Liquid Crystals Pharmaceutical Application: A Review
Imran Tadwee1*, Dr. Sadhana Shahi1, Vivek Ramteke2, Iftequar Syed3*

1 Government college of pharmacy Osmanpura Aurangabad [M.S.] -431005
2. Sharad Pawar College of Pharmacy Hingna Road Nagpur [M.S.]-
3 Y.B. Chavan College of Pharmacy Aurangabad [M.S.] -431001
*Corresponding author: Imran.tpharma@gmail.com, ifte_56@rediffmail.com

Abstract:
Liquid crystals (LC) are substances that flow like liquids but maintain some of the ordered structure characteristics of crystalline solids. Based on the ways that LCs are generated, they can be classified into two types 1) Thermotropic LCs and 2) Lyotropic LCs. The Thermotropic is generated by temperature variation in the liquid state, while the Lyotropic is formed by dissolving the compound in certain solvents. Either way offers the systems sufficient large amplitude molecular mobility so that molecules can change positions and reorient themselves forming LC phases. The thermotropic LCs usually are one-compound systems, while lyotropic LCs are always solutions consisting of multiple compounds containing solute and solvent. The aim of this review article is to scientifically highlight Pharmaceutical Liquid crystals, its importance in current development of targeted drug delivery system. Objective of this review is also to provide in depth information of pharmaceutical liquid crystal technology which include its latest & advanced technology development.

Keywords: Pharmaceutical liquid crystals, Mesomorphs, Liquid crystal Emulsions,

Introduction:
Liquid Crystals are intermediate state between solid and liquid state. It is often called a mesomorphic state which is state of matter in which the degree of molecular order is intermediate between the perfect three-dimensional, long-range positional and orientational order found in solid crystals and the absence of long-range order found in isotropic liquids, gases, and amorphous solids it is also called as meso intermediate. The liquid crystals of thermotropic and lyotropic types lyotropic liquid crystals are induced by the presence of solvent, and have been extensively described elsewhere in the context of emulsion technology; however, other pharmaceutical examples are emerging. Thermotropic liquid crystals are induced by a change in temperature and are essentially free of solvent, where more pharmaceutical applications appear in the literature.

Liquid crystals (LC) are liquids featuring a certain level of orientational order. Specifically, molecules in LCs tend to point to a certain direction, while they still have translational (positional) freedom. Although they are best known for their application in displays, liquid crystals are also an essential part of all life forms. Lyotropic liquid crystals are essential organic substances, DNA, lipids of cellular

Membranes and proteins are some examples of well known liquid crystals. In liquid crystals drug delivery crystalline solids exhibit short as well as long-range order with regard to both position and orientation of the molecules. Whereas liquids are amorphous in general but may show short-range order with regard to position and/or orientation. Liquid crystals show at least orientational long-range order and may show short-range order, whereas positional long-range order disappears.
Accordingly, liquid crystalline phases represent intermediate states and are also called mesophases.8

Applications:

Liquid Crystal Emulsion

A large part of cosmetic products are made in the form of emulsions, a form that allows the simultaneous use of lipophilic and hydrophilic ingredients in the required dosages. A product in the form of an emulsion also has the advantage of having the most convenient appearance and texture that also facilitates its application. They can be formulated to be liquid, milk type emulsions of variable consistency, creams, or even super liquid spray able emulsions. Finally, we should also consider the fact that an emulsion is the best carrier for active ingredients and functional substances.

The theory of stabilising an emulsion through the formation of a network of liquid crystals is different to the HLB theory or the Schulman couple.s theory. The gelification of the water phase obtainable with hydrolysolvatable polymers or with emulsifiers that are able to form a reticular organised structure in liquid crystal form, eliminates the need to use waxy components in large quantities and consistency factors that are no longer in harmony with the modern conception of light and easy to spread emulsions.

Advantage of Liquid crystals in emulsions:

LCs (mesophases) provides the following advantages to emulsion.

1. Increased stability
2. Prolonged hydration
3. Controlled drug delivery

1) Stability: Emulsion stability of the multilayers around the oil droplets act as a barrier to coalescence. If oil droplets coalesce emulsion breaks. This barrier for coalescence acts as increased stability property of the emulsion.

2) Prolonged hydration: Lamellar liquid crystalline and gel network contain water layer, which shows that 50% of the water of oil in water (o/w) emulsion can be bound to such structures. Such water is less prone to evaporation when applied to the skin and permits a long lasting moisturisation / hydrating effect, necessary for drug entry.

3) Controlled Drug delivery: Liquid crystals prevent the fast release of the drug dissolved in the oil phase of an emulsion. This is attributed to the lamellar liquid crystalline multilayer, which reduces the interfacial transport of a drug dissolved within the oil droplets. Microscopic observations under polarized light show the exceptional thickness of liquid crystalline lamellar layer around the oil droplets.

