Novel nanoparticle made of common mineral may help keep tumor growth at bay

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A common over-the-counter drug, chopped down into nanoparticle size, stopped growth in a cancer tumor.

Engineers at Washington University in St. Louis found a way to keep a cancerous tumor from growing by using nanoparticles of the main ingredient in common antacid tablets.

The research team, led by Avik Som, an MD/PhD student, and Samuel Achilefu, PhD, professor of radiology and of biochemistry & molecular biophysics in the School of Medicine and of biomedical engineering in the School of Engineering & Applied Science, in collaboration with two labs in the School of Engineering & Applied Science, used two novel methods to create nanoparticles from calcium carbonate that were injected intravenously into a mouse model to treat solid tumors. The

compound changed the pH of the tumor environment, from acidic to more alkaline, and kept the cancer from growing.

With this work, researchers showed for the first time that they can modulate pH in solid tumors using intentionally designed nanoparticles. Results of the research were recently published online in *Nanoscale*.

"Cancer kills because of metastasis," said Som, who is working on a doctorate in biomedical engineering in addition to a medical degree. "The pH of a tumor has been heavily correlated with metastasis. For a cancer cell to get out of the extracellular matrix, or the cells around it, one of the methods it uses is a decreased pH."The researchers set out to find new approaches to raise the pH of the tumor and do so only in the tumor environment. In water, the pH in calcium carbonate increases as high as 9. But when injected into the body, the team discovered that calcium carbonate only raises the pH to 7.4, the normal pH in the human body. However, working with calcium carbonate presented some challenges.

"Calcium carbonate doesn't like to be small," Som said. "Calcium carbonate crystals are normally 10 to 1,000 times bigger than an ideal nanoparticle for cancer therapy. On top of that, calcium carbonate in water will constantly try to grow, like stalactites and stalagmites in a cave."

To solve this issue, Som worked with other researchers in the School of Engineering & Applied Science to create two unique solutions. Teaming up with researchers in the lab of Pratim Biswas, PhD, the Lucy & Stanley Lopata Professor and chair of the Department of Energy, Environmental & Chemical Engineering, they developed a method using polyethyleneglycol-based diffusion to synthesize 20- and 300-nanometer-sized calcium carbonate.

Working with Srikanth Singamaneni, PhD, assistant professor of materials science, they developed another method to create 100-nanometer-sized calcium carbonate by building on a method known as ethanol-assisted diffusion. By harnessing the complementary expertise of the different labs, the researchers developed a solvent made of albumin to keep the calcium carbonate nanoparticles from growing, allowing them to be injected into the body intravenously.

Commonly, nanoparticles have been made with gold and silver. However, neither are present in the human body, and there are concerns about them accumulating in the body.

"Calcium and carbonate are both found heavily in the body, and they are generally non-toxic," Som said. "When calcium carbonate dissolves, the carbonate becomes carbon dioxide and is released through the lungs, and calcium is often incorporated into the bones."

Som and the team injected the calcium carbonate nanoparticles into the mouse fibrosarcoma model daily, which kept the tumor from growing. However, when they stopped injecting the nanoparticles, it started growing again.

Going forward, the researchers plan to determine the optimal dose to prevent metastasis, improve targeting to tumors and determine if it could be used with chemotherapy drugs.

Provided by Washington University in St. Louis

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