ABSTRACT

Objective: The tricyclic antidepressant drug, Doxepin, is a potent H_1 and H_2 receptor antagonist and also an antidepressant drug with significant antimuscarinic activity which is used for treatment of atopic dermatitis (AD). Conventional formulation of topical doxepin has comparable antihistaminic effects to oral doxepin; however, it is still highly absorbed systemically and causes side effects like blurred vision, dry mouth, and urinary retention. Therefore, a new liposomal formulation of doxepin was investigated to prolong the release of drug and decrease its absorption into the blood.

Methods: Doxepin liposomes of phosphatidylcholine, and cholesterol (w/w ratio 5:1) were prepared by a thin film hydration method and characterized for size, entrapment efficiency (EE%) and morphology.

Results: The particle size of prepared liposomes was 208.7±5.6 nm with a polydispersity index (PDI) of approximately 0.187. The EE% was 79±1.3%. To evaluate the permeation of doxepin through rat skin, an *ex vivo* study was performed over a 30h period using Franz diffusion cell. The results indicate that the accumulation of doxepin entrapped in the liposomal formulation in the skin was 6.3 times greater than the doxepin in plain cream. *Ex vivo* skin permeation studies also showed a significantly higher permeation of doxepin from conventional dosage form (1412±65.7 µg/cm^2) than liposomal cream (338.6±17.2 µg/cm^2).

Conclusion: These results provide evidence for the potential of liposomal based doxepin cream as an effective and easy to use formulation that may improve the treatment of chronic pruritus by accumulating doxepin in the skin rather than absorption to systemic circulation which may result in high side effect and low topical efficacy.

Key words: Doxepin; Liposome; *Ex vivo* study; Atopic dermatitis