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Cubosomes: As a Drug Delivery Carrier

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ABSTRACT

Cubosomes are square and rounded particles with internal cubic lattices visible. The discovery of Cubosomes is a unique story and spans the fields of food science, differential geometry, and biological membranes. Cubosomes are thermodynamically stable; they enclose a structure similar to "Honeycomb" through bicontinuous domains of water and lipid. Inside the surfactant, it is assembled into bilayer and wrapped into a three dimension, periodic and minimal surface, forming a strongly packed structure. Cubosomes dispersions are bioadhesive and biocompatible. Because of their properties, Cubosomes are versatile systems, administrable by different ways such as oral, percutaneous and parenteral. Cubosomes have broad vast applications in many areas and are characterized by various parameters. So, Cubosomes have more beneficial attention by pharmaceutical development sector.

Key words: Cubosomes, Hydrophilic, Honeycomb, Novel Drug delivery.

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INTRODUCTION

Cubosomes are discrete, sub-micron, nanostructured particles of the bicontinuous cubic liquid crystalline phase. Cubosomes are nanoparticles which are self assembled liquid crystalline particles of certain surfactants with proper ratio of water with microstructure. Cubosomes are composed of polymers, lipids and surfactants with polar and non polar components hence said as amphiphilic. There is huge number of vesicular drug delivery systems were developed that allow drug targeting and the sustained or controlled release of conventional medicines. In such a system Cubosomes are also part of the vesicular drug delivery system or lipid based colloidal systems which were discovered in 1980[1]. The cubic phase can fracture and form colloidally and or thermodynamically stable particulate dispersions[2] .Cubosomes have great importance in nanodrug formulation. After formation of the Cubosomes, the dispersion is formulated into a product and then applied to a substrate of interest, usually bodily tissue. Thereafter materials are either absorbed or released via diffusion[3]. Three macroscopic forms of cubic phase are typically encountered: precursor, bulk gel, and particulate dispersions (Cubosomes). The precursor form exists as a solid or liquid material that forms cubic phase in response to a stimulus, such as contact with liquid. Bulk cubic phase gel is an optically isotropic, stiff, solid like material.

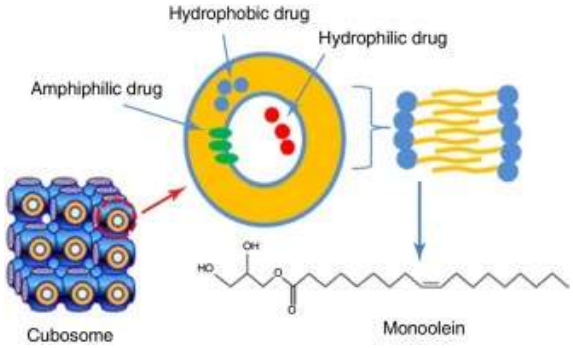

Figure.1 Structure of Cubosomes.

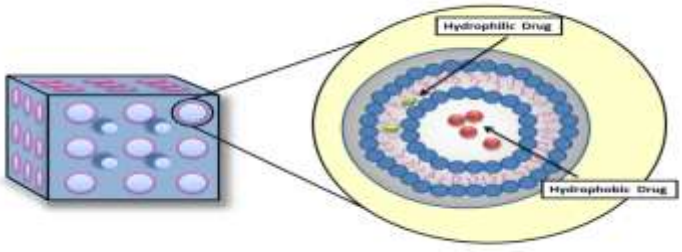

Figure.2: Cubosomes and its membrane composition

Advantages of Cubosomes

- They can be prepared by simple method
- High drug payloads due to high internal surface area and cubic crystalline shapes.
- Cubosomes particles as oil-in-water emulsion stabilizers and pollutant absorbents used in cosmetics.
- Relatively easy method of preparation.
- Biodegradability of lipids.
- Control release of solubilized substance is the most popular application of Cubosomes. Cubic phase is more applicable for control release because of its small pore size (5-10nm)
- Capability of encapsulating hydrophilic, hydrophobic and amphiphilic substances.
- Targeted release and controlled release of bioactive agents.
- Cubosomes address the varied challenges in oral delivery of numerous promising compounds including poor aqueous solubility, poor absorption, and large molecular size[4,5]

Disadvantages of Cubosomes:

- Large scale production is difficult for sometimes because of high viscosity.

