A team is developing an inexpensive biopolymer dressing to heal chronic wounds

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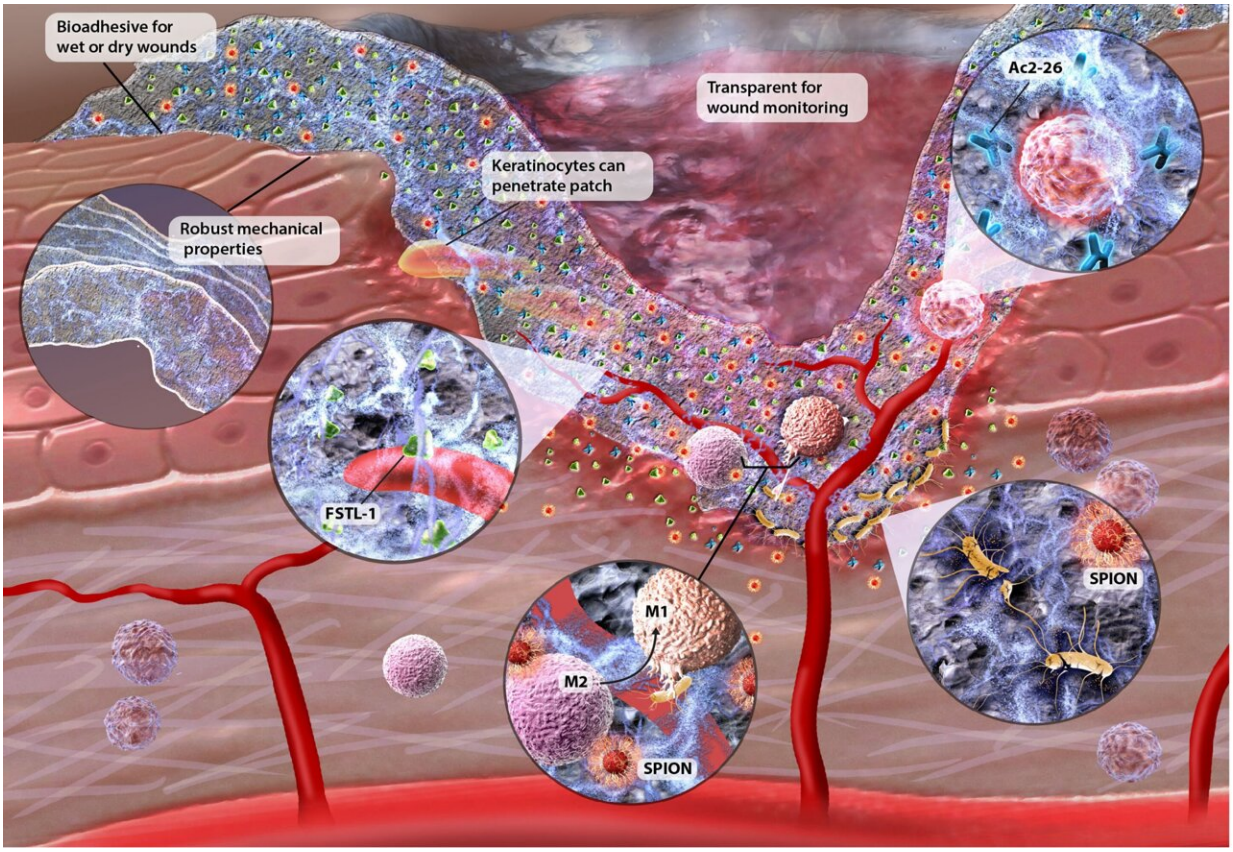


An illustrated schematic shows a potential configuration of the clear bandage that molds to the shape of a wound, which is also part of the illustration that penetrates pink skin tissue and exposes red blood vessels. Insets magnify proteins (green triangles labeled FSTL-1) that help blood vessels regenerate, iron oxide nanoparticles (red orbs labeled SPIONs) that fight bacteria and stimulate immune cells (larger orbs labeled M1 and M2) and peptides (blue crosses) that prevent the immune response from becoming too aggressive. Credit: *The Journal of Molecular Pharmaceutics*

Tens of millions of patients around the world suffer from persistent and potentially life-threatening wounds. For these chronic wounds, which are also a leading cause of amputation, there are treatments, but the cost of existing wound dressings can prevent them from reaching people in need.

