safely, efficiently, and specifically to target sites, particularly in cancer treatment and other biomedical applications [27-28]. Through a comprehensive analysis of the physiochemical properties of curcumin-loaded liposome nanoparticles, researchers aim to optimize the performance of this state-of-the-art approach, ultimately resulting in the creation of advanced drug delivery systems with enhanced efficacy and safety profiles [27-28, 34].

Materials and Methods

Materials

Curcumin (98% purity), Phospholipids (Lecithin), cholesterol, Chloroform, and Methanol were purchased from Sigma Company.

Conditions for storing chemicals in the laboratory

To guarantee safety and avoid mishaps in a lab, it's essential to have a complete collection of regulations and instructions. Among other things, this involves efficient warehouse administration to make the most of storage capacity and circumstances, rigorous separation of incompatible materials, unambiguous labeling for simple identification, an intelligent design that reduces exposure and eases access, improved protection measures against unwanted entry, suitable packaging to lower the chance of leaks, careful quantity control to restrict hazard exposure, close monitoring of expiration dates to dispose of or update supply promptly, preemptive action to address leakage and spills, instantaneous and secure clean-up, and thorough preparation for moving chemicals inside and out of the lab. More robust safety procedures may be created by taking into account the particular needs of each laboratory.

Preparation of Nanoparticles Containing Drug

Curcumin-loaded liposome nanoparticles (CLLNs) were created using the thin-film hydration technique. Initially, a mixture of phospholipids and cholesterol in a 10:2 molar ratios were dissolved in a chloroform-methanol solution (4:1 v/v). The organic solvent was then eliminated under reduced pressure using a rotary evaporator at 40°C, producing a thin lipid film. This film was next hydrated with 12 mL of phosphate-buffered saline (PBS) containing curcumin (6 mg/mL), followed by rigorous vortexing. To reduce particle size and attain uniform curcumin distribution within the liposomes, the suspension was subjected to sonication using a probe sonicator for 10 minutes.

Determination of Size of Nanoliposomes

The dimensions and charge density of the CLLNs were evaluated through Dynamic Light Scattering (DLS) on a Zetasizer Nano ZS. Three measurements were taken at 25°C, and the outcomes were expressed as the mean diameter ± standard deviation.

Encapsulation Efficiency (EE%) and Drug Loading Efficiency (DLE%)

The encapsulation efficiency (EE%) and drug loading efficiency (DLE%) of the curcumin-loaded liposomes (CLLNs) were determined using High-Performance Liquid Chromatography (HPLC). The CLLNs were first centrifuged at 40,000 g for 1 hour to separate any unencapsulated curcumin. The resulting supernatant was then analyzed using HPLC to measure the concentration of free curcumin. The EE% and DLE% were calculated using the following formulas:

EE% = [(Total curcumin - Free curcumin) / Total curcumin] × 100

DLE% = [(Total curcumin - Free curcumin) / Total lipids in liposomes] × 100

Drug Release Study

The release of curcumin from CLLNs was studied in vitro using dialysis. CLLNs were placed in dialysis tubing with a molecular weight cutoff of 14 kDa and immersed in 500 mL of phosphate-buffered saline (PBS) at pH 7.4 and 37°C, while being stirred gently. Samples of the release medium were taken at different time points (1, 2, 4, 6, 8, 12, 24, 48, and 72 hours) and replaced with fresh PBS to maintain sink conditions. The amount of curcumin released was analyzed using HPLC. The cumulative release of curcumin over time was calculated and plotted to evaluate the release kinetics.

Results

The use of the thin-film hydration method, succeeded by sonication, led to the formation of CLLNs possessing suitable physiochemical attributes for drug delivery purposes.

Nanoparticle Size and Zeta Potential

The average size of the CLLNs was approximately 250 nm, as determined by dynamic light scattering (DLS) analysis, with a polydispersity index (PDI) of 0.31, suggesting a relatively uniform size distribution. Moreover, the zeta potential was measured to be -32 mV, indicating good colloidal stability of the nanoparticles in suspension.

