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Review Article

LIQUID CRYSTAL AS ACCELERANT IN DRUG ABSORPTION FROM TOPICAL FORMULATIONS

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ABSTRACT
Topical drug delivery has been one of the major research fields in the area of drug therapy for last few decades. However inspite of its large therapeutic potential market success has been limited. It provides the several advantages over the oral drug delivery. Percutaneous absorption involves the passage of the drug molecule from the skin surface into the stratum corneum under the influence of a concentration gradient and its subsequent diffusion through the stratum corneum and underlying epidermis, through the dermis, and into the blood circulation. Liquid crystal phase has emerged as a novel material for preparation of topical drug delivery systems. It fulfills the requirements for making drug loading and drug absorption faster from the site of application of topical formulations. Liquid crystal has got many phases in itself which can be further exploited to get a better and more efficient drug delivery system. Also a variety of areas in medical and electronics streamline can find its application. There is also a wide scope in respect to the methods by which these liquid crystals can be prepared. Different methods give rise to different kinds of liquid crystals. Topical formulations have emerged as a very useful drug delivery system as it bypasses the first pass metabolism. Also the absorption of drugs depends on the percutaneous absorption of drug from the area of application. Hence it's required to choose such a vehicle which enhances the absorption of drug from the formulation.
KEYWORDS: Topical formulations, Percutaneous absorption, Liquid crystals, Mesophases

INTRODUCTION

There is currently a great deal of world-wide interest in the field of transdermal drug delivery and, consequently, broad classes of drugs are being evaluated for percutaneous absorption potential. The skin is the largest human organ. It ensures that harmful substances and drugs released from topically applied formulations cannot intrude into the organism offhand[1]. The skin is an ever-changing organ that contains many specialized cells and structures as shown in figure 1. Mainly skin composed of three layers such as epidermis, dermis, and subcutaneous tissue. The major barrier for the transport of drugs through the skin is the stratum corneum, with most transport occurring through the intercellular region. Another potential advantage of this type of drug delivery is the optimization of drug concentration at the desirable sites, reducing the chances of side effects[2].

Liquid crystals: A novel topical formulation

The design of new forms that increases the effectiveness of existing drugs is one of new trends observed in pharmaceutical technology in recent years[3]. In this context liquid crystals act as novel dosage forms because of their considerable capacity to solubilize both oil and water soluble compounds[4]. Liquid crystalline phase was formed toward the oil phase, where the spontaneous emulsification took place toward the aqueous phase[5]. Liquid crystals are substances that exhibit a phase of matter possess properties between those of a conventional liquid and solid crystal. For instance, a liquid crystal may flow like a liquid but have the molecules in the liquid arranged and/or oriented in a crystal-like way[6]. The liquid crystalline state combines properties of both liquid and solid states. The liquid state is associated with the ability to flow as shown in figure 2 whereas solids have an ordered crystalline structure[7]. Liquid crystalline phases share features from both liquids and crystalline substances. Due to their intermediate state they are also called as "mesophases"[8]. As shown in the liquid crystalline phase surrounding the droplets is highly viscous, and has an ordered structure and a low interfacial tension. These phases have also a tendency to form a semisolid network extending through the continuous phase of the dispersion. The network slows the movement of the droplets and exhibits a viscoelastic behavior[9]. Liquid crystalline dispersions are prepared by adopting technique like. (1) Cubosomes from pseudo-binary systems. (2) Cubic liquid crystalline phase in the presence of hydrotropes. (3) Cubosomes by nucleation. (4) Dry powder precursor[10].

Types of Liquid crystals

Liquid crystalline transitions can be distinguished into, lyotropic and thermotropic. Materials that form the liquid

crystals by addition of solvents are lyotropic liquid crystals, i.e. when in aqueous solutions the concentration of water-soluble amphiphiles is increased. The amphiphilic molecules must exhibit some chemical complexity; otherwise the solvent will simply dissolve them[11]. Liquid crystal phases are formed by a wide variety of molecules. They can be divided into two classes, thermotropic and lyotropic. Transitions to thermotropic phases are initiated by changes in temperature, while those to lyotropic phases can be initiated by changes in concentration[12]. Liquid crystals can be classified and differentiated in two ways [13]as shown in figure 3.

Lyotropic phases

Lyotropic liquid crystals are also incorporated in special dermatological formulations that exhibit hydrating properties. Most of all, liquid crystals are used as excipients to protect sensitive substances (vitamins, antioxidants, oils). They may enhance the stability of creams while creating a rheological barrier resulting in an increase in the viscosity and a decrease in coalescence by modification of Vander Waals forces[21].

