International Journal of Medical & Pharmaceutical Sciences
DOI: http://dx.doi.org/10.31782/IJMPS.2020.10201

Review Article

IJMPS
Section: Healthcare
SJIF (2019): 7.225

Cubosomes Nanoparticles: Recent Advancements in Drug Delivery

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ABSTRACT

Cubosomes are nanoparticles that are square or rounded and have internal cubic lattices. Cubosomes are a one-of-a-kind creation that combines food science, differential geometry, biological membranes, and digestion into a single entity. Because of its discovery and nomination, self-assembled cubosomes have developed in appeal as excellent drug delivery methods. Cubosomes are thermodynamically stable and contain a honeycomb-like structure of bicontinuous water and lipid domains. It is produced into bilayers inside the surfactant and wrapped into a three-dimensional, intermittent, and minimum surface, resulting in a densely packed structure. The material is a bicontinuous cubic liquid crystalline form that is optically clear and very viscous, with a unique composition in the nanometer range. Overall, cubosomes are critical in nano drug preparations for melanoma treatment because to their intrinsic benefits, which include higher surface area and cuboidal structures, which allow for larger drug payloads. They're easy to make, and their biodegradability allows them to encapsulate hydrophobic, hydrophilic, and amphiphilic chemicals while releasing bioactive substances in a regulated manner. Dispersion of biocompatible and bioadhesive cubosomes Cubosomes are tiny structures that may be administered in a variety of methods, including oral, percutaneous, and parenteral, due to their features. Cubosomes have a wide range of uses and are represented by a number of characteristics. As a result, cubosomes are gaining in popularity in the pharmaceutical testing industry.

Key Words: Cubosomes, Preparation, Mechanism, Composition, Evaluation, Applications

INTRODUCTION

Cubosomes are single, sub-micron-sized nanostructured particles that exist in a bicontinuous cubic liquid crystalline form (Figure 1). Larsson coined the name Cubosomes to describe cubic molecular crystallography and its resemblance to liposomes. Nanoparticles are self-assembled liquid crystalline crystals with surfactants that have the proper water-microstructure ratio. [1] Cubosomes are nanoparticles that self-assemble into liquid crystalline particles with a solid-like rheology and unique practical properties. Cubosomes are most likely made up of amphiphilic polymers, lipids, and surfactants that include both polar and non-polar components. [2] Amphiphilic molecules are drawn into polar liquids by the hydrophobic force, which causes them to spontaneously identify and organise into a nanometer-scale liquid crystal. Cubosomes are bicontinuous cubic liquid phases that include two different water regions separated by bilayers controlled by surfactants. These are all optically isotropic, viscous, and hard, and are similar to cubic crystallographic symmetry liquid crystalline solids. Colloidally and thermodynamically stable particle dispersions are formed using the cubic approach because it has the ability to fragment [3]. When monoolein and poloxamer 407 are hydrated together, they form cubosomes, which are bicontinuous cubic liquid crystalline phases. In nanodrug formulations, they are critical. Dots have a diameter of 10 nm to 500 nm and are square in shape with a slightly round shape. Cubosomes

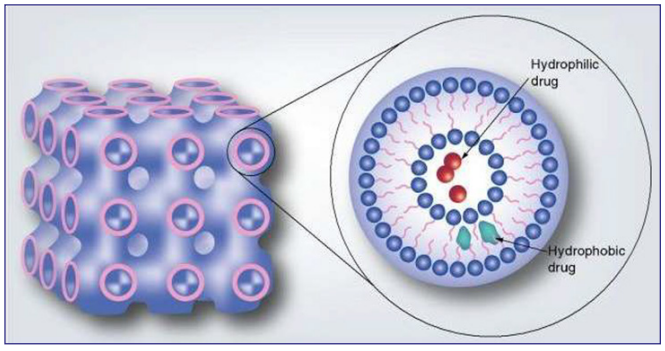

Figure 1: The basic structure of Cubosomes.

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ISSN: 2231-2188 (Print) **ISSN:** 2231-685X (Online)

Received: 05.01.2020 **Revised:** 10.02.2020 **Accepted:** 15.04.2020 **Published:** 10.08.2020

have chemical connections that connect active chemical component molecules to the polar head of the phospholipids. A 1:1 or 2:1 matrix is created by the polymer and the actual medication ingredient, depending on the substance. [4]

CUBIC PHASE STRUCTURE [5]

