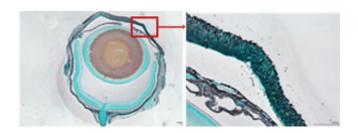


## Stable, inexpensive and easy-to-prepare active ingredients for topical treatments effectively clear fungal eye infection

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Microscope images of a mouse eye (left) show that the polymeric imidazolium compound PIM-45 protects the cornea by reducing fungal invasion into the cornea (right; fungi are stained black). Credit: 2013 A\*STAR Institute of Bioengineering and Nanotechnology

Pathogenic microbes that become encased within a protective and adhesive polymeric coating, forming a biofilm, are among the most difficult forms of infections to treat. Fungal keratitis, for example, is a common form of eye infection caused by fungi that can form a biofilm on the patient's cornea, which if left untreated may lead to blindness. A novel pair of antifungal compounds that clear these biofilms more effectively than existing treatments has now been developed by researchers led by Yugen Zhang and Jackie Ying at the A\*STAR Institute of Bioengineering and Nanotechnology, Singapore.

Zhang, Ying and co-workers developed their compounds from a family



of antimicrobial materials called amphiphilic polymers. These materials incorporate both polar and non-polar subunits, a characteristic that is crucial to their function: the polar group helps to anchor the polymer to the microbe's charged surface, which allows the non-polar tail to then penetrate and rupture the microbe's <u>lipid membrane</u>. The researchers' compounds incorporated a polar unit called an imidazolium group. Interestingly, previously developed imidazolium-based amphiphilic structures simply featured a long-chain non-polar tail. However, in a modification to the usual design, Zhang and Ying's team developed short-chain amphiphilic materials consisting of repeating polar and non-polar subunits.

The researchers showed that the amphiphilic components of these materials—named IBN-1 and PIM-45—make them particularly effective for treating biofilms. In tests against biofilm-protected fungal cells grown on the surface of a contact lens, the team showed that IBN-1 and PIM-45 were more effective than fluconazole and amphotericin B, the drugs currently used to treat these infections. "The amphiphilic structure and its high solubility in water allow our short-chain polymers to better penetrate the biofilms," Ying explains. Using mice, the team then showed that their compounds could curtail fungal growth in the eye itself (see image).

As well as proving more efficacious than current treatments, the compounds also offer several practical advantages. Amphotericin B and fluconazole are fragile structures, requiring careful protection from heat and light. "Once a package of Amphotericin B is opened, it can be used for one to two days only," says Zhang. "In comparison, our compounds can be stored in water or a buffer solution at room temperature for at least six months." In addition, IBN-1 and PIM-45 are easy and inexpensive to prepare, he adds.

The team is currently working with industry to commercialize the



polymer technology, according to Ying. "We will also explore other applications of these materials," she says.

**More information:** Liu, L. et al. Short imidazolium chains effectively clear fungal biofilm in keratitis treatment. *Biomaterials* 34, 1018–1023 (2013). dx.doi.org/10.1016/j.biomaterials.2012.10.050

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