Utilization of PEGylated cerosomes for effective topical delivery of fenticonazole nitrate: *in-vitro* characterization, statistical optimization, and *in-vivo* assessment

باللغة الإنجليزية

In this investigation, we focused on ceramide IIIB, a skin component whose depletion tends to augmentmultiple skin disorders and fungal infections. Ceramide IIIB was included into PEGylated surfactant-based vesicular phospholipid system to formulate 'PEGylated cerosomes' (PCs) loaded withfenticonazole nitrate (FTN). FTN is a potent antifungal agent adopted in thetreatment of mixedmycotic and bacterial infections. The ceramide content of the vesicles may provide protective andregenerative skin activity whereas Brij; the PEGylated surfactant, can enhance drug deposition andskin hydration. Both components are expected to augment the topical effect of FTN.PCs were preparedby thin-film hydration technique. A 23 full-factorial design was applied to study the effect ofceramide amount (X1), Brij type (X2) and Brij amount (X3) on the physicochemical properties of the formulatedPCs namely; entrapment efficiency (EE%;Y1), particle size (PS;Y2), polydispersityindex (PDI;Y3)and zeta potential (ZP;Y4). The optimal formula was selected for further in-vivo dermatokinetic andhistopathological study. The optimal FTN-loaded PC (PC6) showed nanosized cerosomes (551.60 nm)with high EE% (83.00%w/w), and an acceptable ZP value of 20.90 mV. Transmission electron micrographsof the optimal formula illustrated intertwined tubulation form deviated from the conventionalspherical vesicles. Finally, the dermatokinetic study of PC6 showed higher drug concentration andlocalization of FTN in skin layers when compared with FTN suspension and thehistopathological studyconfirmed its safety for topical application. The overallfindings of our study verified the effectivenessof utilizing PEGylated cerosomes to augment the activity of FTN as a topical antifungal agent.