

Diabetes drug could treat leading cause of blindness

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University of Texas Medical Branch at Galveston researchers have discovered that a drug already prescribed to millions of people with diabetes could also have another important use: treating one of the world's leading causes of blindness.

In laboratory rat and cell-culture experiments, the scientists found that metformin, which is commonly used to control blood sugar levels in type 2 diabetes, also substantially reduced the effects of uveitis, an inflammation of the tissues just below the outer surface of the eyeball. Uveitis causes 10 to 15 percent of all cases of blindness in the United States, and is responsible for an even higher proportion of blindness globally. The only treatment now available for the disorder is steroid therapy, which has serious side effects and cannot be used long-term.

"Uveitis has various causes — the most common are infectious diseases and autoimmune disorders— but they all produce inflammation within the eye," said UTMB professor Kota V. Ramana, senior author of a paper on the study now online in the journal *Investigative Ophthalmology & Visual Science*. "Metformin inhibits the process that causes that inflammation."

The scientists discovered metformin's efficacy when they tested it in rats given an endotoxin that mimicked the inflammatory effects of bacterial infection. The results showed clearly that metformin was a very effective anti-uveitis agent.



"We found that the drug is therapeutic as well as preventive — if we gave our rats the drug beforehand, they didn't develop uveitis, and if we gave it after uveitis had developed, it was therapeutic," said UTMB professor Satish Srivastava, also an author of the IOVS paper.

"Metformin's strong anti-inflammatory properties make this possible."

According to the researchers, metformin works by activating an enzyme called AMPK, which in turn damps down the activity of the protein NF-kappa B. The inhibition of NF-kappa B suppresses the production of inflammatory signaling molecules — cytokines and chemokines — needed to initiate and sustain uveitis.

Because metformin is already used so widely as a therapy for diabetes, the UTMB scientists believe that it has a good chance of being rapidly adopted as an anti-uveitis drug.

"I think after a few more pre-clinical studies are done, we can get this drug to patients in a shorter time than usual," Ramana said. "Its safety is already known, so all that we need to see is its efficacy in humans."

Provided by University of Texas Medical Branch at Galveston

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