



International Journal of Pharmaceutics and Drug Analysis

Content Available at www.ijpda.org

ISSN: 2348:8948



AN OVERVIEW ON CUBIC LIQUID CRYSTALLINE NANOPARTICLES-TRIG LIPID DRUG DELIVERY SYSTEM

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Received: 14 Apr 2024 Revised: 27 Apr 2024 Accepted: 28 May 2024

Abstract

This type of complex structure allows them greater drug loading ability, because of increased surface area and cuboidal structures, they have simple method of preparation and have ability to encapsulate hydrophilic, hydrophobic and amphiphilic substances. Cubosomes increases the solubility of poorly soluble drugs. Cubosomal dispersions are bioadhesive and biocompatible in nature. These are versatile systems, administered by different ways such as oral, percutaneous and parental routes. Cubosomes have broad vast applications in many areas and are characterized by various parameters consequently cubosomes are in move forward of awareness by pharmaceutical development division. Cubosomes, sometimes referred to as bicontinuous cubic phase liquid crystals, are spherical, quadruple nanoparticles with an interior cubic lattice mostly composed of certain amphiphilic lipids in a particular proportion. Cubosomes often arise when a solid-like phase is dispersed into smaller particles after a surfactant or polar lipid is hydrated to form a cubic phase. With distinct qualities of practical interest, they exhibit solid like rheology. They are thermodynamically stable, self-assembling drug delivery devices. Water and lipid bicontinuous domains give cubosomes their carvenous structure. Three-dimensional bilayers are formed by tightly twisted honeycomb arrangements.

Keywords: Cubosomes, Nanoparticles, Bicontinuous, Carvenous (honeycomb), Pharmaceutical division.

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DOI: <https://doi.org/10.47957/ijpda.v12i2.595>

Produced and Published by

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Introduction

The term "cubosome," coined by Larsson, refers to unique, nanostructured sub-micron particles of the bicontinuous cubic liquid crystalline phase. Liposomes and cubosomes are similar, which is consistent with cubic molecular crystallography. These are self-assembling liquid crystalline particles that have precise surface active agents and a real microstructure-to-water ratio. Cubosomes resemble solid nanoparticles and possess a distinctive feature related to self-assembling liquid crystalline particles [1]. Lipids, polymers, and amphiphilic surfactants are all integrated into cubosomes. Amphiphilic molecules direct the hydrophobic effect into polar solvent, allowing it to spontaneously identify and assemble into a nanometer-scale liquid crystal. Cubosomes are made of water and

surfactants and are separated by a bicontinuous layer. These have optical properties that resemble liquid crystalline substances with cubic crystallographic symmetry.

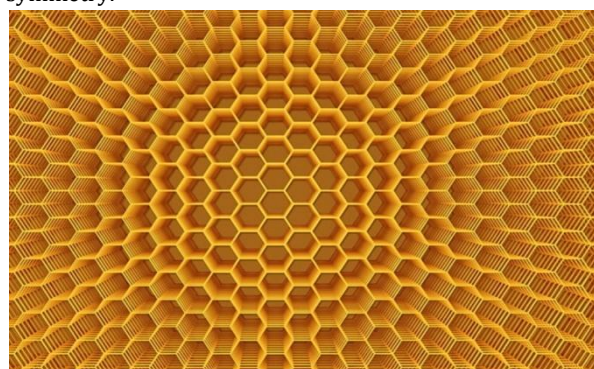


Fig: 1 Carvenous (honeycomb) structure of cubosomes

Because cubosomes are thermodynamically stable, researchers are interested in using them to prepare drugs for topical use, cosmetic preparations, cancer treatment, and other uses. Although cubosome preparation is becoming more popular as a focused drug delivery method due to its stability and versatility, other carrier

systems like as liposomes, niosomes, microparticles, and others are still utilized for targeted delivery.

Narration

Cubosomes from the 1980s exhibit significant levels of intricacy and viscosity, making large-scale manufacturing difficult. It exhibits distinct properties like viscosity, just like solids do. Broken up cubic crystalline phases disperse to form thermodynamically colloidal particles that remain stable for a very long time. Certain surfactants combine with water to generate cubic phases. Husson and Luzzati, [3–8] From 1960 to 1985, researchers Lusatia et al., [9], Larsson [10], and Hyde et al., [11] determined the cubosome's honey comb structure, which is represented in the figure. Larsson is credited with coining the term "cubosome," referring to a structure resembling cubic molecular crystals and liposomes. Attempts are made to enhance the formation of cubosomes. Certain anticancer medications are successfully synthesized and assessed for use using cubosomes [12].

