Review Article

AN OVERVIEW OF CUBOSOMES - SMART DRUG DELIVERY SYSTEM

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ABSTRACT

Cubosomes are square and rounded particles with internal cubic lattices visible. The invention of cubosomes is a distinctive story and spans the fields of food science, differential geometry, biological membranes and digestive processes. Self-assembled cubosomes act as active drug delivery systems; highly accepted, has got importance after innovation and nomination. 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 bilayers and wrapped into a three dimension, periodic and minimal surface, forming a strongly packed structure. Bicontinuous cubic liquid crystalline phase with optically lucid, extremely viscous material and have exclusive structure at the nanometer range. On the whole, cubosome render high importance in nano drug preparations for melanoma treatment outstanding to their potential advantages, including heavy payloads of drug because of increased surface area and cuboidal structures. They have very simple method of preparation; whereas biodegradability of lipids have the capability of encapsulating hydrophobic, hydrophilic and amphiphilic substances meanwhile targeted and controlled release of bioactive agents. Cubosome dispersions are bioadhesive and biocompatible. Because of their properties, cubosome 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. Consequently, Cubosomes are in move forward of awareness by pharmaceutical development division.

***Key words**: Cubosomes, Hydrophilic, Honeycomb, Drug payloads, Pharmaceutical division.*

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INTRODUCTION

Cubosomes are distinct, sub-micron, nano-structured particles of bicontinuous cubic liquid crystalline phase. They contain identical microstructure as that of its parent with high surface area and their dispersions are less viscous than the parent cubic phase.[1]

Most probably cubosomes are composed of polymers, lipids and surfactants with polar and non polar components hence said as amphiphilic. The amphiphilic molecules are driven by the hydrophobic effect into polar solvent to impulsively identify and assemble into a liquid crystal of nanometre scale (Fig.1). Thus cubosomes are bicontinuous cubic liquid phase enclosing two separate regions of water divided by surfactant controlled bilayers.[3] Further these are similar to liquid crystalline substance with cubic crystallographic symmetry and are optically isotropic, viscous and solid too.[4] The cubic phase can fracture and form colloidally and or thermodynamically stable particulate dispersions.[5] Cubosomes have great importance in nanodrug formulations.

Advantages of Cubosomes[6, 7]

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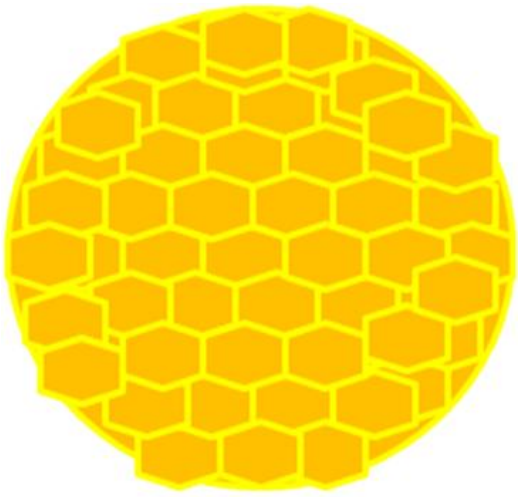

CUBOSOME D

Fig. 1: shows the bulk cubic phase/stage of Diamond (D) cubic lattices cubosomes.

- Because of their high internal surface area and crystalline cubic structures they have high drug payloads.
- They can be prepared by simple method.
- Posses lipid biodegradability.
- They can encapsulate all 3 types like hydrophilic, hydrophobic and amphiphilic substances.
- They render bioactive agents with targeted release and controlled release.

Cubosomes retain their stability even at high dilution which is not possible with other liquid crystalline systems

because they transform into micelles. Thus, being incorporated into formulations easily.[8] Cubosomes are generally produced by the following method: The bulk cubic phase is dispersed by high energy then colloidally stabilized using surfactant polymers.[9] Thus formed cubosomes are formulated into a product and applied topically/ mucosal surface which are absorbed/released via diffusion. They can be modified with protein molecules also. Moreover, companies like L'Oreal, Nivea, Procter and Gamble are interestingly investigating cubosomes for cosmetics applications which will be efficient and also cost effective for the scale up of this technology.