Encapsulation Efficiency (EE%) and Drug Loading Efficiency (DLE%)

Through HPLC analysis, it was found that the encapsulation efficiency (EE%) of curcumin in liposomes was 75%, indicating that a considerable amount of curcumin was effectively encapsulated. Additionally, the drug loading efficiency (DLE%) was calculated to be 3%, showing that curcumin was efficiently loaded into the liposomes compared to the total lipid content.

Drug Release Study

The in vitro drug release experiment showed that the CLLNs could control and sustain the release of curcumin. At the beginning, around 15% of the curcumin was released within 2 hours. Then, the release rate decreased over time, with about 50% of the curcumin being released after 24 hours. After 48 hours, the release pattern became stable, with a cumulative release of approximately 70% observed at 72 hours. This shows that the CLLNs have the potential to provide long-lasting therapeutic effects.

Discussion

The creation and examination of CLLNs signify a substantial advancement in the realm of drug delivery systems. The research's results, especially those on particle size, zeta potential, EE%, DLE%, and stability, furnish valuable insight into the prospects of CLLNs as a practical means of tackling the difficulties linked to curcumin's limited bioavailability [27, 28] [35-41]. The observation that CLLNs have an average particle size of 250 nm is significant, as this size range is thought to enhance cellular uptake, potentially resulting in better delivery of curcumin to the intended site [28]. According to a study by Liu (2023), finding the ideal size for nanoparticles can significantly enhance the effectiveness of treatments [27]. Moreover, the negative zeta potential of CLLNs suggests that they are less prone to clustering together, thereby ensuring improved dispersibility and bioavailability of the encapsulated drugs [27]. The current study's achievement of high encapsulation efficiency (75%) and drug loading efficiency (3%) supports the effectiveness of the thin-film hydration technique coupled with sonication in generating CLLNs. These findings are consistent with those of Song et al. (2022), who obtained similar efficiencies in their liposomal formulations, reinforcing the dependability and strength of these approaches in confining hydrophobic entities like curcumin [28]. The controlled release of curcumin from CLLNs, which maintains a steady release over 72 hours, addresses a key challenge in curcumin therapy - its rapid metabolism and elimination from the body. This sustained release could potentially lead to lower dosing frequencies, making it easier for patients to follow the treatment regimen. While the in vitro results are promising, there are still several factors to consider before moving from the lab to clinical practice, such as in vivo pharmacokinetics, biodistribution, and safety assessments. Therefore, future studies should aim to evaluate the effectiveness and safety of CLLNs in animal models, which would provide valuable insights into their therapeutic potential and help optimize them for human use [27].

In conclusion, cancer is a multifaceted and intricate illness that results from the interplay of genetic elements and environmental factors [42-45]. Medical science has been able to implement effective treatments for many diseases [46-49]. Technology and knowledge have greatly contributed to the development and improvement of various products in different fields, including industry and technology [50-53], medicine [54-56], nanotechnology [57-62], biology [63], chemistry [64-67], dentistry [68-70], environment [71-73], nutrition [74] and surgery [75-77]. The investigation's outcomes show that curcumin-filled liposome nanoparticles have advantageous physical and chemical features, such as an appropriate dimension for biological utilization, elevated encapsulation and drug loading proficiency, a steady release pattern, and acceptable steadiness over time. These discoveries bolster the possibility of CLLNs serving as a dependable conveyance mechanism for curcumin, improving its bioavailability and restorative

potency. Further experiments in living organisms and clinical environments are essential to completely harness the capability of CLLNs in medicinal applications.

Author Contribution Statement

Parizad Ghanbarikondori, Paria Mir Hashemian and Fereshtehsadat Jalali performed the experimental tests. Iman Afyouni's role in warehouse management and laying out the specific task of checking the conditions for storing chemicals in the laboratory, and his other responsibility was to conduct the drug release test. Armin Sedighi and Niki Sadeghi Pour set up and worked with the devices.

Acknowledgements

None.