Structure of Cubosomes

Cubosomes have a huge interfacial area and two internal aqueous channel portions separated by features resembling honeycombs. Cubosomes are liquid crystalline phases that are nanostructured and have cubic crystallographic symmetry, similar to nanoparticles. Molecules that resemble surfactants or are amphiphilic self-assemble to produce cubosomes. Because of their attractive bicontinuous structures that are created by the controlled application of a bilayer of surfactant, the cubic phases have a very high solid viscosity and a distinctive quality [13]. Bicontinuous refers to two different (continuous, but non-intersecting) hydrophilic patches separated by the bilayer, which amphiphilic molecules organize into water and oil channels. The structure's interconnectivity produces a transparent viscous gel with a rheology and look akin to cross-linked polymer hydrogels.

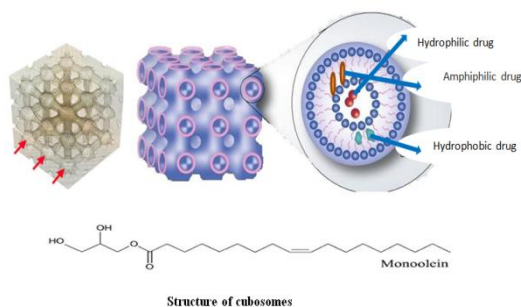


Fig: 2 Structure of cubosomes

Advantages

[23]

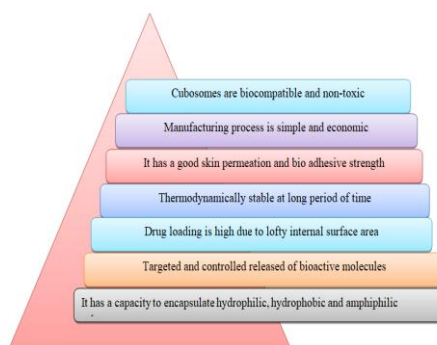


Fig: 3 Advantages of cubosomes
Disadvantages [24, 25]

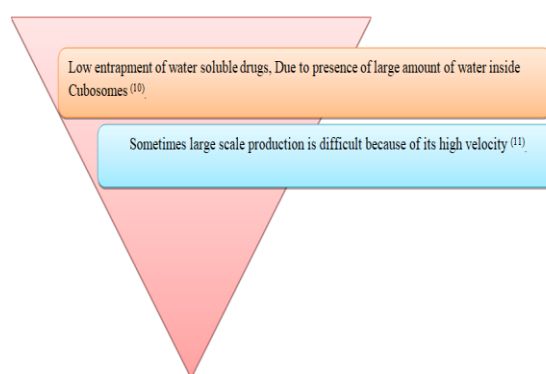


Fig: 4 Disadvantages of cubosomes

Materials used in Cubosomes formation

Bicontinuous cubic phases are found in polymer systems and surfactants in natural lipids [26]. Because monoglycerides naturally generate bicontinuous cubic phases upon the addition of water, monoolein is the most frequently employed lipid to create bicontinuous cubic phases. They are resistant to temperature changes and are comparatively insoluble. The main precursor for the production of cubosomes is monoolein.

Monoolein or glyceryl monooleate is primarily present in a mixture of oleic acid and other fatty acid glycerides [27]. There are two types of monoolein: distilled monoolein and mixed glyceride form.

Distilled monoolein is commonly employed in pharmaceutical applications due to its great purity. Monoolein is a yellow substance that is waxy and has a distinct smell. When submerged in water, it swells and forms many lyotropic liquid crystalline structures. The FDA's list of inactive components includes monoolein, a nontoxic, biodegradable, and biocompatible substance that is also permitted for use in non-parenteral medications in the UK. The mesomorphic phase of this monoolein is crucial since it helps to make the lipid more understandable in terms of its possible medicinal application.

In the presence of water, monoglycerides exhibit distinct phase behaviors. Poloxamer 407 is one of the surface

active chemicals that are utilized in the formation of cubic crystalline phases. Its concentration ranges from 0% to 20% w/w with regard to the disperse phase. Monoglyceried/surfactant concentration mixtures typically range from 2.5% to 10% w/w relative to the total weight of the dispersion. Polyvinyl alcohol can serve as a stabilizing ingredient in the dispersion as an alternative to poloxamer.

