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Surface-modified mucoadhesive microgels as a controlled release system for miconazole nitrate to improve localized treatment of vulvovaginal candidiasis

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ABSTRACT

The use of conventional vaginal formulations of miconazole nitrate (MN) in the treatment of deep-seated VVC (vulvovaginal candidiasis) is limited by poor penetration capacity and low solubility of MN, short residence time and irritation at the application site. Surface-modified mucoadhesive microgels were developed to minimize local irritation, enhance penetration capacity and solubility and prolong localized vaginal delivery of MN for effective treatment of deep-seated VVC. Solid lipid microparticles (SLMs) were prepared from matrices consisting of hydrogenated palm oil (Softisan® 154, SF) and super-refined sunseed oil (SO) with or without polyethylene glycol (PEG)-4000, characterized for physicochemical performance and used to prepare mucoadhesive microgels (MMs) encapsulating MN, employing Polycarbophil as bioadhesive polymer. The MMs were evaluated for physicochemical performance and *in vitro* drug release in simulated vaginal fluid (pH=4.2), whereas mucoadhesive, rheological and stability tests, anticandidal efficacy in immunosuppressed estrogen-dependent female rats and vaginal tolerance test in rabbits were performed with optimized formulation. The amorphicity of 1:9 phytolipid blend (SO:SF) was increased in the presence of PEG-4000. The physicochemical properties of the SLMs and MMs indicated their suitability for vaginal drug delivery. Overall, MN-loaded PEGylated MMs exhibited significantly ($p<0.05$) more prolonged drug release than non-PEGylated MMs. Additionally, optimized PEGylated MMs was stable at 40±2°C over a period of 6 months, viscoelastic, mucoadhesive, non-sensitizing, histopathologically safe and gave remarkably ($p<0.05$) higher reduction in *Candida albicans* load (86.06%) than Daktarin® (75.0%) and MN-loaded polymeric-hydrogel (47.74%) in treated rats in 12 days. Thus, PEGylated MMs is promising for effective and convenient treatment of VVC.

Keywords: Miconazole nitrate (MN), Polycarbophil (PCP), PEGylation, Solid lipid microparticles (SLMs), Vulvovaginal candidiasis (VVC), Mucoadhesive microgels (MMs).

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