A potential game-changer for emergency medicine: Synthetic platelets

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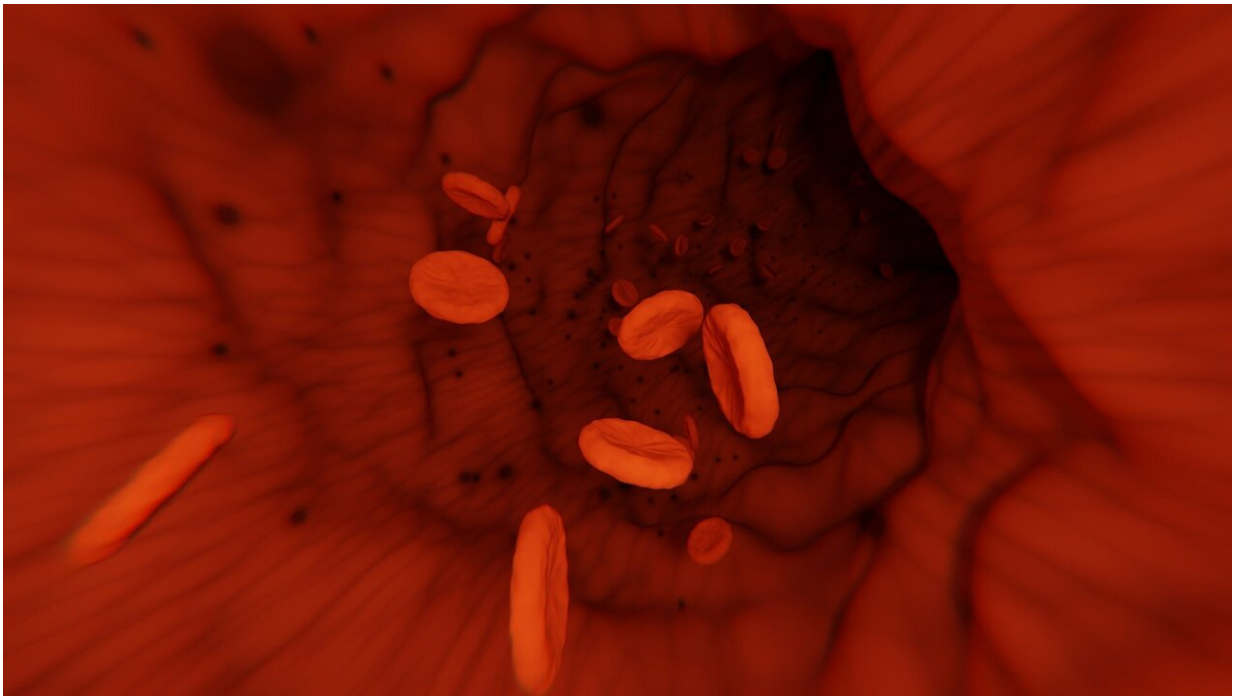

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Imagine being a paramedic treating a trauma patient who's bleeding severely. You know your patient's life is in danger, but there's not much you can do because the patient needs an infusion of blood containing platelets. Platelets encourage clotting, help stop bleeding, and are critical in emergencies like this. Yet on board your ambulance, none are on hand.

As it turns out, it's not an uncommon problem.

Unlike whole blood (plasma, red and white blood cells, and platelets) that can be stored for up to a month under constant refrigeration, platelets by themselves need a different and even more challenging kind of attention. They require constant agitation to keep them from clumping, and they must be kept at room temperature to maintain their clotting function. The increased risk of bacterial contamination at room temperature means they have a shorter shelf life.

"Platelets only last about five days," said Ashley Brown, Ph.D., an associate professor in the joint biomedical engineering program at North Carolina State University and the University of North Carolina at Chapel Hill. "This makes them one of the weakest—yet most critical—links in the chain when you look at blood products we need to access quickly."

And that's just the beginning of the difficulties. Platelets are frequently in short supply as they're harvested from human donors, they're hard to transport, and they can carry contamination risks.

A miracle solution?