Manufacturing of cubosomes

Manufacturing of cubosomes are two types; Bottom up technique and Top down technique

Bottom up technique [28, 29]:

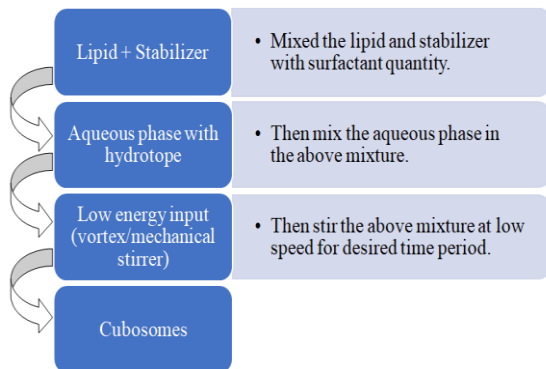


Fig: 5 Manufacturing of cubosomes (Bottom up technique)

Top down technique [28, 29]

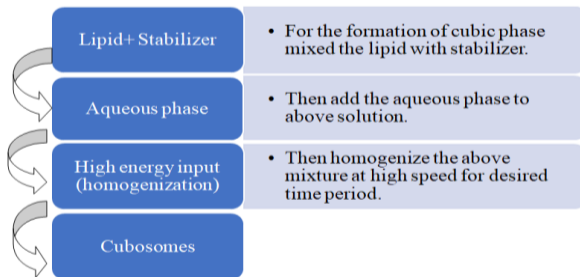


Fig: 6 Manufacturing of cubosomes (Top down technique)

Preparation methods of cubosomes [33, 34]

Emulsification method

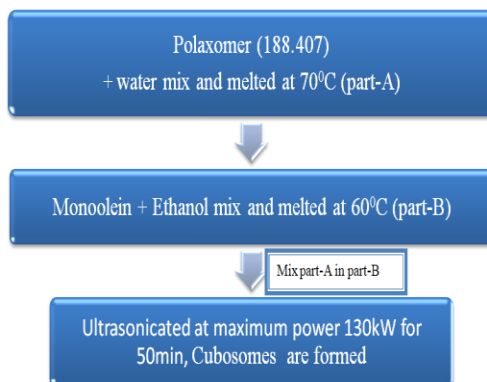


Fig: 7 Preparation methods of cubosomes (Emulsification method)

Fabrication method

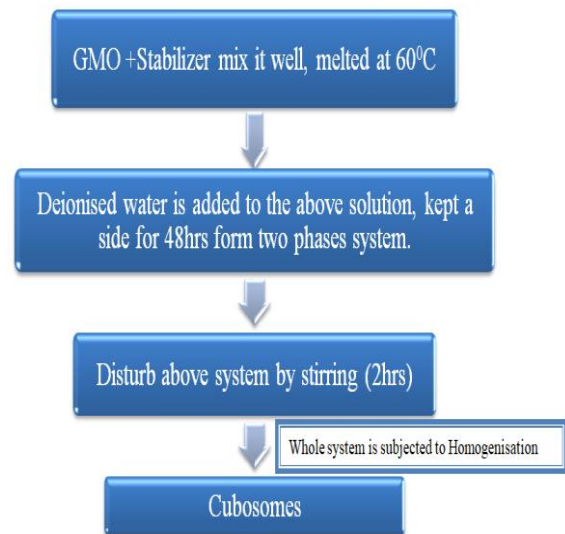


Fig: 8 Preparation methods of cubosomes (Fabrication method)

Evaluation of cubosomes

Visual inspection:

Various optical parameters such as colour, turbidity, homogeneity, microscopic particles are studied by visual observations.

Shape of cubosomes

The shape of cubosomes is observed through Transmission electron microscope.

Particle size distribution

To evaluate the cubosome particle size distribution, Zeta seizer is utilized in conjunction with dynamic laser light scattering. For the sample that was combined with solvent (18), a light scattering intensity of roughly 300 Hz was fixed at 250 c. Utilizing average volume weight size, the gathered data was represented. Data from the polydispersity index was documented in addition to zeta potential.

Zeta potential

The stability of formulation was indicated by Zeta potential. The degree of electronic repulsion between adjust, similarly charge particles gives information about the magnitude of Zeta potential.

Entrapment efficiency

The entrapment efficiency of cubosomes is estimated using ultra filtering techniques [17]. A spectrophotometer is used to measure the amount of drug by subtracting the total amount added from the previously calculated amount of unentrapped drug using a later approach.

Measurement of drug release

Pressure ultra filtration method was performed to determine drug release (17). It is based on that proposed by Magenheim et al. Using an Amicon pressure ultra filtration cell at ambient temperature (22±2) °C fitted with a Millipore membrane.

