DESIGN, PREPARATION AND OPTIMIZATION OF ELASTIC TRANSFERSOMES : A NEW TECHNIQUE FOR TRANSDERMAL DELIVERY OF CLOTRIMAZOLE

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Background: Clotrimazole (CTM) is an imidazole anti-fungal drug which can be used in treatment of candidiasis. Poor aqueous solubility and hepatic first pass metabolism result in low systemic efficacy of CTM. The aim of the present study was to formulate and evaluate Clotrimazole transfersomes (CTM-TF) gel to increase skin permeability and enhance antifungal activity of CTM -TF gel. Canesten® cream 1% where used as a reference.

Methods: CTM-TF different formulae (F1 – F8) were prepared by lipid film hydration technique with slight modification. Different formulations were characterized for vesicle size, zeta potential, polydispersity, entrapment efficiency (EE %) and elasticity measurement. The time required to release 90 % of CTM from TF (t_{90}) was calculated for each formula. The formula showed the least value of (t90) was selected as the optimized formula as it exhibited long duration of action. The optimized formula (F3) was formulated as gel using Hydroxypropyl Methyl Cellulose (HPMC E15) 2% and examined in comparison with a marketed product (Canesten® cream 1%) for spreadability, homogeneity, viscosity measurement, drug content, in-vitro permeation, in-vitro anti-fungal activity, in-vivo anti-fungal activity and Pharmacokinetic study.

Results: The formulated CTM-TF had EE % from (68.55 ± 0.45) to (90.56 ± 0.62) with vesicle size ranged from (64.52 ± 0.24) to (85.42 ± 0.78). The in-vitro release study showed an inverse relationship between EE % and in-vitro release. The kinetic analysis of all in-vitro release formulations followed Higuchi's diffusion model. The optimize formula showed higher antifungal activity than marketed product. Therefore CTM-TF gel can penetrate the skin, overcoming stratum corneum barrier to treat deep fungal infections.

Conclusions: From this study, Formulated CTM-TF have high EE %, low vesicle size and high in-vitro release. So, it could be formulated as gel to penetrate stratum corneum and show high anti-fungal activity compared to marketed product.