Massive hemorrhages are often deadly. Can a perfume ingredient stop the bleed and save lives?

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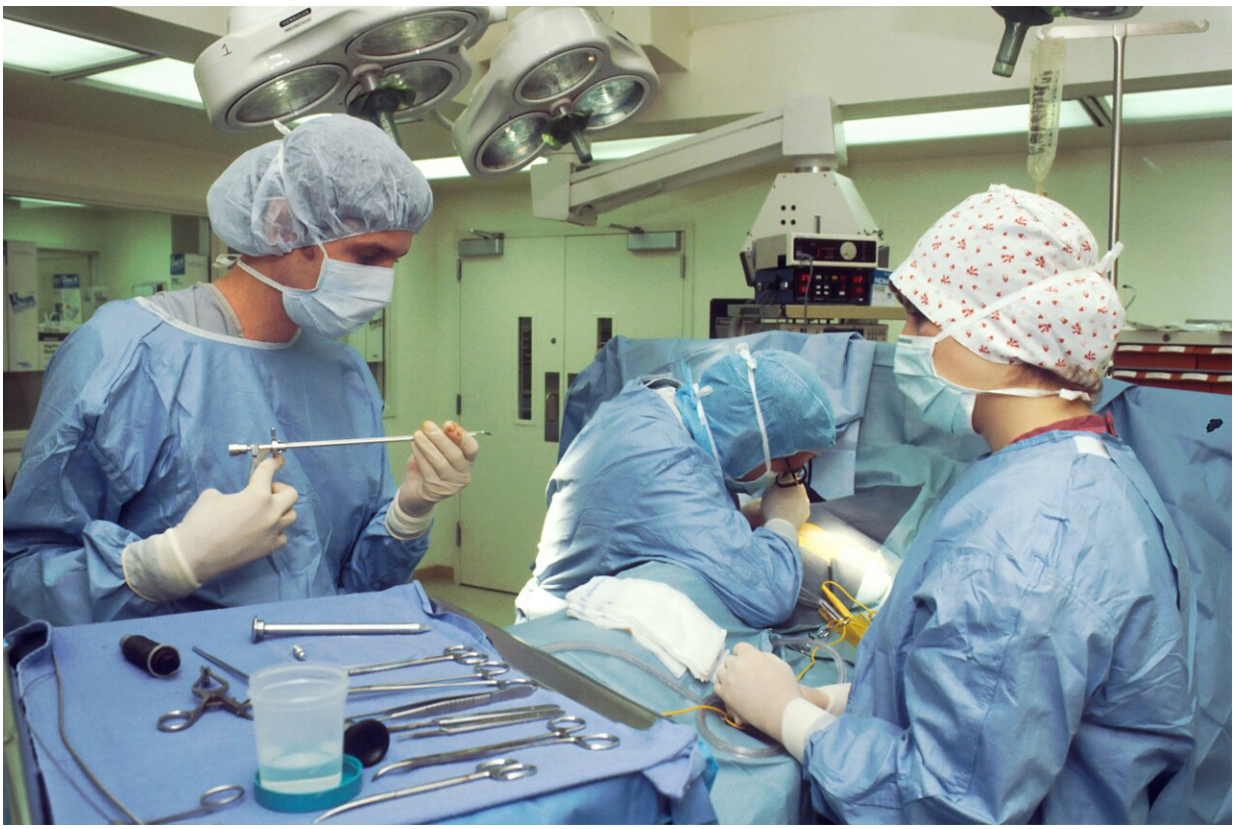

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The chances of surviving massive blood loss from a traumatic injury such as a gunshot wound are around 50%. To survive, a patient needs

two things to happen quickly: a large infusion of blood and coagulation at the wound to stop the bleeding.

The problem is one of these solutions prevents the other. Introducing a large amount of blood to those suffering a massive hemorrhage impairs the blood's ability to clot, a condition known as coagulopathy.

Now, Tulane University researchers have uncovered the cause of coagulopathy in trauma victims receiving a blood infusion. They also found that a synthetic compound called dimethyl malonate—often used in perfume manufacturing—has the potential to stop coagulopathy during a massive hemorrhage. The researchers' findings are part of a new study published in *Science Advances.*

"Coagulopathy of trauma is a major contributor to mortality, but no treatment has shown to be fully effective," said Olan Jackson-Weaver, Ph.D., assistant professor of surgery at Tulane University School of Medicine and corresponding author on the study. "We were getting 60% mortality with our animal model. With dimethyl malonate, we got zero percent mortality, and the coagulopathy completely went away."

Trauma is a leading cause of death in the United States especially for children and young adults as a result gun violence.

Recent studies have shown that coagulopathy during massive hemorrhage treatment is most likely caused by the shedding of the glycocalyx, a barrier of sugars that surrounds and protects cells. In blood vessels, the glycocalyx lines the vessel walls and prevents blood from clotting. However, this is the first study to identify the cellular events that cause the glycocalyx to be ripped apart.

The study found that, during blood loss, a person's cells lack the oxygen to metabolize succinate, a key part of the cell's energy-generating cycle.

Unable to be metabolized, the succinate builds up. When a large amount of blood is infused into a trauma victim—the succinate is metabolized too quickly, which leads to a change in the structure of the plasma membrane lipids. This exposes the glycocalyx, allows it to be chewed up by enzymes, and mixes the shreds into the bloodstream, where it prevents clotting.

"People have been trying to figure out ways to move the needle a little bit on the death rate from massive hemorrhage for the last 20 or so years and nothing has really worked," Jackson-Weaver said. "We're hopeful that understanding these cellular-level events can help to develop something that actually does make a big difference."

In animal models, dimethyl malonate was effective at inhibiting excessive cellular metabolism, which prevented the glycocalyx from shedding and causing coagulopathy.

But Jackson-Weaver said more research needs to be done to determine if dimethyl malonate is safe for humans or if an equivalent drug that targets cellular metabolism can be developed.

"We've established this pathway that causes coagulopathy, so if we can target it therapeutically with a pre-hospital drug or injection, we can hopefully save some lives," Jackson-Weaver said.

More information: Sarah Abdullah et al, Succinate metabolism and membrane reorganization drives the endotheliopathy and coagulopathy of traumatic hemorrhage, *Science Advances* (2023). DOI: 10.1126/sciadv.adf6600. www.science.org/doi/10.1126/sciadv.adf6600

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