New technique can help nanoparticles deliver drug treatments

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A Wayne State University researcher has successfully tested a technique that can lead to more effective use of nanoparticles as a drug delivery system.

Joshua Reineke, Ph.D., assistant professor of pharmaceutical sciences in the Eugene Applebaum College of Pharmacy and Health Sciences, examined how a biodegradable polymer particle called polylactic-co-glycolic acid (PLGA) breaks down in live tissue.

He believes the potential impact of his work is broad, as nanoparticles increasingly have been developed as carriers of drug treatments for numerous diseases and as imaging agents; they also are used in numerous consumer products. The kinetics of nanoparticle biodegradation is an important factor that can control how and where a drug is released, impacting treatment efficacy as well as potential toxicity to nontarget tissues from nanoparticle exposure.

"If nanoparticles given to a patient release a drug before particles can ever get to target tissue, then we get high toxicity and low effect," Reineke said. "Conversely, if particles are drawn to a tissue but don't release the drug until long afterward, then we also don't get the therapeutic effect."

Much previous research has studied nanoparticle biodegradation in vitro, but Reineke and the study's lead author, Abdul Khader Mohammad, Ph.D., a recent WSU graduate, believe they are the first to quantify

biodegradation rates after systemic administration.

Their study, "Quantitative Detection of PLGA Nanoparticle Degradation in Tissues following Intravenous Administration," was published recently in the journal *Molecular Pharmaceutics*. It was supported by funds from the Department of Pharmaceutical Sciences and the Office for the Vice President of Research at Wayne State.

Keeping concentration levels the same, Reineke and Mohammad administered PLGA as particles in sizes of 200 and 500 nanometers (nm) intravenously in mice, an important administration route of nanomedicines for cancer applications, for example, and measured the quantity of the nanoparticles in all tissues and the rates at which it degraded. They then compared those rates to those predicted by in vitro measurements.

Reineke said the 200 nm particles degraded much faster in the body than in vitro, while the 500 nm particles degraded similarly to in vitro analyses. The liver and spleen had the highest concentration of polymers and therefore were easiest to analyze.

Researchers found that 500 nm particles degraded faster in the liver than the spleen, but for the 200 nm size the degradation rate in the liver and the spleen were similar.

"It's known that larger particles degrade differently, and we verified that," Reineke said, "but they didn't quite degrade in vivo the way we would expect. We found that among tissue types there are differences in how they degrade."

"That tells us that in vitro degradation doesn't predict in vivo degradation very well, because we see so many differences."

Reineke said that by in vivo testing of other types of nanoparticles, a mathematical model can be developed to help determine which are most effective and have the lowest toxicity for a given application.

"Optimizing a therapeutic system that utilizes nanoparticles is really about getting that timing correct. In order to do that, we have to know how and when the particles are going to release the drug."

Provided by Wayne State University