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Cubosomes: An Overview

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ABSTRACT

Cubosomes are extremely stable nanoparticles with honeycomb-like or cavernous features. Some amphiphilic lipids are used to create cubosomes, which are then stabilized by a polymer. Bicontinuous cubic phase liquid crystals are what they are called. The two continuous but not intersecting watery zones that are separated by a lipid bilayer are referred to be bicontinuous. Cubosomes are liquid crystalline particles that self-assemble and have a specified water-to-surfactant ratio. Cubosomes that self-assemble function as active medication delivery systems. They exhibit solid-like rheology. Cubosomes have a stable thermodynamic state, and the dispersions they form are both biocompatible and bioadhesive. Cubosomes can be administered orally, topically, mucosally, intravenously, or transdermally for the treatment of skin, hair, or other body tissues. Cubosomes have the ability to encapsulate both hydrophilic and hydrophobic molecules. Nevertheless, several researchers have been pointing out cubosomes' potential as delivery mechanisms. They have various drug-loading techniques and large interior surfaces. Cubosomes also have the ability to target and release bioactive substances under controlled conditions. They can be used as biosensors, artificial cells, membrane bioreactors, and other things as well. They are made using an easy process. Cubosomes have more breaking resistance compared to liposomes. The advanced cubosome preparation techniques are reviewed and discussed in this article.

INTRODUCTION:

In order to establish an effective medication concentration, the drug delivery system delivers the therapeutic agents in a site of action at a specific pace. The therapeutic advantage is promoted while the negative effects are minimized using a controlled drug release formulation. Through sustained medication release, which aids in improving patient compliance, a reduction in the frequency of doses can be accomplished.[1-3] When a drug is enclosed within a vesicle as part of a vesicular drug delivery system, the vesicle acts as a carrier. By doing this, conventional medications can be targeted with drugs and have their release prolonged or controlled. A large variety of vesicular drug delivery systems were identified in 1980, and the cubosome is one of its component elements.[4-5]

Scientist Larsson came up with the word "Cubosomes" to describe the cubic molecular crystals that are comparable to liposomes.[6] Cubosomes are discrete, submicron-sized, bicontinuous, liquid crystalline particles with solid-like rheology that are composed of certain surfactants and water in the right proportions.[7-8] The bulk cubic phases exhibit increased viscosity in contrast to cubosomal dispersion.[9-12] Due to a spectrum of surfactant insolubility, the majority of concentrated surfactants that form cubic liquid crystals lose the phase micelle formation in higher dilutions. The formation of cubosomes involves the employment of a polymer surfactant as a high-energy dispersion of cubic phase with extra water and colloidal stability. Cubosomes are also created via the emulsification method. It is also known as a nanoparticle disperse system and is distinguished by greater biocompatibility and bioadhesivity. [13-15] The main components required for cubosome production are polymer molecules, surfactants, and lipids with amphiphilic properties. The cubic liquid phase is split in two by the surfactant bilayer. Cubosomes are therefore solid-like liquid crystal solids that have cubic crystallographic symmetry, are extremely viscous, and have isotropic optical properties. They are also bicontinuous cubic phases.[6-16] Cubosomes play a significant role in the creation of nano-drugs.[6]

Properties:[17]

- Drug compounds that are hydrophilic, hydrophobic, or amphiphilic can all be contained within cubosomes.
- These have biocompatibility and bioadhesivity qualities.

- In extra water, bicontinuous cubic liquid crystalline phases known as cubosomes are stable.
- They possess properties of prolonged drug release.
- With these cuboidal structures, the bioavailability range of peptides that are water soluble would be increased 20–100 times.
- Cubosomes are a great carrier for preventing enzymatic deterioration of delicate medication.
- Cubosomes display a significant drug carrier capacity for medicines that are sporadically soluble.
- If you compare these to lipid or non-lipid carriers, they are good solubilizers.