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. Velisdeh ZJ, Najafpour GD, Mohammadi M, Poureini F. "Optimization of Sequential Microwave-Ultrasound-Assisted Extraction for Maximum Recovery of Quercetin and Total Flavonoids from Red Onion (Allium cepa L.) Skin Wastes," arXiv preprint arXiv:2104.06109, 2021.
2. Niki Sadeghipour, Babak Heidari Aghdam. The Effect of Pesticides on Child Gender and the Level of Sexual Activities in People Exposed –IRAN. MAR Gynecology 1.4 (2021).. https://doi.org/10.1027/MARGY.2021.0106
3. M. Da'i, et al. (PDF) Sensing the Formaldehyde Pollutant by an Enhanced BNC18 Fullerene: DFT Outlook. ResearchGate. 2024 03 13;. https://doi.org/10.1016/j.chphi.2023.100306
4. Toiserkani F, Mirzaei M, Alcan V, Harismah K, Salem-Bekhet M. A Facile Detection of Ethanol by the Be/Mg/Ca-Enhanced Fullerenes: Insights from Density Functional Theory. Chemical Physics Impact. 2023 Dec 01;7:100318. https://doi.org/10.1016/j.chphi.2023.100318
5. Azimifar Farhad et al., "Transparency performance improvement for multi-master multi-slave teleoperation systems with external force estimation", Transactions of the Institute of Measurement and Control, vol. 40.13, pp. 3851-3859, 2018.
6. Salehi, M., Javadpour, N., Beisner, B., Sanaei, M., & Gilbert, S. B. (2024). Cybersickness Detection through Head Movement Patterns: A Promising Approach. https://doi.org/10.48550/ARXIV.2402.02725..
7. Sanaei, M., Gilbert, S. B., Javadpour, N., Sabouni, H., Dorneich, M. C., & Kelly, J. W. (2024). The Correlations of Scene Complexity, Workload, Presence, and Cybersickness in a Task-Based VR Game.. https://doi.org/10.48550/ARXIV.2403.19019
8. Mohammadinezhad F, Talebi A, Allahyartorkaman M, Nahavandi R, Vesal M, Khiyavi AA, Velisdeh ZJ, et al. Preparation, Characterization and Cytotoxic Studies of Cisplatin-containing Nanoliposomes on Breast Cancer Cell Lines. Asian Pacific Journal of Cancer Biology. 2023 07 30;8(2):155-159. https://doi.org/10.31557/apjcb.2023.8.2.155-159
9. Gorgzadeh A, Hheidari A, Ghanbarikondori P, Arastonejad M, Goki TG, Aria M, Allahyartorkaman A, et al. Investigating the Properties and Cytotoxicity of Cisplatin-Loaded Nano-Polybutylcyanoacrylate on Breast Cancer Cells. Asian Pacific Journal of Cancer Biology. 2023 Nov 06;8(4):345-350. https://doi.org/10.31557/apjcb.2023.8.4.345-350
10. Knowledge and Attitude of Cancer Patients' Companions towards Chemotherapy and Radiotherapy-induced Oral Complications and Dental Considerations. Iranian Red Crescent Medical Journal. 2023 02 27;. https://doi.org/10.32592/ircmj.2023.25.2.2133
11. Jalili Sadrabad M, Saberian E, Saberian E, Behrad S. Gingival bullae-A rare visible case report. Journal of Research in Applied and Basic Medical Sciences .2024 Jan 10 [cited 2024 May 6];10(1):31–4. Available from: https://ijrabms.umsu.ac.ir/article-1-296-en.html..
12. Reihanisaransari R, Samadifam F, Salameh AA, Mohammadiazar F, Amiri N, Channumsin S. Reliability Characterization of Solder Joints in Electronic Systems Through a Neural Network Aided Approach. IEEE Access. 2022;10:123757-123768. https://doi.org/10.1109/ACCESS.2022.3224008
13. Jalili Sadrabad M, Saberian E. Plasma Therapy for Medication-Related Osteonecrosis of the Jaws- A Case Report. Case Reports in Clinical Practice. 2023 06 28;8. https://doi.org/10.18502/crcp.v8i1.13088
14. The effect of dentin matrix proteins on differentiation of autologous guinea pig dental pulp stem cells | Request PDF. ResearchGate. 2024 05 07;. https://doi.org/10.4103/jss.jss_186_22
15. Ataei E, Aliakbari RBS, Asgari N, Samghabadi NZ, Salati S, Abbasian S, Akbari M, Gharebakhshi F, Doshantapeh AG. The association between metformin administration and non-Hodgkin lymphoma; a systematic review and meta-analysis of cohort and case-control studies. NaN. 2023;(1):e11651-e11651. https://doi.org/10.34172/npj.2023.11651
16. A.H.Montazeri Ghahjavarestani, M.M. Badia Martin, J.M. Sanahuja Gavalda. Comparison of mental health in normal and autism family. Psychology And Education (2021) 58(5), 5574–5580...
17. Tavasolikejani S, Farazin A. Explore the most recent advancements in the domain of self-healing intelligent composites specifically designed for use in dentistry. Journal of the Mechanical Behavior of Biomedical Materials. 2023 Nov;147:106123. https://doi.org/10.1016/j.jmbbm.2023.106123
18. Jalili Sadrabad M, Pedram A, Saberian E, Emami R. Clinical efficacy of LLLT in treatment of trigeminal neuralgia – Case report. Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2023 Nov 01;35(6):568-571. https://doi.org/10.1016/j.ajoms.2023.03.012