Cubosomes are nanoparticles with a diameter ranging from 10 to 500 nanometers with the appearance of square, slightly round dots. Using the X-ray scattering method, Luzzati and Husson were the first to discover the presence of pore-containing aqueous phase cubic phases in a lipid water system. Certain monoglycerides, according to Fontwell and Drew, will display cubic phases in ternary configurations of amphiphiles, gasoline, and water. Monoglycerides are polar lipids with aqueous phase behaviour and structural similarities to non-ionic surfactants. Monoglycerides with hydrocarbon chain lengths between C-12 and C-22, particularly monoolein, have a larger cubic phase area, according to Lutton's results. Monoolein is an unsaturated C-18 monoglyceride. Cubic phases are often seen wedged between lamellar and hexagonal liquid crystalline phases in non-ionic surfactant compositions. The monoolein-water technique is unique in that it has a cubic phase region with a broad composition and temperature range. Surfactant packing principles, on the other hand, are becoming more and more similar. Monoolein contains a continuous hydrophilic head and a hydrophobic tail, resulting in reversed or inversed cubic phases, which may be modeled using differential geometry and periodic minimum surfaces. Minimal surfaces are best explained by comparing them to soap films. According to Schwarz's mathematical discovery, three types of minimum surfaces are investigated in cubic phases depending on their curvatures (Figure 2).

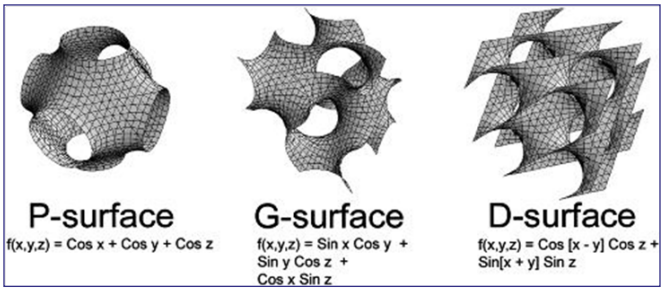

Figure 2: Reported surfaces of Cubosomes.

HISTORY [6]

Due to its dynamic step activity and viscous qualities, cubosomes were challenging to mass-produce despite their early detection (in 1980). Cubic phases have exceptionally strong solid-like viscosities due to their interesting bicontinuous forms. Cubic phases may be fractured and distributed to create colloidally and/or thermodynamically stable particle dispersions with prolonged shelf lives. When such surfactants are mixed with water above a particular concentration, cubic phases form spontaneously. Luzzati and Husson, Luzzati et al., Larsson, and Hyde et al. determined the makeup of their 'honeycomb' between 1960 and 1985. Larsson coined the term "Cubosomes," which alludes to cubic molecular crystallography and its resemblance to liposomes. Efforts are being undertaken to develop scalable technologies for mass-producing cubosomes (Figure 3).

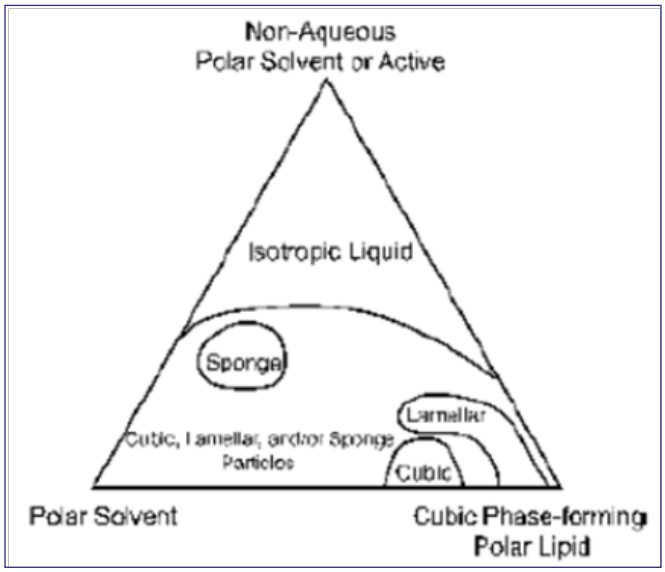

Figure 3: Drug scalable into cubosomes.

PERSPECTIVES [7]

Cubosome nanoparticles show promise in terms of drug delivery and continuous drug release, but further research is required to fully realise their therapeutic potential in a range of disorders, depending on the route of administration, frequency of dosage, and mechanism of drug release. They're also appealing nanocarriers for loading and delivering proteins and peptides, but published research is still in its early stages, and different aspects of these soft nanocarriers' structural and morphological characteristics, as well as their loading and release capabilities, should be discussed. In the future, blood compatibility should be considered early in the formulation of cubosome-based intravenous nanomedicines (Figure 4). Furthermore, there is still a lack of understanding about their persistence in

