

Cubosomes in Drug Therapy – A Review

Akshaya.S, Santhiyapriya, Sivaranjani, Fatima GraceX, Karuna Priyachitra, V.Dhanapal*

Sree Sastha Pharmacy College, Chennai, Tamil Nadu, India 600123.

For Correspondence

Dr.Fatima Grace.X

Professor

Department of Pharmaceutics

Sree Sastha Pharmacy College

Chennai, Tamil Nadu, 600123.

Mobile: 9789003525

CUBOSOMES IN DRUG THERAPY – A REVIEW

ABSTRACT:

Cubosomes are angular and symmetric particles with clearly discernible interior cubic lattices. The development of cubosomes is a unique tale that touches the domains of food science, digestion, biological membranes and differential geometry process. Cubosomes that self-assemble act as active ingredient delivery systems, which are widely used and are significant inventiveness and nominations. The cubosomes are, they surround a structure assembly which resembles the shape of “honeycomb” which is thermodynamically stable. This structure encloses bicontinuous water domains plus liquid. It is put together in the surfactant into bilayers and encased in a periodic, three-dimensional structure with very little surface area, resulting in a densely packed structure. Bicontinuous cubic liquid phase of crystalline structure has a very viscous structural substance that is optically clear and an exclusive nanometre-scale structure.

Keywords: Cubosomes, Honeycomb, encapsulation, nanostructure, novel delivery.

INTRODUCTION:

Cubosomes are prepared in a very straight forward manner, but lipids with biodegradable properties an encapsulate hydrophobic, hydrophilic and amphiphilic molecules which helps in targeted and controlled release of chemical bioactive substance. Bio adhesive cubosomes dispersions are biocompatible.[1-3] Due to their characteristics, cubosomes are flexible system that may be managed in a variety of ways, including such as parenteral, percutaneous and oral. Cubosomes possess applications that are widespread, extensive and are characterized by a number of factors. Consequently, cubosomes are moving towards greater public notice by division for pharmaceutical industries.[4-5]

ADVANTAGES OF CUBOSOMES:[6-9]

- ❖ Even in excess of water, cubosomes have stability in physicochemical.
- ❖ Cubosomes are having excellent solubilizer properties.
- ❖ They have capability to entrap by hydrophilic, lipophilic and amphiphilic substance.
- ❖ Preparation method is simple for cubosomes and it does not require organic solvent for preparation by shear and homogenizer technique.
- ❖ They are non-irritant, non-allergic, non-toxic.
- ❖ They are less cost due to less repeated administration.
- ❖ They have bio-adhesive property in which the polymer presents in cubosomes such as PEG moieties are attached to biological membrane.
- ❖ Polymer present in cubosomes is stabilizers as well as it has controlled & targeted released behaviour.
- ❖ Due to cubic crystalline structure & increase surface area, drug loading capacity is increases.

DISADVANTAGES OF CUBOSOMES:

- ❖ Cubosomes have large amount of water, which affect the entrapment of hydrophilic drug.
- ❖ Due to increase viscosity, it affects the formation of cubosomes.
- ❖ Due to external environment, it may possible to change the phase.
- ❖ Due to increased drug loading it may chance for the growth of particles.

CUBOSOME & USES:

Application of such new materials includes drug delivery vehicles. It is anticipated that the rapidly expanding life science sector will introduce formerly “exotic” delivery methods and chemicals into more mainstream markets, including those for personal care and consumer goods.[10,11] The use of cubosomes particles as an oil-in-water emulsion stabilizer and pollution absorbents in cosmetics is the subject of several studies conducted in conjunction with cosmetic businesses like L'Oréal and Nivea.[12,13] As a result, a variety of medicinal active ingredients and applications have been thoroughly investigated for compatibility with self-assembled surfactant phases.[14,15] Recently, there has been a lot of patent activity on the use of cubosomes in personal care goods

as antiperspirant, skin care, hair care and cosmetics. Numerous medications have been added to cubosomes, and sustained drug release behaviour has also been investigated.[16-19] Because of cubosomes remnant particles cubosome behaviour was perpetuated. Topical and mucosal deposition and drug delivery employ cubic phases because they are more bio-adhesive in nature, which causes them to contain more particles. Cubic phase materials can be created by mixing water and lipids that are compatible with living things, making them ideal for treating skin, hair and other body tissues.[20] Anticancer agents can be delivered orally or topically using cubosomes. Few anticancer medications have recently been successfully cubosome-encapsulated and physico-chemically described. Different strategies have been considered in order to target nanomedicines particularly to tumours, with active and passive targeting of cancer cells both having proven to be effective techniques used in both preclinical and clinical trials.[21]

