



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Cubosomes: A Frontier In Nanotechnology For Enhanced Drug Delivery

Kasturi Pangarkar*

Arnold and Marie Schwartz college of Pharmacy and Health Sciences - Long Island University, 1 University Plaza, Brooklyn, NY 11201 USA.

ARTICLE INFO

Published: 01 Nov 2024

Keywords:

Cubosomes, Nanocarriers, Drug Delivery, Bicontinuous Cubic Phase, Sustained Release, Bio adhesion, Personalized Medicine.

DOI:

10.5281/zenodo.14024554

ABSTRACT

Cubosomes, a class of nanostructured lipid carriers, have emerged as highly versatile systems for drug delivery due to their unique bicontinuous cubic phase structure. Their ability to encapsulate hydrophilic, lipophilic, and amphiphilic drugs, along with their large surface area, makes them ideal for sustained and controlled drug release. Cubosomes can be administered via multiple routes, including oral, ophthalmic, topical, intravenous, intranasal, and pulmonary, each offering specific advantages in terms of bioavailability, targeted delivery, and therapeutic efficacy. Their bioadhesive properties enhance drug absorption, while their nanostructure provides protection against enzymatic and physical degradation. Recent advances in cubosome manufacturing techniques, such as top-down and bottom-up approaches, have improved scalability and stability, making them suitable for large-scale production. The application of cubosomes in theranostics, vaccine delivery, and peptide and protein drugs highlight their potential in advanced therapeutic strategies. Cubosomes hold great promise for future developments in targeted drug delivery, personalized medicine, and multifunctional therapeutic systems.

INTRODUCTION

Cubosomes are a type of lipid-based nanoparticle that have gained significant attention in drug delivery due to their unique structure and benefits. First introduced in the 1980s, cubosomes have a continuous cubic phase structure, allowing them to effectively encapsulate hydrophobic, hydrophilic, and amphiphilic drugs. This cubic arrangement offers a large internal surface area, which

facilitates high drug loading and controlled release. Their versatility makes cubosomes suitable for various drug delivery methods, including oral, topical, and parenteral routes, as well as for use in cosmetics and food products.

Amphiphilic molecules are crucial in drug delivery because they self-assemble into organized structures under certain conditions, enabling the efficient delivery of active compounds. These

*Corresponding Author: Kasturi Pangarkar

Address: Arnold and Marie Schwartz college of Pharmacy and Health Sciences - Long Island University, 1 University Plaza, Brooklyn, NY 11201 USA.

Email ✉: kasturip2204@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



nanocarriers protect drugs from degradation, offer controlled release, and improve bioavailability while minimizing side effects. Among the self-assembled structures, lamellar, hexagonal, and cubic phases form the foundation of lyotropic liquid crystal systems. By dispersing these structures in water, nanoparticles such as liposomes, cubosomes, and hexosomes are formed. Due to their unique ability to encapsulate a wide range of molecules, cubosomes have attracted increasing interest in recent years for their applications in drug delivery. This review will discuss the structure, chemistry, preparation methods, and current applications of cubosomes based on recent developments in the field (1–3).

Components of Cubosomes

Amphiphilic Lipids: The primary lipid used in cubosomes is glyceryl monooleate (GMO), which can self-assemble into a cubic phase in water.

Stabilizers: Polymers like Pluronic F127 are used to prevent aggregation and maintain the nanoscale structure.

Water as a Medium: Water acts as the dispersion medium and helps in forming the cubic mesophase.

Cubic Phase and Its Structure

Bicontinuous Cubic Phase: The cubic phase is a 3D lattice structure that separates hydrophilic regions and offers high surface area for drug encapsulation.

Phase Transitions: The cubic phase can transition to other phases, such as lamellar or hexagonal, depending on factors like water content and temperature.

Cubosome Formation and Nanostructures

Nanostructure Formation: Cubosomes are formed by dispersing cubic liquid crystals into nanostructures with surfactants.

Size and Characteristics: These nanoparticles range from 100 to 300 nm and have a high surface area and low viscosity, making them efficient drug carriers.

Key Lipids in Cubosome Preparation

Glyceryl Monooleate (GMO): GMO is widely used in cubosome formulations for its amphiphilic properties and ability to form lyotropic liquid crystals.

Phytantriol (PHYT): An alternative to GMO, PHYT provides enhanced structural stability due to its resistance to hydrolysis.

