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Review Article

A REVIEW ON: CUBOSOMES DRUG DELIVERY SYSTEM

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ABSTRACT

Cubosomes are the square and round shaped particles with internal visible cubic lattices. The discovery of cubosomes is an extraordinary story and spans the fields of food science, differential geometry, biological membranes, and digestive processes. Cubosomes are thermodynamically stable and they have a "honeycombed" like structures. This honeycombed structure separates two internal aqueous channels and a large interfacial area. Cubosomes are nanoparticles which are together liquid crystalline particles of certain surfactants with proper ratio of water with microstructure that provides excellent properties. Bicontinuous cubic liquid crystalline phase is visually clear and very viscous material has the unique structure at nanometer scale. The word bicontinuous refers to the breakup of two continuous but non-intersecting aqueous regions by lipid bilayer that is wicked into space filling structure. Hydrating a surfactant or polar lipid that forms cubic phase and then dispersing a solid like phase into smaller particles normally forms a cubosomes. Self-assembled cubosomes as active drug delivery systems are receiving more and more concentration and interest after the first discovery and selection. They show different internal cubic structure and composition with different drug-loading technique. It has high internal surface area and cubic crystalline structures, adequately simple preparation process, biodegradability of lipids, the ability of encapsulating hydrophobic, hydrophilic and amphiphilic substances, targeting and controlled release of bioactive agents. Cubosomes are having broad range of uses in various fields and they can be characterized by various evaluation parameters. So, Cubosomes have more beneficial attention by pharmaceutical development sector.

Keywords: Cubosomes, Honeycombed, Drug-loading, Hydrophobic, Hydrophilic, Amphiphilic.

INTRODUCTION

Cubosomes are distinct, sub-micron, nano-shaped particles of bicontinuous cubic liquid crystalline stages. They contain identical microstructure with high surface area and their dispersions are less viscous than the parent cubic phase. Mostly cubosomes are composed of polymers, lipids and surfactants with polar and non-polar constituents hence said to be amphiphilic. The amphiphilic molecules are move by the hydrophobic effect into polar solvent to impulsively recognise and unite into a liquid crystal of nanometer scale. Thus, cubosomes are bicontinuous cubic liquid phase surrounded by two separate regions of water divided by surfactant controlled bilayers. Further these are parallel to liquid crystalline substance with cubic crystallographic symmetry and are visually isotropic, viscous and solid too.The cubic phase can break and form thermodynamically stable particulate dispersions.Cubosomes has great importance in nanodrug formulations.

ADVANTAGES OF CUBOSOMES:

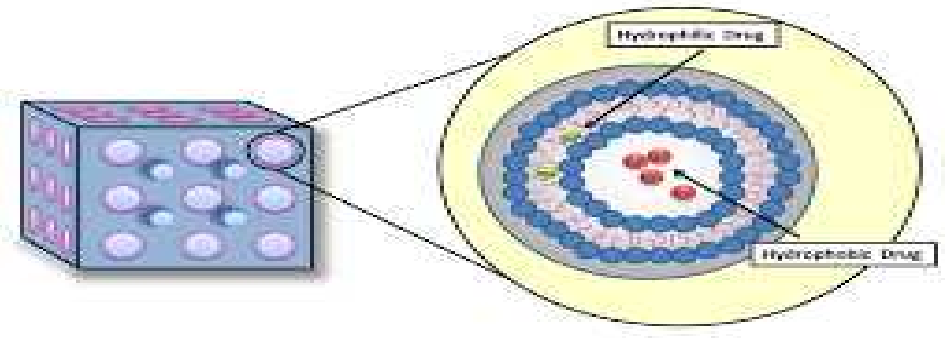
- High drug payloads due to high internal surface area and cubic crystalline shapes.
- Relatively easy method of preparation.
- Biodegradability of lipids.
- Capability of encapsulating hydrophilic, hydrophobic and amphiphilic substances.
- Targeted release and controlled release of bioactive agents.

DISADVANTAGES OF CUBOSOMES:

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

STRUCTURE OF CUBOSOMES:

Cubosomes have honeycombed structures whose size range from 10–500 nm in diameter. They appear like dots, which are slightly spherical in shape. Each dot corresponds to the presence of pore contains aqueous cubic phase in lipid water system. It was first identified by Luzzati and Husson using X-ray scattering technique.