The disadvantages of the cubosomes are that they do not offer controlled drug delivery on their own compared with polymer based drug delivery. It is very difficult to load water soluble active ingredients during the formation of cubosomes, due to large amounts of water already present in it. Furthermore, researchers find it as a challenging task on production of large scale cubosome due to its high viscosity.

Recently, scientists are interested in preparing cubosomes for the treatment of cancer therapy, topical applications, cosmetics preparations and other drug delivery systems. Even though liposomes, niosomes, nanocochleates, micro sponges, micro particles and other carrier systems have been used as targeted / novel drug delivery systems, the cubosomes are more thermally stable. So, the authors suggest that preparation of cubosomes may be helpful in future by targeting the drug to a particular site and achieve therapeutic efficacy and also improve patient compliance.

Narration / The Past:

Early in 1980's, cubosomes manufacture in large scale was difficult because of their complexity and high viscosity. They are unique as they have viscosity similar to solids. These cubic phases can be broken and spread to thermodynamically/ colloidal particulates which are stable for a longer time. At certain concentrations, some surfactants form cubic phases suddenly when mixed with water. Luzzati and Husson,[10] Lusatia et al., [11] Larsson[12] and Hyde et al.,[13] determined the honey comb structure of cubosomes between 1960 and 1985 as represented in the figure 2 (a) and (b).

The word "Cubosome" was coined by Larsson, since the structure resembles cubic molecular crystals and liposomes. Attempts were made in scaling up the production of cubosomes. In practice very few anticancer drugs are being successfully formulated and characterized as cubosomes.[14]

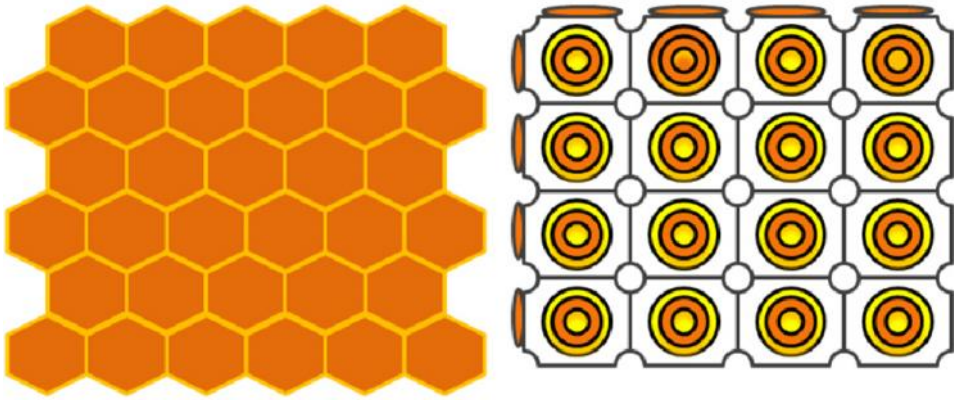

Fig. 2: (a) shows the honey comb structures, (b) shows the structures of primitive (P) cubic cubosomes which is similar to honeycomb.

Cubosomes and their Uses:

A universal application is as drug delivery vehicles and although bulk cubic phases achieve controlled release frequently, the first patent on cubosomes was to specify its medical and controlled release applications.[15,16] As a result, self-assembled surfactant phases are extensively examined for compatibility through various medical dynamic ingredients and their applications.[17] The quick development of the life-sciences industry is likely to drive beforehand "exotic" delivery vehicles and ingredients interested in broader market places, such as personal care and consumer products.[18] An area under modern development by L'Oreal is the use of cubosomal particle as oil-in-water emulsion stabilizers and pollutant absorbents in cosmetics.[19-22] They revealed that a second amphiphile, glycerol monooleate and phytantriol have an aqueous phase behaviour sufficiently close to that of monoolein to form cubosomes.

Interests on cubosomes being formulated as cosmetics products like skin care, hair care, antiperspirants has been increased and Nivea had filed patent too.[23-25] In spite of new activity, there resides a need on the practical problems like scale up and material customization with the purpose of necessary to lead formulators to believe using cubosomes in commercial

products.

