Sprayed NIR-responsive black phosphorus-based gel treats diabetic ulcers

Diabetic ulcers (DUs) are a common chronic complication of diabetes mellitus and appear as chronic wounds that form on feet and legs, and less commonly on other locations on the skin. For treating DUs, an international research group has developed a series of smart black phosphorus (BP)-based gels that are responsive to near-infrared light (NIR), which can be rapidly sprayed on the affected regions. This work is published in a recent issue of *PNAS* (<https://doi.org/10.1073/pnas.2016268117>).

The study targets the complex and challenging wound-healing milieu associated with DUs, including chronic wounds, impaired angiogenesis (growth of new blood vessels), persistent pain, bacterial infection, and exacerbated

inflammation. Both *in vitro* and *in vivo* results show that this BP-based gel can simultaneously and effectively treat the individual features associated with this condition.

“Owing to its significant analgesic effects and wound-healing properties, this functional gel could be a huge boon for diabetic patients, improving their life quality,” says Wei Tao of Harvard Medical School, the work’s principal investigator. “The greatest advantages of this sprayed BP-based gel are its superior biosafety, simple administration, and excellent therapeutic efficacy,” Tao tells *MRS Bulletin*.

The functionalized gel contains (i) fibrinogen (protein) and thrombin (enzyme), FDA-approved ingredients that have unique advantages such as good biocompatibility, amenability to a simple spray-coating approach, and wound healing through promoting angiogenesis; (ii) BP nanosheets, which can easily degrade into nontoxic phosphate

ions and serve as active photothermal agents under NIR laser irradiation (808 nm); and (iii) FDA-approved anesthetic lidocaine hydrochloride.

The gel wound dressing can be easily formed to cover DUs using a dual-cartridge sprayer (as shown in the **Figure**). Tao says, “Regardless of the different shapes or areas of the wounds, the developed technology can be quickly mixed and sprayed at the DU site to form wound-healing gels *in situ*. Besides, this approach can avoid the toxic effects associated with the systemic administration of drugs.” The sprayed gel serves as an artificial “skin” to temporarily shield the tissue from the external environment and facilitate wound healing by elevating the proliferation of endothelial cells, vascularization, and angiogenesis.

Also, it can act as a drug “reservoir” to store curative BP and pain-relieving lidocaine hydrochloride. Within several minutes of NIR laser irradiation, the gel

generates local heat to facilitate microcirculatory blood flow, regulate the release of loaded anesthetic for on-demand pain relief, eliminate bacterial infection, and alleviate inflammation. In addition to DU treatment, this work may also enlighten future development of pain-relief nanotechnology in biomedical applications and greatly expand research areas for BP-based materials.

“We are interested in the bench-to-bed translation of this technology in the future,” Tao says. “Our next step is to carry out more studies to (i) achieve high-yield production, and (ii) access the long-term safety of these gels, which are both the basis of future possible clinical applications.”

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Schematic illustration of *in situ* sprayed near-infrared light (NIR)-responsive, pain-relieving gel for accelerated wound healing in diabetic ulcers. Lid is lidocaine hydrochloride; NS is nanosheet; BP is black phosphorus; and PTT is photothermal therapy. Credit: Wei Tao.

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