MANUFACTURE OF CUBOSOMES:

There are two methods for the manufacture of cubosomes they are

1. Top down technique
2. Bottom up technique

TOP DOWN TECHNIQUE:

It is the most widely used technique initially reported in 1996 by Ljusberg- Wahren. Bulk cubic phase is first manufacture and by use of high energy such as high pressure homogenization it is processed into cubosomes nanoparticles. Bulk cubic phase mimic a clear rigid gel formed by water-swollen crosslinked 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 then seperates 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.

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 monooleinethanol solution with aqueouspoloxamer 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 dextran 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 cubosome 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.

DRUG LOADING CAPACITY OF CUBOSOMES:

The cubosomes generally have different internal cubic structure along with alternative composition related to the drug loading modalities. The cubosomes have enormous potential in drug nano formulations for melanoma therapy due to their potential applications consists of high drug payloads.

METHODS FOR CHARACTERIZATION AND EVALUATION OF CUBOSOMES

1. Gel permeation chromatography or ultra filtration techniques & UV spectrophotometer or HPLC analysis:

Entrapment planning and drug loading of cubosomes can be determined by using gel permeation chromatography or ultra filtration methods. In the later technique, un entrapped drug concentration was determined, which is subtracted from the total amount of drug added. The amount of drug is analyzed by using UV spectrophotometer or HPLC analysis.

2. Photon correlation spectroscopy:

Particle size distributions of cubosomes is majorly determined by dynamic laser light scattering technique using Zeta Sizer (Photon correlation spectroscopy). The sample was diluted with a suitable solvent and adjusted to light scattering intensity of about 300 Hz and measured at 25°C in triplicate. The data can be collected and normally shown by using average volume weight size. The zeta potential and polydispersity index can also be recorded.

3. Polarized light microscopy:

Polarized light microscopy can be used to release the optically birefringent (possibly vesicular) surface coating of the cubosomes and also well known between anisotropic and isotropic
Substances.

4. X-ray scattering:

Small angle X-ray scattering can be used to determine the cubic arrangements of different groups in the sample. The diffraction patterns obtained are converted into plots of intensity versus q value, which enable the identification of peak positions, and their conversion to Miller Indices. The Miller Indices can be correlated with known values for different liquid crystalline structures and space groups to identify the internal nanostructure of the sample.

5. Transmission electron microscopy:

Transmission electron microscopy can be used to aspect the shape of the cubosomes, described that the suspensions of cubic phase nanoparticles are negatively stained with freshly prepared phosphortungstic acid solution (2%, pH 6.8) and was transferred into a carbon coated grid (200 mesh) and air dried at room temperature. The electron microphotographs were taken on an electron microscope. SEM analysis may not be performed on cubosomes or some vesicular systems since the integrity and robustness of the formulation may be lost during the procedure while exposing to electron array.

6. Pressure Ultrafiltration Method:

Drug release measurement of cubosomes can be done by pressure ultrafiltration technique. It is based closely on that proposed by Magenheim, using an Amicon pressure ultrafiltration cell fitted with a Millipore membrane at ambient temperature (22±2) °C.

7. Stability studies:

The physical stability can be studied by the investigation of organoleptic and morphological aspects as a function of time. Particle size distribution and drug content can be evaluated at different time intervals can also be used to evaluate the possible variations by time.

8. Visual inspection:

About 1 week after preparation, the dispersions were visually evaluated for optical appearance (e.g., colour, turbidity, homogeneity, presence of macroscopic particles).

9. Lightmicroscopy:

Samples of the prepared cubosomes was suitably diluted with deionized water and examined using an optical microscope and calibrated with a micrometer slide at magnification of x 400 and x1000.

10. Viscosity:

The viscosity of the prepared formulations was determined at different angular velocities at 250C using a rotary viscometer (Brookfield). The rotation speed was 20 rpm, with spin # 18. The average of three readings was used to calculate the viscosity of the samples.

CONCLUSION

Cubic phase materials can be formed by simple combination of biologically compatible lipids and water and are thus well suited for the pharmaceutical and body tissue. The capacity to form cubosomes either in use, during formulation, or during manufacture offers greatly increased flexibility for product development efforts. The precursor forms enhance its further scope in technological field. Moreover, the literature reviews also specifics cubosomal utility as a controlled release drug carrier.

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