Role of Stabilizers in Cubosome Stability

Poloxamer 407 (P407): The most commonly used stabilizer, crucial for maintaining the nanostructure and influencing phase behavior.

Effect on Particle Size: Higher stabilizer concentrations reduce particle size and prevent coalescence, ensuring colloidal stability.

Polymers derived from castor oil, specifically those rich in ricinoleic acid, offer promising potential as key components in the development of stable cubosomes. The unique combination of hydroxyl, carboxylic, and double bond groups in ricinoleic acid enables chemical modifications that enhance the stability and functionality of cubosome formulations. These renewable, biocompatible polymers not only improve the structural integrity of cubosomes but also contribute to their environmentally friendly nature, making them an ideal choice for sustainable drug delivery systems. By incorporating castor oil-based polymers, cubosome formulations can achieve greater stability, enhanced drug encapsulation, and controlled release profiles (4).

Applications of Cubosomes

Drug Delivery Systems: Cubosomes are used for sustained drug release, enhancing the stability and bioavailability of active compounds.

Cosmetics and Biosensors: Beyond pharmaceuticals, cubosomes are also used in cosmetics for skin delivery and in biosensor development (5,6).

Advancements in Cubosome Research

Lipid Combinations: Research continues on optimizing lipid and stabilizer combinations to improve cubosome efficiency and stability.

The incorporation of herbal drugs into advanced delivery systems like cubosomes offers a novel approach to enhancing their therapeutic efficacy. For instance, *Moringa oleifera* Lam., known for its anti-asthmatic properties, can benefit from cubosomal encapsulation (7).

Cubosomes offer a promising platform for the formulation and standardization of polyherbal treatments, such as those used for managing Type 2 Diabetes Mellitus. By encapsulating polyherbal formulations within cubosomes, it is possible to achieve better control over the release profiles of active compounds, enhancing their bioavailability and therapeutic effectiveness. The use of cubosomes also supports improved quality control by providing a more stable environment for herbal ingredients, protecting them from degradation and ensuring consistency in dosage. This approach can lead to more reliable and effective polyherbal formulations for diabetes management (8).

Emerging Applications: Novel uses include mucosal, transdermal, and periodontal drug delivery, showcasing cubosomes' versatility.

Manufacturing Techniques of Cubosomes

Producing cubosomes with uniform particle size and stability is crucial for pharmaceutical applications. Two main approaches are utilized: the top-down and bottom-up methods. Both techniques require a colloidal stabilizer, such as Poloxamer 407, to prevent aggregation.

1. Top-Down Approach

In the top-down method, a bulk cubic phase is first formed by mixing lipids and stabilizers. This bulk phase is then broken down into nanoparticles through high-energy processes like sonication or high-pressure homogenization. This approach is effective for producing uniform cubosomes but can be energy-intensive and unsuitable for temperature-sensitive compounds, such as

proteins and peptides. While the top-down method ensures stable cubosomes for up to a year, it can result in coexisting vesicles and requires high energy for dispersing the cubic phase into smaller nanoparticles.

2. Bottom-Up Approach

The bottom-up method involves the self-assembly of cubosomes from lipids and water, aided by stabilizers. Techniques like solvent evaporation or the liquid precursor method, where lipids dissolve in a hydrotrope, are commonly used. This approach is more energy-efficient than the top-down method and better suited for temperature-sensitive materials. Additionally, it produces smaller particles with long-term stability and higher encapsulation efficiency. However, controlling the dilution process is critical for success, and this method may also result in the formation of unwanted vesicles.

3. Emerging Methods

Innovations such as using phosphate-buffered saline (PBS) to modify lipid curvature have shown potential for producing cubosomes without hydrotropes. This method adjusts the bilayer curvature by adding charged lipids, offering a way to tailor cubosomes to specific requirements.

4. Spray Drying and Freeze Drying

These techniques are used to convert cubosomes into dry powders, which can be rehydrated when needed. This approach enhances the stability and shelf-life of cubosome formulations, making them easier to store and transport.

In conclusion, while both the top-down and bottom-up approaches have their advantages, the bottom-up method is generally more efficient for large-scale production, especially when working with sensitive materials. New techniques like charge-shielding offer promising avenues for improving cubosome manufacturing (9,10).

Analytical Approaches for Cubosome Characterization



Characterizing cubosomes is essential to understand their physicochemical properties, stability, and effectiveness in drug delivery. Various analytical techniques are used for this purpose:

Small-Angle X-ray Scattering (SAXS): This is the gold standard for confirming the cubic phase structure of cubosomes. It provides detailed information about lattice parameters and the internal structure.

