Team customizes nanoparticles to better transport therapeutic drugs

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A UNL team has unveiled an extremely compact yet fully loaded vehicle that can brave conditions and navigate terrain its predecessors could not.

It features a protein frame with a citric acid finish. It's the size of a typical bug—viral, not Volkswagen. And it might just help fight cancer.

The team recently published a study detailing the performance of a custom nanoparticle made from zein, a corn-based protein whose biological properties make it an appealing vehicle for delivering therapeutic drugs throughout the body.

Despite their advantages, however, zein and other proteins typically erode when passing through the spleen and liver en route to their destinations.

In response, the UNL researchers chemically "crosslinked" their zein nanoparticles with citric acid before loading them with the cancer drug 5-FU and injecting them into mice.

The authors found that citric acid prevented the spleen and liver from breaking zein's molecular bonds before it reached the kidney, a common target for drugs such as 5-FU. As a result, the crosslinked nanoparticles delivered larger doses of 5-FU to the kidney than did those without the citric acid buffer.

The citric acid also gave the nanoparticles a larger negative electrical

charge, increasing their mutual repulsion and reducing the accumulation that accelerates their breakdown.

Co-author Yiqi Yang said the findings could prove useful to physicians looking for more efficient means of treating cancer and similarly intrusive diseases.

"What we are doing is letting doctors know that we may have a better candidate (for drug delivery) than what they have now," said Yang, Charles Bessey Professor of biological systems engineering and of texiles, merchandising and fashion design. "This is just the beginning, and it may lead to further studies and opportunities for collaboration."

The crosslinking process could also be calibrated to target specific organs within the body, Yang said, by increasing or decreasing the levels of citric acid introduced to the nanoparticles.

"Sometimes you want the nanoparticle to dissipate quickly; other times, you want it to dissipate slowly," he said. "Because we wanted it to reach the kidney, we had to crosslink it more to allow it to pass through the spleen and liver without it being wiped out."

Though researchers have tested numerous chemicals as crosslinking agents, the majority have buffered nanoparticles less effectively, degraded more quickly or produced toxic carcinogens that citric acid does not, according to Yang.

Yang noted that the nanoparticles' zein shell also offers many inherent advantages, including the ability to carry both positive and negative charges that can attract oppositely charged drugs.

The source of that protein—and the backdrop for his research—has further inspired Yang's interest in zein, he said.

"We're in the middle of a lot of corn, so we'd like to add value to those products," Yang said. "When we use corn for industrial applications, the distilled grain that's left is a zein-rich co-product.

"Hopefully, one day, our farmers can say, 'Look! This is not just for food and fuel. It's also a tool to help treat cancer.'"

Yang's co-authors included Helan Xu, research assistant professor of textiles, merchandising and fashion design; Lan Xu, laboratory manager in agronomy and horticulture; and Li Shen, a former UNL postdoctoral researcher now at Donghua University in Shanghai.

The team's study appeared in the February edition of the journal *Biomedical Microdevices.*

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