Chemists develop nanoscale bioabsorbable wound dressing

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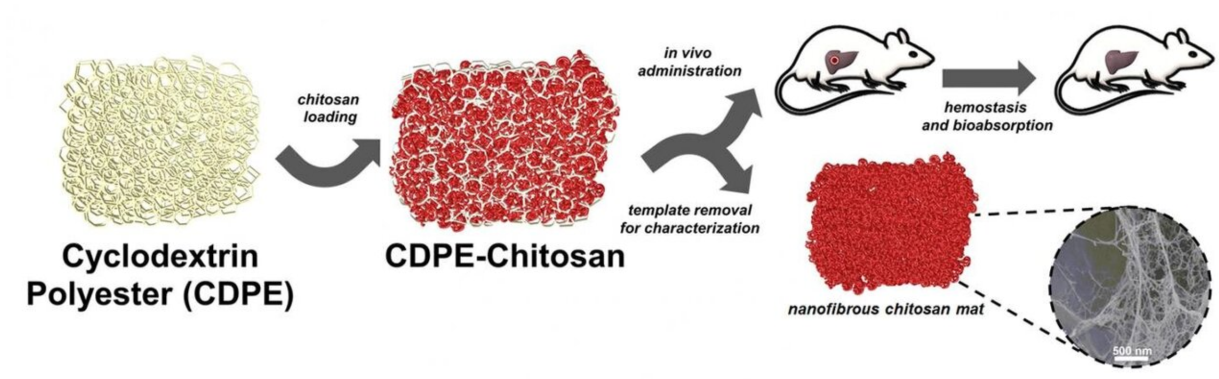

A Texas A&M University-led team successfully encapsulated highly entangled chitosan nanofibers within a sugar-based hydrogel template scaffold that, when applied to liver injury sites in animals, dissolves in as little as seven days, eliminating the need for subsequent physical removal and any chance of re-injury in the process. Credit: Texas A&M University

Scientists at Texas A&M University are harnessing the combined power of organic nanomaterials-based chemistry and a natural product found in crustacean exoskeletons to help bring emergency medicine one step closer to a viable solution for mitigating blood loss, from the hospital to the battlefield.

Hemorrhage is a leading cause of death in traumatic injuries, ranking fourth in the United States at a total cost of $671 billion in 2013.

Working with an interdisciplinary team involving collaborators from Assiut University in Egypt, Texas A&M chemist Karen Wooley's research group has developed a bioabsorbable wound dressing that builds on the already proven blood-flow-staunching properties of chitosan—a natural material widely used in commercial wound dressings—by taking them nanoscale to boost their effectiveness and impact.

Wooley's team, led by Texas A&M chemistry Ph.D. student and NASA Space Technology Research Fellow Eric Leonhardt, successfully encapsulated highly entangled nanofibers of chitosan within a sugar-based hydrogel that dissolves in as little as seven days, leaving behind a significantly larger available wound-healing surface while eliminating the need for subsequent physical removal. Their results are published in *Nature Communications*.

"Bioabsorbable wound dressings that can be applied and left in the injury site are desirable for a variety of blood loss scenarios—for example, to control bleeding in traumatic injuries and to save lives on both civilian and military fronts," said Leonhardt, who served as first author on the team's paper. "The composite materials we've developed are malleable and could be easily administered to wound sites. They have also performed significantly better in terms of reducing the amount of blood loss and the time required to achieve hemostasis against commercially available bioabsorbable wound dressing in several animal models."

Team members in addition to Leonhardt include Texas A&M materials science and engineering Ph.D. student Nari Kang; Dr. Mahmoud Elsabahy, assistant director of the Texas A&M Laboratory for Synthetic-Biologic Interactions and director of the Assiut Clinical Center of Nanomedicine at Al-Rajhy Liver Hospital; and Dr. Mostafa A. Hamad, a professor in the Department of Surgery within the Assuit Faculty of Medicine.

Elsabahy recognized that, while chitosan is a desirable option in such dressings due to its proven efficacy in slowing blood flow and because it offers bonus antimicrobial properties, it also has a tendency to clump, rendering it difficult to incorporate into a bioabsorbable material. The team overcame that obstacle by loading chitosan into a nanostructured template scaffold to better disperse it and increase its interaction with blood components, thereby speeding up both absorption and healing.

As a first step in their breakthrough discovery process, the researchers developed hydrogels from cyclodextrins—a type of saccharide with hydrolytically degradable linkages—designed with sites that were capable of ionically interacting with and binding to chitosan molecules. After freeze-drying the resulting composite material, they exposed it to a solution that removed the template scaffold. They then used scanning electron microscopy to further analyze the chitosan, which they determined had assembled into mats of highly entangled nanofibers measuring about 10-to-20 nanometers in diameter.

"Not only are these fibers considerably smaller than what has been previously reported for chitosan, they also are highly desirable, given that the corresponding increase in surface area is expected to greatly enhance hemostatic effect," said Elsabahy, who conceived the project. "We believe this work will enhance the scope of chitosan as a hemostatic technology through the demonstration of its fabrication and use as a bioabsorbable wound dressing."

To date, the team has applied their composite wound dressings to liver injuries in rats, rabbits and pigs, measuring the amount of blood loss, time to hemostasis and mean arterial pressure in each case to gauge effectiveness. The dressings also were implanted in the liver and imaged after seven days to evaluate the biodegradation of the composite materials. No residues could be observed in any of the settings.

"Hemorrhage is responsible for more than 35 percent of pre-hospital deaths and more than 40 percent of deaths within the first 24 hours of injury," Leonhardt said. "Hemostatic dressings have the potential to reduce morbidity and mortality through the early control of hemorrhage. These dressings can be included in first aid kits and carried by soldiers to save lives in the battlefield, and they can be also utilized to control bleeding in various injury scenarios and surgical procedures in hospitals. Absorbable hemostatic dressing can be left in the injury site and eliminate the necessity for carrier removal, which reduces the risk of re-bleeding—in case of carrier removal of non-absorbable dressings—and decreases the duration required for the surgical interventions."

Wooley intends to extend this initial work to the evaluation of the materials in studies that simulate lethal hemorrhage scenarios, followed by clinical trials. In addition, she would like to conduct future fundamental studies to further explore the mechanism of chitosan nanofiber formation within the template scaffolds, with the aim of ultimately achieving control over the assembly to enable tuning and optimization of the resulting morphology of the wound dressings.

More information: Eric E. Leonhardt et al, Absorbable hemostatic hydrogels comprising composites of sacrificial templates and honeycomb-like nanofibrous mats of chitosan, *Nature Communications* (2019). DOI: 10.1038/s41467-019-10290-1

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