Silk microneedles deliver controlled-release drugs painlessly

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Bioengineers at Tufts University School of Engineering have developed a new silk-based microneedle system able to deliver precise amounts of drugs over time and without need for refrigeration. The tiny needles can be fabricated under normal temperature and pressure and from water, so they can be loaded with sensitive biochemical compounds and maintain their activity prior to use. They are also biodegradable and biocompatible.

The research paper "Fabrication of Silk Microneedles for Controlled-Release Drug Delivery" appeared in Advanced Functional Materials December 2 online in advance of print.

The Tufts researchers successfully demonstrated the ability of the silk microneedles to deliver a large-molecule, enzymatic model drug, horseradish peroxidase (HRP), at controlled rates while maintaining bioactivity. In addition, silk microneedles loaded with tetracycline were found to inhibit the growth of Staphylococcus aureus, demonstrating the potential of the microneedles to prevent local infections while also delivering therapeutics.

"By adjusting the post-processing conditions of the silk protein and varying the drying time of the silk protein, we were able to precisely control the drug release rates in laboratory experiments," said Fiorenzo Omenetto, Ph.D., senior author on the paper. "The new system addresses long-standing drug delivery challenges, and we believe that the technology could also be applied to other biological storage applications

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The Drug Delivery Dilemma

While some drugs can be swallowed, others can't survive the gastrointestinal tract. Hypodermic injections can be painful and don't allow a slow release of medication. Only a limited number of small-molecule drugs can be transmitted through transdermal patches. Microneedles—no more than a micron in size and able to penetrate the upper layer of the skin without reaching nerves—are emerging as a painless new drug delivery mechanism. But their development has been limited by constraints ranging from harsh manufacturing requirements that destroy sensitive biochemicals, to the inability to precisely control drug release or deliver sufficient drug volume, to problems with infections due to the small skin punctures.

The process developed by the Tufts bioengineers addresses all of these limitations. The process involves ambient pressure and temperature and aqueous processing. Aluminum microneedle molding masters were fabricated into needle arrays of about 500 µm needle height and tip radii of less than 10 µm. The elastomer polydimethylsiloxane (PDMS) was cast over the master to create a negative mold; a drug-loaded silk protein solution was then cast over the mold. When the silk was dry, the drug-impregnated silk microneedles were removed. Further processing through water vapor annealing and various temperature, mechanical and electronic exposures provided control over the diffusity of the silk microneedles and drug release kinetics.

"Changing the structure of the secondary silk protein enables us to 'pre-program' the properties of the microneedles with great precision," said David L. Kaplan, Ph.D., coauthor of the study, chair of biomedical engineering at Tufts and a leading researcher on silk and other novel biomaterials. "This is a very flexible technology that can be scaled up or down, shipped and stored without refrigeration and administered as easily as a patch or bandage. We believe the potential is enormous."

More information: Tsioris, K., Raja, W. K., Pritchard, E. M., Panilaitis, B., Kaplan, D. L. and Omenetto, F. G. (2011), Fabrication of Silk Microneedles for Controlled-Release Drug Delivery. *Advanced Functional Materials*. doi: 10.1002/adfm.201102012

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