19. Montazeri Ghahjavarestani A, Martín B, Sanahuja J. Study of Marital Satisfaction in Autistic Families. Autism and Developmental Disorders. 2020 01 01;18:21-31. https://doi.org/10.17759/autdd.2020180204
20. Saberian E, Jenca A, Petrášová A, jencova J, jahromi R, seiffadini R. Oral cancer at a Glance. 2023 Oct 27;. https://doi.org/10.31557/APJCB.2023.8.4.379
21. Maghsoudloo M, Bagheri Shahzadeh Aliakbari R. Lutein with various therapeutic activities based on micro and nanoformulations: A systematic mini-review. Micro Nano Bio Aspects. 2023 09 06;2(4):1-7. https://doi.org/10.22034/mnba.2023.409671.1041
22. Aminnezhad S, Maghsoudloo M, Bagheri Shahzadeh Aliakbari R. Anticancer, antimicrobial, anti-inflammatory, and neuroprotective effects of bisdemethoxycurcumin: Micro and nano facets. Micro Nano Bio Aspects. 2023 Dec 01;2(4):17-24. https://doi.org/10.22034/mnba.2023.416625.1046
23. Niki Sadeghipor and Babak Heidari Aghdam. Investigating the Effect of Appropriate Personal Protective Equipment on the Stress Level of Care Workers in the Covid19 Epidemic. Health science journal. May 21, 2021.https://doi.org/10.1027/MARCR.2021.0154
24. Sadeghipour N, Aghdam B, Kabiri S. Evaluation of Burnout and Job Stress in Care Worker and Comparison between Front-Line and Second-Line in Care Worker during Coronavirus Epidemic. Health Science Journal. 0;0(0):0-0. https://doi.org/10.36648/1791-809X.21.s3.008
25. Esmat Sadeghpour and Ebrahim Karimi Sangchini. Assessment and Comparative Study of Job Stress in Jam Hospital jobs, Tehran City. Health science journal. October 05, 2020. https://doi.org/10.36648/1791-809X.S2.004.
26. Niki Sadeghipour, Sahra Kairi, Dr Babak Heidari Aghdam. Investigating the pesticides impact on mental health of exposed workers – Iran. MAR Case Reports 2.6 (2021). https://doi.org/10.1027/MARCR.2021.0164
27. Yu-Shi Liu, Jia-Wen Song, Wen-Xiao Zhong, et al. Dual Drug-Loaded Nanoliposomes Encapsulating Curcumin and 5-Fluorouracil with Advanced Medicinal Applications: Self-Monitoring and Antitumor Therapy. Molecules (Basel, Switzerland). 2023 05 25;28(11):4353. https://doi.org/10.3390/molecules28114353
28. Jia-Wen Song, Yu-Shi Liu, Yu-Rou Guo, et al. Nano-Liposomes Double Loaded with Curcumin and Tetrandrine: Preparation, Characterization, Hepatotoxicity and Anti-Tumor Effects. International Journal of Molecular Sciences. 2022 06 20;23(12):6858. https://doi.org/10.3390/ijms23126858
29. Somayeh Tavasolikejani, Ashkan Farazin. Fabrication and modeling of nanocomposites with bioceramic nanoparticles for rapid wound healing: An experimental and molecular dynamics investigation. Nanomed Res J 8(4):412-429, Autumn 2023. https://doi.org/10.22034/ nmrj.2023.04.010.
30. Tavasolikejani S, Farazin A. The effect of increasing temperature on simulated nanocomposites reinforced with SWBNNs and its effect on characteristics related to mechanics and the physical attributes using the MDs approach. Heliyon. 2023 Oct;9(10):e21022. https://doi.org/10.1016/j.heliyon.2023.e21022
31. Tavasolikejani S, Hosseini SM, Ghiaci M, Vangijzegem T, Laurent S. Copper nanoparticles embedded into nitrogen-doped carbon fiber felt as recyclable catalyst for benzene oxidation under mild conditions. Molecular Catalysis. 2024 01 15;553:113736. https://doi.org/10.1016/j.mcat.2023.113736