HISTORY / NARRATION:

Due to its intricacy and high viscosity, cubosome manufacturing on a widescale was challenging in the earlier 1980's. This cubic phase may be split and distributed, based on thermodynamics and high stability. They stand out because of the similar viscosity as that of solids. Depending on the concentration, when combined with surfactants, cubic phases emerge quickly. Larsons, Lusatia et al., Luzzati and Husson and Hyde et al., identified these structure of honeycomb between 1960 to 1985. Larsson came up with the term 'cubosome' since its design is similar to cubic molecular crystals and liposomes. There were attempts to scale up the making of cubosomes. Few anticancer drugs are rarely used as cubosomes.[22]

CURRENT STATUS OF KNOWLEDGE:

The medication delivery method known as cubosomes is innovative and biocompatible.[23] These Nano particles used in controlled release have significant implications for pharmacy and cosmetics industries. In the first example, Leal et al., demonstrated that the Gyroid cubic phase grew to Lattice parameter above 20nm when 15 mol% of the positively charged lipid DOTAP was added to cubosomes made of monoolein in OptiMEM media.[24] Spicer et al., first described the dilution method. They created a monoolein-water-ethanol phase diagram and thus demonstrated that cubosome creation employing nucleation processes.[25] Elnagger et al., Created piperine-loaded cubosomes with integrated monoolein to combat Alzheimer's illness. [26]

According to Dian et al., a GMO-based piperine cubosomes has a safer effect on brain cells than a free medication and improves cognitive performance in Alzheimer's disease.[27]

METHOD OF PREPARATION;[28]

Cubosomes can be prepared by High pressure homogenizer, Emulsifier, Spray drying etc.

Prepared by two techniques

Top down technique

Bottom up technique

TOP DOWN TECHNIQUE:

Monoolein (lipid) + poloxamer 407(stabilizer)

↓ mixed

Aqueous phase

↓ High energy input

Homogenizer

↓

Cubosome

ADVANTAGES:

Organic solvent is not used, so it is simple method.

DISADVANTAGE:

Heat sensitive drugs are not used in homogenizer.

BOTTOM UP TECHNIQUE:

Monoolein(lipid)+Poloxamer407(stabilizer)+sodium benzoate(hydrotropes)

↓ Mix

Aqueous phase

↓ low energy input

Vortex

↓

Cubosome

ADVANTAGES:

Low energy and less time are consumed.

DISADVANTAGES:

Causes allergy due to hydrotropes.

CONCLUSION:

Cubosomes as cubic phase materials are made from a straight forward lipid and water mixture that is compatible with living organisms, as a result it is suitable for pharmaceutical and body tissues. The primary use of cubosome are regulated or controlled release several of medications like for the treatment of cancer, devices for administering medication orally and intravenously,

methods and techniques for applying drugs topically. The ability to sculpt cubosomes during production and utilization during manufacturing gives enormous flexibility for creating products. In addition, the story or the reviews from the past attest to cubosomes usefulness as a controlled release drug delivery system.

ACKNOWLEDGEMENT

The Authors appreciate and thank Sree Sastha Pharmacy College administration's assistance and for their whole hearted support.