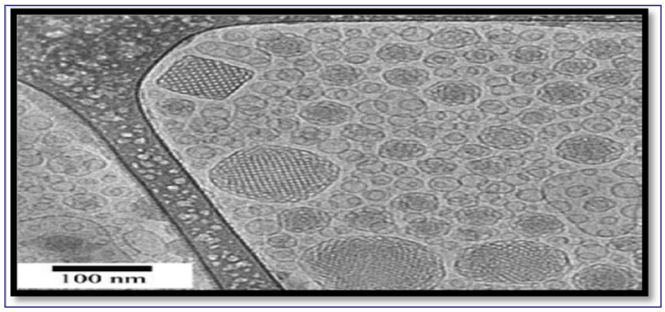

Figure 4: Diversely shaped Cubosomes.

biological fluids and biological factors that control drug release from cubosomes, structural transformation upon contact with biological fluids such as plasma, interactions with cell membranes, and infusion-related reactions, to name a few. Although the use of cubosomes for intravenous drug administration is ambitious, these nanocarriers may be used to deliver poorly water-soluble medicines through oral, ophthalmic, and topical routes, giving a cost-effective option in formulation development.

ADVANTAGES OF CUBOSOMES [8]

1. It is inexpensive.
2. It is non-toxic and biocompatible.
3. The process for preparation is simple.
4. It has exceptional bio-adhesive qualities.
5. It enhances the skin's permeability.
6. They have a longer duration of thermodynamic stability.
7. Molecules that are hydrophilic, hydrophobic, or amphiphilic may be enclosed.
8. Bioactive compounds are dispersed in a controlled and precise way.
9. Due to the large interior surface area and cubic crystalline formations, medication loading is considerable.

DISADVANTAGES OF CUBOSOMES [9]

1. Due to the large amount of water present, there is little trapping of water-soluble medicines inside cubosomes.
2. Because of the high viscosity, large-scale processing is often challenging.
3. Large-scale processing may be difficult at times due to the high viscosity.

STRUCTURE OF CUBOSOME [10]

Cubosomes have a honeycombed structure with a wide interfacial region between the two internal water channels. Cubosomes are nanoparticles, or more precisely nanostructure particles, that are generated when amphiphilic or surfactant-like molecules self-assemble in liquid crystalline phases with cubic crystallographic symmetry (Figure 5). The cubic phases exhibit a high solid-like viscosity, which is a unique attribute, due to their interesting bicontinuous structures, which surround two different areas of water separated by a balanced bilayer of surfactant usage. Amphiphilic molecules create bicontinuous water and oil channels, with bicontinuous referring to two distinct (but non-intersecting) hydrophilic areas split by the bilayer. The structure's interconnectedness produces a transparent viscous gel with the rheology and appearance of cross-linked polymer hydrogels.

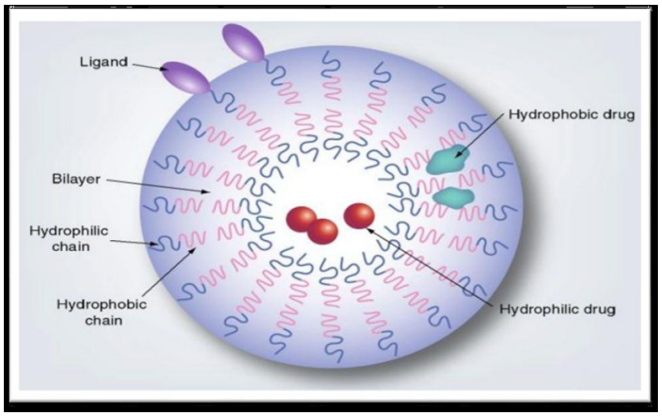

Figure 5: Structure of drug-loaded Cubosomes.

Solid Cubosomes Precursors

Honeycombed (cavernous) features with sizes ranging from 10 to 500 nm characterise cubosomes. They have a spherical form and resemble round dots. Each dot in the lipid water system corresponds to the presence of an aqueous cubic phase-containing pore. Using the X-ray scattering approach, Luzzati and Husson were the first to find it.

Liquid Cubosome Precursors

Cubosomes produced by the hydrotrope dilution process are smaller and more compact. The processes of nucleation and growth, which are employed in crystallisation and precipitation, generate particles. This is accomplished by dissolving the monoolein in a hydrotrope that precludes liquid crystalline formation, such as ethanol. The cubosomes spontaneously "crystallise" or precipitate after further dilution of this mixture. Because the liquid precursor step eliminates bulk solids processing and possibly destructive high-energy processes, cubosome preparations can readily be scaled up (Figure 6).