Cryo-Electron Microscopy (Cryo-EM): This high-resolution imaging technique allows for direct visualization of cubosome structures, offering insights into their morphology and confirming the presence of cubic phases.

Dynamic Light Scattering (DLS): DLS measures the size distribution and polydispersity index of cubosome dispersions, both of which are critical for assessing the stability of the formulation.

Zeta Potential Analysis: This method evaluates the surface charge of cubosomes, providing information about their colloidal stability and potential interaction with biological membranes (11,12).

Cubosomes And Related Formulation For Various Therapeutic Applications

Cubosomes are versatile drug delivery systems capable of encapsulating hydrophilic, lipophilic, and amphiphilic drugs. Their structure allows for targeted compartmentalization: hydrophilic drugs can be stored in the aqueous channels, lipophilic drugs in the lipid bilayer, and amphiphilic molecules at the lipid–water interface. Key features of cubosomes in drug delivery include:

Solubilization of various drug types: Cubosomes can encapsulate hydrophilic, lipophilic, and amphiphilic drugs.

Bioadhesion: Their adhesive properties enable prolonged contact with biological membranes, improving drug absorption.

Sustained drug release: Cubosomes provide controlled, sustained release of drugs over time.

Protection from degradation: They protect drugs from enzymatic or physical degradation, enhancing stability.

Biocompatibility: The materials used in cubosomes are non-toxic, making them suitable for various therapeutic applications.

Poly(lactic-co-glycolic acid) (PLGA) is a popular biodegradable polymer used in drug delivery systems due to its biocompatibility and customizable properties (13).

Recent advancements have expanded the use of cubosomes in theranostics, combining therapy and diagnostics. For example, cubosomes loaded with both anticancer drugs and near-infrared (NIR) imaging agents have been developed for cancer treatment. Targeting capabilities can be enhanced by functionalizing cubosomes with ligands like folate, allowing for specific targeting of cancer cells.

Cubosomes are particularly effective for delivering peptide and protein drugs, which are prone to rapid degradation. By encapsulating these molecules in cubosomes, they are protected and can be released in a controlled manner. Additionally, cubosomes show promise in vaccine delivery, where they can enhance the immune response by incorporating adjuvants and antigenic substances (14).

Lipoidal vesicular drug delivery systems, such as liposomes, ethosomes, and transferosomes, have revolutionized targeted drug delivery by offering improved bioavailability, controlled release, and enhanced targeting of specific tissues. These systems share similarities with cubosomes in their ability to encapsulate a wide variety of drugs while protecting them from degradation. Characterization methods, including particle size analysis, surface charge determination, and release studies, are critical for optimizing the performance of these vesicular carriers (15,16).

Cubosomes offer a versatile platform for delivering proteins due to their ability to



encapsulate and protect sensitive biomolecules. The characterization of proteins encapsulated within cubosomes is crucial to ensure their stability and functionality. One of the key methods for analyzing the secondary structure of proteins is Circular Dichroism (CD) spectroscopy. This technique allows for the examination of protein folding, particularly the α -helices and β -sheets that form through hydrogen bonding in the polypeptide backbone. For accurate structural analysis, several factors must be optimized, including solvent selection to preserve the protein's native state, sample concentration, and path length to ensure high signal quality. Proper data processing, including baseline correction and conversion to mean residue ellipticity, is essential to obtain reliable insights into the protein's secondary structure. By integrating CD spectroscopy into the characterization of protein-loaded cubosomes, researchers can ensure that the encapsulated proteins maintain their functional integrity, enhancing the therapeutic potential of these nanocarriers (17–20). Cubosomes provide an innovative delivery system for peptide therapeutics, offering enhanced stability and controlled release. However, the accurate analysis of peptides encapsulated within cubosomes is critical for ensuring their efficacy and quality. Peptides are known for their hygroscopicity and sensitivity to environmental conditions, making their assay challenging. To address these issues, the use of well-characterized, lyophilized peptide working standards is essential to ensure precise quantification. Proper standardization, stability testing, and stringent quality control metrics are required to obtain reproducible results across different instruments, analysts, and laboratories. By incorporating these analytical strategies into the development of peptide-loaded cubosomes, it becomes possible to ensure the reliability and therapeutic potential of these formulations in clinical applications (21,22).

