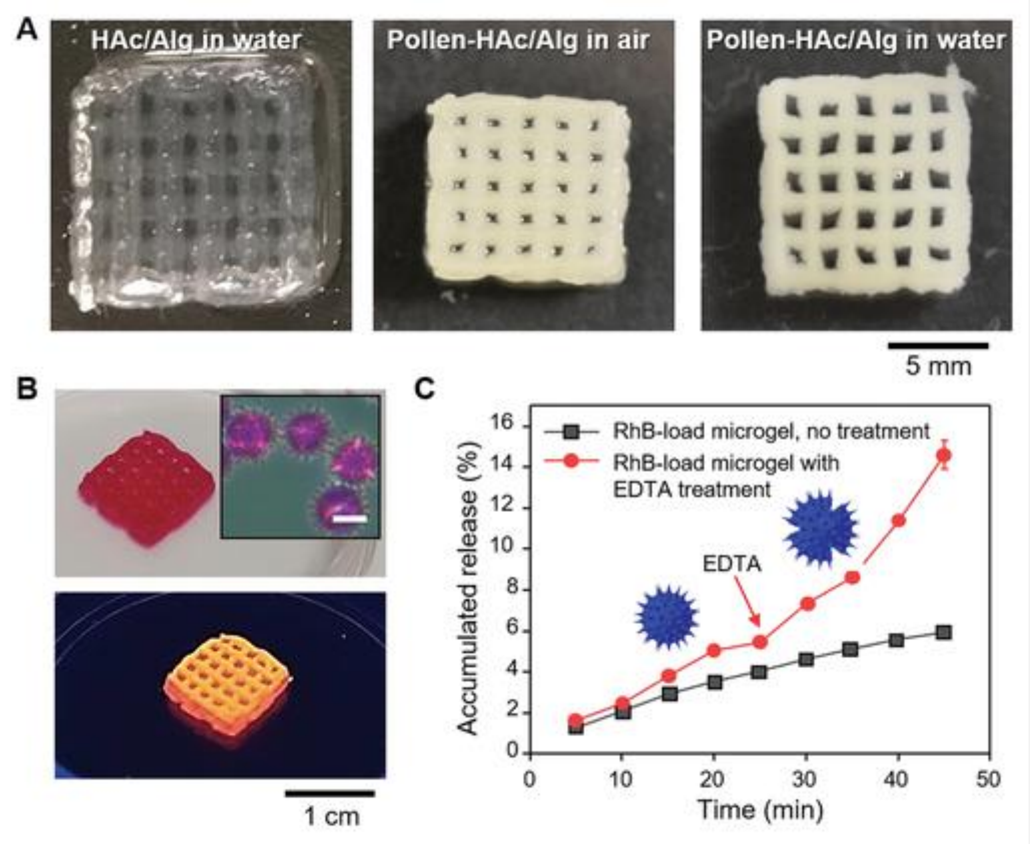
Pollen-Based Bioink Heralds New Potential for Bioprinting Drugs

13 hoursby Michael Molitch-Hou3D Printing3D Printing Materials3D Printing ResearchBioprintingSustainability

Bioprinting has made its way out of the lab and…into other labs. We still haven't seen a true bioprinted organ implant, but the technology has so evolved and proliferated that a wide variety of printers and materials are being sold, mostly to university and corporate labs around the world. So, while the technology is on the precipice of a market explosion, we're witnessing numerous advances take place. One recent example is that of a bioprinting ink created by researchers at Nanyang Technological University, Singapore (NTU Singapore) using sunflower pollen.