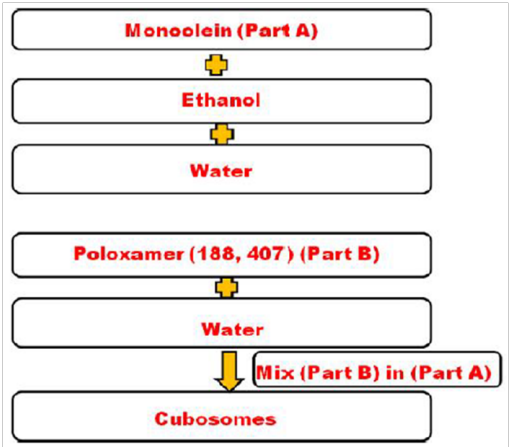

Figure 6: Liquid Cubosome Precursors..

Powdered Cubosome Precursors

Dehydrated surfactant is coated with polymer in powdered cubosome precursors (Figure 7). Compared to liquid phase hydrotropic cubosome precursors, such powders have advantages. As indicated by light scattering and cryo-TEM, the hydration of the precursor powders produced cubosomes with a mean particle size of 600 nm. Cubosomes are made up of waxy, sticky compounds called lipids. The waxy lipid is coated with a non-cohesive water-soluble starch that prevents agglomeration and enables for particle size control. Spray drying is an excellent option for his requirements.

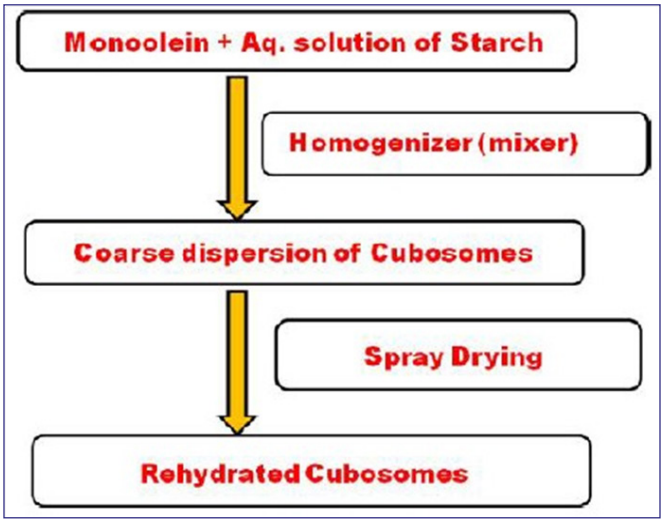

Figure 7: Powdered Cubosome Precursors.

MECHANISMS OF DRUG TRANSPORT [11]

Drug distribution across the biological membrane is influenced by the essence of the carrier's activity and structure, as well as the morphology and physiology of the skin (Figure 8). Small ions pass through hair follicles, skin membrane pores, and close junctions with little difficulty. In skin membrane transport systems, intra (trans) and inter (para) cellular transports are also active. Controlling carriers may inject drugs into the heart or make them an integral component of the vesicles. Paracellular diffusion is the transport of a medication via a membrane between two cells rather than between two cells. This is a passive process regulated by pore size, as well as the size and shape of the xenobiotic. Transcellular diffusion is the process of a medication moving through a cell. When intestinal absorption occurs by transcellular diffusion, the substance is exposed to the enzymes within the cell, as well as any efflux pumps present on the apical part of the membrane. As a result, the amount of drug entering the systemic circulation may be lowered. Diffusion between cells may be passive, passively aided, or aggressively aggressive. Transcellular movement, which involves drug passing through cells, is the most common method of medication administration. Some drugs, on the other hand, are too polar to pass through the lipoidal cell membrane and must rely on the paracellular route to link the cells.

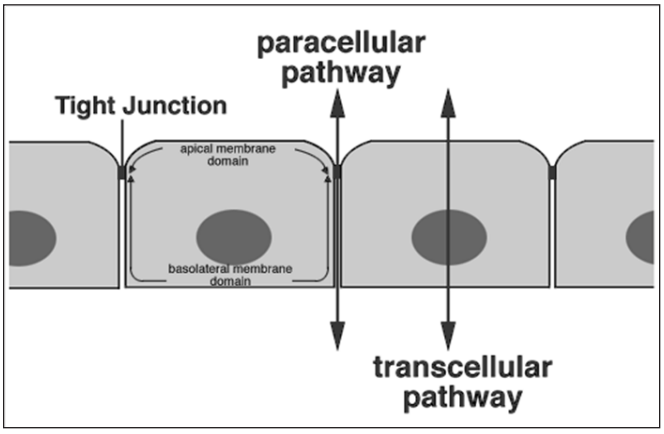

Figure 8: Mechanism of drug transport.

