Liposomes Containing Voriconazole (VOR) for Ocular Drug Delivery
1 Universidade de Brasilia, 2 Universidade Federal de Goias

Purpose
To prepare and characterize liposomes for the topical ocular drug delivery of voriconazole (VOR) for the treatment of fungal keratitis.

Methods
Liposomes containing VOR were prepared using the thin film hydration method and were subsequently characterized for various vesicle-specific attributes (i.e., size, zeta potential yield and entrapment efficiency). Ex vivo permeation experiments from the selected formulation were performed using porcine cornea in a modified Franz diffusion cell model for 30 min.

Results
Liposomes composed of soy phosphatidylcholine (PC) containing voriconazole in a drug-lipid ratio of 1:3 w/w were successfully developed presenting an average size of 116.6 ± 5.9 nm and a narrow size distribution (PdI of 0.17 ± 0.06). The entrapment efficiency was 86.8 ± 0.1% with a yield of 105.6 ± 0.1%. Zeta potential was -1.16 ± 3.64 mV. There was no enhancement in the entrapment efficiency with changing the amount of VOR from 5 mg to 20 mg, while keeping the amount of lipids fixed (30 mg). However, at higher drug concentrations, i.e. when a drug-lipid ratio of 1:1.5 w/w was used, the yield dropped to 43.8 ± 1.0%. The addition of 10 to 20 % w/w of cholesterol to the formulation led to lower entrapment efficiency (76.7 ± 0.2 % and 79.7 ± 0.6, respectively). Ex vivo permeation studies revealed that 53.68 ± 2.52 µg of drug penetrated the cornea after only 30 min of liposomal formulation contact. Such drug levels are higher than the minimal inhibitory concentrations (MIC) of several fungi species isolated from clinical cases of corneal keratitis.

Conclusion
Overall study suggests that VOR can be effectively incorporated in liposomes and could be used for the topical treatment of fungal keratitis. More evidence demonstrating the benefits of VOR liposomal formulation under clinical conditions and determining the therapeutic regime require further investigation.