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Green Synthesis of Cubosomes

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ABSTRACT

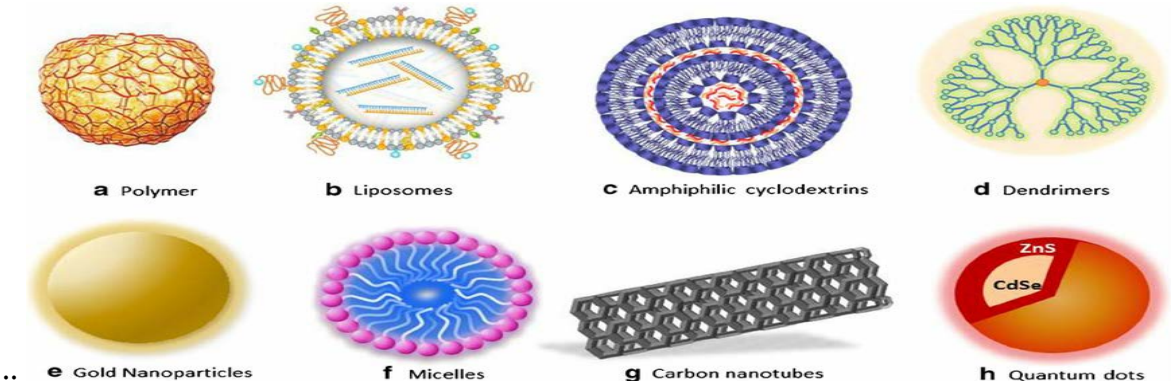
An existing drug's evolution from a conventional dosage form to novel drug delivery system can impact the drug compliance, release properties, safety, and efficacy. There is a need to deliver drugs to a patient with less side effects and more benefits. Our present article work focus on the concept of formulating cubosomes by green synthesis. Green synthesis is gaining a huge popularity in the recent years due to the tremendous advantages it has over physical and chemical synthesis of cubosomes.

Keywords: green synthesis, cubosomes

1)INTRODUCTION:

Nano technology also known as molecular nanotechnology aims at precisely manipulating atoms and molecules for fabrication of macromolecules. National nanotechnology initiative defined nanotechnology as "the manipulation of matter with atleast one dimension sized 1 to 100 nanometers". Nanotechnology includes various fields such as "semi-conductor physics, molecular biology, molecular engineering, pharmacy, microfabrication, organic chemistry and surface chemistry.

Nanoparticles are classified based on there size, method of preparation, physical and chemical properties. It includes liposomes, nanosomes, neosomes, mesosomes, dendrimers, cubosomes , carbon nanotubes, gold nanoparticles, silver nanoparticles, etc..



2) CUBOSOMES

Cubosomes are of recent interest to research investigators as they have several advantages over the conventional nanoparticles

A definite proportion of amphiphilic liquids knowns as bicontinuous lipid phased liquid crystals are assembled to create discrete nanostructured particles called as cubosomes whose size ranges between 10-500nm. Their complex three-dimensional honeycomb structure and thermodynamic stability gives them a greater drug loading ability [1].

In the mid-1980s, Kåre Larsson referenced cubosomes in his review on cubic phases in water system in which he had discussed the utilization of X-ray diffraction and NMR diffusion measurements studies to analyse the structures formed in the monoolein water framework[2]. Pursuing this further, Larsson was the first to establish work on cubosomes[3].

The formation of highly organized and stable submicron particles like cubosomes relies on the concept that amphiphilic molecules have the ability to self-assembly forming liposomes upon dispersion in water and also protect the drug from degradation. In other words, the self-assembling property of a lipid mixture and a suitable stabilizer loaded with the protein of interest results in the formation of lipid bicontinuous cubic phase structures known as cubosomes. Such nanoparticles serve as a decent drug delivery system and an effective therapeutic approach [4].

Cubosomes exhibit sterling properties such as excellent bio-adhesiveness, encapsulation of hydrophilic, amphiphilic and hydrophobic substances, effective and controlled release of bioactive agents on the targets, biocompatibility, protects the drug from physical, chemical of the drug, non-toxic nature and high drug loading competence[4] [5].

The ability of Glycerol monooleate (GMO) and phytantriol (PHYT) to self-assemble in an aqueous media makes them ideal amphiphilic lipids to employ in the formulation of cubosomes. Owing to their remarkable properties, cubosomes are attracting noteworthy attention in the therapeutic field. Application of cubosomes as nanocarriers for drug delivery has been recently employed in cancer, ocular, oral and dermatological therapy [5].

Lamellar and non-lamellar are the two distinct classes of lipids which drive the formation of planar lipid bilayers and bicontinuous or hexagonal cubic phases, respectively. Formation of three types of lipid-bicontinuous cubic phases which differ in their structure and stability are observed as a result of dispersion of non-lamellar lipids in water [6]. *Pn3m*, *Im3m* and *Ia3d* are the liquid crystalline organisations observed in lipid membrane systems. These are also referred as the double diamond (Q_{II}^{D}), the primitive (Q_{II}^{P}) and the gyroid (Q_{II}^{G}) phases respectively [6][7].