Thermotropic phases

- Nematic Liquid Crystal Phase
- Chiral Nematic Liquid Crystal Phase
- Smectic Liquid Crystal Phases
- Discotic Liquid Crystal Phases

A liquid crystal id defined as liquid which has a nature of crystal in showing optical and other physical anisotropies caused by the structure. The liquid crystalline phase is also known as mesophase between the solid state and the liquid state[14]. This phase can appear in either of the two ways one in a given temperature range while other in given concentration range. They are called thermotropic and lyotropic phases respectively. In case of thermotropic liquid crystal a solid changes into an optically opaque liquid crystalline phase above the melting point. Being heated further the liquid becomes an optically clear isotropic phase at a temperature which is called the clearing point[15].

Nematic crystal phase

The simplest example of nematic phase is as shown in figure 4 for which the rod-like molecules translate randomly through space (as in a fluid), while pointing on average in a particular direction (this direction is called the nematic director).[16,17]

Chiral and nematic crystal phase

Chiral molecules (molecules lacking a center of symmetry) can assume a cholesteric phase, also called a chiral nematic phase. In this mesophase the molecules have helical arrangements as shown in figure 5. The pitch is the distance along a longitudinal axis corresponding to a full turn of the helix[18-20].

Smectic phase

Another liquid crystalline phase is the smectic phase as shown in the figure 6, which consists of a sandwich-like structure of homogenous two-dimensional layers of oriented molecules, stacked on top of each other. Because of the periodicity in the direction of the director, the smectic phase can be seen as crystalline in one direction and liquid-like in the other two directions. The properties of these liquid crystalline phases are in between those of liquids and crystals[16, 17].

DRUG LOADING AND RELEASE

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. In simplified view, higher affinity of the active constituents for the liquid crystal leads to higher loading. It was demonstrated that changing the ionization state of active constituents alter their solubility and consequently its loading in liquid crystalline phases, at low pH, the active constituents is more hydrophobic and can be loaded to higher levels, while the vice versa is also true. This was observed for a wide range of active constituents including lidocaine, prilocaine and clomethiazole and phenol butyl amine. A wide variety of drugs with different physicochemical properties have been incorporated in glycerol monooleate based cubic phases, as well as their sustained releases were also studied. The drugs clindamycin phosphate[22], clomethiazole[23], clotrimazole[24], gramicidin[25], indomethacin[26], insulin[25], isosorbide mononitrate[26], lidocaine hydrochloride[26], nitroglycerin[27], oestriol[27], 4-phenylbutylamine, prilocaine[28].include 2-amino-1-phenylpropanol hydrochloride[27], cefazolin[28] and cefuroxime[28]. The Solubility of a drug determines the concentration presented to the absorption site, and the water/lipid partition coefficient influences the rate of transport and inverse relationship appears to exist between the absorption rate and the molecular rate. Small molecules penetrate more rapidly than large molecules but within a narrow range of molecular size. There exists little correlation between size and the penetration rate[29]. The total therapeutic effect of percutaneous preparations depends not only on the action of the drug itself, but also on other factors related to the structure of the vehicle[30].

APPLICATIONS

Liquid crystal technology has a major effect in many areas of science and engineering, as well as device technology. Applications for this special kind of material

are still being discovered and continue to provide effective solutions to many different problems[31].

Liquid crystal displays

The most common application of liquid crystal technology is liquid crystal displays (LCDs). This field has grown into a multi-billion dollar industry, and many significant Liquid Crystal Thermometers

As demonstrated earlier, chiral nematic (cholesteric) liquid crystals reflect light with a wavelength equal to the pitch. Because the pitch is dependent upon temperature, the color reflected also is dependent upon temperature.

Liquid crystals make it possible to accurately gauge temperature just by looking at the color of the thermometer. By mixing different compounds, a device for practically any temperature range can be built.

The "mood ring", a popular novelty a few years ago, took advantage of the unique ability of the chiral nematic liquid crystal.

Special liquid crystal devices can be attached to the skin to show a "map" of temperatures. This is useful because often physical problems, such as tumors, have a different temperature than the surrounding tissue.

Liquid crystal temperature sensors can also be used to find bad connections on a circuit board by detecting the characteristic higher temperature[19, 20].

Orthopedic applications

The substance is unique in that the molecule is neither in a three dimensional array as in a solid nor in a free form as in a liquid.

Instead, cholesteric liquid crystals form layers which are free to slide over one another or revolve around a fixed axis.

