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# Liquid salts by-pass skin to treat infections

**'Ionic liquids' can disrupt microbial biofilms or penetrate outer skin layers.**

**Nicole Skinner**

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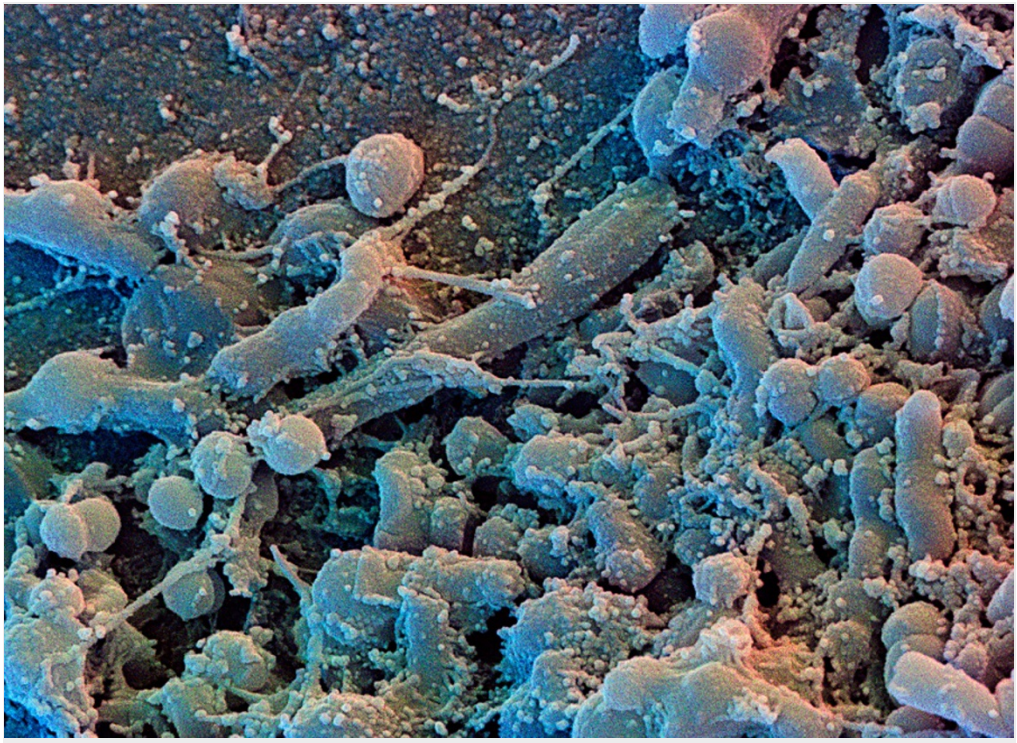

*David Scharf/Corbis*

Dental plaque is a biofilm that forms on teeth.

Liquid salts can improve the treatment of skin infections by killing bacteria and enhancing antibiotics' ability to penetrate the skin's outer layer, a new study finds.

A team led by Samir Mitragotri, a chemical engineer at the University of California, Santa Barbara, has demonstrated this strategy in principle in a study published this week in *Proceedings of the National Academy of Sciences*[1].

**Penetrating the barriers**

Four-fifths of all human infections are associated with biofilms. These are densely packed communities of microbial cells that grow on both living and inert surfaces, including human skin and catheters. When bacteria form biofilms, they secrete and surround themselves with a dense matrix of polymers that renders them 50–1,000 times more resistant to treatment with antibiotics.

Another obstacle to treating bacterial infection is skin itself. The stratum corneum — the outermost layer of the skin and a natural barrier that protects the underlying tissue from infection, dehydration, and injury — can also make it hard for topical drugs (drugs applied to the skin surface) to reach an underlying infection. Skin infections are among the most common reasons for hospital visits, accounting for almost one out of every ten visits.

**Liquid salts**

Ionic liquids are salts — neutrally charged compounds of a positively charged and a negatively charged component — in liquid form. Some, including the ones used in the new study, have an organic component and are liquid below 100 ºC, and some down to room temperature. “Essentially, they are liquids that can be used instead of organic solvents, which tend to be toxic,” explains Mitragotri. “That’s one of their main advantages for pharmaceutical applications.”

Mitragotri and his team synthesized a variety of ionic liquids and screened them for their ability to penetrate skin and biofilms. They

then tested 12 of their ionic-liquid formulations on the human pathogens *Pseudomonas aeruginosa* and *Salmonella enterica*, and found that at least one possessed strong antimicrobial activity, decreasing biofilm survival by more than 99.9%.

**Multipurpose activity**

After additional tests for skin toxicity and irritation, one ionic liquid — choline geranate — emerged as a multipurpose vehicle, showing antimicrobial activity, minimal toxicity and enhanced delivery of the broad-spectrum antibiotic cefadroxil.

The researchers then tested the effectiveness of choline geranate as an antibiotic-delivery vehicle in an *in vitro* skin model that was wounded and infected with biofilm-forming *Pseudomonas aeruginosa*. Less than 5% of the bacteria survived when the antibiotic ceftazidime was paired with choline geranate, compared with 80% when the antibiotic was used on its own.

According to Mark Prausnitz, a chemical engineer at the Georgia Institute of Technology in Atlanta, this work is an interesting application of ionic liquids to treat microbial skin infections and "it opens the door to other possible applications of ionic liquids in medicine". Mitragotri and colleagues are already thinking in that direction, "Given that ionic liquids show antibiotic activity, we can see applications wherever surfaces need to be treated."

Brendan Gilmore, a pharmaceutical microbiologist at Queen's University Belfast, UK, says that "the individual parts of this research have been demonstrated before, but this study draws them together in a very coherent strategy".

Gilmore adds that ionic liquids such as those described might be attractive candidates for increasing the activity of conventional antibiotics, including some that are no longer regarded as clinically useful.

The next step for Mitragotri and his team will be to expand the panel of target bacteria and test ionic liquids *in vivo*.

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## References

1. Zakrewsky, M. *et al. Proc. Natl Acad. Sci. USA* http://www.pnas.org/cgi/doi/10.1073/pnas.1403995111 (2014).