GMR
The Original

AN OVERVIEW OF LIPOSOMES IN ENDODONTICS: A LITERATURE REVIEW

Dr. Geonath Immanuel. K[1], Dr. Sachith Jayavardhan[2], Dr. Kirubnath Gold[3], Dr. Prasanti Kumari Pradhan[4], Dr. Varshinee Vijayakumar[5], Dr. Vikas Singh[6]

[1]Postgraduate Trainee, Department of Conservative Dentistry and Endodontics, Kalinga Institute of Dental Sciences, University name: KIIT deemed to be University, Bhubaneswar, Odisha, India geoimmanuelkibu@gmail.com
[2]Postgraduate Trainee, Department of Periodontology, JSS Dental College & Hospital, JSS Academy of Higher Education & Research, Mysore, Karnataka, India, sachithj3@gmail.com
[3]General Dental Practitioner, Trust Dental Clinic, Chennai, Tamilnadu, India, trustdentalclinic.chennai@gmail.com
[4]Professor, Department of Conservative Dentistry and Endodontics, Kalinga Institute of Dental Sciences, KIIT deemed to be University, Bhubaneswar, Odisha, India, drprasanti@rediffmail.com
[5]Postgraduate Trainee, Department of Orthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamilnadu, India drvarshineepv@gmail.com
[6]Professor, Department of Public Health Dentistry, Teerthanker Mahaveer Dental College & Research Centre, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India
*Corresponding Author: Prasanti Kumari Pradhan, drprasanti@rediffmail.com

ABSTRACT

Liposomes are versatile nanoscale drug delivery systems known for their biocompatibility, ability to encapsulate diverse therapeutic agents, and potential for targeted delivery. This manuscript provides a comprehensive overview of liposomes, including their composition, preparation methods, and mechanisms of interaction with microbial biofilms. Emphasis is placed on their applications in dentistry and endodontics, particularly in the management of biofilm-associated infections. Liposomal formulations have demonstrated enhanced penetration into biofilm matrices, sustained release of antimicrobial agents, and improved therapeutic outcomes compared to conventional treatments. Specific applications in periodontal therapy, dental tissue engineering, and root canal disinfection are discussed. Emerging strategies, such as stimuli-responsive systems and hybrid nanocarriers, are highlighted as future directions for optimising liposomal delivery in clinical settings. This article attempts to review the existing literature on the different liposomes in dentistry and endodontics. Relevant scientific literature related to the topic was searched in PubMed, Google Scholar, and Scopus, critically analysed, and the data were extracted.

INTRODUCTION

Liposomes are spherical vesicles composed of lipid bilayers, extensively utilised as nanocarriers in drug delivery systems due to their biocompatibility, stability, and capacity to encapsulate both hydrophilic and hydrophobic therapeutic agents. First identified in the 1960s by Alec Bangham, these structures mimic biological membranes, facilitating their application across various fields, notably in medicine and dentistry.

Their ability to enhance the therapeutic index of drugs, target specific sites, and minimise adverse effects has garnered significant attention. The adaptability of liposomes in drug formulation addresses challenges associated with resistant infections and complex biofilm structures.[1]

There has been a significant surge in the development of liposome-based therapeutic strategies within dentistry, especially in areas where biofilm resistance and deep tissue penetration are critical concerns. However, most available literature remains scattered across various domains of pharmacology, microbiology, and dental research. This review aims to consolidate current knowledge, highlight recent advancements, and provide a unified perspective on the role of liposomes in endodontics and broader dental applications. It serves as a reference point for clinicians and researchers aiming to integrate nanocarrier systems into endodontic practice and research.

A comprehensive literature search was conducted to identify studies relevant to the application of liposomes in dentistry and endodontics. Sources included PubMed, Google Scholar, and Scopus databases. Search terms included "liposomes", "dentistry", "endodontics", "liposomal drug delivery", and related keywords. Inclusion criteria were peer-reviewed articles, systematic reviews, and relevant clinical or in vitro studies focusing on liposomal formulations in dentistry. Exclusion criteria involved non-English articles and studies irrelevant to the current topic.