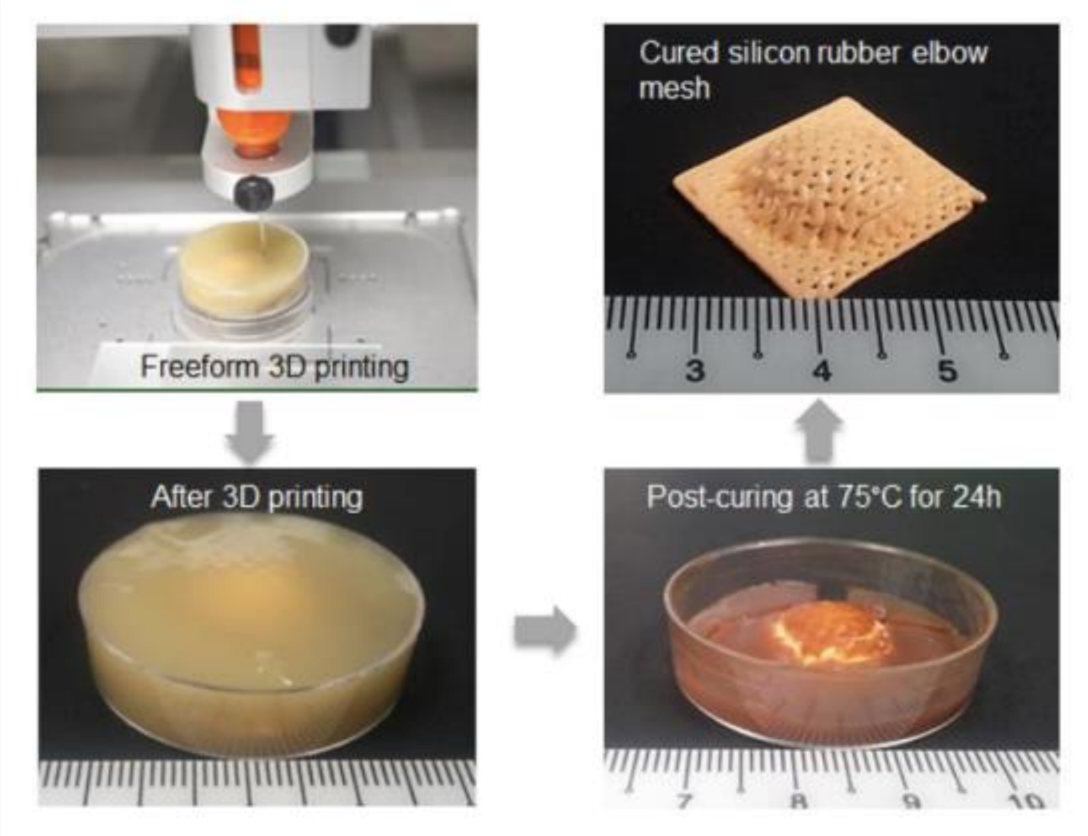
The new material is capable of maintaining its shape upon deposition onto a substrate, opening up the possibility of using it as an alternative to other bioprinting inks. Many bioprinting materials—such as hydrogels, cells, and biopolymers—are soft and delicate, presenting difficulties for retaining the desired shape of the print as ink is deposited. In turn, they require support matrix into which they might be extruded during the printing process. This results in waste, as the support material is not used after printing.



"3D-printed pollen microgel–hydrogel scaffolds for drug loading and release. A) Optical images of hyaluronic acid (HAc)/alginate (Alg) scaffolds printed in gelatin supporting matrix with or without pollen microgels. All scaffolds were post-cured under UV irradiation after printing. B) Optical images of a Rhodamine B (RhB)-loaded pollen–HAc/Alg hybrid scaffold printed and crosslinked under UV irradiation. The inset displays RhB-loaded pollen microgels. The scale bar represents 10 µm. C) Dye release of RhB-loaded pollen microgels mimicking drug release. Accumulated release as a function of time." Image courtesy of Advanced Functional Materials.

Song Juha, co-lead author of the study published in *Advanced Functional Materials* and assistant professor at the NTU School of Chemical and Biomedical Engineering, elaborated: "Previous research efforts were focused on developing special bioinks for efficient deposition and printability through mixing hydrogels with fibres or particles. The main drawback of such hydrogel composite inks is nozzle clogging, which is a more significant issue in inks with a higher content of such fibres or particles. The pollen-based hybrid ink we have developed, in contrast, is mechanically strong enough to retain its structure without jamming the printer."