MATERIALS USED IN CUBOSOME FORMATION [12]

Bicontinuous cubic phases may also be seen in normal lipids, cationic and non-ionic surfactants, and polymer structures. Monoglycerides form bicontinuous cubic phases spontaneously when water is added, are generally insoluble, and are resistant to temperature changes. Monoglycerides are the most often employed lipid in the creation of bicontinuous cubic phases. The most significant precursor for cubosome development is monoolein. Monoolein, commonly known as glyceryl monooleate, is a fatty acid composed mostly of monooleate and oleic acid glycerides (Figure 9). Blended glyceride and distilled monoolein are the two types of monoolein, with the latter being employed for therapeutic purposes owing to its high purity. Monoolein is a yellow waxy substance with a distinctive odour. When exposed to water, it expands and forms numerous lyotropic liquid crystalline shapes. Monoolein is a nontoxic, biodegradable, and biocompatible chemical included in the FDA's inactive ingredients guide and nonparenteral medications allowed in the United Kingdom. Monoolein's mesomorphic mechanism is crucial to comprehending the lipid's potential therapeutic uses. When monoglycerides are exposed to sunshine,

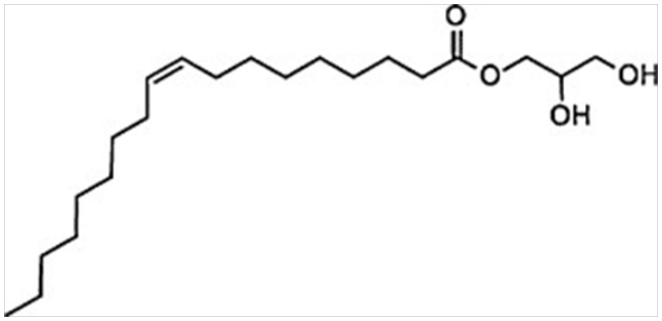

Figure 9: Structure of monoolein or glyceryl monooleate.

they exhibit a wide range of processes. Poloxamer 407 is a surfactant that is used in the dispersion process of cubosomes in concentrations ranging from 0% to 20% w/w. The monoglyceride/surfactant combination concentration in terms of total weight of the dispersion is normally between 2.5 percent and 10% w/w. Instead of poloxamer, polyvinyl alcohol was utilized to stabilize the dispersion.

METHOD OF PREPARATION [13]

Cubosomes may be made using a variety of methods:

Top-down Technique

It was initially reported by Ljusberg-Wahren in 1996 and is the most often used approach. Bulk cubic phase is generated initially, then cubosomes nanoparticles are created utilizing high-energy processes such high-pressure homogenization. The bulk cubic process, which resembles a translucent stiff gel, is shaped by water-swollen cross-linked polymer chains. Cubic phases are distinct from other thermodynamic phases because they are made up of a single thermodynamic phase with a periodic liquid crystalline structure. The amount of energy required to rupture cubic phases parallel to the shear direction is related to the number of ruptured tubular network branches (Figure 10).

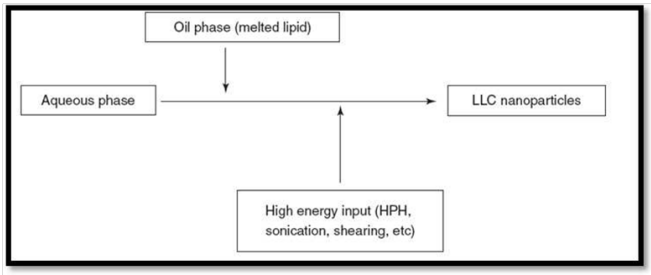

Figure 10: Structure of monoolein or glyceryl monooleate.

Bottom-up Technique

In this procedure, cubosomes are allowed to form or crystallize from precursors. The bottom-up process starts with the creation of nanostructure building blocks, which are then put together to create the final substance. It's a more contemporary way of cubosome formation that permits molecular precursors to combine and crystallize into cubosomes. A key component of this technique is hydrotrope, which may breakdown water-insoluble lipids into liquid precursors. This is a dilution-based strategy that manufactures cubosomes with little energy consumption, as opposed to a top-down approach (Figure 11). Several strategies were used to disperse nanoparticles created during cubosome formation:

1. Sonication
2. Spray drying
3. High-pressure homogenization
4. Spontaneous emulsification
5. Sonication and high-pressure

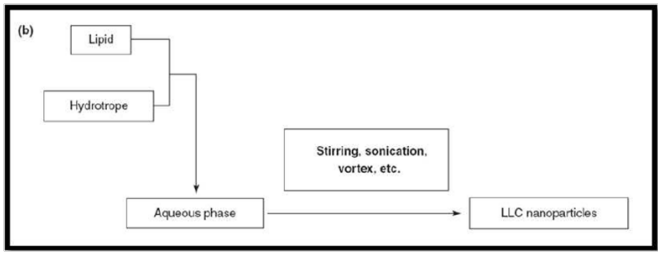

Figure 11: Bottom-up approach method.

