Thesis Title: **"TOPICAL GEL DECORATED WITH TERBINAFINE HYDROCHLORIDE NANOMICELLES FOR ENHANCED DERMAL DRUG DELIVERY"**

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ABSTRACT

Human skin, the largest organ of the body, serves as the primary barrier against environmental insults and microbial invasion. However, disruption of this barrier predisposes the skin to fungal infections, which affect millions worldwide and are often persistent, recurrent, and difficult to treat. Effective therapy requires efficient delivery of antifungal agents across the skin barrier to achieve adequate drug concentrations at the site of infection.

Terbinafine hydrochloride (HCl), a Biopharmaceutics Classification System (BCS) Class II antifungal drug, inhibits squalene epoxidase, thereby disrupting ergosterol biosynthesis and inducing fungal cell death. Despite its established clinical efficacy, conventional topical formulations are limited by poor aqueous solubility, inadequate skin penetration, suboptimal drug localization, recurrent infections, and prolonged treatment duration. The present study aimed to enhance the aqueous solubility and topical bioavailability of terbinafine HCl through the development of Soluplus®-based polymeric nanomicelles incorporated into a chitosan gel for improved localized antifungal therapy.

Terbinafine HCl-loaded nanomicelles were prepared by the dissolution method and optimized based on particle size and encapsulation efficiency. The optimized formulation exhibited a hydrodynamic diameter of 61 ± 0.2 nm, an encapsulation efficiency of 95.04 ± 0.75%, and a drug loading capacity of 19.05%. Zeta potential and morphological analyses confirmed formulation stability, while Fourier-transform infrared spectroscopy (FTIR) demonstrated the absence of drug–polymer incompatibility. Differential scanning calorimetry (DSC) confirmed thermal stability, and energy-dispersive X-ray (EDX) analysis verified successful drug encapsulation within the nanomicelles.

The optimized nanomicelles were incorporated into a chitosan gel, exploiting the polymer's intrinsic antifungal activity, biocompatibility, and skin permeation-enhancing properties. In vitro antifungal evaluation against *Candida albicans* demonstrated a 31 ± 1.6 mm zone of inhibition, approximately two-fold greater than the commercially available terbinafine cream (Lamisil®). Ex vivo fluorescence microscopy revealed superior skin retention and localization of the nanomicellar gel compared with the marketed formulation. Histopathological evaluation in rats demonstrated preservation of normal skin architecture without evidence of irritation or residual fungal elements, confirming excellent biocompatibility and therapeutic efficacy. A significantly greater reduction in fungal infection was observed with the developed formulation compared with Lamisil®.

Overall, the developed Soluplus®-based terbinafine HCl nanomicelles incorporated into a chitosan gel represent a safe, biocompatible, and efficient topical drug delivery platform capable of overcoming the limitations of conventional antifungal therapy. By enhancing drug solubility, skin permeation, local bioavailability, and antifungal efficacy, this nanomicellar system offers a promising strategy for the effective management of fungal skin infections and establishes a versatile platform for the topical delivery of poorly water-soluble antifungal agents.