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Drug-embedded microparticles bolster heart function in animal studies

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Researchers at Emory University and Georgia Institute of Technology have developed tiny polymer beads that can slowly release anti-inflammatory drugs and break down into non-toxic components.

When injected into rats' hearts after a simulated heart attack, the drug-embedded "microparticles" reduce inflammation and scarring, the researchers found.

Injecting the particles could cut the area of scar tissue formed after the heart attack in half and boost the ability of the heart to pump blood by 10 percent weeks later.

The results are published online this week and are scheduled for publication in the Oct/Nov issue of *Nature Materials*.

Doctors believe that certain anti-inflammatory drugs, if delivered directly into the heart after a heart attack, could prevent permanent damage and reduce the probability of heart failure later in life.

Fulfilling this idea -- getting drugs to the right place at the right time -- is more challenging than simply swallowing an aspirin, says senior author Michael Davis, PhD, assistant professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University.

"If you look at previous studies to see what it would take to get enough

of these drugs into the heart, they did things like direct injections twice a day," he says. "And there are clear toxicity issues if the whole body is exposed to the drug."

As an alternative, Davis and graduate student Jay Sy, the first author of the paper, turned to microscopic particles made of a material called polyketals, developed by co-author Niren Murthy, PhD, assistant professor of biomedical engineering.

The microparticles break down over a few weeks in the body, releasing the experimental drug SB239063. This drug inhibits an enzyme, MAP kinase, which is important during the damaging inflammation that occurs after a heart attack.

Davis says the drug gradually leaches out of the polyketal particles – half is gone after a week of just sitting around in warm water. In addition, the microparticles are broken down by white blood cells called macrophages.

"These are actually cells we're trying to reach with the drug, because they're involved in the inflammatory response in the heart," he says. "The macrophages can surround and eat the particles, or fuse together if the particles are too big."

Davis says polyketals have an advantage over other biodegradable polymers, in that they break down into neutral, excretable compounds that aren't themselves inflammatory.

Polyesters such as PLGA (polylactic-co-glycolic acid) are approved for use in sutures and grafts. However, when they are made into particles small enough to be broken down in the body, polyesters cause inflammation – exactly what the drugs are supposed to stop, he says.

When the particles were injected into rats' hearts, the researchers could see an inhibition of the MAP kinase enzyme lasting for a week. However, the effect on heart function was greater after 21 days. Davis says this result suggests that the main way the particles helped the heart was to prevent the scarring that sets in after the initial tissue damage of a heart attack.

He and Murthy are exploring polyketal particles as delivery vehicles for drugs or proteins in several organs: heart, liver, lungs and spinal cord.

Source: Emory University