Lipoidal systems have been widely explored in areas such as cancer therapy, infectious disease treatment, gene therapy, and transdermal applications. Despite facing challenges related to stability, scalability, and precise targeting, ongoing advancements in formulation techniques and nanotechnology continue to expand the potential of these systems. The integration of innovative manufacturing methods has opened new pathways for the development of versatile, efficient, and patient-specific drug delivery platforms. Incorporating these advances into the field of cubosome research could further enhance their role in complex therapeutic strategies, such as theranostics and personalized medicine (23,24). Nanotechnology has significantly advanced biomedicine, particularly in drug delivery systems, by utilizing the unique properties of nanoparticles to improve therapeutic outcomes. The precise control of nanoparticle size, surface charge, and structure enables enhanced drug targeting, bioavailability, and controlled release. Nanoparticle-based drugs, including several FDA-approved therapies, demonstrate the potential of nanotechnology in clinical settings. However, as the use of nanoparticles expands, there are growing concerns about the long-term safety and potential risks of nanoparticle exposure, highlighting the need for ongoing research and careful evaluation in therapeutic applications (25–27). Cell-based *in vitro* models play a crucial role in early drug development, providing cost-effective methods to study drug absorption. These models utilize immortalized epithelial cells to replicate barriers like the gut, lung, and skin, allowing for the analysis of absorption rates and mechanisms. A key challenge remains in aligning *in vitro* findings with real-world human absorption, and refining these models is essential for optimizing drug discovery and advancing promising therapeutic candidates (28).



Microspheres and cubosomes represent advanced drug delivery systems that offer enhanced control over drug release and stability. While microspheres, such as those designed for acetazolamide using the Box-Behnken method, allow for precise drug encapsulation and sustained release, cubosomes provide additional benefits with their unique bicontinuous cubic phase structure. Integrating cubosomal technology with microsphere formulations can further improve drug bioavailability, stability, and release profiles, offering a powerful combination for optimizing therapeutic outcomes in various pharmaceutical applications (29,30). Cubosomes, as advanced nanocarriers, offer significant potential for enhancing the delivery of traditional chemotherapeutic agents like alkylating compounds. Drugs such as cisplatin, an alkylating agent widely used in cancer treatment, can benefit from cubosome encapsulation by improving their stability, bioavailability, and targeted delivery. Cisplatin exerts its anticancer effects through DNA crosslinking and apoptosis induction, but its conventional use is often associated with systemic toxicity and side effects. By incorporating cisplatin into cubosomes, it is possible to achieve controlled release, reduce toxicity, and enhance the drug's effectiveness by delivering it directly to tumor cells. This approach not only maximizes the therapeutic potential of alkylating agents but also aligns with the goal of cubosome-based drug delivery to improve cancer treatment outcomes (31). Cancer treatment often faces challenges in targeting tumors and ensuring controlled drug release. Niosomes, self-assembled vesicular systems, have emerged as a promising solution for advanced drug delivery in cancer therapy. They offer advantages such as enhanced drug stability, controlled release, and targeted delivery, outperforming some conventional and other vesicular delivery methods. Similarly, cubosomes, with their unique cubic phase structure, provide

enhanced drug encapsulation and sustained release capabilities. Both niosomes and cubosomes hold great potential for improving cancer treatment outcomes, though further research is needed to overcome their respective limitations and optimize their use in clinical settings (32,33).

Routes of Administration for Cubosomes (3,10)

Cubosomes are versatile nanocarriers that can be administered through various routes depending on the therapeutic goal. Their ability to encapsulate a wide range of drugs, coupled with their bioadhesive properties and controlled release potential, makes them suitable for different administration pathways. Here are the primary routes through which cubosomes are delivered:

1. Oral Administration

Cubosomes are emerging as promising carriers for oral drug delivery, particularly for poorly water-soluble drugs. Their unique nanostructure allows for improved solubilization of lipophilic drugs in the gastrointestinal (GI) tract. The bioadhesive nature of cubosomes promotes prolonged contact with the intestinal mucosa, enhancing absorption. Additionally, cubosomes can protect drugs from the harsh environment of the GI tract, preventing degradation. Studies have shown that drugs like ibuprofen and anticancer agents such as protopanaxadiol (PPD) demonstrate enhanced bioavailability when delivered via cubosomes.