REFERENCES

- Bhosale RR, Osmani RA, Harkare BR, Ghodake PP. Cubosomes. The Inimitable Nanoparticulate Drug Carriers. *Sch Acad J Pharm* 2013; 2:481-86.
- Wu H, Li J, Zhang Q, Yan X, Guo L, Gao X et al. A novel small Odorrana lectin - bearing cubosomes: preparation, brain delivery and pharmacodynamics study on amyloid- β 25-35- treated rats following intranasal administration. *Ear J Pharm Bio Pharm* 2012; 80:368-78.
- Scriven LE. Equilibrium bicontinuous structure. *Nature* 1976;263:123-25.
- Madhurilatha T, Paruchuri SK, Suria Prabha K. Overview of Cubosomes: A Nano Particle. *IJRPC* 2011; 1:535-41.
- Spicer P. Cubosome Processing Industrial Nanoparticle Technology Development. *Chem. Eng. Res. Des* 2005;83:1283-86.
- Rizwan SB, Dong YD, Boyd BJ, Rades T, Hook S. Characterisation of bicontinuous cubic liquid crystalline systems of phytantriol and water using cryo field emission scanning electron microscopy (cryo FESEM). *Micron* 2007;38:478-85.
- Bei D, Meng J, Youan BC. Engineering nanomedicines for improved melanoma therapy: progress and promises. *Nano medicine (Lond)* 2010;5:1385-99.
- Gustafsson J, Ljusberg Wahren H, Almgren M, Larsson K. Cubic lipid - water phase dispersed into submicron particles. *Langmuir* 1996;12:4611-13.
- Landh T. Phase behavior in the system pine needle oil monoglycerides-Poloxamer 407- Water at 20. *J Phys Chem* 1994;98:8453-67.
- Luzzati V, Husson F. The structure of the liquid-crystalline phases of lipid water systems. *J Cell Biol* 1962; 12: 207-19.
- Ribier A, Biatry B. Cosmetic Compositions Comprising a Stable Aqueous Dispersion of Phytantriol-Based Gel Particles Containing a Long Chain Surfactant as Dispersant and Stabilizer. *Eur. Pat. Appl.* 1995; 13.
- Ribier A, Biatry B. Cosmetic or Dermatologic Oil/ Water Dispersion Stabilized with Cubic Gel Particles and Method of Preparation. *Eur. Pat. Appl.* 1996; 16.
- Ribier A, Biatry B. Oily Phase in Aqueous Phase Dispersion Stabilized by Cubic Gel Particles and Method of Making. *Loreal (Paris, FR), USA.* 1998.
- Biatry B. Cosmetic and Dermatological Emulsion Comprising Oily and Aqueous Phase, *Eur. Pat. Appl. (Loreal, Fr.), Ep.* 2000.
- Schreiber J, Albrecht H. Cosmetic Cleaning Products with a Content of Disperse Phase Liquid Crystals Which Form Cubic Phases. *Ger. Offen. (Beiersdorf AG, Germany) De* 2002.
- Schreiber J, Eitrich A. Deodorant and Antiperspirant Products with a Content of Disperse Phase Liquid Crystals Which Form Cubic Phases. *Ger. Offen. (Beiersdorf AG, Germany) De.* 2002.
- Schreiber J, Schwarzwaelder C, Cassier T. Skin Care Products with a Content of Disperse Phase Liquid Crystals Which Form Cubic Phases. *Ger. Offen. (Beiersdorf AG, Germany) De.* 2002.
- Deepak P, Dharmesh S. Cubosomes: A Sustained Drug Delivery Carrier. *Asian J Res Pharm Sci* 2011; 1: 59- 62
- Patrick TS. Bicontinuous Cubic Liquid Crystalline Phase and Cubosome Personal Care Delivery Systems. 1-27.
- Yosra SRE, Samar ME, Doaa AA, Ossama YA. Novel piperine - loaded tween - integrated monoolein cubosomes as brain-targeted oral nanomedicine in Alzheimer's disease: pharmaceutical, biological and toxicological studies. *Int J Nanomedicine* 2015, 10: 5459-73.
- Sergio M, Sara B, Angela MF, Sandrina L, Vito L, Valeria M et al. Drug-Loaded Fluorescent Cubosomes: Versatile Nanoparticles for Potential Theranostic Applications, *Langmuir* 2013;29:6673-79.
- Ruchi S, Gurbinder K, Deepak NK, Fluconazole loaded cubosomal vesicles for topical delivery. *Int J Drug Dev & Res* 2015, 7: 032-041.
- Hyde ST, Anderson S, Ericsson B, Larsson K. A cubic structure consisting of a lipid bilayer forming an infinite periodic minimal surface of the gyroid type in the glycerol monooleate water system. *Z Kristallogr.* 1984; 168:213-19.
- Vinod KR, Sravya K, Sandhya S, Banji D, Anbazhagan S, Prameela RA. Tailoring active compounds across biological membranes by cubosomal technology: an updated review. *J China Pharm Sci* 2013; 22:303-11.
- Longley W, McIntosh TJ. A bicontinuous tetrahedral structure in a liquid-crystalline lipid. *Nature* 1983; 303: 612-14.
- Boyd BJ. Characterisation of drug release from cubosomes using the pressure ultrafiltration method. *Int J Pharm* 2003; 260: 239-47,
- Drummond CJ, Fong C. Surfactant Self-Assembly Objects as Novel Drug Delivery Vehicles. *Curr Opin Colloid Interface Sci* 2000; 4:449-56.
- Enriquez J, Goldberg R. Transforming Life, Transforming Business: The Life-Science Revolution. *Harvard Bus Rev* 2000; 96-104.