Now, a Michigan State University researcher is leading an international team of scientists to develop a low-cost, practical biopolymer dressing that helps heal these wounds.

"The existing efficient technologies are far too expensive for most health care systems, greatly limiting their use in a timely manner," said Morteza Mahmoudi, an assistant professor in the Michigan State University College of Human Medicine and the Precision Health Program. "An economically accessible, practical and effective technology is needed."

To develop that new technology, Mahmoudi tapped into years of experience and expertise, having studied advanced materials to heal heart tissue, fight infections and support immune systems. But the team also kept an eye on cost, working to develop a product that could be made available to as many patients as possible, even in resource constrained markets.

"My goal is always to make something that works and is practical," Mahmoudi said. "I want to see my research become clinical products that help patients."

With his latest work, published July 19 in the journal *Molecular Pharmaceutics*, Mahmoudi is getting closer to that goal. He's working with partners in the United Kingdom who have started a company to oversee the development and approval of the new technology.

"We are building an experienced and expert team in the U.K. who will be able to efficiently commercialize the dressing," Mahmoudi said. "The company has just won a very competitive Eurostar grant to accelerate product development."

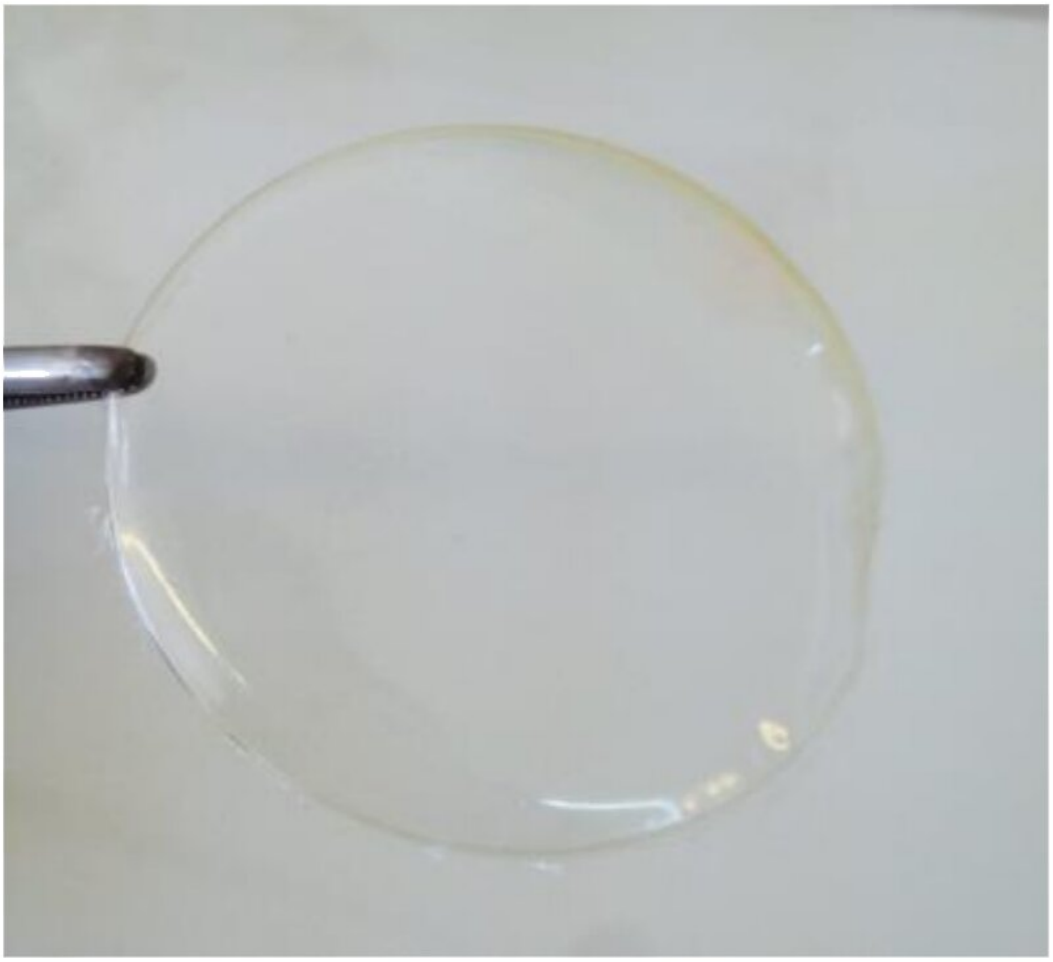
Working with his collaborators, Mahmoudi conducted a small pilot trial of the wound dressing with 13 patients with chronic wounds, all of whom were cured, he said.

