Nanoparticles offer hope for common skin allergy

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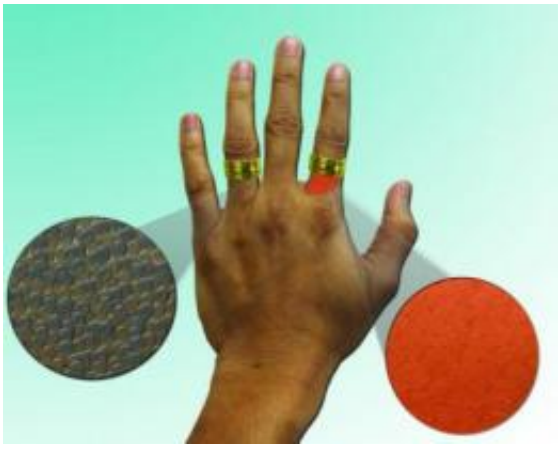


Researchers from Brigham and Women's Hospital (BWH) believe that nanoparticles added to a cream or coated on a nickel-containing object could prevent the itchy redness associated with an allergy to the nickel found in everyday objects like rings. In this cartoon, a nanoparticle cream applied to the ring finger prevents inflammation from the nickel in a ring (brownish particles represent a thin barrier layer of nanoparticles). The forefinger, without the cream, is inflamed after exposure to the ring and its nickel. Credit: Praveen Kumar Vemula, Karp lab, BWH

Tiny particles only billionths of a meter in diameter—about two thousand would fit across the width of a human hair—could offer big hope in a small package to the many millions of people who are allergic to the nickel in everything from jewelry to coins and cell phones, say scientists at Brigham and Women's Hospital (BWH).

In the April 3 online issue of *Nature Nanotechnology,* the team will report a new approach to preventing the common skin allergy.

Approximately ten to fifteen percent of the US population, or over 30 to 45 million people, plus many more worldwide, are allergic to the nickel found in many everyday objects. For these people the metal causes a red, itchy rash when it comes into contact with their skin. You can see many examples through a quick google search for nickel-induced dermatitis.

However, even though some countries regulate the amount of the metal in certain products to limit exposure, there is no good solution to the problem. "There have been approaches to developing creams with agents that bind the nickel before it can penetrate the skin, but these are not effective in most patients and can even be toxic when the agents themselves penetrate the skin, as most do," says Jeffrey Karp, leader of the work and co-director of the Center for Regenerative Therapeutics at BWH. He adds, "People also sometimes coat their jewelry with nail polish to create a barrier between the skin and nickel ions, but this won't prevent all exposures, such as handling coins or wearing a watch."

Karp, who also holds appointments through Harvard Medical School, Harvard Stem Cell Institute (HSCI), and the Harvard-MIT Division of Health Sciences and Technology (HST), is himself allergic to nickel.

Now he and colleagues including R. Rox Anderson, a dermatologist at Harvard Medical School and Massachusetts General Hospital, have found that nanoparticles containing calcium could offer a safe solution to the problem. When applied to the skin in a cream, the nanoparticles efficiently capture the nickel, preventing it from making its way into the body. Further, the nanoparticles themselves were designed so that they cannot penetrate the skin. The cream with its nickel can then be easily washed off with water.

Says Anderson, "Despite barrier creams, anti-inflammatory drugs, and attempts to avoid nickel, this [metal] is still the most common cause of allergic skin reactions. Nanoparticles that bind to [the nickel] allergens but do not penetrate the skin offer a new strategy. Big hope in a small package!"

"We expect that a person could simply apply the cream just as they would hand cream," says Praveen Kumar Vemula of BWH, HMS, HSCI, and HST. Vemula is first author of the paper.

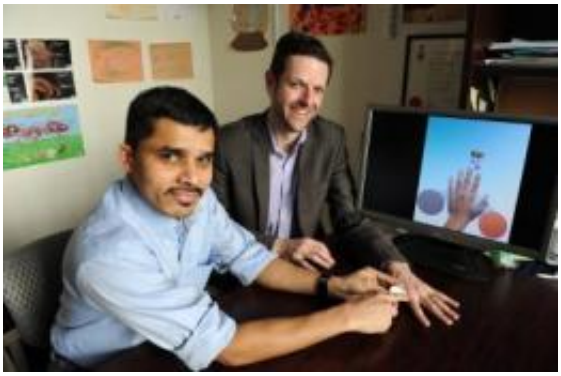
Toward a Solution

The idea for tackling the problem began when Karp, a specialist on nanoparticles, met Anderson at a dinner. Afterward, Karp sat at his computer thinking about how he could potentially work with the accomplished dermatologist to tackle medical problems. As he pondered, he looked at his hands, which were red and itchy from his nickel allergy. Could he and Anderson find a nontoxic, practical way to prevent nickel from penetrating the skin using nanoparticles?

The team began by focusing on compounds containing calcium, which are known to sequester nickel (some are used in the treatment of water). Next, they explored whether these compounds were available as nanoparticles. Karp knew that the tiny particles could potentially allow very efficient nickel capture thanks to their very high surface area.

The team limited their search to nanoparticles within a certain size range. "We wanted them to be large enough so they could not penetrate the skin, yet small enough to present a very large surface area for capturing nickel," Vemula says. (They ultimately decided on particles between 70 and 500 nanometers.) Finally, to cut the time involved in bringing a new technology to market, the team only explored nanoparticles already designated by the Food and Drug Administration

as being generally recognized as safe (GRAS) for use in humans.



Researchers at Brigham and Women's Hospital (BWH) believe nanoparticles could prevent the itchy, red rash millions suffer from because they are allergic to the nickel found in many everyday objects. Here Praveen Kumar Vemula of BWH and Jeffrey Karp, co-director of the Center for Regenerative Therapeutics at BWH, sit next to a graphic describing their team's approach. Vemula holds a small jar representative of a cream containing the nanoparticles. He points to Karp's finger as an example of where the cream could be applied; many people are exposed to nickel through jewelry like rings. Credit: Brigham and Women's Hospital, Donna Coveney.

They found two compounds that met these criteria (calcium carbonate and calcium phosphate), added them to a common emollient to create a cream, and tested them under a variety of experimental conditions. For example, they applied the cream to samples of animal skin and to living animals, and tested it in the presence of artificial sweat (sweat is known to exacerbate the allergy, accelerating the release of nickel). Further, they conducted the tests with concentrations of nickel much higher than would be found in everyday situations.

"We were able to demonstrate that the particles could indeed capture nickel with high efficiency and prevent inflammation in nickel-

sensitized animals," Karp says. Further, "we needed 11-fold less nanoparticles to get the same effect" as another common nickel-capture agent. (A significant drawback of the latter: it can penetrate the skin, and even small amounts can cause local and systemic toxicity.)

All results "suggest that nanoparticles can effectively prevent the penetration of nickel into the skin, and may therefore abrogate nickel-induced contact dermatitis," the team concluded in the Nature Nanotechnology paper.

Provided by Brigham and Women's Hospital