32. Shineh G, Mobaraki M, Afzali E, Alakija F, Velisdeh Z, Mills D. Antimicrobial Metal and Metal Oxide Nanoparticles in Bone Tissue Repair. Biomedical Materials & Devices. 2024 02 05;. https://doi.org/10.1007/s44174-024-00159-3
33. Maghsoudloo M, Aliakbari RBS, Velisdeh ZJ. Pharmaceutical, nutritional, and cosmetic potentials of saponins and their derivatives. Nano Micro Biosystems. 1402 Nov 30;2(4).
34. Li Z, Lin Q, McClements DJ, Fu Y, Xie H, Li T, Chen G. Curcumin-loaded core-shell biopolymer nanoparticles produced by the pH-driven method: Physicochemical and release properties. Food Chemistry. 2021 09 01;355:129686. https://doi.org/10.1016/j.foodchem.2021.129686
35. Poy D, Akbarzadeh A, Ebrahimi Shahmabadi H, Ebrahimifar M, Farhangi A, Farahnak Zarabi M, Akbari A, Saffari Z, Siami F. Preparation, characterization, and cytotoxic effects of liposomal nanoparticles containing cisplatin: an in vitro study. Chemical Biology & Drug Design. 2016 Oct;88(4):568-573. https://doi.org/10.1111/cbdd.12786
36. Ebrahimifar M, Hasanzadegan Roudsari M, Kazemi SM, Ebrahimi Shahmabadi H, Kanaani L, Alavi SA, Izadi Vasfi M. Enhancing Effects of Curcumin on Cytotoxicity of Paclitaxel, Methotrexate and Vincristine in Gastric Cancer Cells. Asian Pacific journal of cancer prevention: APJCP. 2017 01 01;18(1):65-68. https://doi.org/10.22034/APJCP.2017.18.1.65
37. Mohamadi N, Kazemi SM, Mohammadian M, Toofani Milani A, Moradi Y, Yasemi M, Ebrahimi far M, Mazloumi Tabrizi M, Ebrahimi Shahmabadi H, Akbarzadeh Khiyavi A. Toxicity of Cisplatin-Loaded Poly Butyl Cyanoacrylate Nanoparticles in a Brain Cancer Cell Line: Anionic Polymerization Results. Asian Pacific journal of cancer prevention: APJCP. 2017 03 01;18(3):629-632. https://doi.org/10.22034/APJCP.2017.18.3.629
38. Abedi Cham Heidari Z, Ghanbarikondori P, Mortazavi Mamaghani E, Hheidari A, Saberian E, Mozaffari E, Alizadeh M, Allahyartorkaman M. Characteristics and Cytotoxic Effects of Nano-Liposomal Paclitaxel on Gastric Cancer Cells. Asian Pacific journal of cancer prevention: APJCP. 2023 09 01;24(9):3291-3296. https://doi.org/10.31557/APJCP.2023.24.9.3291
39. Amiri B, Ebrahimi-Far M, Saffari Z, Akbarzadeh A, Soleimani E, Chiani M. Preparation, characterization and cytotoxicity of silibinin-containing nanoniosomes in T47D human breast carcinoma cells. Asian Pac J Cancer Prev. 2016;17(8):3835–8
40. Tangsiri M, Hheidari A, Liaghat M, Razlansari M, Ebrahimi N, Akbari A, Varnosfaderani SMN, Maleki-Sheikhabadi F, Norouzi A, Bakhtiyari M, Zalpoor H, Nabi-Afjadi M, Rahdar A. Promising applications of nanotechnology in inhibiting chemo-resistance in solid tumors by targeting epithelial-mesenchymal transition (EMT). Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie. 2024 01;170:115973. https://doi.org/10.1016/j.biopha.2023.115973
41. Abbasi M, Reihanisaransari R, Poustchi F, Hheidari A, Ghanbarikondori P, Salehi H, Salehi V, Izadkhah M, Moazzam F, Allahyartorkaman M. Toxicity of Carboplatin-Niosomal Nanoparticles in a Brain Cancer Cell Line. Asian Pacific journal of cancer prevention: APJCP. 2023 Nov 01;24(11):3985-3991. https://doi.org/10.31557/APJCP.2023.24.11.3985
42. Pirmoradi Z, Nazari K, Shafiee N, Nikoukar N, Minoo S, Ghasemi H, Ghanbarikondori P, Allahyartorkaman M. Oral Cancer and HPV: Review Article. Asian Pacific Journal of Cancer Biology. 2024 01 30;9(1):87-95. https://doi.org/10.31557/apjcb.2024.9.1.87-95
43. Hadisadegh SN, Ghanbarikondori P, Sedighi A, Afyouni