Fabrication method

Cubic gel of GMO/p407 In a hot water bath at 60°C, GMO 5% and P407 1.0 percent were melted, then the required amount of medicine was added and agitated frequently until thoroughly dissolved. Deionized water is added drop by drop, and the vortex is set to homogenization. The optically isotropic cubic gel was formed and shattered by mechanical stirring blunt dispersion, which was then fragmented for 20 minutes at a cold temperature of 20°C in a water bath using a sonicator probe with energy of 200 W.

Emulsification method

The GMO and P407 are dissolved in water and ultrasonically separated into 5% GMO, 1% P407, and 5% ethanol in 89 percent water in this procedure. The GMO and P407 were melted and mixed at 60°C, and the ethanolic solution was used to speed up the melting process. The resultant mixture is put into 70°C deionized water and ultrasonicated for 50 minutes at the same temperature. The distributed solution is kept at room temperature and out of direct sunlight.

EVALUATION OF CUBOSOMES [14]

Visual inspection

The cubosomes' optical appearance is assessed visually (e.g. color, turbidity, homogeneity, presence of macroscopic particles).

Shape of the cubosome

The morphology of cubosomes may be studied using transmission electron microscopy.

Particle size distribution

Using a Zeta sizer and dynamic laser light scattering, the particle size distributions of cubosomes are determined (Photon correlation spectroscopy). At 25°C, with a light scattering rate of roughly 300 Hz, the sample is combined with an appropriate solvent and calibrated in triplicate. An

average volume weight size may be used to collect and display the data. The zeta potential and polydispersity index may also be reported.

Entrapment efficiency

Cubosome entrapment efficiency may be measured using ultrafiltration technologies. In the aforementioned procedure, the concentration of unentrapped medicine is measured and deducted from the total amount of drug added. The volume of medicine present is measured using a spectrophotometer.

Polarized light microscopy

Polarized light microscopy will reveal the optically birefringent (potentially vesicular) surface layer of the cubosomes, as well as distinguish anisotropic and isotropic substances.

X-ray scattering

Small-angle X-ray scattering may be used to identify the spatial structures of distinct classes in the research (SAXS). The diffraction patterns are transformed to strength versus q-value plots, enabling peak sites to be detected and converted to Miller Indices. To assess the sample's dominant internal nanostructure, the Miller Indices will be compared to documented values for different liquid crystalline structures and space groups.

Measurement of drug release

The pressure ultrafiltration technology might be used to liberate drugs from cubosomes. It focuses on the work of Magenheim et al., who employed a Millipore membrane with an Amicon pressure ultrafiltration cell at ambient temperature.

Stability studies

Organoleptic and morphological parameters may be used to assess physical consistency throughout time. To assess possible variations over time, particle size distribution and medicine content may be studied at different time intervals.

APPLICATIONS [15]

Oncotherapy

Any anti-cancer drugs have lately been successfully encapsulated in cubosomes, and their physicochemical characteristics have been determined (Figure 12). Because of the unique properties of this potential nanocarrier, it may be employed to treat melanoma. Different strategies for guiding nanomedicines directly to tumors have been developed, with passive and active cancer cell targeting showing to be successful in preclinical and clinical studies.

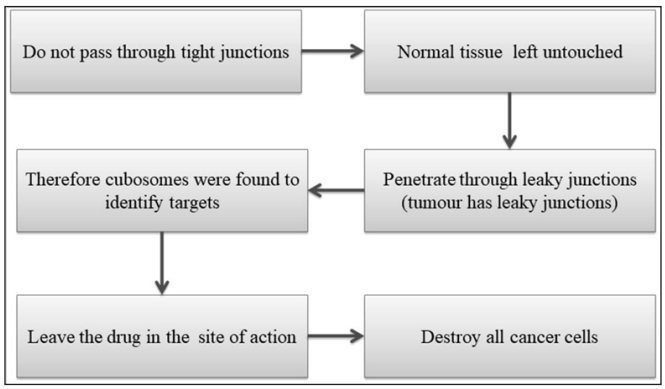

Figure 12: Role of Cubosomes in treating cancer.

Oral drug delivery

Cubosomes solve problems including limited water solubility, poor diffusion, and large molecular size in the oral distribution of a wide range of drugs. In one example, a wide range of proteins were encapsulated for local activity in the gastrointestinal system. Pharmaceuticals may be given at diverse absorption locations, such as the upper or lower intestine, thanks to cubosome technology, which is useful for therapies with a restricted absorption window.

Intravenous drug delivery

Lipid nanoparticles having internal liquid crystal frameworks and curved lipid membranes are utilised to solubilize, encapsulate, and distribute medications to disease locations inside the body. Cubosome nanoparticles may carry more peptides, proteins, and numerous insoluble tiny molecules than emulsions and liposomes, making them good carriers for injection.