The cubic aggregates formed from lipid cubic phase, when dispersed in aqueous media exhibit kinetically unstable nature. In addition, such nanoparticles exhibit certain degree of cytotoxicity against erythrocytes. Therefore, stabilizing these cubic agglomerations with certain polymer based stabilizing agents' knowns as Pluronic's will aid in producing thermodynamically stable biocompatible formulations with improved bio accessibility of the drug [8].

Conglomeration of polyethylene oxide (PEO) and poly propylene oxide (PPE) arranged in PEO-PPO-PEO order forms the tri block Pluronic compound. Temperature and hydrophobicity of Pluronic compounds are the major factors governing the binding of Pluronic's to the cell membrane. Pluronic's are the most ideal gold standard stabilizing agents as they exhibit potential to lower the membrane viscosity and aid in transmembrane transport of low molecular drugs [9]. The most used Pluronic stabilizer is a non-ionic surfactant known as poloxamer 407, also referred as Pluronic F127 [10]. Although Pluronic F127 is the most prominent copolymer used in formulations of cubosome drug carrier system, a study by

Uyama, M, et al, 2009 suggests that hydroxypropyl methylcellulose acetate succinate (HPMCAS), a modified cellulose polymer shows potential to act as emulsifiers for cubosomes without causing any modification. [11].

2.1 ADVANTAGES OF CUBOSOMES:

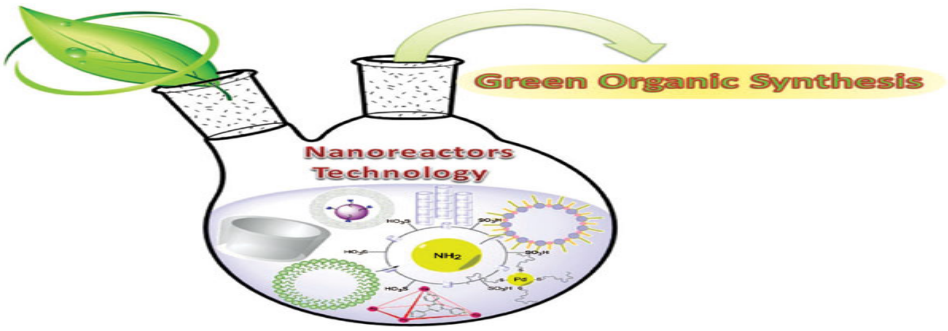
- These are composed of biodegradable lipids
- Preparation is simple and inexpensive
- They can encapsulate different type of drugs which may be hydrophilic, hydrophobic, or amphiphilic in nature
- High drug load capacity due to high internal surface
- Provides protection to the drug from physical and chemical degradation

2.2 DISADVANTAGES OF CUBOSOMES:

- Entrapment of water-soluble drugs is difficult as it has high water content in their structure
- Production in large quantity is difficult as it has high viscosity in cubic phase

3) GREEN SYSNTHESIS OF CUBOSOMES:

Green synthesis of nanoparticles is done to reduce the waste generated and implement sustainable process. In this process mild reaction conditions and nontoxic precursors are used. It does not require expensive and harmful chemicals; we can synthesize various metallic nanoparticles by this method. It can be done by one step using various biological organisms such as bacteria, algae, yeast, molds and plants or their products. We can also use molecules from plants and microorganisms like phenolic compounds, amines, proteins and alkaloids. It is free from toxic compounds, different parts of the plant can be used for synthesis of nanoparticles



Green synthesis of cubosomes by using plant extracts has drawn a considerable attention. We can also extract reducing and stabilising agents from plants to synthetize metallic nanoparticles.

Various components can be extracted from plants and used in the synthesis of cubosomes such as curcuma longa, capsicum, neem plant, tulasi herb, red onion, moringa oleifera, lippia citriodora, alium sepa, eucalyptus, tridax procumbens etc.

The basic method of preparation includes either top down approach or bottom up approach

3.1 TOP DOWN APPROACH

The most widely used technique is top down approach. It involves two steps:

1) Mixing the cubosomes forming lipids with suitable stabilizer to form bulk cubic viscous aggregates
2) Dispersion of cubic viscous aggregates in aqueous medium by application of high pressure

Cubosomes prepared by this method are more stable, however it has a drawback that high energy is required in this process for incorporation of temperature sensitive bioactive agents specially peptides and proteins.

3.2 BOTTOM UP APPROACH

This is also called as solvent dilution method. The process includes dispersion of mixture containing cubosome forming lipid, hydrotrope and a stabiliser in excess of water. Hydrotrope is very important in this process as it is added to water insoluble lipids to form lipid precursors and prevents the formation of crystals at high concentration. Ex: sodium alginate, sodium benzoate and urea.

Characterisation of cubosomes prepared by green synthesis can be done by the following methods: optical microscopy, entrapment efficiency, particle size analysis, zeta potential analysis

CONCLUSION: Green synthesis is a best alternate method for preparation of nanoparticles over the physical and chemical methods available. It avoids the release of harmful compound which are injurious to human health and environment. It is simple, cost effective way.

The biological method of synthesis of nanoparticles is still under developing stage, further research has to be carried out in this field.

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