

Researchers develop microneedles to accelerate diabetic wound healing

Zhaki Abdullah
Correspondent

Each day, about four people face having their lower limbs amputated because of non-healing diabetic wounds in Singapore, where some 400,000 people live with the disease.

To tackle this problem, researchers from NUS have developed two technologies which have shown to be effective in accelerating diabetic wound healing, thus reducing the risk of amputation.

Diabetic wounds can take a longer time to heal as a result of factors such as impaired blood circulation, a weakened immune system and chronic inflammation.

The new technologies use microneedle patches to accelerate diabetic wound healing in preclinical models by preserving the functions of growth factors – proteins that stimulate cell growth and tissue repair – and wound healing.

Microneedles are miniature needles whose tips can be as thin as one micrometre, or 0.001mm – less than the width of a human hair.

Microneedles are also used in

dermatology to treat acne scars and facial wrinkles.

They can also be used to administer drugs and vaccines, with benefits such as being safer and less painful for patients, as well as having a lower risk of infection compared with regular needles.

The team that developed the two innovations is led by Assistant Professor Andy Tay from the biomedical engineering department at NUS' College of Design and Engineering.

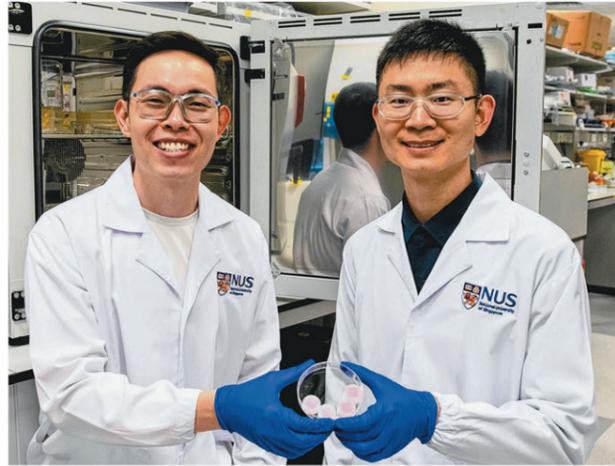
Although growth factors are important in wound healing, Prof Tay pointed out that other enzymes known as proteases quickly break them down in diabetic wounds, significantly slowing down the healing process.

Diabetic wounds are also characterised by persistently high levels of inflammation, he added.

The use of microneedles can help tackle both issues, said Prof Tay.

"It is minimally invasive, can be fabricated with precision, and allows for the active compounds to be painlessly administered directly into wounds," he said.

In the first method, sucralfate microneedles were developed to



Microneedles, made from a type of biodegradable polymer that can be used in the sustained delivery of drugs, being produced with a mould.

NUS researchers Andy Tay (far left) and Le Zhicheng are part of the team that developed the two innovations. PHOTOS: NUS

deliver a protein known as interleukin-4 (IL-4) to stimulate the production of growth factors in diabetic tissue.

IL-4 helps regulate immune response and promote tissue regeneration, while the use of sucralfate – a medication commonly used to treat gastrointestinal ulcers – protects growth factors from degradation.

This approach has several advantages over existing methods, such as applying hydrogel to such wounds to deliver growth factors.

For example, the microneedles dissolve, allowing IL-4 and sucralfate to be delivered directly to the wound.

Additionally, the localised delivery system minimises systemic side effects and also avoids secondary damage to delicate, newly formed tissues commonly caused by traditional adhesive dressing.

The researchers found that the

sucralfate microneedles also significantly accelerated wound healing, doubling its rate when compared with traditional treatments.

Prof Tay noted that while medications used to treat wounds are typically applied to the surface, the use of microneedles allows for them to be administered to inflammation deep within the tissue.

The team's findings were published in the peer-reviewed scientific journal *Biomaterials* in July 2024.

The second innovation meanwhile involves microneedles being employed to extract undesirable pro-inflammatory proteins and immune cells.

Exploring the use of different materials, the researchers decided on the use of heparin-coated porous microneedles to address the issue of persistent inflammation in skin wounds.

Heparin is a drug that acts as an

anticoagulant, or blood thinner, that is typically used to treat and prevent blood clots.

Previous studies have shown heparin readily binds to chemokines – molecules that select and guide monocytes, a type of white blood cell, in wound tissues.

While monocytes play a crucial role in fighting infections, they also contribute to inflammation.

The researchers found that heparin-coated porous microneedles could effectively deplete chemokines and monocytes from wound sites, leading to a 50 per cent reduction in tissue inflammation, as well as a 90 per cent reduction in wound size by the 14th day of treatment.

These initial findings point to the potential use of heparin-coated porous microneedles in the treatment of inflammatory skin disorders, common in diabetics.

Such microneedles can remove

chemokines and inflammatory cells deep within the skin tissue, the study found.

The technology could also be further developed for personalised wound care, as well as personalised treatment of inflammatory skin conditions such as psoriasis, the researchers said.

This study was published in *Advanced Functional Materials* in July 2024.

For now, the researchers are focused on their work with extractive microneedles, Prof Tay said.

This includes exploring the use of 3D-printing to make microneedle patches, which would allow such patches to be made to the exact shape of a wound to allow for more customised treatment for patients.

The technology would also allow for the creation of microneedles with more controllable pore sizes.

The team is also looking at integrating antibacterial properties into the microneedles to tackle the risk of infections.

Prof Tay said the researchers hope to establish such developments before proceeding to clinical trial, adding that the researchers have also received a \$300,000 grant from A*Star for their research.

The use of microneedles to treat non-healing diabetic wounds could also help ease healthcare inequality, Prof Tay said, noting those in lower-income groups tend to be disproportionately affected by such wounds and face having their limbs amputated.

"It's very important that we try to find a solution like microneedles that is quite simple to use and relatively cheap to make," he said.

azhaki@sph.com.sg