Optimization of transdermal atorvastatin calcium ï Loaded proniosomes: Restoring lipid profile and alleviating hepatotoxicity in poloxamer 407-induced hyperlipidemia

Dalia Samuel Shaker Kirolos,Maha Osama Abdelaziz Mohamed Elkayal,Yasmin El Tellawy ,Yasmin A Eltellawy, Maha El-Kayal, Rehab F Abdel-Rahman, Salwa Salah, Dalia S Shaker

Abstract

In an attempt to optimize the anti- hyperlipidemic effect and reduce statins induced hepatotoxicity, Atorvastatin Calcium (ATC) transdermal proniosomal gel (PNG) was developed. Different non-ionic surfactants (NISs) (Spans, Tweens, Cremophor RH 40 and Brij 52) were incorporated in the vesicleôs lipid bilayer, in combination with lecithin. PNG formulae were characterized for encapsulation efficiency percent (% EE), vesicle size, polydispersity index (PDI) and zeta potential (ZP). Ex-vivo permeation study was performed using full thickness rat skin measuring drug flux and skin permeability coefficients. The pharmacodynamic performance of optimized transdermal ATC- PNG on both lipid profile and liver biomarkers was assessed and compared to oral ATC administration in poloxamer 407-induced hyperlipidemic rats. The liver tissues were subjected to histological examination as well. The results revealed nano-size range vesicles with relatively high ATC entrapment efficiency. Ex-vivo results demonstrated the permeation superiority of ATC proniosomes over free drug. Pharmacodynamic study revealed that transdermal administration of ATC- PNG succeeded in retaining the anti-hyperlipidemic efficacy of orally administered ATC without elevating liver biomarkers. The histological examination signified the role of optimized ATC-PNG in hindering statin- induced hepatocellular damage. The obtained results suggested a promising, easy-to-manufacture and effective ATC proniosomal gel for safe treatment of hyperlipidemia.

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