To develop an alternative, the NTU team turned to sunflower pollen, which the group has already explored as a natural and renewable resource for other projects, such as eco-friendly paper and biodegradable sponges for cleaning up oil. The process began with the incubation of sunflower pollen in an alkaline solution for six hours to create a pollen microgel. This was then combined with other hydrogels, such as seaweed-derived alginate or hyaluronic acid.



Using pollen microgel as the support structure for freeform 3D printing, the
NTU scientists successfully fabricated a silicon elbow mesh. Image courtesy of NTU Singapore.

Cho Nam-Joon, co-lead author of the study and professor of the NTU School of Materials Sciences and Engineering, said: “Bioprinting can be challenging because the material of the inks used is typically too soft, which means the structure of the envisioned product may collapse during printing. Through tuning the mechanical properties of sunflower pollen, we developed a pollen-based hybrid ink that can be used to print structures with good structural integrity. Utilising pollen for 3D printing is a significant achievement as the process of making the pollen-based ink is sustainable and affordable. Given that there are numerous types of pollen species with distinct sizes, shapes, and surface properties, pollen microgel suspensions could potentially be used to create a new class of eco-friendly 3D printing materials.”

To test the potential of this pollen-based material, the team 3D printed a five-layer tissue scaffold, a process that took about 12 minutes. Collagen was added to the scaffold before it was seeded with human cells with a high cell-seeding efficiency of 96 to 97%, similar to that of more commonly used inverted colloidal crystal hydrogels.

In addition to demonstrating the durability of the material, the researchers explored several other possible advantages of sunflower pollen bioink. One exciting possibility was the use of bioprinted scaffolds for drug delivery. Because pollen responds to changes in acidity or alkalinity, the team tested the possibility of printing a stimulus-responsive drug delivery system. To do so, they dripped red dye onto the scaffold, noting that the pollen microgel released the die into the scaffold gradually. When acid was added, more dye was released more quickly, opening up the potential for a controlled release system for medications.

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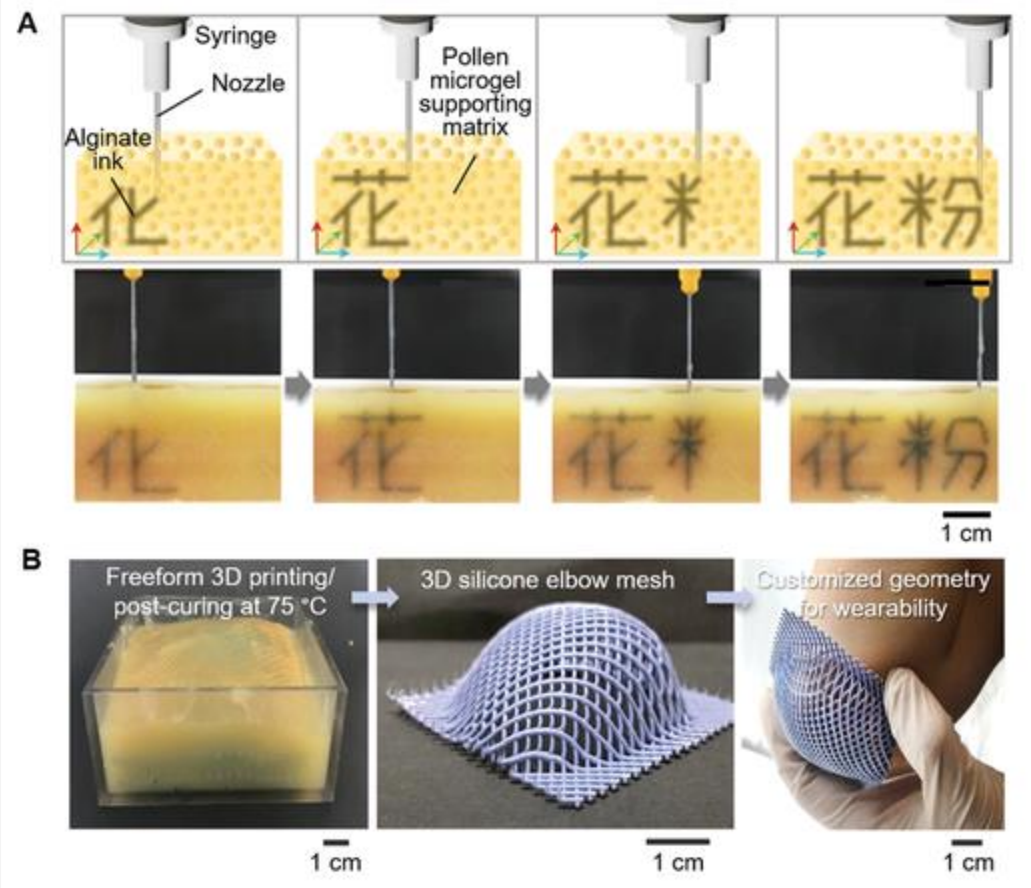

