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Study Shows Buckyballs Penetrate Deeper, Faster When Skin is Flexed

FOR IMMEDIATE RELEASE

Researchers at North Carolina State University have discovered that repetitive flexing movements increase the speed and depth at which tiny particles are absorbed through the skin, a finding that could have major implications in medical, consumer and industrial fields.

Dr. Nancy Monteiro-Riviere, professor of investigative dermatology and toxicology at NC State's College of Veterinary Medicine, and graduate student Jillian Rouse, working with Dr. Andrew R. Barron, professor of chemistry and materials science at Rice University, made the discovery by exposing the tiny particles – the soccer-ball shaped materials known as fullerenes or buckyballs which are much smaller than the head of a pin – to pig skin.

The research findings will be published in the Jan. 10 edition of *Nano Letters*, a journal published by the American Chemical Society. The study was funded by the Environmental Protection Agency, the National Academies Keck Futures Initiative and the Robert A. Welch Foundation.

"Our results confirm that repetitive motion can speed the passage of nanoparticles through the skin," Monteiro-Riviere says. "As more nanoparticles find their way into the workplace and consumer goods, and as scientists look for innovative ways to use nanoparticles to deliver drugs into the body, it is critical that the nanoscience community identify these types of external exposure factors."

Researchers conducted the in vitro experiment by adding a fullerene-derived amino acid to portions of pig skin, which has physiological and structural similarities to human skin. The skin was placed on a machine that repeatedly flexed the samples for either 60 or 90 minutes, while control samples were not flexed. Scientists measured the intake of the nanoparticles eight hours after exposure and again at 24 hours after exposure.

The non-flexed and flexed samples all showed some degree of fullerene penetration, but the amount and depth of nanoparticle penetration increased the longer the skin was

flexed, the paper reports. Penetration was also deeper in each experimental group after 24 hours than after eight hours, but the deepest penetration was observed in the skin flexed for 90 minutes.

The nanomaterial used in the study were Bucky amino acids (Baa), which are spherical, soccer-ball shaped molecules comprised of 60 carbon atoms and an amino acid chain. The average size of the Bucky amino acids used in the study were .7 nanometers. One nanometer is one-billionth of a meter in size, which is much smaller than the head of a pin. A pin head is 1 million nanometers wide. Each Baa was also tagged with a fluorescent marker so it could be traced through the skin.

The study also suggests that fullerenes penetrate the skin between rather than through cells on the outer, or epidermal, skin layer. The fact that some particles penetrated to the dermal layer further suggests that nanomaterials could get absorbed by capillaries and transported elsewhere in the body.

In drug-delivery applications, the ability of nanoparticles to access the body's circulatory system has important implications. Although there are many potential benefits to the use of nanomaterials in the treatment of diseases, little is currently know about the potential risks involved with the uptake of nanoparticles through the skin and into the body.

"Many physicians believe the potential for using nanomaterials in drugs to target diseases is the greatest thing," Monteiro-Riviere says. "Yet the implication is that no one knows what happens when nanoparticles are filtered through the body. There is still a lot of research that must be done."

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Note to editors: An abstract of the *Nano Letters* paper follows:

"Effects of Mechanical Flexion on the Penetration of Fullerene Amino Acid-Derivatized Peptide Nanoparticles through Skin"

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Abstract: Dermatomed porcine skin was fixed to a flexing device and topically dosed with 33.5 mg-mL-1 of an aqueous solution of a fullerene-substituted phenylalanine (Baa) derivative of a nuclear localization peptide sequence (Baa-Lys(FITC)-NLS). Skin was flexed for 60 or 90 min or left unflexed (control). Confocal microscopy depicted dermal penetration of the nanoparticles at 8 h in skin flexed for 60 and 90 min, whereas Baa-Lys(FITC)-NLS did not penetrate the dermis of the unflexed skin until 24 h. TEM analysis revealed fullerene-peptide localization within the intercellular spaces of the stratum granulosum.