Liposomes: Structural Features and Composition

Liposomes are primarily constructed from natural or synthetic phospholipids, sterols such as cholesterol, and occasionally polymers. These constituents influence their stability, size, and drug-carrying capacity. Based on their structure and size, liposomes are categorised into:

- **Small Unilamellar Vesicles (SUVs)**
- **Large Unilamellar Vesicles (LUVs)**
- **Multilamellar Vesicles (MLVs)**

• **Multivesicular Vesicles (MVVs)**

Incorporation of cholesterol enhances bilayer stability and modulates membrane fluidity. The hydrophilic inner compartments and hydrophobic bilayers of liposomes enable the encapsulation of diverse drugs. Surface modifications, such as the addition of targeting ligands, polyethylene glycol (PEG), or other polymers, facilitate site-specific drug delivery, confer stealth properties, and extend circulation time.[1,2]

Types of Liposomes

1. **Conventional Liposomes**: Comprising natural or synthetic phospholipids, often stabilised with cholesterol.
2. **Charged Liposomes**: Anionic or cationic variants that enhance stability and target specificity.
3. **Stealth Liposomes**: Coated with polymers like PEG to prolong circulation time.
4. **Targeted Liposomes**: Functionalized with ligands for receptor-mediated delivery.
5. **Stimuli-Responsive Liposomes**: Designed to release drugs in response to environmental triggers such as pH or temperature.[3]

Fabrication Techniques

Several methods are employed for liposome preparation:

1. **Thin Film Hydration**: Lipids dissolved in organic solvents form a thin film upon evaporation, which is subsequently hydrated to create vesicles.
2. **Reverse-Phase Evaporation**: Lipids are dissolved in an organic phase, mixed with an aqueous solution to form emulsions, and then evaporated.
3. **Solvent Injection**: Lipid solutions are rapidly injected into an aqueous phase, leading to liposome formation.
4. **Microfluidic Techniques**: Liposomes are formed by continuous mixing of lipid and aqueous phases within micro-channels.
5. **Freeze-Thaw and Lyophilisation**: Techniques employed to enhance encapsulation efficiency and stability.
6. **Dehydration-Rehydration Method**: An organic solvent-free approach to produce LUVs using sonication. This method involves dispersing lipids at low concentrations into an aqueous solution containing drug molecules, followed by sonication.

Advanced methods like supercritical fluid processing and detergent removal offer scalability and high encapsulation efficiency, making them suitable for industrial applications.[4]

Liposome Characterisation

Characterising liposomes is crucial to ensure their efficacy, stability, and safety as drug delivery systems. Key parameters include:

• **Particle Size**: Typically measured by dynamic light scattering (DLS), influencing circulation time and cellular uptake.

• **Zeta Potential**: Indicates surface charge and colloidal stability.

• **Morphology**: Assessed via transmission electron microscopy (TEM) or scanning electron microscopy (SEM), providing insights into shape and lamellarity.

• **Encapsulation Efficiency**: Determines the proportion of drug successfully loaded into liposomes.

• **In Vitro Drug Release Profiles**: Evaluates the release kinetics under physiological conditions.

• **Stability Studies**: Assess the maintenance of these properties over time under various storage conditions.

These characterisation techniques collectively ensure the reproducibility and performance of liposomal formulations in therapeutic applications.[5]

Complexity of endodontic biofilm

Microbial biofilms within the root canal exhibit strong resistance to the various irrigants and intracanal medicaments commonly employed in endodontic procedures. The intricate and often variable anatomy of the root canal system, combined with the presence of diverse microbial communities, significantly complicates the complete elimination of these biofilms.[6]

The microbes in the biofilm are polymicrobial and are extremely resilient to conventional treatment procedures and irrigating solutions. Hence, the need for targeted drug delivery using nanocarriers was established.[7]

Liposomes in Biofilm Management

Liposomes present a promising solution for biofilm-related infections due to their ability to penetrate biofilm matrices and deliver antimicrobial agents effectively. Biofilms are microbial communities embedded in extracellular polymeric substances (EPS), which confer resistance to conventional antimicrobial agents.[8,9,10]

