

# Fumarate greatly reduces heart attack damage in mice

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Fumarate showed promise in protecting the heart in mice.

(Medical Xpress) -- Boosting levels of the simple compound fumarate in mice significantly reduces damage from a heart attack, an Oxford University-led study has shown.

Fumarate, which comes in the form of simple pills to swallow, is already known to be safe and well-tolerated in humans from trials of the drug in multiple sclerosis and psoriasis.

The researchers say that clinical trials in humans could now go ahead to see if fumarate can reduce injury to the heart in a range of conditions. They are beginning to plan for a trial in patients undergoing heart surgery.

The Oxford University researchers, along with colleagues from the UK, Denmark and the USA, published their findings in the journal [Cell Metabolism](#).

They showed that fumarate greatly reduces the amount of [heart tissue](#) damage occurring in a [mouse model](#) of a [heart attack](#). In mice given fumarate, the amount of dead heart tissue after the heart attack was 9.3% of the whole heart volume. In untreated mice, it was 36.9%.

Dr. Houman Ashrafian of the Department of [Cardiovascular Medicine](#) at Oxford University, who led the study, said: "We have shown that heart attack size in mice can be reduced substantially by boosting their fumarate levels."

Coronary heart disease is still the biggest killer in the UK. It occurs when blocked arteries reduce the blood flow to the heart. The [lack of oxygen](#) reaching the [heart muscle](#) results in [tissue damage](#).

A heart attack is caused by a sudden block in the blood flow and rapid treatment is needed to remove the blood clot and re-open the artery. Despite modern treatments contributing to a reduction in [death rates](#), there are still many patients that sustain significant [heart damage](#).

There is a need for additional treatments that can help protect the heart – not just in heart attacks but also in patients with a range of conditions whose hearts may be exposed to other causes of injury.

Fumarate is a simple chemical compound or metabolite that forms part of the normal metabolic pathway the body uses to break down food and release energy – the process known as the citric acid or Krebs cycle. But metabolites can also have roles in biological pathways that control the responses of cells to stress, such as low oxygen.

For example, increased levels of fumarate have been implicated in allowing some cancer cells to thrive in the low oxygen levels that surround them.

Some seals that can dive to great depths under the Antarctic where there is little oxygen appear to activate similar biological pathways that employ fumarate.

These lines of evidence led the Oxford University researchers to become interested in whether there was any role of fumarate in heart cells' response to stress, and whether fumarate could be protective against low oxygen levels.

As well as showing the reduction in heart attack size in mice, the researchers also identified the biological pathways triggered by increased levels of fumarate which appeared to result in the extra protection for the heart.

"The advantages of fumarate are that it would present a relatively safe, cheap drug that wouldn't need to be given for very long," says Dr. Ashrafian. "It could be used upfront to protect the heart ahead of surgery or other predictable insults. Potentially it may also be beneficial in heart attacks in addition to standard treatments.

"But let's be clear: it's great to show we can reduce heart attack damage in mice. It's another thing altogether to show that fumarate is protective in humans. But it is now ready to test in clinical trials."

Dr. Ashrafian has applied for patents on the use of fumarate in [heart surgery](#) and [coronary heart disease](#) through Isis Innovation, the University of Oxford-owned technology transfer company.

Professor Jeremy Pearson, Associate Medical Director at the British

Heart Foundation (BHF), which was the major funder of the study, said: "This very promising study shows that fumarate, already safely trialled in patients for other conditions, including multiple sclerosis, might be repurposed for the benefit of heart patients. It provides strong foundations to build on in the future, and we look forward to seeing the results of the first clinical trials."

Provided by Oxford University

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