METHOD OF PREPARATIONS:

There are two methods for the manufacture of Cubosomes they are

1. Top down technique
2. Bottom up technique

1. Top down technique

It is the most widely used procedure initially reported in 1996 by Ljusberg- Wahren. Bulk Cubic phase is first produced and by application of high energy such as high pressure homogenization. it is processed into Cubosomes nanoparticles. Bulk cubic phase resembles a clear rigid gel formed by water-swollen cross linked polymer chains. The cubic phases differ in that they are a single thermodynamic phase and have periodic liquid crystalline structure. Cubic phases break in a direction parallel to the shear direction; the energy required is equivalent to the number of tubular network branches that breaks. It is the most broadly used in research area, where the bulk cubic phase is first manufacture and the separates by high energy processing in to Cubosomes Nano particles. Bulk cubic phase is mimic a clear rigid gel formed by water swollen cross Linked polymer chains whereas cubic phases are like liquid crystalline shapes. The cubic Phases reveal yield stress that increases with increasing amount of bilayer forming surfactants and oils. Warr & Chen gave the cubic phases may behave as lamellar phases during dispersion with increasing shear, dispersed liquid

crystalline particles are forming at transitional shear rates, where overcome free bulk phase reforms at higher shear rates. Based on most existing studies similar to dispersion produced by Sonication and high-pressure homogenization suggests the formation of complex dispersions containing vesicles and Cubosomes with time dependent ratios of each particle. Coarse Cubosomes on micron scale hold the same D-surface structure as their develop bulk cubic phase, but after homogenization, the P-surface dominates because of added polymers.

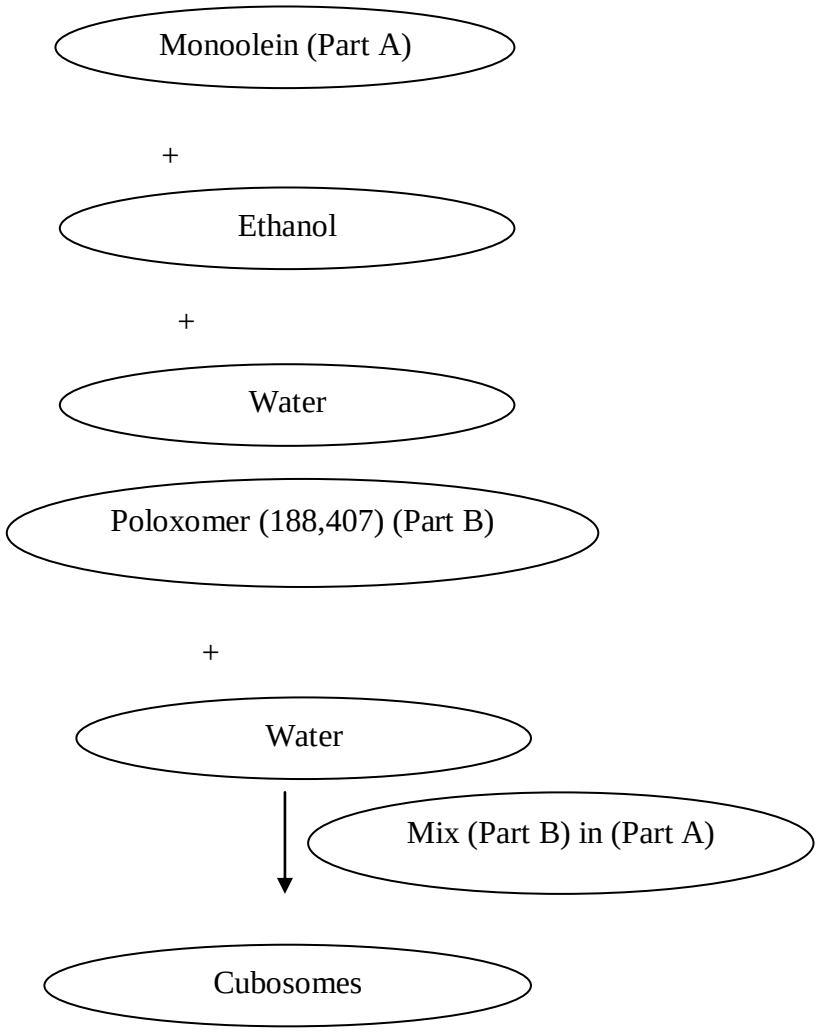

Figure.3: Flow chart of Cubosomes formed by dilution of an isotropic solution.

