

Study reveals how diabetes drug delays ageing in worms

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A widely prescribed type 2 diabetes drug slows down the ageing process by mimicking the effects of dieting, according to a study published today using worms to investigate how the drug works.

Following a calorie-restricted diet has been shown to improve health in later life and extend lifespan in a number of animals, ranging from the simple worm to [rhesus monkeys](#). The type 2 [diabetes drug](#) metformin has been found to have similar effects in animals but until now it was not clear exactly how the drug delays the ageing process.

Researchers supported by the Wellcome Trust and Medical Research Council looked at the effects of metformin on *C. elegans* worms that were grown in the presence of *E. coli* bacteria, a relationship similar to that which humans have with the 'healthy' bacteria in our gut. They found that the worms treated with metformin lived longer only when the *E. coli* strain they were cultured with was sensitive to the drug.

Dr Filipe Cabreiro from the Institute of Healthy Ageing at UCL, who led the research, explains: "Overall, treatment with metformin adds up to 6 days of life for the worm which is equivalent to around a third of its normal lifespan. It seems to work by altering metabolism in the bacteria that live in the worm, which in turn limits the nutrients that are available to the worm host and has a similar effect to restricting the diet."

Bacteria living in the gut have an important role in helping the [host organism](#) to digest and extract nutrition from food. Defects in gut

bacteria have been linked to [metabolic diseases](#) such as obesity, diabetes, [inflammatory bowel disease](#) and cancer. It has also been suggested that [gut bacteria](#) may have an impact on the [ageing process](#), but this is the first study to suggest a mechanism for how this works.

The team used strains of *E. coli* with defects in genes that are linked to metabolism and tweaked the levels of nutrients available to tease out which [metabolic pathways](#) might be affected by the drug. They found that treatment with metformin disrupted the bacteria's ability to metabolise folate, a type of B-vitamin, and methionine, one of the building blocks of proteins. This limits the nutrients that are available to the worm and mimics the effects of dietary restriction to enable the worms to live longer.

However, when they added an excess of sugar to the diet, the team found that the life-extending effects of metformin were cancelled out. As the drug is used as a treatment for diabetes caused by elevated glucose levels in the blood, this finding is particularly relevant for understanding how the drug works in people.

Professor David Gems, who directed the study, said: "We don't know from this study whether metformin has any effect on human ageing. The more interesting finding is the suggestion that drugs that alter bacteria in the gut could give us a new way of treating or preventing metabolic diseases like obesity and diabetes."

[Metformin](#) is currently one of the most widely prescribed drugs and the findings should help to inform how it is used in patients.

The study was published today, Thursday 28 March, in the journal *Cell*.

More information: F. Cabreiro et al. Metformin Retards Aging in *C. elegans* by Altering Microbial Folate and Methionine Metabolism. *Cell*,

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Provided by Wellcome Trust

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