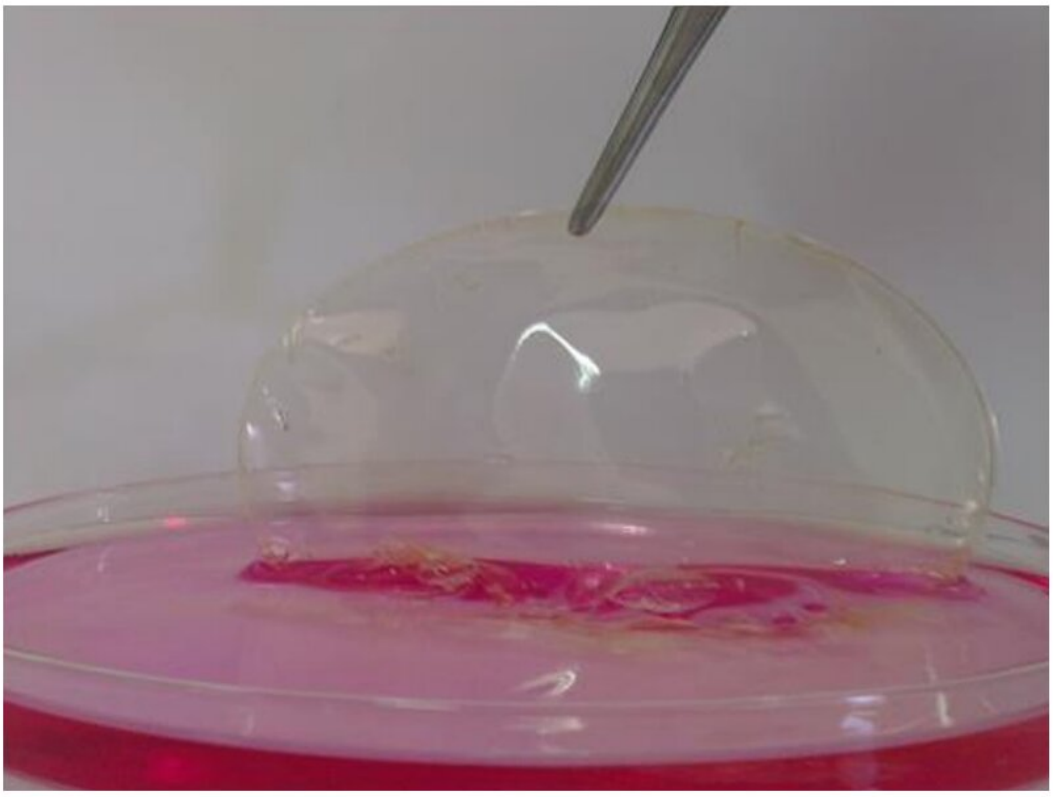
Patients with advanced chronic wounds—those which do not respond to traditional therapies—are estimated to number over 45 million globally, making this one of the world's most pressing and urgent health care needs, Mahmoudi said.