Topical drug delivery

Cubosomes are designed to be more bioadhesive, making them suited for topical and mucosal medication delivery. The remarkable characteristics of liquid crystal and liquid crystal nanoparticle technologies are being leveraged to produce topical delivery systems. Topical drug delivery systems are bioadhesive liquid crystal systems that form in situ and distribute drugs to mucosal surfaces such as the buccal, ocular, and vaginal mucosa in a controlled and efficient manner.

Drug delivery vehicle

One of the most common applications for such novel materials is as a medication delivery vehicle. Cubosome particles are being investigated in cosmetics in partnership with companies like L'Oreal and Nivea to determine whether they can be utilised as oil-in-water emulsion stabilisers and pollutant absorbents.

Controlled or sustained release behavior

Cubosomes have been loaded with a range of medicines with

diverse physicochemical features, and their long-term opioid release behavior has been studied. The cubosomes' long-term action was attributed to cubosome residue particles. Monoglyceride-based cubosomes may be used topically for percutaneous or mucosal applications.

Treatment of viral diseases

Monoglycerieds may be utilized to produce intravaginal therapies for sexually transmitted illnesses caused by viruses (e.g., HSV, HIV) or bacteria (e.g., Chlamydia trachomatis and Neisseria genorrticae) owing to their microbicidal characteristics.

Current application

One technique Loreal® is now working on is the use of cubosome particles as oil-in-water emulsion stabilizers and pollution absorbents in cosmetics.

SPECIFIC EXAMPLES OF CUBOSOME FORMULATIONS

The creation of several therapeutically active cubosome formulations by integrating diverse natural products and synthetic medication components is fully illustrated in Table 1 by multiple worldwide researchers. Table 2 also includes a list of recently submitted and authorised patents for different cubosome compositions.

Table 1. Drugs incorporated into cubosome forms.

Drugs	Study Objectives	Study Outcomes	Ref
Amphotericin B	Using cubic nanoparticles to improve amphotericin B solubilization and bioavailability	Amphotericin B may be delivered orally using this formulation. Cubosomes were used to produce a controlled release of amphotericin B for oral delivery.	16
Antimicrobial peptide LL37	Cubosomes were used to test the anti-bacterial properties of LL37 in in vitro and ex vivo skin irritation models	Cubic nanoparticles protect LL-37 from enzymatic degradation and have a strong bactericidal impact when released in a regulated manner. The skin irritation caused by LL-37 is reduced by LL-37 produced cubic nanoparticles.	17
Cisplatin and Paclitaxel	Method assessment and anti-tumor efficacy of a dual drug-loaded system	The top-down method resulted in small aggregates with a higher surface area and homogeneous drug encapsulation without crystallization.	18
Cyclosporine A	To obtain better in vitro corneal penetration with decreased ocular irritation, cubic nanoparticles were produced for ocular administration of Cyclosporine A	A tiny cubic nanoparticle with a greater drug loading was created. Cubosomes increased corneal permeability in vitro, had a higher retention effect, and were less irritating to the eyes.	19
Dapsone	Using cubic nanoparticles, improve dapsone skin permeability	The increased levels of dapsone were obtained while decreasing systemic adverse effects, resulting in better therapeutic action at the targeted region.	20
Docetaxel	Docetaxel-loaded thermosensitive depot cubosomes for control release development and assessment	Cubosome preparation was free flowing at room temperature and converted to the depot at body temperature, allowing for progressive drug release.	21
Doxorubicin	In vitro cell line experiments showed that phytonadione cubosomes reduced doxorubicin cardiotoxicity and improved intestinal permeability	Cubosomes made with doxorubicin had greater drug loading, pH sensitivity, and controlled release at the target location. The carrier system improves cell cytotoxicity while minimizing unfavorable side effects.	22
Elesclomol	Elesclomol cubosomes for mitochondrial targeting: in vitro testing with A549 and A431 cancer cell lines	Nanoparticles were easily absorbed by the A549 and A431 cancer cell lines, leading in improved localized distribution. Elesclomol and copper complexation have a greater cytotoxic impact when delivered through cubosomes.	23

