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Bio-inspired, blood-repelling tissue glue could seal wounds quickly

A new adhesive that mimics the sticky substance barnacles use to cling to rocks may offer a better way to treat traumatic injuries

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Summary: Engineers have designed a strong, biocompatible glue that can seal injured tissues and stop bleeding, inspired by the sticky substance that barnacles use to cling to rocks.

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FULL STORY

Inspired by the sticky substance that barnacles use to cling to rocks, MIT engineers have designed a strong, biocompatible glue that can seal injured tissues and stop bleeding.

The new paste can adhere to surfaces even when they are covered with blood, and can form a tight seal within about 15 seconds of application. Such a glue could offer a much more effective way to treat traumatic injuries and to help control bleeding during surgery, the researchers say.

"We are solving an adhesion problem in a challenging environment, which is this wet, dynamic environment of human tissues. At the same time, we are trying to translate this fundamental knowledge into real products that can save lives," says Xuanhe Zhao, a professor of mechanical engineering and civil and environmental engineering at MIT and one of the senior authors of the study.

Christoph Nabzdyk, a cardiac anesthesiologist and critical care physician at the Mayo Clinic in Rochester, Minnesota, is also a senior author of the paper, which appears today in *Nature Biomedical Engineering*. MIT Research Scientist Hyunwoo Yuk and postdoc Jingjing Wu are the lead authors of the study.

Natural inspiration

Finding ways to stop bleeding is a longstanding problem that has not been adequately solved, Zhao says. Sutures are commonly used to seal wounds, but putting stitches in place is a time-consuming process that usually isn't possible for first responders to perform during an emergency situation. Among members of the military, blood loss is the leading cause of death following a traumatic injury, and among the general population, it is the second leading cause of death following a traumatic injury.

In recent years, some materials that can halt bleeding, also called hemostatic agents, have become commercially available. Many of these consist of patches that contain clotting factors, which help blood to clot on its own. However, these require several minutes to form a seal and don't always work on wounds that are bleeding profusely.

Zhao's lab has been working to address this problem for several years. In 2019, his team developed a double-sided tissue tape and showed that it could be used to close surgical incisions. This tape, inspired by the sticky material that spiders use to capture their prey in wet conditions, includes charged polysaccharides that can absorb water from a surface almost instantaneously, clearing off a small dry patch that the glue can adhere to.

For their new tissue glue, the researchers once again drew inspiration from the natural world. This time, they focused their attention on the barnacle, a small crustacean that attaches itself to rocks, ship hulls, and even other animals such as whales. These surfaces are wet and often dirty -- conditions that make adhesion difficult.

"This caught our eye," Yuk says. "It's very interesting because to seal bleeding tissues, you have to fight with not only wetness but also the contamination from this outcoming blood. We found that this creature living in a marine environment is doing exactly the same thing that we have to do to deal with complicated bleeding issues."

The researchers' analysis of barnacle glue revealed that it has a unique composition. The sticky protein molecules that help barnacles attach to surfaces are suspended in an oil that repels water and any contaminants found on the surface, allowing the adhesive proteins to attach firmly to the surface.

The MIT team decided to try to mimic this glue by adapting an adhesive they had previously developed. This sticky material consists of a polymer called poly(acrylic acid) embedded with an organic compound called an NHS ester, which provides adhesion, and chitosan, a sugar that strengthens the material. The researchers froze sheets of this material, ground it into microparticles, and then suspended those particles in medical grade silicone oil.

When the resulting paste is applied to a wet surface such as blood-covered tissue, the oil repels the blood and other substances that may be present, allowing the adhesive microparticles to crosslink and form a tight seal over the wound. Within 15 to 30 seconds of applying the glue, with gentle pressure applied, the glue sets and bleeding stops, the researchers showed in tests in rats.

One advantage of this new material over the double-sided tape the researchers designed in 2019 is that the paste can be molded to fit irregular wounds, while tape could be better suited to sealing surgical incisions or attaching medical devices to tissues, the researchers say. "The moldable paste can flow in and fit any irregular shape and seal it," Wu says. "This gives freedom to the users to adapt it to irregular-shaped bleeding wounds of all kinds."

Better bleeding control

In tests in pigs, Nabzdyk and his colleagues at the Mayo Clinic found that the glue was able to rapidly stop bleeding in the liver, and it worked much faster and more effectively than the commercially available hemostatic agents that they compared it to. It even worked when strong blood thinners (heparin) were given to the pigs so that the blood did not form clots spontaneously.

Their studies showed that the seal remains intact for several weeks, giving the tissue below time to heal itself, and that the glue induced little inflammation, similar to that produced by currently used hemostatic agents. The glue is slowly resorbed within the body over months, and it can also be removed earlier by applying a solution that dissolves it, if surgeons need to go in after the initial application to repair the wound.

The researchers now plan to test the glue on larger wounds, which they hope will demonstrate that the glue would be useful to treat traumatic injuries. They also envision that it could be useful during surgical procedures, which often require surgeons to spend a great deal of time controlling bleeding.

"We're technically capable of carrying out a lot of complicated surgeries, but we haven't really advanced as fast in the ability to control especially severe bleeding expeditiously," Nabzdyk says.

Another possible application would be to help stop bleeding that occurs in patients who have plastic tubes inserted into their blood vessels, such as those used for arterial or central venous catheters or for extracorporeal membrane oxygenation (ECMO). During ECMO, a machine is used to pump the patient's blood outside of the body to oxygenate it. It is used to treat people with profound heart or lung failure. Tubes often remain inserted for weeks or months, and bleeding at the sites of insertion can lead to infection.

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1. Hyunwoo Yuk, Jingjing Wu, Tiffany L. Sarrafian, Xinyu Mao, Claudia E. Varela, Ellen T. Roche, Leigh G. Griffiths, Christoph S. Nabzdyk, Xuanhe Zhao. **Rapid and coagulation-independent haemostatic sealing by a paste inspired by barnacle glue**. *Nature Biomedical Engineering*, 2021; DOI: 10.1038/s41551-021-00769-y
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