

## **Antioxidants: New Kid On The Block For Pain Relief?**

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Antioxidant-based pain killers may one day become a viable alternative to addictive medications such as morphine. Researchers found that synthetic antioxidants practically eradicated pain-like behavior in nearly three-quarters of mice with inflamed hind paws.

"When it comes to pain killers, there aren't many choices between overthe-counter pain relievers like ibuprofen and aspirin and prescription opiates like morphine," said Robert Stephens, a professor of physiology and cell biology at Ohio State University. He's the lead author of a study examining the effects of antioxidants as pain killers.

"We need drugs that fall somewhere between these two extremes," Stephens said. "Someone suffering from chronic pain can become dependent on, or even addicted to, heavy-duty pain killers like morphine."

The study appears in a recent issue of the journal *Behavioural Brain Research*.

Chronic pain is such a formidable problem that, in 2000, Congress passed a bill designating January 1, 2001 as the beginning of the "Decade of Pain Control and Research."

Antioxidants neutralize free radicals, substances that damage cells. While our bodies constantly produce free radicals, healthy tissues inactivate these damaging substances and keep their levels in check. It's



when free-radical production somehow exceeds the body's natural defenses that problems occur. Researchers have linked this excessive production to diseases like cancer and Alzheimer's.

A handful of studies published in the last 10 years suggest that free radicals may also contribute to chronic pain. Left unchecked, free radicals build up in the body and can further damage already-injured tissue.

An equally small number of studies, including those by Stephens, suggest that antioxidants may fight chronic pain by helping the body to break down free radicals.

"Studying the pain-killing effects of antioxidants is an emerging area of research," Stephens said. "The FDA hasn't approved antioxidants for the treatment of chronic pain. But down the road we may see some drugs that contain antioxidants."

Stephens and his colleagues first injected one of three different synthetic antioxidants into mice. An additional group of control mice received only saline. The antioxidants used in this study – PBN (phenyl-N-tert-butylnitrone), TEMPOL

(4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxy) and NAC (N-acetyl-Lcysteine) – aren't the same as those found in fruits and vegetables, and two, PBM and TEMPOL, are currently only available for scientific purposes. NAC is available as a dietary supplement.

"Right now we're trying to show that antioxidants are viable pain killers," Stephens said. "Similar work by other researchers suggested that these antioxidants were the best available. And while certain foods likely contain pain-killing antioxidants, these agents have not been systematically tested as pain relievers."



Shortly after the antioxidant or saline injections, the researchers injected formalin, an irritant, into the left hind paw of each mouse. Formalin causes inflammation, which provokes pain-like behavior in mice. Researchers then spent the next 30 minutes studying how much time an animal spent licking and biting its injured paw. This kind of behavior suggests that the animal is in pain or discomfort.

The researchers divided the 30-minute observation session into three distinct periods – a five-minute acute phase, when the body first senses and reacts to pain, followed by a 5- to 15-minute period of relative stillness, as the body uses its own mechanisms to try to inhibit the pain, and ending with a 15- to 30-minute period called the tonic phase, during which a mouse starts to again vigorously lick or bite its irritated paw, suggesting that it still feels pain or discomfort.

The three antioxidants significantly reduced the amount of time that mice spent biting and licking their injured paw during both the acute and tonic phases. The researchers reported a 70- to 90-percent reduction in pain-related behaviors during the acute phase, and a 78- to 98-percent reduction in such behavior during the tonic phase.

"We were surprised to see such a major decrease in pain in the mice, particularly during the acute phase," Stephens said. "The antioxidants seem to preempt pain-like behavior.

"Other investigators have given antioxidants to rodents after experimentally inducing pain and have found that the drugs relieve pain to a similar extent."

Stephens conducted the study with researchers from Ohio State and from Ataturk University in Erzurum, Turkey.

Source: Ohio State University



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