To overcome these obstacles, Brown and her team have come up with something novel that just might check all the boxes: synthetic platelets. The synthetic platelets they have designed have a long shelf life, can be stored under a variety of conditions, and don't carry contamination risks in the animal models they've so far been tested on.

The platelets are created using hydrogel nanoparticles—gels invisible to the naked eye that are formed through a mixture of water and a tiny bit of polymer molecules to give them structure. Brown calls the magical result "Jell-O at the microscale"—except for one enhancement.

"We designed the platelets in a way that makes them extra squishy," Brown said. "It was really important for us to mimic features of natural platelets."

One area where these synthetic platelets really shine is their ability to focus on the site of injury after injecting them intravenously, said Ronald Warren, Ph.D., a program director in the Division of Blood Diseases and Resources at NHLBI. "Other methods to treat internal hemorrhage can run the risk of off-target clot formation, which could lead to stroke, heart attack, or pulmonary embolism," he explained.

Brown's platelets are engineered to incorporate antibody fragments on the surface of the hydrogel that bind to a protein, called fibrin, that is naturally produced when the body is injured. The platelets use the antibody like a homing mechanism to go directly to the injury site. The fibrin's job is to generate a mesh-like substance to enhance clot formation. The researchers found that the synthetic platelets can help stiffen the clot and stabilize it, which then aids the wound-healing process after clotting happens.

"This was a really exciting finding and a total surprise when we first discovered it," Brown said. She explained that if a person is bleeding excessively, the body isn't able to make enough fibrin. But when her platelets are infused, they can actually speed up fibrin formation.

After they reach the site of the injury and become active, the platelets, due to their squishiness, can also change shape—from being rounded to being more star-like, mimicking what natural platelets do in the body. This change encourages a process called clot retraction, or the shrinking of a blood clot to allow the edges of the injured blood vessel wall to be slowly brought together again for repair.

The squishiness of the platelets gives them another advantage at the end

of the process. "They can squeeze through pores that are way smaller than their size, allowing them to be excreted by the kidneys," Brown said. "Normally they would accumulate in the liver, which could have harmful effects."

Still testing—and showing promise

Brown and her research team have been testing the synthetic platelets in a variety of animal models, and so far the results have been positive. In mice with liver injuries, the synthetic platelets went directly to the injury site and had the lowest levels of blood loss when compared to mice given normal platelets or a control solution of saline. At seven days after injury, mice given the synthetic platelets also had the smallest wounds, a sign of improved healing. Testing in rats with an injury to the blood vessel instead of the liver, the researchers found similarly promising results.

But Brown said that pigs are the gold standard, for their ability to provide greater insight into how synthetic platelets might work in humans. When given immediately after a liver injury in pigs, the synthetic platelets traveled to the site of injury and reduced blood loss. They also didn't cause any measurable allergic or immune system reactions, and began to be excreted by the kidneys in as little as two hours after injection.

"We think that synthetic platelets could be the best thing since sliced bread, but that's yet to be determined through further testing," Brown said. Her team is still experimenting to find the ideal conditions to store the platelets for the best results. Currently, testing shows they can be stored as a freeze-dried powder, which could be useful in ambulances or similar trauma situations such as on the battlefield, or suspended in a solution that may be better for hospital use.

While they continue testing storage conditions, Brown has launched a company with her colleague Seema Nandi, Ph.D. serving as the CEO. SelSym Biotech is focused on completing all the necessary steps, such as manufacturing, pre-clinical studies, and clinical trials, to get synthetic platelets into clinical use. It will evaluate the long-term stability and safety of the platelets, as well as work out the processes for scaling up production after testing in humans shows they are safe and effective. Brown expects those trials to begin in about two years.

"By developing a new generation of treatment options for emergency medicine, this research may help improve patient outcomes while potentially reducing health care costs," Warren said. "Unlike donated platelets, which can vary in quality, synthetic platelets could potentially be produced in large quantities with uniform quality and performance."

Brown said she is hopeful the platelets will find their way to emergency medical service vehicles, military medic kits, and hospitals soon, so that her "extremely motivating" work to save lives finally pays off.

"So many people die from unnecessary bleeding injuries," she said. "I'm hopeful that this work could have a big impact."

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