Researchers develop promising drug for inflammation

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Aspirin, ibuprofen and other non-steroidal anti-inflammatory drugs (NSAIDs) remain the most common treatment to relieve symptoms of arthritis and other inflammatory disorders. But despite their widespread use (around 2.5 million Canadians have osteoarthritis) these medications are also known to cause severe, sometimes life-threatening adverse effects within the body, particularly in the gastrointestinal tract.

A novel anti-inflammatory drug being developed and commercialized by an inflammation expert at McMaster University has shown promise in relieving symptoms of inflammation, while substantially reducing the incidence of bleeding and intestinal damage often caused by NSAIDs.

The research is published in the March issue of the British Journal of Pharmacology.

John Wallace, a pharmacologist and director of the Farncombe Family Digestive Health Research Institute at McMaster University, compared naproxen, a commonly used NSAID, to a novel anti-inflammatory drug, ATB-346, which he developed in collaboration with a team of Italian chemists and is now commercializing through his company, Antibe Therapeutics Inc.

ATB-346 is a derivative of naproxen which releases hydrogen sulfide. Evidence from animal studies suggests that in small quantities, hydrogen sulfide can protect the stomach from injury and can accelerate the healing of pre-existing ulcers.

"I've been working on NSAIDs for over 20 years," said Wallace, a professor of medicine in the Michael G. DeGroote School of Medicine at McMaster University. "This particular drug is, by far, the shining star. We've tested it in every model where it should fail, and it has performed exceptionally well."

To examine the gastrointestinal safety and anti-inflammatory effectiveness of ATB-346, Wallace and his co-investigators tested the drug in healthy rats as well as those with arthritis and inflammation. The researchers also examined the impact of the drug on rats with compromised gastrointestinal tracts, a model which mimicked the clinical scenario in which NSAIDs are frequently used and have caused damage such as bleeding and ulcers.

"From the beginning, we decided that we were going to do the most rigorous testing of any NSAID that's ever been done," Wallace said. "We very deliberately tested the drug in models where NSAIDs fail."

The researchers found that ATB-346 was at least as effective as naproxen in relieving inflammation in animal models. They also discovered that ATB-346 was in the order of 100 times safer than naproxen, causing little or no damage to the stomach and small intestine.

When given to rats with impaired gastrointestinal tracts, ATB-346 did not cause any gastric damage. Moreover, the researchers observed that it enhanced, rather than inhibited, healing of pre-existing ulcers.

Finally, unlike naproxen, ATB-346 had no effect on blood pressure in rats with hypertension, suggesting the drug may have less cardiovascular risks than conventional NSAIDs.

The researchers concluded that H2S-releasing NSAIDs appear to represent a promising alternative to existing therapies for the treatment

of inflammation and pain. Future research will focus on the potential cardiovascular benefits of these drugs.

Provided by McMaster University