Fluconazole	Fluconazole-loaded cubosomes delivered intraocularly for the treatment of keratomycosis	Ocular tolerance and histological investigations in rats showed that FCZ laden cubosome dispersion was efficient and safe in the treatment of induced keratomycosis.	24
Flurbiprofen	Flurbiprofen cubic nanoparticles are delivered ophthalmically to enhance bioavailability while reducing skin irritation	Cubic nanoparticles enhanced the transport of flurbiprofen to the cornea and increased its bioavailability.	25
Indomethacin	Anti-inflammatory activity of indomethacin-fabricated cubosomes was tested	With extended administration of lipophilic medication via the skin, a homogenized monoolein and poloxamer containing cubosomes formulation was effectively produced.	26
Ketorolac	Monoolein and poloxamer cubic nanoparticles for ketorolac ocular administration	Ketorolac-loaded cubosomes with an optimized formulation produced nano-sized particles with greater ketorolac encapsulation. Cubosomes containing ketorolac also enhanced trans corneal penetration and retention of ketorolac.	27
Pilocarpine nitrate	Improved corneal permeability with ophthalmic administration of pilocarpine nitrate	The bioavailability of nanoparticles made from pilocarpine nitrate was superior to that of the commercial formulation. When compared to a commercial formulation, cubic nanoparticles had improved in vitro release and ex vivo penetration.	28
Rapamycin	Psoriasis therapy with transdermal and regulated administration of rapamycin-loaded cubosomes	The rapamycin-carrying particles were ultimately incorporated into a polymeric matrix made up of microneedle pads that dissolve rapidly. The designed microneedles successfully pierced and deposited the loaded cubosome-like particles on a skin-like agarose gel. The findings show that cubosome-like particles may be transported into the skin and help with the continuous release of rapamycin.	29
Resveratrol	Topical administration of resveratrol-loaded cubosomes for melanoma was developed	In the epidermal layers of mice, the RC-Gel exhibited higher drug permeability and deposition. An in vivo bioavailability investigation revealed that RC-Gel had a high proclivity for skin localisation. RC-gel cubosomes were shown to be an effective topical drug delivery carrier for the treatment of melanoma in the trials.	30
Silver sulfadiazine	Cubosome hydrogels were tested for their antibacterial capabilities using cubic nanoparticles for topical burn therapy	The cubic liquid crystalline nanoparticles (cubosomes) Formulation was created of SSD dispersions to circumvent the cytotoxic effects of silver by regulating the release of SSD. When compared to the commercial formulation, it helped lower the dosage of SSD to 0.2% and showed improved and better healing with less adverse effects.	31
Tropicamide	Cubic nanoparticles containing tropicamide were produced for ocular use	With tropicamide loaded cubic nanoparticles, there was a faster start of level and a greater intensity of mydriatic effects.	32

Table 1. Recent studies on niosomes drug delivery systems.

Patent Number	Summary	Ref
KR102013804B1	A skin-protecting cosmetic formulation incorporating cubosomes containing ceramide and phytosphingosine as active ingredients. The cubosomes, in particular, enhance the moisturizing impact of the skin.	33
US20070176143A	Cubic-like nanoscale symmetry in a ternary system. The ternary system, which may be disseminated and utilized as a solubilizing medium for hydrophobic and hydrophilic compounds, can be used.	34
US6936187B2	Cubic precursors, including as gels, dispersions, and cubic gel particles, are employed to transport active chemicals to substrates.	35
US6994862B2	The creation of a new solubilizing compound combining monoglycerides, emulsifiers, and organic solvents has been awarded a US patent. The liquid formulation that emerged was claimed to disperse in water without the need of physical force.	36
US7807188B2	When applied to undamaged skin, this composition promotes skin development and healing while also acting as a water resistant barrier and moisturizing agent.	37
WO2007140510A1	Cubosome liquid crystal particles containing phytantriol and a stabilizer in an agrochemical formulation.	38
WO2010060131A1	The current patent covers the development of a lyotropic liquid crystal phase contrast agent for diagnostic imaging, in which the lyotropic liquid crystal phase is distributed as nanodroplets, as well as a stabiliser to prevent the nanodroplets from re-aggregating.	39

CONCLUSION

Cubosomes are nanoparticles that, rather than being rigid crystals, are self-assembled liquid crystalline particles that may contain a broad variety of hydrophilic and lipophilic medicines and distribute them in a controlled and targeted way. Top-down and bottom-up methodologies may be utilised to create cubosomes utilizing ultrasonication operations or high-pressure homogenization. Cubosomes are found in a wide range of pharmaceuticals, hormones, resistant compounds, and cosmetics. Due to its possible site-specificity, cubosomal preparations may be routinely utilized as selective drug delivery methods for ophthalmic, diabetic, and anti-cancer treatment. Because cubosome technology is new and has a high yield, there is plenty of space for development into new economically and industrially feasible formulations.

CONFLICT OF INTEREST

The author declares no conflict of interest.

ACKNOWLEDGEMENTS

The author provides acknowledgment to the college management and colleagues for providing guidance and essential facilities for this study.

FUNDING INFORMATION

No agency provided funding support in this study.

AUTHOR'S CONTRIBUTION

All authors have equally contributed to this manuscript. All authors did the literature survey from standard databases, collected all essential elements, and wrote this manuscript collectively.

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