The United States is home to about 5% of this population, yet more than 90% of the sales of "active" wound care technologies happen in the U.S. That essentially means that the rest of the world is left out, Mahmoudi said.

Venous leg ulcers and pressure ulcers associated with immobility in older and paralyzed patients are also major causes of chronic wounds, but perhaps the best-known examples of this type of injury being diabetic foot ulcers. Worldwide, there are more than 400 million people living with diabetes, and some studies have estimated that up to a quarter of those patients will develop foot ulcers within their lifetime.

Even with the high level of care available in the U.S., more than 30% of patients who develop a diabetic foot ulcer will die within five years of its onset. For reference, that percentage is higher than breast cancer, prostate cancer and colon cancer.





The transparent wound dressing is shown against a white background (above) and on a simulated wound (below). Credit: Michigan State University

Diabetic foot ulcers also illustrate many of the reasons why chronic wounds can be so challenging to treat.

Patients with diabetes can be dealing with restricted blood flow and other factors that slow their immune response, compromising the body's ability to heal the wound on its own. They can also have nerve damage that dulls the wound's pain and can delay patients from seeking treatment. When wounds heal more slowly and stay open longer, bacteria have more opportunities to cause infections and lead to serious complications. Put bluntly, there's a lot going wrong in a chronic wound.

"Chronic wounds are some of the most complicated things doctors have to treat," Mahmoudi said. "If you want to make a dressing that works, it has to address all those problems. And in order to be relevant to the majority of patients in the world, it has to be easy to use, practical and inexpensive as well."

There are many technologies available to support healing in chronic wounds, but those that can stimulate tissue regeneration are typically derived from harvested natural tissues. This is complex and expensive, resulting in products that cost upwards of $1,000, putting them out of reach for many patients and health care systems.

To attack those problems, Mahmoudi drew on a wealth of experience in developing new materials for biomedical applications. By designing a product that can be manufactured from readily available biopolymers,

production costs can be kept low, and the team could add various other materials to lead to improved healing.

The team starts with a flexible framework of nanofibers—exceedingly thin threads—of natural polymers, including collagen, a structural-support protein found in our skin and cartilage. The framework provides a three-dimensional scaffold that fosters cell migration and the development of new blood vessels, essentially replicating the function of the extracellular matrix, the natural support system found in healthy, living tissue.

"It's important that the physical and mechanical properties of the dressing are really close to that of skin," Mahmoudi said. "In order to heal, the new cells have to feel like they're at home."

To that framework, the team can incorporate proteins, peptides and nanoparticles that not only spur the growth of new cells and blood vessels but also fight off bacteria by encouraging a patient's own immune system to join the charge. (The team's experiences on these elements were documented in earlier publications in *Nature Nanotechnology* and *Trends in Biotechnology*).

The dressing also degrades over time, meaning that nobody would have to change or remove it and potentially aggravate the wound site. And at roughly $20 apiece, Mahmoudi believes that the dressings—if and when approved by regulatory agencies—will be affordable to even resource-strapped health care systems faced with treating these serious wounds.

Although there are many existing wound care products, Mahmoudi is optimistic that the new dressing will stand out thanks to its low cost, high performance and another piece of research he did years ago.

For this previous project, though, he wasn't developing any new

technology. He was interviewing hundreds of health care workers around the U.S., asking them what they wanted and needed in a wound dressing.

"We developed this dressing to solve the problems they were having. One of the clinicians told me, "When you see too many products on the market, that means none of them works,'" said Mahmoudi, a researcher driven to make things that work.

More information: Rahimeh B. Atashgah et al, Restoring Endogenous Repair Mechanisms to Heal Chronic Wounds with a Multifunctional Wound Dressing, *Molecular Pharmaceutics* (2021). DOI: 10.1021/acs.molpharmaceut.1c00400

Provided by Michigan State University