Advantages of Liposomal Drug Delivery for Biofilms

• **Enhanced Penetration**: Liposomes can traverse the EPS barrier, delivering drugs directly to microbial cells. Their bilayer structure protects encapsulated agents from enzymatic degradation, environmental stress, and premature release. For instance, a soy lecithin–cholesterol liposome formulation extended the stability of cinnamon oil by 96 hours and enhanced its anti-biofilm activity against MRSA tenfold compared to the free compound.[11]

• **Targeted Delivery**: Modified liposomes reduce off-target effects and improve therapeutic outcomes. Wheat germ agglutinin-modified liposomes have shown enhanced delivery of clarithromycin, overcoming phenotypic resistance mechanisms such as cell wall thickening and efflux pump overexpression.[12]

• **Reduced Resistance Development**: Encapsulation can prevent premature drug degradation and reduce the likelihood of resistance development. Liposomes can obscure antimicrobial agents from bacterial detection until release at the target site.[13]

Mechanisms of Biofilm Interaction

Liposomes interact with biofilms through electrostatic forces, fusion with bacterial membranes, and active targeting using ligands. Their design flexibility allows for specific customisation based on the type of biofilm and infection.[8,14]

Literature Review:

Dental Applications of Liposomes

Liposomes have been explored for various dental applications, including:

1. **Antimicrobial Therapy**: Liposomal formulations have demonstrated efficacy against biofilms of oral pathogens like *Streptococcus mutans* and *Fusobacterium nucleatum*. Nano-liposomal chlorhexidine (CHX) formulations exhibited sustained drug release and superior penetration into dentinal tubules, resulting in enhanced antimicrobial action. These formulations reduced bacterial loads in treated areas and offered prolonged protection against recolonisation. Liposomes loaded with agents like chlorhexidine or cinnamon oil showed superior biofilm disruption, prolonged retention on enamel surfaces, and reduced damage to gingival cells.[15]
2. **Periodontal Therapy**: Cationic and anionic liposomes have been utilised to deliver drugs for periodontitis treatment, exhibiting improved biofilm eradication compared to free drugs. For instance, triclosan-loaded liposomes demonstrated specific targeting to biofilms on dental surfaces, offering significant reductions in microbial counts and inflammation.[16]
3. **Dental Tissue Engineering**: Injectable hydrogels combined with liposome-encapsulated agents like curcumin and α-tocopherol have shown potential for dental tissue repair and regeneration. These systems offer controlled release of bioactive agents, promoting tissue integration and healing.[17]
4. **Local Anaesthesia**: A study compared an infiltration of liposomal bupivacaine with bupivacaine for postoperative pain control in symptomatic patients diagnosed with pulpal necrosis experiencing moderate to severe preoperative pain. The authors found that a 4.0-mL infiltration of liposomal bupivacaine had some effect on soft tissue numbness, pain, and use of non-narcotic medications, but it was not clinically significant.[18]

Additional Applications:

• **Tooth Remineralisation**: Liposomes can be used as carriers for fluoride or calcium phosphate, enabling deeper and more sustained delivery into enamel lesions, thus promoting remineralisation.[19]

• **Implantology**: In dental implantology, liposomal drug carriers have been utilised for local antibiotic delivery around implants to prevent peri-implantitis. These formulations aid in reducing bacterial colonisation at the implant-tissue interface and enhance healing.[20]

Role of Liposomes in Endodontics

Liposomes have demonstrated valuable potential in endodontics due to their ability to encapsulate and deliver antimicrobial agents directly into root canals, biofilms, and dentinal tubules.

