Flexible nano-sized lipid vesicles for the transdermal delivery of colchicine; in vitro/in vivo investigation

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Abstract

Colchicine (CL) is the most effective treatment of acute gout, however, it is associated with side effects in 80% of the patients at therapeutic doses, in addition, it's a water-soluble strong base (pKa 12.8) which ionizes at physiological gastrointestinal pH resulting in low oral bioavailability of 44%. This work employed enhancing the bioavailability and reducing the side effects of CL through combining the benefits of the transdermal route together with those of elastic lipid nano-vesicles. Transfersomes (TRs) have been studied as vehicles for transdermal drug delivery, however, poor encapsulation of drugs and drug leaking of the vesicles required complexation of CL with ɓ-cyclodextrin (ɓ-CD) before formulation. The composition of the designed CL-ɓ-CD-TR was studied to balance the flexibility of the vesicles to their entrapment ability. CL-ɓ-CD-TR were characterized for their shape, size, entrapment efficiency, elasticity, release profile, ex vivo skin permeation, pharmacological efficacy, and histopathological effect. Encapsulation efficiency of CL-ɓ-CD complex in the vesicular formulations ranged from 42.3% to 93.8%. Particle size ranged from 70.6 nm to 138.5 nm and zeta potential ranged from 16.1 mV to 23.4 mV. The in vitro release of CL from the selected CL-ɓ-CD-TR formulation (F3) showed a controlled, biphasic profile. Ex vivo study reported the great potential of F3 (CL-ɓ-CD-TR) for skin permeation. In vivo experiment demonstrated that F3 (CL-ɓ-CD-TR) possessed high biological efficacy with reduced skin irritation.

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