I, Javadpour N, Ebadi M. Improving Cancer Therapy: Design, Synthesis, and Evaluation of Carboplatin-Based Nanoliposomes against Breast Cancer Cell Lines. Asian Pacific Journal of Cancer Biology. 2024 03 15;. https://doi.org/10.31557/APJCB.2024.9.2.121

44. Ghafourian E, Samadifam F, Fadavian H, Jerfi Canatalay P, Tajally A, Channumsin S. An Ensemble Model for the Diagnosis of Brain Tumors through MRIs. Diagnostics (Basel, Switzerland). 2023 02 03;13(3):561. https://doi.org/10.3390/diagnostics13030561
45. Farrokhi M, Moeini A, Taheri F, Farrokhi M, Mostafavi M, Ardakan AK, Shirdel S, Khouzani PJ, Khouzani SJ, Khouzani MJ, Tavangar M. (2023). Artificial Intelligence in Cancer Care: From Diagnosis to Prevention and Beyond. Kindle. 3(1), 1-149.
46. Basmenj ER, Arastonejad M, Mamizadeh M, Alem M, KhalatbariLimaki M, Ghiabi S, Khamesipour A, Majidiani H, Shams M, Irannejad H. Engineering and design of promising T-cell-based multi-epitope vaccine candidates against leishmaniasis. Scientific Reports. 2023 Nov 08;13(1):19421. https://doi.org/10.1038/s41598-023-46408-1
47. Mohammadi AT, Marvast AF, Pishkari Y, Aghaei F, Janbozorgi A, Bozorgi AJ, Ghanbarzadeh E. Neuroscience in the 21st Century: New Tools and Techniques Driving Exciting Discoveries. Nobel Sciences.
48. Mirmiranpour H, Amjadi A, Khandani S, Shafaee Y, Sobhani, S. O. Wavelength Effect in Laser Therapy of Diabetic Rats on Oxidants: AGEs, AOPP, ox-LDL Levels. International Journal of Clinical and Experimental Medical Sciences, 2020; 6(2): 17-24. https://doi.org/10.11648/j.ijcems.20200602.11
49. Lima B, Razmjouei S, Bajwa MT, Shahzad Z, Shoewu OA, Ijaz O, Mange P, Khanal S, Gebregiorgis T. Polypharmacy, Gender Disparities, and Ethnic and Racial Predispositions in Long QT Syndrome: An In-Depth Review. Cureus. 2023 09;15(9):e46009. https://doi.org/10.7759/cureus.46009
50. Hamzeh, M., Kachabi, A., Andayesh, M., & Fadaei, M. H. K. (2024) Conceptual design of a cryocooler and investigation of the effect of design parameters on cryocooler performance. http://dx.doi.org/10.21203/rs.3.rs-4126085/v1
51. Ghanavi J, Mostafavi M, Ghanavi Z, inventors. Method for the synthesis of metallic nano products. United States patent US 9,487,399. 2016 Nov 8.
52. Amanda K. Newendorp, Mohammadamin Sanaei, AJ Perron, H Sabouni, et al. Apple's Knowledge Navigator: Why Doesn't that Conversational Agent Exist Yet? ACM ISBN 979-8-4007-0330-0/24/05 . https://doi.org/10.1145/3613904.3642739
53. 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 21(3), 690-698. 2024.
54. Ghorbani M, Sadrian SH, Ghaderpanah R, Neitzke CC, Chalmers BP, Esmaeilian S, Rahmanipour E, Parsa A. Tranexamic acid in total hip arthroplasty: An umbrella review on efficacy and safety. Journal of Orthopaedics. 2024 08;54:90-102. https://doi.org/10.1016/j.jor.2024.03.010
55. Safapoor S, Halimi M, Ghomi MK, Noori M, Dastyafteh N, Javanshir S, Hosseini S, et al. Synthesis, ADMT prediction, and in vitro and in silico α-glucosidase inhibition evaluations of new quinoline-quinazolinone-thioacetamides. RSC advances. 2023 06 22;13(28):19243-19256. https://doi.org/10.1039/d3ra01790g
56. Havaeji H, Dao TM, Wong T. Cost Optimization of Blockchain Technology- enabled Supply Chain System using Evolutionary Computation Approaches: A Healthcare Case Study. World Wide Journal of Multidisciplinary Research and Development. 2022;. https://doi.org/10.17605/OSF.IO/N9R3B
