# Stopping liver failure from painkiller overdose

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Tylenol 500 mg capsules. Credit: Wikipedia

(Medical Xpress)—University of Adelaide researchers have identified a key step for the future prevention of liver failure resulting from taking too much of the everyday painkiller paracetamol (also known as acetaminophen).

Published today in the *Proceedings of the National Academy of Sciences* (*PNAS*), the study pinpoints a target for new treatments to prevent the potentially lethal consequences of paracetamol overdose.

"Paracetamol is the most frequently used over-the-counter pain medication," says Dr Grigori Rychkov, Senior Research Fellow in the University's School of Medical Sciences.

"Overdose of paracetamol is the most common cause of acute liver failure and the leading cause of liver damage requiring transplantation in developed countries. The precise mechanisms of liver toxicity due to paracetamol overdose, however, have remained unclear."

It has been known for a long time that paracetamol overdose is associated with toxic levels of calcium in liver cells but nobody has known how the calcium gets into the cells.

The University of Adelaide researchers have identified a channel transporting calcium across the cell membrane that is triggered by paracetamol overdose, known as Transient Receptor Potential Melanostatine2 (TRPM2). Once the channel is activated, the cells become overloaded with calcium, leading to cell death. If this continues and enough cells die, it can lead to liver failure.

The research, conducted by PhD student Ehsan Kheradpezhouh, showed in laboratory studies that when the TRPM2 channel was missing or blocked, liver cells were protected from paracetamol damage.

"We now have a potential drug target for treating paracetamol overdose and possibly some other liver-damaging poisonings," says Dr Rychkov.

Currently paracetamol overdose can be effectively treated – but only if caught within 18 hours.

"If we can block the TRPM2 channel we might be able to prevent the toxicity or extend this timeframe. If we can stop the calcium uptake and cell death, we'll be giving the liver a better chance for recovery and, hopefully, preventing complete liver failure," says Dr Rychkov.

The study was conducted in collaboration with Flinders University.

**More information:** "TRPM2 channels mediate acetaminophen-induced liver damage," by Ehsan Kheradpezhouh, Llinlin Ma, Arthur Morphett, Greg J. Barritt, and Grigori Y. Rychkov, *PNAS*, 2014.

Provided by University of Adelaide