Stability studies

By investigation of organoleptic and morphological characteristics as a function of time physical stability can be studied. Drug release and particle size distribution is performed at different time intervals [19].

Applications [30-43]

a) In cancer therapy:

Anti-cancer medications are successfully encapsulated in cubosomes to evaluate their physicochemical characteristics [20]. Propose the use of a nano carrier in melanoma therapy due to its distinct structure. Nanomedicines employ a variety of strategies, including passive and active techniques, to target tumor cells. Preclinical and clinical research have demonstrated the validity of anticancer medications incorporating cubosomes.

b) Oral drug delivery

Cubosomes face several difficulties when it comes to the oral distribution of various chemicals, such as high molecular size, poor absorption, and low aqueous solubility. Large proteins have been encapsulated to obtain the local action in the gastrointestinal tract [21]. For medications with a limited window of absorption, cubosomal technology's release of the medicine at distinct absorption sites—such as the upper or lower intestine—is significant.

c) Intravenous route drug delivery systems:

In order to solubilize, encapsulate, and transport drugs to disease locations within the body, lipid nanoparticles with internal liquid crystal architectures of curved lipid membranes are employed [22]. In comparison to emulsions and liposomes, cubosomal nanoparticles exhibit enhanced payloads of peptides, proteins, and several insoluble small molecules, making them suitable injectable carriers.

d) Topical drug delivery systems

Due to their bioadhesive qualities, cubosomes are a practical way to deliver many medications topically and through mucous membranes. The basis of topical delivery systems is the application of the special qualities of liquid crystal and liquid crystal nanoparticle technologies. Bioadhesive liquid crystal systems are being formed by topical drug delivery systems to expedite and regulate the administration of drugs to mucosal surfaces such as the vaginal, ocular, and buccal.

e) Drug delivery vehicle

The traditional use of novel materials is in drug delivery vehicles. Research on cubosome particles as pollution absorbents and stabilizers for oil-in-water emulsions is being conducted by cosmetic businesses such as L'Oreal and Nivea [23].

f) Drug release behavior

Every medication has unique physicochemical characteristics. It has been integrated with cubosomes and how they release drugs. Because cubosomes contain leftover particles, they exhibit persistent behavior.

Cubosomes have monoglycerides; they can be applied topically, i.e., mucosally or percutaneously.

g) In treatment of viral diseases

Due to their microbicidal characteristics, monoglycerides are employed in the intravaginal treatment of STDs brought on by bacteria (*Neisseria gonorrhoea*) and viruses (HSV, HIV) [24].

Future prospects

Cubosomes have a unique role in the treatment of different infections in the field of drug delivery systems and sustain medication release. To provide a better therapeutic effect in treating various diseases, more research is needed in a number of areas, including the frequency of dosing, manner of drug release, and route of administration [25]. Various forms of nano vehicles are available for the loading and delivery of proteins and peptides; nevertheless, investigations are still reported at fundamental levels [26]. The structural and morphological properties of these soft nano carriers, the loading capacity of bio macromolecules, and their release are only a few more things that need to be made very apparent. In order to advance cubosome development, blood compatibility should be examined and discussed throughout the early phases of formulation development.

A brief overview of their stability in biological fluids, biological factors regulating drug release from cubosomes, structural transformation upon contact with biological fluids like plasma, interactions with cell membranes, and infusion-related reactions, to mention a few, are also provided by additional information [27]. Cubosomes for intravenous administration might be easy or challenging. Nano carriers offer numerous opportunities for diverse applications through different routes, including topical, ocular, and oral delivery of poorly soluble pharmaceuticals at a very economical procedure of producing a dosage form by selecting an alternative way.

Conclusion

Cubosomes, like solid nanoparticles, can have certain properties. Self-assembling liquid crystalline particles known as cubosomes can carry a wide range of hydrophilic and lipophilic medications and demonstrate targeted, prolonged drug delivery. It is possible to generate cubosomes by ultrasonication techniques using two simple methods: powder cubosome precursor, or top down methodology, and cubosomes dispersion, formed by dilution of an isotropic solution, or bottom up technique with the aid of high pressure homogenization. Cubosomes are important for proteins, immunological components, and cosmetics. Because of this caution, cubosomes can be widely used as targeted drug delivery devices for diabetes, cancer treatment, and ocular conditions. Due to its novelty and high output, cubosomal technology expands the field of study for creating novel formulations with feasibility.

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