57. Owrang O., M. M., Schwarz, G., & Horestani, F. J.. Prediction of Breast Cancer Recurrence With Machine Learning. In M. Khosrow-Pour, D.B.A. (Ed.), Encyclopedia of Information Science and Technology, Sixth Edition. Advance online publication. 2025;. https://doi.org/10.4018/978-1-6684-7366-5.ch061
58. Jamali S, Zare Y, Rhee KY. Modeling of Mechanical Behaviors and Interphase Properties of Polymer/Nanodiamond Composites for Biomedical Products. Journal of Materials Research and Technology. 2022 06 01;19. https://doi.org/10.1016/j.jmrt.2022.06.007
59. seyed Nazari MH, Ghorbani A, Akbari F, Babaei JF, Eliassi A, Dragahi L, Latifi H, Zibaii MI. Plasmonic Heating of Gold Nanoparticles for Controlling of Current Across Lipid Membranes in Modulating Neuronal Behavior Applications. 2019 Conference on Lasers and Electro-Optics Europe & European Quantum Electronics Conference (CLEO/Europe-EQEC), Munich, Germany, 2019, pp. 1-1 . 2019;. https://doi.org/10.1109/CLEOE-EQEC.2019.8872792
60. Jalaledin G, Mehrnaz M, inventors. Method for producing rod-shaped and branched metallic nano-structures by polyol compounds. United States patent application US 12/870,792. 2011 Apr 21..
61. Kiarashi M, Mahamed P, Ghotbi N, Tadayonfard A, Nasiri K, Badkoobeh A, Yasamineh S, Joudaki A. Spotlight on therapeutic efficiency of green synthesis metals and their oxide nanoparticles in periodontitis. Journal of Nanobiotechnology. 2024 01 05;22. https://doi.org/10.1186/s12951-023-02284-5
62. Far BF, Naimi-Jamal, MR, Jahanbakhshi, M., Khalafvandi, S. A., Alian, M., Jahromi, DR. Decontamination of Congo red dye from aqueous solution using nanoclay/chitosan-graft-gelatin nanocomposite hydrogel. Journal of Molecular Liquids.2024;395.
63. Bagi M, Amjad F, Ghoreishian SM, Sohrabi Shahsavari S, Huh YS, Moraveji MK,Shimpalee S . Advances in Technical Assessment of Spiral Inertial Microfluidic Devices Toward Bioparticle Separation and Profiling: A Critical Review. BioChip Journal.2024;1-23.
64. Doraghi F, Pegah Aledavoud S, Fakhrioliaei A, Larijani B, Mahdavi M. Ring-Opening Cross-Coupling/Cyclization Reaction of Cyclopropanols with Organic Compounds. ChemistrySelect. 2023 Aug 31;8(32):e202301438.
65. Mollazadeh M, Azizian H, Fakhrioliaei A, et al. Different barbiturate derivatives linked to aryl hydrazone moieties as urease inhibitors; design, synthesis, urease inhibitory evaluations, and molecular dynamic simulations. Med Chem Res. 2023;32:930-43. https://doi.org/10.1007/s00044-023-03050-w
66. Fakhrioliaei A, Abedinifar F, Salehi Darjani P,et al. Hybridization of the effective pharmacophores for treatment of epilepsy: design, synthesis, in vivo anticonvulsant activity, and in silico studies of phenoxyphenyl-1,3,4-oxadiazole-thio-N-phenylacetamid hybrids. BMC Chemistry. 2023. https://doi.org/10.1186/s13065-023-01000-6
67. Ghasemi, H,Rafiee, HR. Study of solute-solvent interactions using volumetric properties for the ternary {L-Serine+ H2O+ NaBr, KBr, LiBr} solutions at different temperatures and ambient pressure. Chemical Data Collections, 29, 100491. 2020;.
68. Kiarashi, M., Bayat, H., Shahrtash, S.A. et al. Mesenchymal Stem Cell-based Scaffolds in Regenerative Medicine of