1. **Antimicrobial Activity of Liposomal CHX**: Nano-liposomal formulations of chlorhexidine (CHX) have shown increased antibacterial activity against *Enterococcus faecalis*, a pathogen commonly found in failed root canal treatments. Compared to conventional CHX, liposomal CHX displayed enhanced substantivity and greater penetration into biofilm structures, reducing the risk of reinfection.[15,21]
2. **Curcumin-Loaded Liposomes**: Curcumin, a natural compound with anti-inflammatory and antimicrobial properties, has poor aqueous solubility. Encapsulating curcumin into liposomes improves its bioavailability and enables controlled release. In endodontics, curcumin-loaded liposomes demonstrated significant biofilm disruption and anti-inflammatory effects when applied to infected root canals or periapical tissues. Nanocurcumin-coated gutta-percha had a significantly better antibacterial activity when compared with conventional gutta-percha against E. faecalis and Staph. Aureus.[17,22,23,24,25]
3. **Photodynamic Therapy (PDT)**: Liposome-assisted photodynamic therapy enhances the delivery and activation of photosensitizers within the root canal system. Studies have shown that liposomal encapsulation of photosensitising agents such as methylene blue or curcumin improves their solubility and enables better light absorption, resulting in higher reactive oxygen species (ROS) production and more effective bacterial eradication.[23,26]

In this systematic review, the inclusion of nanoparticle-mediated photodynamic therapy compared to conventional and traditional techniques was found to be effective in reducing the bacterial load when used as a disinfection method, although the heterogeneity was high. This gives a future prospective direction for further research using nanoliposome-mediated photodynamic therapy.[27]

4. **Magnetic Liposomes for Targeted Delivery**: Magnetic liposomes, synthesised by incorporating superparamagnetic iron oxide nanoparticles into liposomes, allow for site-specific targeting through external magnetic fields. These have been explored for delivering antibiotics and anti-inflammatory agents within complex root canal anatomies. Once directed into the canal system, the magnetic field maintains its position while the drug is released locally.[28]

5. **Interaction with Restorative Materials**: Liposomes may also interact with dental materials such as adhesives and sealers. Some studies suggest that the inclusion of liposome-loaded antibacterial agents within restorative materials enhances their antimicrobial properties without compromising bond strength or material integrity. This dual function sealing and antimicrobial action, adds value to restorative procedures.[29]
6. **Caries Vaccine:** The anti-idiotype vaccine aimed at antibodies against S. mutans, when administered orally in liposomes to rats, has significantly reduced caries and its colonisation in the oral cavity.[30]

Clinical Applications Beyond Dentistry
Beyond dental and endodontic use, liposomes are widely utilised in medical fields including oncology, ophthalmology, dermatology, and vaccines. For example:
• **Oncology**: Liposomal formulations like Doxil® (liposomal doxorubicin) reduce cardiotoxicity while improving antitumor activity.[31]
• **Vaccinology**: Liposomes are used as adjuvants to enhance immune responses; for instance, in hepatitis and COVID-19 vaccine platforms.[32]
• **Ophthalmology**: Liposomal eye drops enable prolonged drug retention and improved comfort in treating conditions like dry eye or conjunctivitis.[33]
These broader applications underline the versatility and adaptability of liposomes as a drug delivery platform.

Challenges and Future Prospects
Despite their many benefits, liposomal drug delivery systems face certain limitations and challenges:
1. **Stability**: Liposomes are prone to degradation, oxidation, and leakage of encapsulated drugs, especially during storage or upon exposure to biological fluids. Ensuring long-term stability remains a major concern in formulation science.[34]
2. **Toxicity and Biocompatibility**: While composed of biocompatible lipids, some formulations—especially those incorporating cationic or synthetic lipids—can elicit cytotoxic or immunogenic responses. Ensuring safety in sensitive oral or periapical tissues requires extensive biocompatibility testing.[35]
3. **Scalability and Cost**: Manufacturing liposomes at an industrial scale with consistent size, encapsulation efficiency, and batch-to-batch reproducibility can be technically challenging and expensive. Methods like microfluidic-based synthesis and lyophilisation are being optimised for better scalability.[4,36]
4. **Controlled Release Mechanisms**: Achieving precise control over drug release timing and location within oral tissues remains difficult. Research into stimuli-responsive liposomes—activated by pH changes, enzymes, or temperature—is ongoing to address this challenge.[36,37]
5. **Biofilm Penetration and Retention**: Although liposomes can penetrate biofilms, their retention and sustained action are influenced by factors such as surface charge, lipophilicity, and the biofilm's composition. Engineering liposomes to maintain prolonged presence and activity within the oral cavity and root canals is an area of active development.[38]