This property is responsible for the color changes associated with differentials in temperature to the areas on which they are applied.

Normally the liquid is colorless, but the molecules realign themselves in response to temperatures of adjacent substances[33].

The diagnosis of an actual disease condition is not made using this technique but it is a valuable adjunct in determining and delineating the extent of the pathology to be encountered[34].

Other Applications

Liquid crystals have a multitude of other uses. They are used for nondestructive mechanical testing of materials under stress.

This technique is also used for the visualization of radio frequency waves in waveguides. They are used in medical applications where, for example, transient pressure transmitted by a walking foot on the ground is measured.

Low molar mass liquid crystals have applications including erasable optical disks, full color "electronic slides" for computer-aided drawing, and light modulators for color electronic imaging.

As new properties and types of liquid crystals are investigated and researched, these materials are sure to gain increasing importance in industrial and scientific applications[32].

CONCLUSION

The major barrier in skin permeation is outer stratum corneum due to presence of the intercellular lipids, arranged in lamellar sheets. The total therapeutic effect of percutaneous preparations depends not only on the action of drug itself, but also on other factors related to the structure of vehicles. Liquid crystals enhance the permeation of the drug by reacting with these intercellular lipids.

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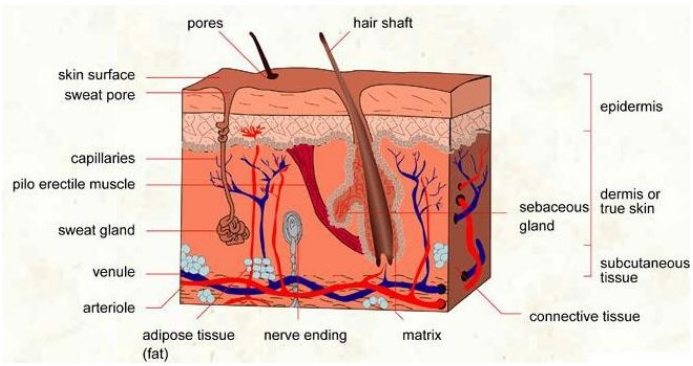

Figure 1: Cross Section of Skin.

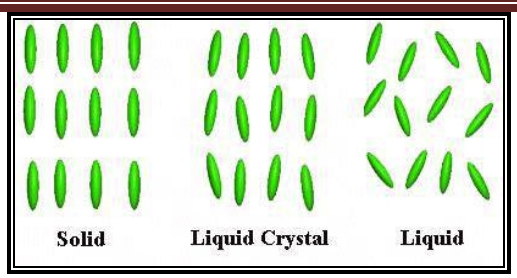

Figure 2: Average Alignment of Molecules in Each Phase

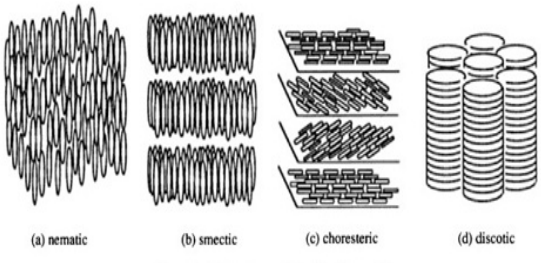

Figure 3: Molecular Models of Liquid Crystals

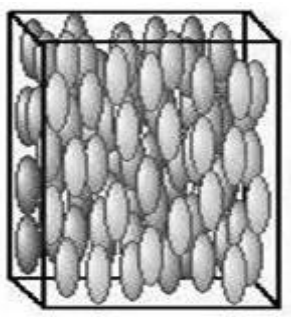

Figure 4: Schematic Representation of Nemetic Phase

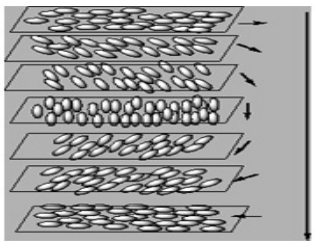

Figure 5: Schematic Representation of Chiral and Nemetic Crystal Phase

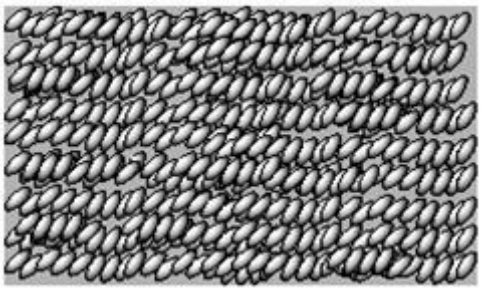

Figure 6: Schematic Representation of Smectic Crystal Phase