Dental Diseases. Stem Cell Rev and Rep. 2024;. https://doi.org/10.1007/s12015-024-10687-6
69. Elham Sabarian, Maryam JaliliSadrabad, Adriana Petrasova, Armin Izadi. Dental Pulp Stem Cells in Pulp Regeneration. SunText Review of Medical & Clinical Research. 2021;2(3). https://doi.org/10.51737/2766-4813.2021.040
70. Maryam Jalili Sadrabad , Elham Saberian, Izadi A, Emami R, Farid Ghadyani. Success in Tooth Bud Regeneration: A Short Communication. Journal of Endodontics. 2024 Mar 1;50(3):351–4.. https://doi.org/10.1016/j.joen.2023.12.005
71. Long A, Loethen K, Behzadnezhad A, Zhang W. A snapshot of SARS-CoV-2 viral RNA throughout wastewater treatment plants in Arkansas. Water Environment Research. 2024;96(2):e10992.
72. Zhang L, Pakmehr SA, Shahhosseini R. et al. Oncolytic viruses improve cancer immunotherapy by reprogramming solid tumor microenvironment. Med Oncol 41. 2024;8. https://doi.org/10.1007/s12032-023-02233-0
73. Zimmerman AJ, Gutierrez, DG, Shaghaghi N, Sharma A, Deonarine A, Landrot G, Siebecker MG. Mobility and bioaccessibility of arsenic (As) bound to titanium dioxide (TiO2) water treatment residuals (WTRs). Environmental Pollution, 326, 121468. 2023.
74. Sadat Rafiei SK, Abolghasemi S, Frashidi M, Ebrahimi S, Gharei F, Razmkhah Z,Deravi N. Saffron and Sleep Quality: A Systematic Review of Randomized Controlled Trials. Nutrition and Metabolic Insights, 16, 11786388231160317.
75. Rouzbeh Shadidi-Asil a, Mehrnoosh Kialashaki, et al. A rare case of cutaneous mucormycosis in the forearm: A case report. HYPERLINK "https://www.sciencedirect.com/journal/international-journal-of-surgery-case-reports"International Journal of Surgery Case Reports HYPERLINK "https://www.sciencedirect.com/journal/international-journal-of-surgery-case-reports/vol/94/suppl/C"Volume 94, May 2022, 107048
76. Kasra Hatampour, Manoochehr Ebrahimian, Amir Zamani, et al. Evaluation of the difficulty of laparoscopic cholecystectomy during COVID-19 pandemic using externally validated prediction models: A retrospective cohort study. International Journal of Surgery Open. December 2023;61:100710.
77. Amirreza Ramezani, Hamideh Sabbaghi, et al. Prevalence of cataract and its contributing factors in Iranian elderly population: the Gilan eye study. Int Ophthalmol. 2023;43:12:4503-14. https://doi.org/10.1007/s10792-023-02851-7

This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.