FUTURE DIRECTIONS
• **Multifunctional Liposomes**: Combining targeting ligands, imaging agents, and therapeutic compounds into a single liposomal system offers prospects for theranostics (therapy + diagnostics).[39]
• **Smart Liposomes**: The development of stimuli-responsive liposomes that release contents in response to local environmental cues (e.g., acidic pH in infected tissues) can enhance treatment specificity.[40]
• **Gene Delivery**: Liposomes are being explored as carriers for gene editing technologies like CRISPR or for delivering siRNA to downregulate pathogenic gene expression in oral diseases.[41]
• **Combination Therapies**: Liposomes may be co-loaded with multiple drugs (e.g., antibiotic + anti-inflammatory) for synergistic effects in complex dental conditions like periodontitis or necrotic pulp infections.[42]

CONCLUSION
Liposomes represent a highly versatile and biocompatible platform for the targeted delivery of therapeutic agents in dental and endodontic applications. Their capacity to encapsulate a wide range of active compounds, from antimicrobials to anti-inflammatories, allows for enhanced treatment efficacy, especially in managing persistent infections and biofilm-related conditions. Technological advancements in liposome formulation, surface modification, and delivery strategies continue to push the boundaries of their clinical utility.
Despite challenges such as stability and manufacturing scalability, ongoing research into smart and multifunctional liposomal systems holds great promise for improving dental care outcomes. As dental science moves towards more personalised and minimally invasive therapies, liposome-based drug delivery stands as a cornerstone technology with immense potential for future innovation.

REFERENCES
1. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. *Heliyon*. 2022 May 1;8(5):e09333.

2. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo SW, Zarghami N, et al. Liposome: classification, preparation, and applications. *Nanoscale Res Lett*. 2013 Dec;8:102.
3. Alavi M, Karimi N, Safaei M. Application of various types of liposomes in drug delivery systems. *Adv Pharm Bull*. 2017 Apr 13;7(1):3-9.
4. Mozafari MR. Liposomes: an overview of manufacturing techniques. *Cell Mol Biol Lett*. 2005 Jan 1;10(4):711-9.
5. Dwivedi C, Verma S. Review on preparation and characterization of liposomes with application. *Int J Sci Innov Res*. 2013 Mar;2:486-508.
6. Bhagat N, Salam S, Garg A, Venkatesan V, Hardik S, Hardik SG, Kumar S, Kashwani R. Use of Liposomal Curcumin for Oral Cancer Treatment: A Systematic Review and Meta Analysis. Nanotechnology Perceptions. 2024 Jun 22:342-59.doi: https://doi.org/10.62441/nano-ntp.vi.1019
7. Garg A, Mala K, Kamath PM. Biofilm models in endodontics—a narrative review. *J Conserv Dent*. 2021;24:2-9.
8. Wang Y. Liposome as a delivery system for the treatment of biofilm-mediated infections. *J Appl Microbiol*. 2021 Dec 1;131(6):2626-39.
9. Liu P, Chen G, Zhang J. A review of liposomes as a drug delivery system: current status of approved products, regulatory environments, and future perspectives. *Molecules*. 2022 Feb 17;27(4):1372.
10. Makhlouf Z, Ali AA, Al-Sayah MH. Liposomes-based drug delivery systems of anti-biofilm agents to combat bacterial biofilm formation. *Antibiotics (Basel)*. 2023 May 8;12(5):875.
11. Cui H, Li W, Li C, Vittayapadung S, Lin L. Liposome containing cinnamon oil with antibacterial activity against methicillin-resistant *Staphylococcus aureus* biofilm. *Biofouling*. 2016 Feb 7;32(2):215-25.
12. Yang K, Gitter B, Rüger R, Albrecht V, Wieland GD, Fahr A. Wheat germ agglutinin modified liposomes for the photodynamic inactivation of bacteria. *Photochem Photobiol*. 2012 May;88(3):548-56.
13. Ferreira M, Ogren M, Dias JN, Silva M, Gil S, et al. Liposomes as antibiotic delivery systems: a promising nanotechnological strategy against antimicrobial resistance. *Molecules*. 2021 Apr 2;26(7):2047.
14. Sugano M, Morisaki H, Negishi Y, Endo-Takahashi Y, Kuwata H, et al. Potential effect of cationic liposomes on interactions with oral bacterial cells and biofilms. *J Liposome Res*. 2016 Apr 2;26(2):156-62.
15. Shirur KS, Padya BS, Pandey A, Hegde MM, Narayan AI, et al. Development of lipidic nanoplatform for intra-oral delivery of chlorhexidine: characterization, biocompatibility, and assessment of depth of penetration in extracted human teeth. *Nanomaterials (Basel)*. 2022 Sep 27;12(19):3372.
16. Pinon-Segundo E, Ganem-Quintanar A, Alonso-Pérez V, Quintanar-Guerrero D. Preparation and characterization of triclosan nanoparticles for periodontal treatment. *Int J Pharm*. 2005 Apr 27;294(1-2):217-32.
17. Atila D, Dalgic AD, Krzemińska A, Pietrasik J, Gendaszewska-Darmach E, et al. Injectable liposome-loaded hydrogel formulations with controlled release of curcumin and α-tocopherol for dental tissue engineering. *Adv Healthc Mater*. 2024 Sep;13(23):2400966.
18. Bultema K, Fowler S, Drum M, Reader A, Nusstein J, Beck M. Pain reduction in untreated symptomatic irreversible pulpitis using liposomal bupivacaine (Exparel): a prospective, randomized, double-blind trial. *J Endod*. 2016 Dec 1;42(12):1707-12.
19. Skrinda-Melne M, Locs J, Grava A, Dubnika A. Calcium phosphates enhanced with liposomes–the future of bone regeneration and drug delivery. *J Liposome Res*. 2024 Jul 2;34(3):507-22.
20. Angellotti G, Presentato A, Murgia D, Di Prima G, D'Agostino F, et al. Lipid nanocarriers-loaded nanocomposite as a suitable platform to release antibacterial and antioxidant agents for immediate dental implant placement restorative treatment. *Pharmaceutics*. 2021 Dec 3;13(12):2072.
21. Raddi S, El Karmy B, Martinache O, Richert R, Colnot C, et al. Development of chlorhexidine-loaded lipid nanoparticles incorporated in a bioceramic endodontic sealer. *J Endod*. 2024 Aug 1;50(8):1134-42.
22. Ferreira S, Grenho L, Fernandes MH, Lima SA. Curcumin-loaded lipid nanoparticles: a promising antimicrobial strategy against *Enterococcus faecalis* in endodontic infections. *Pharmaceutics*. 2025 Jan;17(1):108.
23. Afrasiabi S, Partoazar A, Chiniforush N. In vitro study of nanoliposomes containing curcumin and doxycycline for enhanced antimicrobial photodynamic therapy against *Aggregatibacter actinomycetemcomitans*. *Sci Rep*. 2023 Jul 18;13(1):11552.
24. Panwar D, Sidhu K, Bhushan J, Kakkar V, Mehta M, Sharma J. Evaluation of antimicrobial efficacy of nanocurcumin-coated gutta-percha against *Enterococcus faecalis*: an in vitro study. *J Conserv Dent*. 2023;26:1604.
25. Sharma J, Panwar D, Bhushan J, Mehta M, Sidhu K, Jhamb S, et al. An in vitro evaluation of antibacterial effect of curcumin-loaded chitosan nanoparticle-coated gutta-percha against *Staphylococcus aureus*. *J Conserv Dent Endod*. 2023;26:5603.
26. Alfirdous RA, Garcia IM, Balhaddad AA, Collares FM, Martinho FC, et al. Advancing photodynamic therapy for endodontic disinfection with nanoparticles: present evidence and upcoming approaches. *Appl Sci*. 2021 May 22;11(11):4759.
27. Yarlagadda S, Selvakumar RJ, Parashar SR, Arockiam S, Natanasabapathy V. Comparative evaluation of the antimicrobial efficacy of nanoparticle-mediated photodynamic therapy versus photodynamic therapy and