"Freeform 3D printing of alginate hydrogel and silicone rubber inks in pollen microgel for complicated and flexible 3D architectures. A) 3D printing of Chinese characters 花粉 (meaning pollen) using alginate hydrogel ink within a pollen microgel supporting matrix. B) 3D printing of a complex 3D elbow mesh with various curvatures. Optical images of 3D printing of silicone rubber (PDMS) elbow mesh within pollen microgel after curing and fitting onto the human elbow." Image courtesy of Advanced Functional Materials.

"Pollen microgel particles have a hollow shell structure, which means they could potentially be used to carry drugs, cells, or biomolecules in drug delivery platforms with customised 3D structures. We are now looking at how we can use these pollen microgel scaffolds for 3D cell culture platforms in various biomedical applications," Cho explained. "There is also potential for the pollen-based scaffold to be used as a smart drug carrier, given pollen's stimulus-responsive nature. For instance, we can further slow down the release of drugs by coating the pollen-based scaffold with a thin layer of alginate, and stimulate the release by introducing an acid."

Another advantage they found was that the material could potentially be used as a recyclable support matrix. 3D printing a silicon rubber mesh, the researchers relied on pollen microgel as a support structure. The print was then cured at 75°C (167°F) for 24 hours within the pollen matrix. Once cured, the mesh could be removed and shaped to the curvature of the human elbow and maintained physical properties similar to traditional cast elbow meshes.

Song discussed the possibilities of such an approach, saying, "Our findings could open new doors to customised flexible membranes that fit the human skin's contours exactly, such as wound dressing patches or facial masks. Such soft and flexible membranes are usually manufactured based on flat geometry, thus resulting in problems such as fractures in the layers or a poor fit when applied on large surface areas of skin, such as the face or areas that see frequent movement like the joints. Using our pollen-based 3D printing ink, which is biocompatible, flexible, and low in cost, we can fabricate membranes that are tailored to the contours of the human skin and are capable of bending without breaking."

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In addition to developing sustainable materials, NTU has as a 2025 plan to commercialize its research in order to enhance the country's economy and quality of life. In turn, the researchers are looking to work with industry partners to perfect their 3D printing technique and bring it closer to commercialization.

There are a number of companies we could imagine being interested in this development. Bico Group (previously known as Cellink), is a quickly growing biomedical company that has made a string of acquisitions that could be excited about the possibilities of a sustainable bioink. 3D Systems, too, has been rapidly increasing its presence in the bioprinting space. Korea's ROKIT Healthcare may be a bit closer in terms of physical location. There's an entire global map of bioprinting businesses that could be great partners for such a project. Regardless of who takes this opportunity, the research is yet a further demonstration of the exciting work that is coming out of NTU Singapore.

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