

## Antifungal Hydrogels

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**INTRODUCTION:** Fungi are increasingly identified as major pathogens in bloodstream infections, often involving indwelling devices. Materials with antifungal properties may provide an important deterrent to these infections. Here we describe amphogel, a dextran-based hydrogel into which amphotericin B is adsorbed. Amphogel kills fungi within 2 h of contact and can be reused for at least 53 days without losing its effectiveness against *Candida albicans*. The antifungal material is biocompatible *in vivo* and does not cause hemolysis in human blood. Amphogel inoculated with *C. albicans* and implanted in mice prevents fungal infection. Amphogel also mitigates fungal biofilm formation. An antifungal matrix with these properties could be used to coat a variety of medical devices such as catheters as well as industrial surfaces.

**METHODS:** Dextran-based hydrogels (10-mm diameter and 1-mm thickness, before swelling) were obtained by a photopolymerization reaction of aqueous solutions of dextran acrylate.

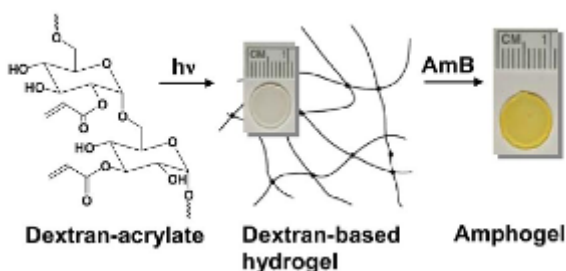


Fig. 1: Dextran-based hydrogels were noncovalently loaded with the antifungal drug amphotericin B.

6 polymer disks were immersed in 16 ml of a solution of DMF: triethylamine (15:1) containing 20 mg of AmB (Sigma-Aldrich, St. Louis, MO) and 5 mg of 4-dimethylaminopyridine. The loading was performed for 12 h, and then the gels were washed with DMF (3 days) followed by PBS (pH 7.2; 3 days).

The polymer disks (1 cm diameter) were placed in the wells of a 24-well tissue culture plate with 1 ml

of the *Candida* suspension ( $1 \times 10^7$  cells in YNB). The disks were incubated for 2 h, at 37°C while shaking at 100 rpm. Then the disks were removed, and the remaining medium was vigorously stirred then diluted to a concentration of 1:1,000. Next, 200  $\mu$ l of the diluted medium was plated on YEP agar plates. The disks were washed gently in 3 x 1 ml of fresh PBS to remove any nonadherent cells. The disks were crushed and vigorously stirred in 1 ml of PBS, and the suspension was diluted to a concentration of 1:1,000. Then, 200  $\mu$ l of the diluted suspension was plated on YEP-agar plates. The YEP plates were incubated at 37°C for 24 h, and yeast colonies were counted.

**RESULTS:** Amphogel kills *C. albicans* within 2 h of contact and remains biologically active for at least 53 days. The system was equally active when implanted in an animal model.

**DISCUSSION & CONCLUSIONS:** We found an unanticipated adsorption of AmB to a specific hydrophilic matrix resulting in a very simple manufacture process, and a marked killing of *C. albicans* in the absence of detectable release of fungicidal activity. As fungi appear to gain entry into patients via percutaneous devices, the ability to reduce entry through these portals could prevent the introduction of the microorganism and thereby reduce the probability of ensuing disease.

**REFERENCES:** <sup>1</sup> A. Zumbuehl, L. Ferreira, D. Kuhn, A. Astashkina, L. Long, T. Iaconis, M. A. Ghannoum, G. R. Fink, R. Langer, D. S. Kohane (2007) *Proc. Natl. Acad. Sci. USA* **104**: 12994–12998.

**ACKNOWLEDGEMENTS:** This work was supported by a Swiss National Science Foundation Postdoctoral Fellowship (A.Z.), Fundacao para a Ciencia e a Tecnologia Fellowship SFRH/BPD/ 14502/2003 (L.F.), National Science Foundation Grant BES-0507449, and National Institutes of Health Grants GM035010 (to G.R.F.), NIH DE017846 (to M.G.), NSF BES-0507449 (to R.L. and D.S.K.), and GM073626 (to D.S.K.).