Advantages: [18]

- Cubosome preparation is rather easy.
- Both hydrophilic and hydrophobic as well as amphiphilic compounds can be encapsulated by them.
- Cubosomes have characteristics that make them both biocompatible and bioadhesive.
- Comparatively speaking to traditional lipids or non-lipid carriers, cubosomes are good solubilizers.
- Cubosomes can be used to treat a variety of promising drugs that have low aqueous solubility, poor absorption, and high molecular sizes.
- High internal surface area and cubic crystalline formations make it possible to achieve high drug payloads.
- Cubosome particles are employed in cosmetics as stabilizers and pollution absorbents for oil-in-water emulsions.
- Due to the relative insolubility of cubic phase-forming lipids in water, cubosomes remain stable at most any dilution level, unlike the majority of liquid crystalline systems, which change into micelles at higher levels of dilution. Therefore, cubosomes can be easily added to product compositions.

- Cubosomes' fragmented and scattered cubic phase produces particle dispersions that are more thermodynamically and/or colloidally stable over time.
- Proteins and peptides, which are sensitive medications, can be shielded from enzymatic and in-vivo breakdown by cubosomes.
- Low cost of raw materials.
- Reduces the chance of drug abuse and misapplication while increasing effectiveness.
- The bioavailability of peptides that are water-soluble is increased 20–100 times by the cuboidal system.
- Convenience and compliance are increased by cubosomes.

Disadvantages:[18-21]

- Due to the cubosomes' high water content, water-soluble medicines are only minimally trapped inside of them.
- Due to their high viscosity, cubosomes are challenging to produce.
- Due to drug loss from preparation during transportation, preservation, and ineffective drug loading, it only has a restricted number of applications.
- Cubosomes' main issue, their stability, operates as a barrier to their utilization by causing low drug loading efficiency and drug leakage throughout synthesis, preservation, and transport in vivo.
- It can be challenging to produce these materials on a big scale because of their high viscosity.
- The lattice structure of the bicontinuous liquid crystalline phase can be damaged by medications, and some large drugs cannot enter the channels.

Structure of Cubosome:

The preparation of the cubosomes is simple and consists of three essential components such as amphiphilic lipids, stabilizer, and water.

Amphiphilic Lipids:

Phytantriol and glyceryl mono-oleate both are amphiphilic lipids used for Cubosomes preparation. The two amphiphilic lipids that are most frequently employed in the production of cubosomes are GMO and phytantriol. GMO is a man-made substance that is made up of a combination of glycerides of oleic acid and other fatty acids. Monooleate, a member of the class of amphiphilic lipids with the capacity to form a variety of lyotropic liquid crystals, makes up the majority of these fatty acids. GMOs have both hydrophilic and hydrophobic properties at the same time because they contain hydroxyl groups in the head region that can form H-bonds with water in an aqueous solution and hydrocarbon chains in the tail. According to Lutton's findings, monoglycerides with hydrocarbon chains between 12 and 22 have a strong propensity to crystallize in cubic phases. PHYT, a compound with a phytanyl chain, exhibits phase behavior when the water content rises. PHYT, 3, 7, 11, 15- tetramethyl-1, 2, 3-hexadecanetriol is a frequently found component in cosmetic products. Given that PHYT offers good structural stability, it is proposed as an excellent substitute for GMO in the manufacture of cubosomes. While the two substances' characteristics and molecular compositions are different, X-ray diffraction analysis has shown that they behave in phases that are comparable when the water content and temperature are increased. At room temperature, reversed micellar, lamellar, Q230, and Q224 phases appear in that order as the water concentration is increased. When the temperature is raised to 44 C, the cubic phase transforms into a hexagonal structure.[22-23] PHYT Cubosomes are in equilibrium with water, which is a prerequisite for Cubosome production. Additionally, liquid crystalline matrices based on PHYT make excellent sustained drug delivery systems.[24-25]

Stabilizers:

For cubosomes to have colloidal stability, surfactant is crucial. There are numerous active projects to introduce and use in cubosome preparation. The most common surfactant utilized in the manufacture of cubosomes is poloxamer 407 (P407), a PEO99-PPO67-PEO99tri-block copolymer. Both PPO sections and PEO chains make up the P407, with PPO portions being found either on the cubosomes' surface or inside the bilayer structure, and PEO chains being exposed to the water around them. P407 is applied up to a concentration of 20% w/w depending on the dispersed phase, and depending on the weight of the dispersion, the monoglyceride-polymer mixture is typically in the concentration range between 2.5 and 10%