Current Status of Knowledge:

Cubosomes are biocompatible drug delivery system and is a novel approach. The controlled release application of these nanoparticles is of a great significance in cosmeceutical and pharmaceutical fields. Cubosome have become an attractive vehicle for *in-vivo* drug delivery due to their low cost, versatility and potential for controlled release and functionalization. The personal care industry show particular interest on cubosomes due to their unique features. Deepak Prashar et al. and Patrick T. Spicer et al. studies substantiate the use of cubosome during manufacture / formulation enhanced the flexibility for product development.[26, 27] Cubosome formulations have been revealed to be safe in brain targeted drug delivery reported by Yosra SR Elnaggar et al and also Sergio Murgia et al have successfully exploited single living cell imaging by preparing drug loaded fluorescent cubosomes.[28, 29] Besides, Ruchi Sharma et al have reported the preparation of cubosomal gels of fluconazole which resulted in enhanced pay load, entrapment efficiency, drug permeability compared with conventional gels.[30]

DISCUSSION

Preparation / Manufacture of Cubosomes[31]

There are two methods in preparing cubosomes

i) Bottom up technique (Fig.3)

ii) Top down technique (Fig.4)

Cubosome dispersion formed by dilution of an isotropic solution (Bottom up technique)

Powder cubosomes precursor (Top down technique)

The merits of cubosomes preparations are:

* Easy method of preparation.

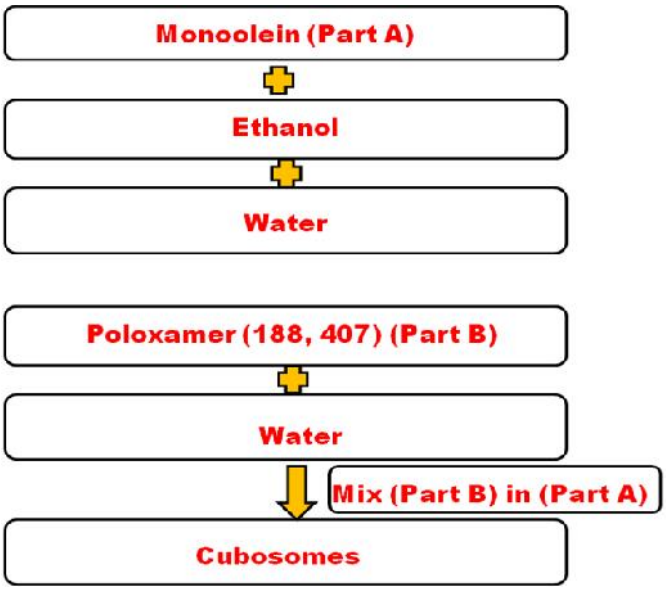

Fig.3: shows the flow chart preparation of cubosomes formed by dilution of an isotropic solution.

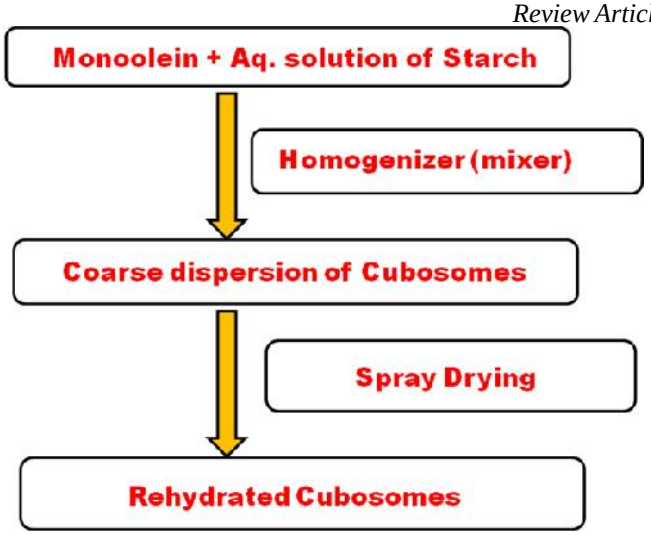

Fig.4: shows the flow chart preparation of powdered cubosomes precursor.

* Cost effective procedure.

* Less time consumption.

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 main applications of cubosomes are controlled release of various drugs, in melanoma (cancer) therapy, oral drug delivery systems, intravenous drug delivery systems and topical drug delivery systems. 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 cubosome as a controlled /sustained release drug carrier.

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