Function & properties of the liquid crystal system

LCs When present at the oil/water interface, the liquid crystals help give the system rigidity and, by limiting the fluctuation of the components at the interface, give the emulsion great stability. Furthermore, the liquid crystal system enhances the moisturising ability of the emulsion; in this special network. The quantity of inter-lamellar water can be extremely high and become immediately available when the cream is applied to the skin. For these reasons these emulsions have a shiny surface, a fresh and original feel and they leave a light and pleasant sensation on the skin.

In recent years, the moisturising effect of creams and lotions has become increasingly more important and cosmetic chemists are constantly searching for better methods of retaining water in the superior layers of the skin. The evaporation of the bonding water in emulsions containing anistropic lamellar phases is slower and permits a hydroretentive action that prolongs the moisturising effect. The associations that are formed because of the excess water are particularly interesting; in these cases the ability of the crystalline phase to swell is strictly linked to the stability and the behaviour of the emulsion because, in a liquid crystal system, the quantity of inter-lamellar water and of hydrophile elements can amount to 70% of the total external phase.

Fig. 1 Image of Liquid crystal
Controlled Release of Bioactive Materials:
The release of the active substance from liquid crystalline delivery systems is often controlled by diffusion, and some systems using the photoinduced or thermal phase transition of the liquid crystals as the release for bioactive materials\textsuperscript{14}

Drug loading
According to the nature of the drug, it can be added in both the aqueous as well as oil phase. Loading totally depends on solubility of active constituents and their partition between existing phases.

Drug can be incorporated in liquid crystal technology:\textsuperscript{15}

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drugs</th>
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<tbody>
<tr>
<td>Cefazolin</td>
<td>Cefuroxime</td>
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<tr>
<td>Clomethiazole</td>
<td>Clindamycin phosphate</td>
</tr>
<tr>
<td>4-Phenylbutylamine, prilocaine</td>
<td>Oestriol</td>
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<tr>
<td>Isosorbide mononitrate</td>
<td>Insulin</td>
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<tr>
<td>Indomethacin</td>
<td>Clotrimazole gramicidin</td>
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<tr>
<td>Nitroglycerin</td>
<td>Lidocaine Hydrochloride</td>
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Patents with Liquid Crystals Applications:

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Title of Patent</th>
<th>Patent No / Date</th>
<th>Abstract</th>
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<tbody>
<tr>
<td>1</td>
<td>Liquid crystals containing cosmetic and pharmaceutical compositions and methods utilizing such compositions</td>
<td>US 4,999,348 / Mar.12, 1991</td>
<td>Cosmetic and pharmaceutical compositions and methods comprising delivery systems for the controlled release and enhanced penetration of biologically active material (e.g. Vitamin A) to the skin. The delivery systems comprise cholesteric liquid crystals wherein the active material is retained within the lamellar molecular structure (i.e. between the molecular sheets) of the cholesteric liquid crystals\textsuperscript{3}</td>
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<tr>
<td>Number</td>
<td>Description</td>
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<td>2</td>
<td>Liquid crystals emulsion type pharmaceutical composition containing cyclosporine and therapeutic method of treating cutaneous disease therewith</td>
<td>US 2010/190695 A/ July 29,2010</td>
<td>A dermal external pharmaceutical composition that excels in feeling at application or after application and that by enhancing of the transdermal absorption of cyclosporine exerts medicinal benefits at low concentration. There is provided a liquid crystals emulsion- type pharmaceutical composition comprising cyclosporine a hydrophilic nonionic surfactant, a lipophilic nonionic surfactant, an oil a fatty acid that is insoluble in the oil at room temperature, a solid fatty alcohol that is insoluble in the oil at room temperature and a water soluble polyhydric alcohol that is immiscible with the oil at room temperature, and a method of testing cutaneous diseases with the use of the pharmaceutical composition. 4</td>
</tr>
<tr>
<td>3</td>
<td>Drug delivery system utilizing liquid crystal structure</td>
<td>US 5,891,845/ April 6,1999</td>
<td>Vitamin E TPGS/drug composition and method are provided which obviates the need for surfactants or non evaporated co solvents because the active drug component is dissolved directly into vitamin E TPGS to form a true molecular solution –not an emulsion or a micro emulsion the invention provides a slowly dissolving TPGS/Drug matrix that absorbs gastrointestinal fluid into the matrix at crystal is formed. This gel front forms a liquid crystals boundary where drug dissolution is highest. At this liquid crystals/GI fluid boundary, synchronization takes place in which the rate of formation of liquid crystals equals the dissolution rate of liquid crystals at the water interface thereby giving controlled order release of the drug into the GI tract. The rate of dissolution is also controlled by the geometry of the dosage form. The solid vitamin E TPGS/ drug matrices of the inventions can be solidified and compressed into tablets or filled into capsules, with other excipients, binder and /or fillers. The solid TPGS/drug solution of the invention also can be made into an immediate release liquid formulation upon addition of water or into a controlled release system solid tablet by the use of impermeable or semi permeable barriers or coating surroundings portions of the tablet. 5</td>
</tr>
<tr>
<td>4</td>
<td>Transdermal pharmaceutical composition</td>
<td>10/575,145/June 1, 2010</td>
<td>The invention relates to a liquid crystal gel containing polyoxyethylene-glyceryl-trioleate, propylene-glycol, isopropyl myristate and a hyaluronic acid salt or complex for use in the manufacture of transdermal pharmaceutical compositions and healing cosmetics. The invention also relates to transdermal pharmaceutical composition consists of an estrogen and a progestin component as well as a liquid crystal gel containing polyoxyethylene-</td>
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glyceryl-trioleate, propylene-glycol, isopropyl myristate and a hyaluronic acid salt or complex. The invention can be applied for transdermal hormone replacement therapy and for other transdermal depending on the active principles included.

