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Microemulsion-based hydrogels of itraconazole: evaluation of characteristics and stability

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Itraconazole (ITZ) is a broad spectrum triazole antifungal drug and commercially available as oral forms. However, effective topical forms are interesting to avoid systemic adverse effects, to directly deliver antifungal drugs to the target sites and to enhance patient compliance [1]. Microemulsion-based hydrogel (MBH), semisolid form of microemulsion (ME), is one of novel formulations practically used as topical drug carriers [2]. This study aimed to develop formulations of ITZ-loaded MBHs having advantageous properties and high stability.

Phase diagram of a system containing Tween 80 (T80), propylene glycol (PG), ethyl oleate (EO) and water (W) was constructed by water titration method to obtain ME region. Blank oil-in-water (o/w) ME was selected from the region and prepared by simply mixing. Blank MBHs were then produced by combining ME with a hydrophilic gelling agent (carbomer 934 (C934), hydroxypropyl methylcellulose HPMC) or xanthan gum (XG) at various concentrations. They were characterized for appearance, pH, conductivity and viscosity. Satisfied formulations were incorporated with 0.5% ITZ. Subsequently, ITZ-loaded MBHs were evaluated for physical and chemical properties before and after being stored in clear glass containers at room temperature for 8 weeks. The drug content was quantitatively determined by UV spectrophotometric technique [3]. Briefly, ITZ in each sample was extracted with methanol and then measured absorbance against methanol at 262 nm. The drug content of the sample was calculated using the calibration curve. All experiments were performed in triplicate. Selected o/w ME was composed of 50% 3:1 T80:PG, 8% EO and 42% W as shown in Fig. 1(A). MBHs prepared from 1% HPMC or 1% XG were desirable in term of physical characteristics. Thus, ITZ-HPMC-MBH and ITZ-XG-MBH containing 0.5% ITZ were prepared and evaluated. Both ITZ-loaded MBHs were translucent yellowish gels. Their results of physical stability were exhibited in Fig. 1(B). A slightly decrease in the pH of both formulations with significantly increasing conductivity and viscosity (p-value < 0.05, paired t-test) was observed during storage. After stability study, the percent ITZ remaining in ITZ-HPMC-MBH and ITZ-XG-MBH dramatically reduced to be 46.65% and 87.45%, respectively. The results indicated that type of hydrophilic gelling agent affected characteristics and stability of the obtained ITZ-loaded MBHs.

Keywords: Itraconazole; Microemulsion-based hydrogels; Gelling agent; Stability
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References


Fig. 1. Phase diagram of studied system (A) and characteristics of ITZ-HPMC-MBH and ITZ-XG-MBH at before (clear bar) and after (opaque bar) stability study (B).