2. Bottom up technique

Cubosomes are allowed to form or crystallize from precursors. The formation of Cubosomes by dispersing L2 or inverse micellar phase droplets in water at 80°C, and allow them to cool slowly, gradually droplets get crystallizes into Cubosomes. This is more vigorous in large scale production of Cubosomes. The cubosomes at room temperature is by diluting monoolein ethanol solution with Aqueous poloxamer 407 solution. The Cubosomes are automatically formed by emulsification. Another procedure is also developed to produce the Cubosomes from powdered precursors by spray

drying method. Spray dried powders including monoolein coated with starch or dextrin form Cubosomes on simple hydration. Colloidal stabilization of Cubosomes is spontaneously provided by the polymers. In this Cubosomes are allowed to form or crystallize from precursors. The bottom-up approach first forms the nanostructure building blocks and then gather them into the final material. It is more recently developed method of Cubosomes formation, allowing Cubosomes to form and crystallize from precursors on the molecular length scale. The key factor of this method is hydrotrope that can dissolve water insoluble lipids into liquid precursors. This is a dilution based approach that Produces Cubosomes with less energy input when compared top down technique[6].

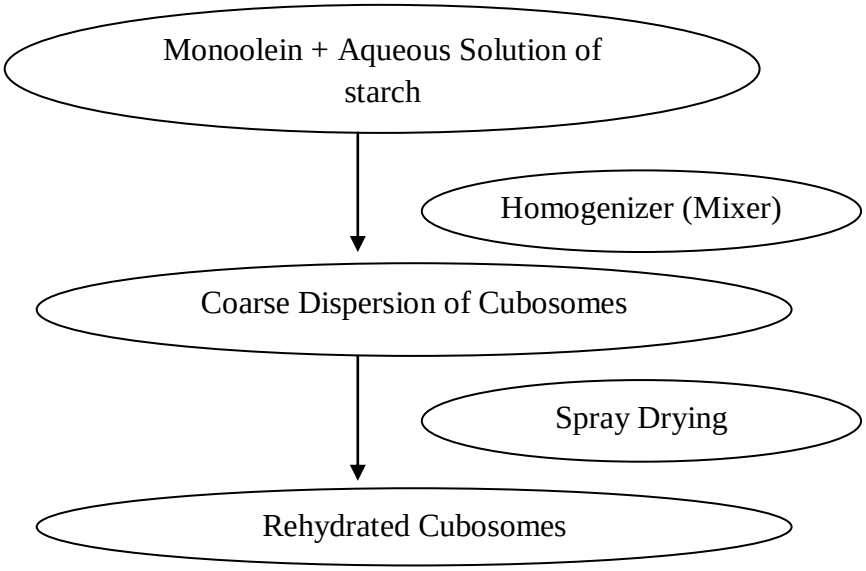

Figure.4: Flow chart preparation of powdered Cubosomes precursor.

Evaluation of Cubosomes[7,8,9]

1. Gel permeation chromatography
2. Polarized light micro scopy
3. Photon correlation spectroscopy
4. X-ray scattering
5. Viscosity
6. Transmission electron microscopy
7. Pressure Ultra filtration Method
8. Visual inspection
9. Light microscopy
10. Stability studies

CONCLUSION

Cubic phase materials formed with simple mixture of biologically compatible lipids and water and are consequently well suited for pharmaceutical and body tissue. The capability to shape

Cubosomes both in use, throughout formulation or throughout manufacture offer great extent of flexibility for product development. Furthermore, the narrative or the past reviews states the effectiveness of Cubosomes as a controlled /sustained release drug carrier.

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