Key advantages of oral administration include:

- Improved solubility of poorly water-soluble drugs
- Enhanced intestinal absorption due to bioadhesion
- Protection of drugs from degradation in the GI tract

2. Ophthalmic Delivery

Topical ocular drug delivery is challenging due to the eye's protective mechanisms, such as blinking and tear production, which limit drug retention and absorption. Cubosomes offer a solution by adhering to the corneal surface and providing sustained release of drugs. Their nanostructure allows for better penetration through the corneal



barrier. Cubosome-based formulations for drugs like flurbiprofen and dexamethasone have shown improved bioavailability and longer retention in the eye compared to conventional eye drops. Key advantages of ophthalmic administration include: Increased drug retention and prolonged contact with the eye Enhanced transcorneal drug permeability Reduced irritation and improved patient compliance

3. Topical Delivery

Cubosomes are well-suited for transdermal and topical delivery, particularly for drugs that need to penetrate the skin barrier. The lipid bilayer of cubosomes can interact with the stratum corneum, enhancing drug permeation. This makes cubosomes effective for the treatment of skin conditions and for delivering drugs such as silver sulfadiazine for burn wounds or antifungal agents like clotrimazole. Additionally, cubosomes can be combined with microneedles to improve skin penetration and drug delivery. Key advantages of topical administration include: Improved skin penetration of drugs Ability to deliver both hydrophilic and lipophilic drugs

Sustained release of drugs over time

4. Intravenous (IV) Administration

Cubosomes can be administered intravenously for systemic drug delivery. However, their formulation must be carefully controlled to ensure colloidal stability and prevent aggregation. Surface modifications, such as PEGylation, can improve the circulation time of cubosomes in the bloodstream and minimize interactions with plasma proteins. Cubosomes have been investigated for the delivery of anticancer drugs, contrast agents for imaging, and other therapeutic molecules via IV administration. Key advantages of intravenous administration include: Rapid systemic distribution of drugs Ability to deliver drugs to specific organs or tissues Surface modifications can enhance circulation time and target specificity

5. Intranasal Administration

Cubosomes have shown potential in intranasal drug delivery, particularly for bypassing the blood-brain barrier (BBB) and delivering drugs directly to the brain. This route offers a non-invasive alternative for treating central nervous system (CNS) disorders, such as Alzheimer's disease and Parkinson's disease. Surface-engineered cubosomes, such as those functionalized with odorranalectin, have been shown to enhance the delivery of therapeutic peptides and proteins to the brain through the nasal cavity. Key advantages of intranasal administration include: Direct drug delivery to the brain, bypassing the BBB Non-invasive route for CNS therapies

Potential for treating neurodegenerative diseases

6. Pulmonary Delivery

Cubosomes can also be delivered via the pulmonary route for the treatment of respiratory diseases. Their nanoscale size allows them to be efficiently aerosolized and delivered to the lungs. This route is especially useful for delivering drugs that target the respiratory system, such as anti-inflammatory agents for asthma or chronic obstructive pulmonary disease (COPD). Cubosomes can also be used for systemic delivery through the alveolar epithelium. Key advantages of pulmonary administration include: Direct delivery to the respiratory system for localized treatment Potential for systemic drug delivery via the lungs Efficient drug deposition in the alveoli

CONCLUSION

Cubosomes represent a highly promising and versatile nanocarrier system for drug delivery, owing to their unique structural properties and ability to encapsulate a wide variety of therapeutic agents, including hydrophilic, lipophilic, and amphiphilic drugs. Their bicontinuous cubic phase structure provides an extensive internal surface area, enabling high drug loading capacity and controlled, sustained drug release, which are



essential for improving drug efficacy and patient outcomes. The different routes of administration that cubosomes can support—oral, ophthalmic, topical, intravenous, intranasal, and pulmonary—highlight their adaptability across a range of medical applications. Each route offers specific advantages: oral delivery benefits from enhanced bioavailability, ophthalmic delivery sees improved drug retention and absorption, and topical formulations experience increased skin permeability. Intravenous and intranasal routes allow for systemic and targeted delivery, especially for drugs that need to bypass biological barriers such as the blood-brain barrier, while pulmonary administration offers effective treatment for respiratory diseases. Cubosomes have demonstrated considerable potential in not only conventional drug delivery but also in advanced therapeutic strategies, including theranostics—where drug delivery is coupled with diagnostic capabilities. Additionally, cubosomes offer protection for sensitive molecules, such as peptides, proteins, and vaccines, shielding them from enzymatic and physical degradation while facilitating their controlled release. Furthermore, innovative manufacturing techniques such as the top-down and bottom-up approaches have enabled the efficient production of cubosomes with stable particle size and structure. While challenges remain, such as scale-up limitations and stability concerns, advancements in surface modifications, like PEGylation and ligand attachment, have further enhanced the targeting capabilities and therapeutic efficacy of cubosome formulations. In conclusion, the versatility, biocompatibility, and potential for surface functionalization make cubosomes a cutting-edge platform for future drug delivery systems. Their ability to be tailored for specific therapeutic needs opens doors to personalized medicine, improved treatment efficacy, and reduced side effects. As research progresses, cubosomes are poised to play a central