(w/w) When it comes to PHYT cubic phase, P407 is adsorbed onto the surface, however when it comes to GMO cubic phase, it is incorporated into the liquid crystalline structures.[28]

Structure of Cubosome:

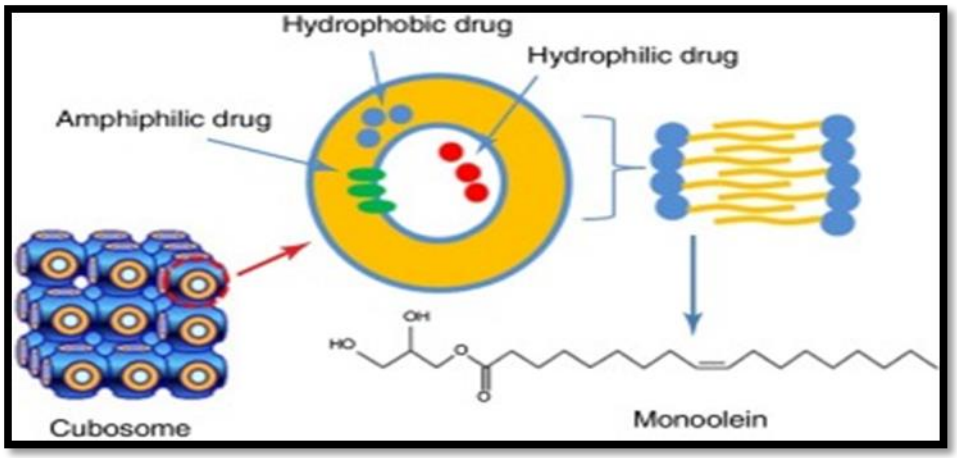

Fig: 1

Types of cubosomes

The following are the types of cubosomes.

Liquid cubosome precursors:

Hydrotrope dilution is a method that produces smaller, more stable cubosomes. Particles can form during the nucleation process and expand through the crystallization and precipitation processes. The monoolein dissolves correctly in a hydrotrope like ethanol. Therefore, diluted mixtures can spontaneously crystallize or cumbersome precipitation can occur quickly. The quid precursor procedure, which avoids handling bulk solids, is the most straightforward method of cubosome preparation.[29-30]

Powdered cubosome precursor:

Powdered cubosome precursors, the second type of cubosome, are made using dehydrated surfactants that have been polymer-coated. The hydration of precursor powders results in cubosomes with a mean particle size of 600 nm, which is verified by Cryo-TEM and the light scattering method. Cubosome lipids have a waxy consistency and are glumpy. In order to manage the particle size of cubosomes due to minimal agglomeration, these waxy and sticky lipids are coated with water-soluble starch. Spray drying is an effective approach for this.[31]

Method of preparation of cubosomes:

Based on their microscopic shapes, cubic phases are often divided into three types, such as particle dispersion, precursor, and bulk gel. When the precursor form comes into contact with liquid, it either becomes liquid or solid and forms a cubic phase. The later phase, known as the bulk form, is a rigid gel with solid-like cubosomes that are evenly dispersed throughout the water. There are several methods for the preparation of cubosomes such as solvent evaporation, shearing, homogenization, dispersion of bulk phase using sonication, mechanical stirring, and incorporation of hydrotropes via dilution method. Cubosome nanoparticles are created using two different techniques: bottom-up and top-down. To avoid aggregation in both methods, P407 is required as a colloidal stabilizer.[32-43]

1. Top-Down technique
2. Bottom Dowm technique
3. High Shear Homogenization technique

Evaluation Of Cubosomes:

1. Particle size
2. Zeta Potential
3. Entrapment Efficiency

CONCLUSION:

Cubosomes are liquid crystalline nanoparticle structures that self-assemble. Due to advantages like a larger surface area and a method of preparation that is straightforward, bioadhesive, biocompatible, and flexible enough to incorporate hydrophobic, amphiphilic, or hydrophilic drugs in drug delivery as a carrier system over other types of nanoparticles, their interest in the pharmaceutical industry is continuously rising. This technique is new with a high output and a wide research scope for the creation of novel formulations or dosage forms with industrial and commercial viability.

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