

Popular painkiller ibuprofen affects liver enzymes in mice

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The popular painkiller ibuprofen may have more significant effects on the liver than previously thought, according to new research from the University of California, Davis. The study in laboratory mice also shows marked differences between males and females.

The work is published Feb. 25 in *Scientific Reports*.

Ibuprofen belongs to a group of drugs called [nonsteroidal anti-inflammatory drugs](#), or NSAIDs, widely used over the counter to treat pain and fever. It's well-established that [ibuprofen](#) can cause [heart problems](#) and increase stroke risk, but the effects on the liver were less well understood, said Professor Aldrin Gomes, Department of Neurobiology, Physiology and Behavior in the UC Davis College of Biological Sciences.

Gomes, postdoctoral researcher Shuchita Tiwari and colleagues dosed mice with a moderate amount of ibuprofen for a week—equivalent to an adult human taking about 400 mg of the drug daily. Then they used advanced mass spectrometry at

UC Davis' Proteomics Core Facility to capture information on all the [metabolic pathways](#) in liver cells.

"We found that ibuprofen caused many more protein expression changes in the liver than we expected," Gomes said.

At least 34 different metabolic pathways were altered in male mice treated with ibuprofen. They included pathways involved in metabolism of amino acids, hormones and vitamins as well as production of reactive oxygen and [hydrogen peroxide](#) inside cells. Hydrogen peroxide damages proteins and stresses [liver cells](#).

Different effects in male and female mice

The researchers found that ibuprofen had different, and in some cases opposite, effects in the livers of male and female mice. For example, the proteasome—a waste-disposal system that removes unwanted proteins—responded differently in males and females. Ibuprofen elevated activity of cytochrome P450, which breaks down drugs, in females but decreased it in males.

"The elevation in cytochrome P450 could mean that other drugs taken with ibuprofen could stay in the body for a longer duration in males and this has never been shown before. No drug is perfect, as all drugs have side effects. However, many commonly used drugs such as ibuprofen are being overused and should not be used for certain conditions such as mild pain," Gomes said.

In the long term, it is important for the scientific community to start addressing differences between males and females with respect to drug metabolism and effects, he said.

More information: Shuchita Tiwari et al, Gender-specific changes in energy metabolism and protein degradation as major pathways affected in livers of

mice treated with ibuprofen, *Scientific Reports*
(2020). DOI: [10.1038/s41598-020-60053-y](https://doi.org/10.1038/s41598-020-60053-y)

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