Bioavailability and hypocholesterolemic effect of proniosomal simvastatin for transdermal delivery.

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Abstract

ABSTRACT
Objective: Simvastatin (SIM) existing oral formulations suffer from poor bioavailability (less than 5%) as a result of extensive first-pass effect as well as dissolution rate-limited in vivo absorption. In the present study, a proniosomal system was designed for SIM transdermal delivery.
Methods: In vitro evaluation of proniosomal SIM was performed in different aspects; drug entrapment, vesicle size, zeta potential, vesicular morphology, in vitro release, skin permeation and stability. The optimized formula was assessed for transdermal permeation in rats and for hypocholesterolemic effect in hypercholesterolemic rats compared to oral SIM dispersion.
Results: The proniosomal formula consisted of lecithin: Tween 20 in molar ratio of 1:9 exhibited significantly ($P<0.05$) lower vesicular size, high SIM entrapment, sustained release pattern as well as significantly higher skin permeation. The topical application of optimized proniosomal SIM showed significantly ($P<0.05$) higher values of AUC0–8 and Tmax, and significantly ($P<0.05$) lower values of Cmax compared to SIM oral dispersion. The mean relative bioavailability of proniosomal SIM to oral dispersion was 120.40 ± 11.44%. The investigated proniosomal SIM showed a significantly ($P<0.05$) higher hypocholesterolemic effect compared to oral SIM dispersion in treatment of hypercholesterolemic rats.
Conclusion: The obtained results were very encouraging and offered an alternative approach to enhance the bioavailability and the hypocholesterolemic effect of SIM.
Keywords: Proniosomes, Simvastatin, Bioavailability, Hypocholesterolemic effect, Transdermal delivery.

Int J Pharm Pharm Sci. - 2013, June