conventional disinfection in endodontics: a systematic review and meta-analysis. *J Conserv Dent Endod*. 2023;26:50213.
28. Di Turi G, Riggio C, Vittorio O, Marconcini S, Briguglio F, et al. Sub-micrometric liposomes as drug delivery systems in the treatment and periodontitis. *Int J Immunopathol Pharmacol*. 2012 Jul;25(3):657-70.
29. Nguyen S, Adamczak M, Hiorth M, Smistad G, Kopperud HM. Interactions of liposomes with dental restorative materials. *Colloids Surf B Biointerfaces*. 2015 Dec 1;136:744-51.
30. Cherukuri G, Veeramachaneni C, Rao GV, Pacha VB, Balla SB. Insight into status of dental caries vaccination: a review. *J Conserv Dent*. 2020 Nov-Dec;23(6):544-9.
31. Rivankar S. An overview of doxorubicin formulations in cancer therapy. *J Cancer Res Ther*. 2014 Oct 1;10(4):853-8.
32. Attia MA, Essa EA, Elebyary TT, Faheem AM, Elkordy AA. Brief on recent application of liposomal vaccines for lower respiratory tract viral infections: from influenza to COVID-19 vaccines. *Pharmaceuticals (Basel)*. 2021 Nov 17;14(11):1173.
33. Fujisawa T, Miyai H, Hironaka K, Tsukamoto T, Tahara K, et al. Liposomal diclofenac eye drop formulations targeting the retina: formulation stability improvement using surface modification of liposomes. *Int J Pharm*. 2012 Oct 15;436(1-2):564-7.
34. Sopyan I, Gozali D. A review: a novel of efforts to enhance liposome stability as drug delivery approach. *Syst Rev Pharm*. 2020 Jun 1;11(6):765-71.
35. Inglut CT, Sorrin AJ, Kuruppu T, Vig S, Cicalo J, et al. Immunological and toxicological considerations for the design of liposomes. *Nanomaterials (Basel)*. 2020 Jan 22;10(2):190.
36. Barenholz Y. Liposome application: problems and prospects. *Curr Opin Colloid Interface Sci*. 2001 Feb 1;6(1):66-77.
37. Aghdam MA, Bagheri R, Mosafer J, Baradaran B, Hashemzaei M, et al. Recent advances on thermosensitive and pH-sensitive liposomes employed in controlled release. *J Control Release*. 2019 Dec 10;315:1-22.
38. Panthi VK, Fairfull-Smith KE, Islam N. Liposomal drug delivery strategies to eradicate bacterial biofilms: challenges, recent advances, and future perspectives. *Int J Pharm*. 2024 Mar 29:124046.
39. Cheng X, Gao J, Ding Y, Lu Y, Wei Q, et al. Multi-functional liposome: a powerful theranostic nano-platform enhancing photodynamic therapy. *Adv Sci (Weinh)*. 2021 Aug;8(16):2100876.
40. Li T, Takeoka S. Smart liposomes for drug delivery. In: Smart nanoparticles for biomedicine. Amsterdam: Elsevier; 2018. p. 31-47.
41. Zylberberg C, Gaskill K, Pasley S, Matosevic S. Engineering liposomal nanoparticles for targeted gene therapy. *Gene Ther*. 2017 Aug;24(8):441-52.
42. Meng J, Guo F, Xu H, Liang W, Wang C, et al. Combination therapy using co-encapsulated resveratrol and paclitaxel in liposomes for drug resistance reversal in breast cancer cells in vivo. *Sci Rep*. 2016 Mar 7;6:22390.