role in the next generation of targeted, efficient, and multifunctional drug delivery system.

CONFLICT OF INTEREST

The author declares that there are no conflicts of interest regarding the publication of this article.

REFERENCES

1. Singhal K, Kaushik N, Kumar A. Cubosomes: Versatile Nanosized Formulation for Efficient Delivery of Therapeutics. *Curr Drug Deliv.* 2021;19(6).
2. Garg G, Saraf S, Saraf S. Cubosomes: An overview. Vol. 30, *Biological and Pharmaceutical Bulletin.* 2007.
3. Karami Z, Hamidi M. Cubosomes: Remarkable drug delivery potential. Vol. 21, *Drug Discovery Today.* 2016.
4. Vashi AS. Renewable Resource-Based Polymers And Properties Of Interpenetrating Polymer Networks Based On Castor Oil. *International Research Journal of Modernization in Engineering Technology and Science.* 2024;6(04):7074–9.
5. Elakkad YE, Younis MK, Allam RM, Mohsen AF, Khalil IA. Tenoxicam loaded hyalucubosomes for osteoarthritis. *Int J Pharm.* 2021;601.
6. Sivadasan D, Sultan MH, Alqahtani SS, Javed S. Cubosomes in Drug Delivery—A Comprehensive Review on Its Structural Components, Preparation Techniques and Therapeutic Applications. Vol. 11, *Biomedicines.* 2023.
7. Patel BA, Sachdeva Pd. Evaluations Of Anti-Asthmatic Activity Of Roots Of Moringa Oleifera Lam. In *Various Experimental Animal Models. Inventi Impact: Planta Activa.* 2011;
8. Vijapur LS, Singh G, Pandey J, Patel BA, Kanna J, Konda S, et al. Formulation Standardization And Quality Control Of Polyherbal Formulation For Treatment Of