Silicone liquid crystals, silicone vesicles, and silicone gels are formed by combining (i) an amine functional silicone or an organic amine compound, (ii) an organic epoxide containing at least two epoxy groups or an epoxy functional silicone containing at least two epoxy groups, and (iii) a fluid such as water, a silicone fluid other than a silicone used in (i) and (ii), and a polar organic compound or nonpolar organic compound other than organic compounds used in (i) and (ii) in which the polar and nonpolar organic compound are present at a concentration to provide a level of solids less than 40 percent by weight based on the weight of (i)-(iii). These silicone liquid crystals, silicone vesicles, and silicone gels are useful in personal care for preparing various skin, hair, and underarm products.

The present invention relates to a delivery system based on a film of an imine forming liquid crystalline phase, mixed with at least with one biologically active substance, to which a constant or variable electric field can be applied. The delivery system can be used as a delivery system for biologically active substances such as flavors, fragrances, bactericides, fungicides, insecticides, insect attractants or repellents, agrochemicals or pharmaceuticals.

Conclusion:
Liquid crystals technique for drug delivery can be an effective and useful for delivering the drug with desired target. This technique can be utilized largely in topical delivery of the drug as it posses the advantages of smooth feel and drug loading of incompatible molecule. Day by day various patents are coming in this liquid crystals technique. This technique of drug loading is a new & immerging techniques requires attention further for its practice in real scientific industries to deliver a quality outcome for a society

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3) Gheorge Cioca, Lake Grove, James Hayward, Port jeffeson, Manuel L.Tan, Glen Clove, Morris Herstein scarsdae, N.Y.walter, Stamford, conn
“Liquid crystals containing cosmetic and pharmaceutical compositions and methods for utilizing such compositions” US 4,999,348 March 12, 1991
5) Garry Myers, Kingsport, Tenn. “Drug delivery system utilizing liquid crystal structure” US 5,891,845 April 6, 1999
Abstract. Pharmaceutical co-crystals are novel class of pharmaceutical substances, which possess an apparent probability of advancement of polished physical properties offering stable and patentable solid forms. Liquid Crystals Materials (LCMs) are mesophase pomp equivocation between profound and clear nation. It is mostly assemble a mesomorphic plight which is nation of moment in which the gradation of brownian arrangement is intervene between the three dimensional, belong-wander mealy and orientation attitude found in grave crystals and the destitution of hunger-sift direction found in isotropic liquids, gases, and uncристallized compact [1]. LCMs are finding rhythmical applications that of their ability to veer orientation of molecules in answer to very soft physical and alchemical humor, such as e...Â. Liquid crystals pharmaceutical application: A review. J Int Pharm Res Allied Sci 2012;1:6-11. 2 Liquid crystals emulsion type pharmaceutical composition containing cyclosporine and therapeutic method of treating cutaneous disease therewith US 2010/190695 A1/ July 29,2010 A dermal external pharmaceutical composition that excels in feeling at application or after application and that by enhancing of the transdermal absorption of cyclosporine exerts medicinal benefits at low concentration.Â Cite this article Imran Tadwee, Dr. Sadhana Shahi, Vivek Ramteke, Syed Iftequar Liquid Crystals Pharmaceutical Application: A Review Int. J. of Pharm. Res. & All. Lyotropic liquid crystal (LLC) systems that commonly consist of amphiphilic molecules and solvents can be classed into lamellar (La), cubic, hexagonal mesophases, and so on. In recent years, LLC systems have received considerable attention because of their excel-lent potential as drug vehicles.Â To widen the applications of cubosomes in pharmaceutical eld, dry powder precursors can be fabricated by spray drying and used for the preparation of oral solid formulations and inhalants. This approach was originally proposed and investigated by Spicer et al.Â This review mainly discusses the current applications of reversed cubic and hexagonal mesophases as drug vehicles, with a major focus on their applications in vivo.