GD-Forum „Young Scientists“

Stability studies and rheological behavior of liquid poloxamer 407-based formulations containing sertaconazole nitrate

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Introduction

Fungal infections of skin and nails are common, with a lifetime prevalence of 70% for tinea pedis[1] and a prevalence of 10% for onychomycosis[2], increasing with age.
Simultaneous treatment of tinea pedis and onychomycosis is desirable as both often occur at the same time. However, due to the different physicochemical behavior of stratum corneum and human nail plate, no such treatment currently exists.

Semisolid poloxamer 407-based formulations have shown to allow drug permeation into and through both human nail and stratum corneum[3]. Formulations with the model API ciclopirox-olamine could effectively inhibit growth of T. rubrum in an infected nail plate model as well as in an infected stratum corneum model[4] [5].

Based on these results, liquid formulations containing sertaconazole nitrate are being developed as an option for simultaneous treatment of tinea pedis and onychomycosis.
In this study, the physical and chemical stability of the formulations as well as their rheological behavior was examined.

Methods

Various poloxamer 407-based formulations containing 0.3% up to 1% (w/w) sertaconazole nitrate were manufactured and stored for 24 weeks at 30°C. The ingredients were varied within a pseudoternary phase diagram, with a fixed ratio of poloxamer 407 and medium chain triglycerides on one side, a fixed ratio of isopropylic alcohol and propylene glycol on the second side, and water on the third side. Chemical stability of sertaconazole nitrate was determined using an HPLC method. Physical stability was assessed by the following criteria: Macroscopic appearance (consistency, occurrence of creaming), microscopic appearance (crystal formation, size of emulsion droplets). The size of emulsion droplets was determined with a microscope camera and the image processing software ImageJ. Rheological behavior was measured with a rheometer using a cone-plate 60mm 1° geometry in rotational mode. The apparent viscosity was determined at 4°C, 20°C and 32°C.

Results
The API content of all formulations remained above 95% of the declared content after 24 weeks. The formulations showed creaming within one day or up to one week, depending on their viscosities. The homogeneity was restored by manually shaking the vial. No crystallization of API was observed under the microscope. The size of the emulsion droplets increased over time, depending on the specific composition. A high amount of poloxamer 407 + medium chain triglycerides and a low amount of isopropylic alcohol + propylene glycol resulted in smaller droplets after 24 weeks. Most formulations behaved like Newtonian fluids, only those with a high amount of poloxamer 407 showed a yield point at low shear stress. The viscosity ranged between 20mPa*s and 1010mPa*s at 20°C.

Conclusion
Six liquid Poloxamer 407-based formulations with up to 1% sertaconazole nitrate were developed. All six formulations were physically and chemically stable over 24 weeks at 30°C.
A broad range of viscosities was found, with medium to high viscosities offering a compromise between ease of application and adherence at the site of action. Creaming occurred within one week after manufacture and was reversible by shaking the vial. No coalescence of the emulsion droplets was observed, however the droplet size increased to various extent depending on the composition.

References
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