Relative Precipitation Potential of Current Injectable Azole Antifungal Products Containing CycloDEXTRINS
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Introduction
Cyclodextrins (CDs) containing products are growing in the market. Worldwide, 36 different drugs are marketed as an injectable solution based on cycloextrin containing formulations. Cyclodextrins and their derivatives are readily used to enhance the aqueous solubility and stability of the polar drugs. The advantage of injectable cycloextrin products is to create a monolithic system of monodisperse micelles, the micelle formation of which depends on the pH, ionic strength, surfactant, and temperature. The monolithic micelle can be either the core of a micellar sponge or the shell of a micellar cage, and contains the surfactant and a drug as a guest molecule. Various surfactants of either neutral CDs (n-CDs), anionic Cs-CDs, or cationic Cs-CDs might be incorporated into this system. The unique physical and chemical properties of guest molecules, cyclodextrins are successfully utilized by drug carriers for improving in aqueous solubility, chemical and physical stability, and bioavailability of the active pharmaceutical ingredients (APIs).

Objective
The purpose of this study was to determine the effect of added bovine serum albumin (BSA) on the potential for o/w precipitation of current injectable antifungal products formulated with cycloextrinsics using an in-vitro dynamic precipitation model.

Results and Discussion

Density of Precipitation Pharmacophores
For the evaluation of aqueous antifungal products; Vfend®, Cordaine Injection (USP normal saline) and Dormyocin Injection (USP) were evaluated in order to understand and further quality this experimental set. These two products were evaluated by Yang et al. (2007). The condensation of cycloextrinsics is a pH function which increases in the range of 4 to 5 pH. As a result, their precipitation is seen to be pH-dependent.

Method
The dynamic precipitation study was performed following the procedure developed by Yang et al. (2007). Each set of samples described below was prepared by the method of Yang et al. (2007). Sample tubes were prepared at a rate of 5 mL. The samples were prepared with 5 mL of 1:400 dilution of cycloextrin and 1 mL of guest molecule solution in a normal saline medium at pH 7.4 and was diluted with sterile saline to prepare a 1:400 dilution of cycloextrin. After this, 1 mL of 5% BSA (w/v) was added to the sample set. The vortexing was performed with the help of a vortexer (Vortex model 7620) for 30 sec. After vortexing, the samples were incubated at 37°C for 24 h.

Figure 1. Dynamic in Vivo Apparatus

Figure 2. UV Determinations upon the Injection of Normal Saline (A) and Dormyocin Injection (B)

Figure 3. UV Determinations upon the Injection of Vfend (A) and Sporanox (B)

Figure 4. Vfend Ex-Cuante Samples after 3 Hours with BSA or without BSA

Figure 5. Sporanox Ex-Cuante Sample with BSA or without BSA

Conclusion
This dynamic precipitation model proved to be a useful in vitro screen to evaluate and understand antifungal formulations containing cyclodextrins. Adding alcohol to the cycloextrin-based systems can raise additional interactions such as protein binding that can also play a role in preventing precipitation from these sustained systems.

Materials
Injection Fluids:
Vfend®: Voxonplus for injection, Pfizer, LOT A01097
Dormyocin®: Cordaine Injection (USP normal saline) and Dormyocin Injection (USP) were evaluated in order to understand and further quality this experimental set. These two products were evaluated by Yang et al. (2007).

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References

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