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Mini Review

Characterizations of Liquid Crystals as A Transdermal Drug Delivery System

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Abstract

The outermost layer of skin, the stratum corneum, has a role as the primary barrier against water evaporation from the body and drug entry through skin into the body. Thus, overcoming the stratum corneum barrier is important to develop transdermal drug delivery systems. Transdermal administration of drugs represents an excellent alternative to conventional pharmaceutical dosage forms. However, insufficient penetration of the active pharmaceutical substance through the skin is a common problem. Thus, in the present review we discussed the characterizations and the skin permeation enhancing ability of liquid crystal (LC) topical formulations.

Introduction

Liquid crystals (LCs) are semisolids made of lipids with crystalline structures combining the properties of both crystal and liquid states. Molecules in crystal are highly ordered, while those in liquid are free to diffuse in a random way. Thus, molecules in LC phases diffuse like the molecules in liquid but contain some degree of order [1-4]. A generally used term is the mesophase for LC, indicating such a unique structure is between those of true liquid and solid crystals [5]. In general, LCs can be classified into two categories, i.e., thermotropic and lyotropic. Thermotropic LCs are formed by a change in temperature, whereas lyotropic phases are obtained when mixed with some solvent. Lyotropic LCs usually consist of amphiphilic substances like surfactants and solvents. Amphiphilic substances become micelle at a low concentration, having cluster of molecules with their polar groups oriented in the water. This is a liquid isotropic phase, where isotropic means identical properties of the structure in all directions. More ordered structures such as hexagonal, lamellar and cubic phases are formed at higher concentrations. These structures are formed, due to insufficient water to fill up spaces between the spherical or elongated micelles [6,7]. Depending on the solvent concentration and the polarity of solvated mesogen, these systems can undergo phase transitions and structure modifications. Thus, their consistencies and rheological properties can be systematically changed as required [5,8]. Lyotropic LCs formed with aqueous surfactants can absorb water from the environment, inducing spontaneous phase-transition and forming lamellar phase (Lα), cubic phase (V2) and hexagonal phase (H2) [9,10]. Among them, cubic phase and hexagonal phase have received much attention due to their highly ordered internal structures, and can be used as a slow release matrix for active pharmaceutical ingredients with various molecular sizes and polarities [11,12]. Cubic and hexagonal LCs are often spontaneously formed by addition of certain amphiphilic lipids in an aqueous environment [13]. When these LCs are dispersed into nanoparticles by addition of excess water with the stabilizers such as Pluronic copolymers and Myrj series [14], they form stable colloidal dispersions which are termed cubosomes and hexosomes, respectively [15-18]. During the last few decades, increasing attention has been paid to LC formulations including cubosomes and hexosomes because of their remarkable structural complexity and usefulness in diverse applications [19].

LC phase structures:

The confirmation of LC phase structures can be undertaken by Small-Angle X-Ray Scattering (SAXS). The typical reflection patterns; for dispersed LC formulation at nearly √2, √3, √4, √6, √8, √9, revealed the presence cubosomes. On the other hand, the typical reflection patterns at nearly √1, √3, √4, √7, √9 revealed the presence of a hexagonal phase in all prepared LC formulations [20, 21]. In general, if there was any material with high birefringence, the light output by the top layer, a linear polarizer, may cause optical anisotropy to appear on the displayed image, depending on the orientation of the viewer with respect to the display.

Particle size and zeta potential of LC

Zeta potential and particle size are important parameters for the evaluation of stability and bio-distribution. By increasing the LC concentration, the particle size tended to be smaller and the zeta potential became more negative, suggesting that the number of LC forming particles can be increased with an increasing of LC concentration. Stable nano-formulations of LC should own small particle sizes ranged between 220 and 280 nm, and the zeta potential of these formulations should range between -17 and -30 mV [22]. In addition, no significant changes should be observed in particle size or zeta potential at 10 days after their preparation. LC formulations characterized by small particle size with high surface charges and electrical repulsion between the particles, can prevent their aggregation even 10 days after preparation. The zeta potential present strong negative values for LC formulations, indicating the predominance of repulsive forces. The reason why LC formulations show negative zeta potential values is due to the present of free oleic acid in the lipid phase may give rise to the negative charge of the particles. In addition, the negative charge can also be explained by preferential adsorption of hydroxyl ions at the lipid-water interface [22, 23].