- Type 2 Diabetes Mellitus. *Nanotechnol Percept.* 2024;20(11):775–83.
9. Nanjwade BK, Hundekar YR, Kamble MS, Srichana T. Development of Cuboidal Nanomedicine by Nanotechnology. *Austin Journal of Nanomedicine & Nanotechnology* . 2014;2(4).
 10. Abourehab MAS, Ansari MJ, Singh A, Hassan A, Abdelgawad MA, Shrivastav P, et al. Cubosomes as an emerging platform for drug delivery: a review of the state of the art. Vol. 10, *Journal of Materials Chemistry B*. 2022.
 11. Almoshari Y, Alam MI, Bakkari MA, Salawi A, Alshamrani M, Sabei FY, et al. Formulation, Characterization, and Evaluation of Doxorubicin-loaded Cubosome as a Cytotoxic Potentiator against HCT-116 Colorectal Cancer Cells. *Indian Journal of Pharmaceutical Education and Research*. 2022;56(3).
 12. Meikle TG, Dyett BP, Strachan JB, White J, Drummond CJ, Conn CE. Preparation, Characterization, and Antimicrobial Activity of Cubosome Encapsulated Metal Nanocrystals. *ACS Appl Mater Interfaces*. 2020;12(6).
 13. Vashi A. Comprehensive Review On The Characterisation And Quantification Of Plga In Pharmaceutical Drug Products. *World J Pharm Pharm Sci*. 2024;13(08):116–44.
 14. Patel HK, Suthar RM, Jadeja MB. Penetration Enhancers: An Important Tool for Transdermal Drug Delivery. [https://www.google.com/books/edition/Penetration_Enhancers/YMW4NAEACAAJ ...](https://www.google.com/books/edition/Penetration_Enhancers/YMW4NAEACAAJ...); 2012.
 15. Vashi A. Innovative approaches in characterizing and developing methods for lipoidal vesicular drug delivery systems. *GSC Advanced Research and Reviews*. 2024;20(1):427–38.
 16. Jadeja M, Patel R. Development And Evaluation Of Phosphatidylcholine Complexes Of Arbutin As Skin Whitening Agent. *Int J Pharm Sci Res*. 2021;12(2):917–27.
 17. Kuril AK, Vashi A, Subbappa PK. A comprehensive guide for secondary structure and tertiary structure determination in peptides and proteins by circular dichroism spectrometer. *Journal of Peptide Science*. 2024;e3648.
 18. Micsonai A, Wien F, Kernya L, Lee YH, Goto Y, Réfrégiers M, et al. Accurate secondary structure prediction and fold recognition for circular dichroism spectroscopy. *Proc Natl Acad Sci U S A*. 2015;112(24).
 19. Whitmore L, Wallace BA. Protein secondary structure analyses from circular dichroism spectroscopy: Methods and reference databases. *Biopolymers*. 2008;89(5).
 20. Bertocchi F, Sissa C, Painelli A. Circular dichroism of molecular aggregates: A tutorial. *Chirality*. 2023;35(10).
 21. Kuril AK, Vashi A. Identifying Trending Issues in Assay of Peptide Therapeutics During Stability Study. *Am J Biomed Sci Res*. 2024;22(4):501–4.
 22. Bousmail D, Amrein L, Fakhoury JJ, Fakhir HH, Hsu JCC, Panasci L, et al. Precision spherical nucleic acids for delivery of anticancer drugs. *Chem Sci*. 2017;8(9).
 23. Vashi A. Innovative approaches in characterizing and developing methods for lipoidal vesicular drug delivery systems. *GSC Advanced Research and Reviews*. 2024;20(1):427–38.
 24. Alam MK. Nanocarrier-Based Drug Delivery Systems using Microfluidic-Assisted Techniques. Vol. 3, *Advanced NanoBiomed Research*. 2023.
 25. Vashi A. Nanoparticle Based Liposomes For Drug Delivery: A Review Of

- Physicochemical Considerations. *International Research Journal of Modernization in Engineering Technology and Science*. 2024;6(5):9028–38.
26. Edgar JYC, Wang H. Introduction for Design of Nanoparticle Based Drug Delivery Systems. *Curr Pharm Des*. 2016;23(14).
27. Duan L, Li X, Ji R, Hao Z, Kong M, Wen X, et al. Nanoparticle-Based Drug Delivery Systems: An Inspiring Therapeutic Strategy for Neurodegenerative Diseases. Vol. 15, *Polymers*. 2023.
28. Vashi A. Cell-Based In Vitro Models: Emerging Technologies For Enhanced Drug Permeability Prediction. *International Research Journal Of Modernization in Engineering Technology and Science*. 2024;6(4):6389–97.
29. Abbas Ali Ghoto Kalyan Chakravarthy Janjanam Jeganathan Kannan Shyamala Praveencumar Ramachandr Ganesh Kumar Varsha Deva SanjayKumar Patel AV. Formulation Designing And Optimizing Acetazolamide Microspheres Using A Box-Behnken Method. *Nanotechnol Percept*. 2024;20(S11):1008–18.
30. Suthar RM, Thumar RM, Jadeja MB, Lad BN. AN OVERVIEW ON SUSTAINED DRUG Delivery System. *Inventi Rapid: Pharm Tech*. 2010;
31. Vashi A, Kuril Ak. Cisplatin: A Beacon Of Hope In Cancer Treatment-Unveiling The Potent Alkylating Antineoplastic Agent. *European Journal Of Pharmaceutical And Medical Research*. 2024;11(06):197–203.
32. Patel Ba. Niosomes: A Promising Approach For Advanced Drug Delivery In Cancer Treatment. *International Research Journal Of Modernization In Engineering Technology and Science*. 2024;6(4):2747–52.
33. Rao L, He Z, Meng QF, Zhou Z, Bu LL, Guo SS, et al. Effective cancer targeting and imaging using macrophage membrane-camouflaged upconversion nanoparticles. *J Biomed Mater Res A*. 2017;105(2)

HOW TO CITE: Kasturi Pangarkar, Cubosomes: A Frontier In Nanotechnology For Enhanced Drug Delivery, *Int. J. of Pharm. Sci.*, 2024, Vol 2, Issue 11, 27-36. <https://doi.org/10.5281/zenodo.14024554>