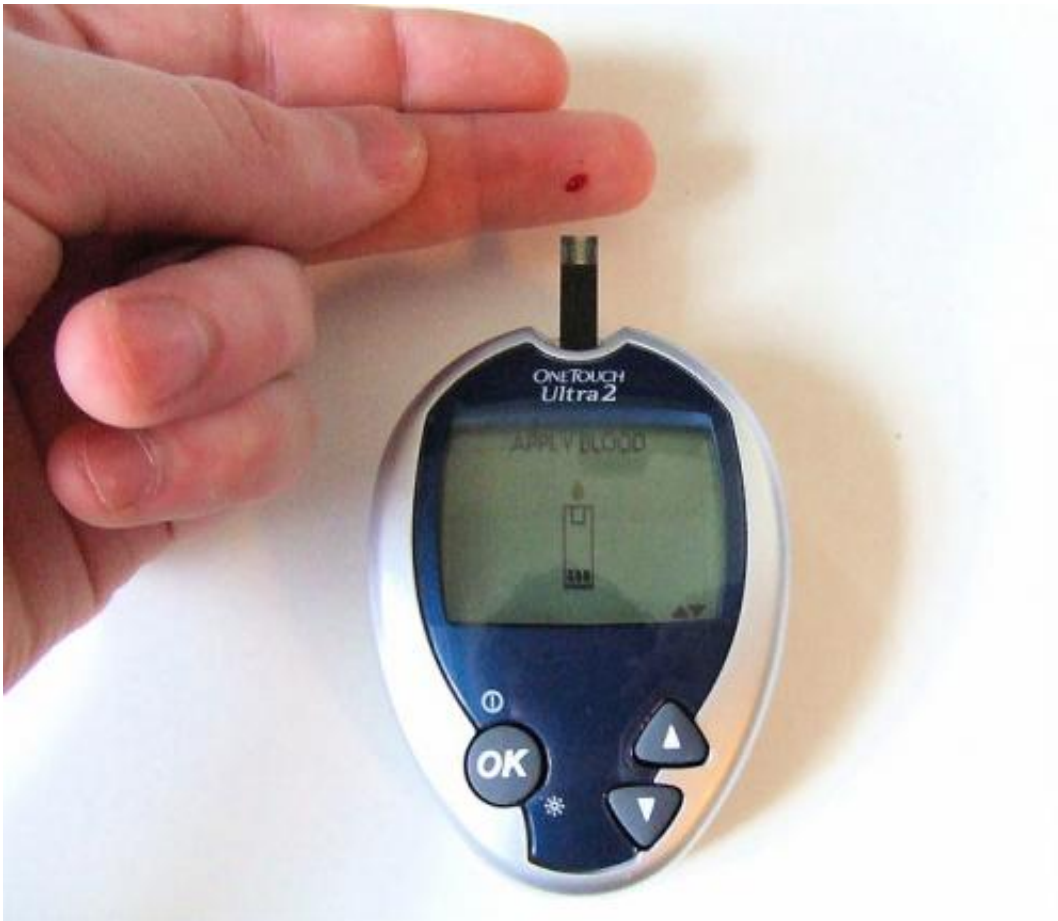


Diabetes drug metformin's primary effect is in the gut, not the bloodstream

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Blood glucose monitoring. Credit: Wikipedia

Although metformin was introduced as a treatment for type 2 diabetes nearly 60 years ago and is now the recommended first-line treatment for

newly diagnosed patients, researchers still debate precisely how the drug works. Now, a study published online today in *Diabetes Care* by researchers at the University of North Carolina School of Medicine, Elcelyx Therapeutics, and other leading endocrinologists provides strong evidence that metformin's primary effect occurs in the gut, not the bloodstream. The paper outlines results from phase 1 and phase 2 studies involving the investigational drug Metformin Delayed Release (Metformin DR), which is designed to target the lower bowel and limit absorption into the blood.

"Our clinical trials show that [metformin](#) works largely in the lower intestine, reversing half a century of conventional thinking," said John Buse, MD, PhD, first author of the paper, professor of medicine, and director of the Diabetes Care Center at the University of North Carolina School of Medicine. "These findings create an opportunity to develop a new metformin [treatment option](#) for the 40 percent of [patients](#) that currently can't take this first-line drug of choice."

Buse added, "One of the top reasons metformin isn't used for all people with [type 2 diabetes](#) is that patients with impaired kidneys accumulate too much drug in the blood, and this can result in life-threatening lactic acidosis. These studies provide evidence that delivering Metformin DR to the lower bowel significantly reduces the amount of metformin in the blood, while maintaining its glucose-lowering effect."

Because of this, Metformin DR may prove to be a treatment option for the four million type 2 diabetes patients in the United States with impaired kidney function.

In the phase 1 study, single daily doses of Metformin DR were compared to immediate-release metformin (Metformin IR) and extended-release metformin (Metformin XR) in healthy volunteers. The amount of metformin in the bloodstream after Metformin DR treatment was

approximately half the amount seen with Metformin IR or Metformin XR. The phase 1 randomized study involved 20 healthy subjects.

In the phase 2 study, various doses of Metformin DR were compared to placebo or Metformin XR in patients with type 2 diabetes. Metformin DR exhibited a 40 percent increase in apparent potency compared to Metformin XR. Also, Metformin DR exhibited statistically significant and sustained reductions in fasting plasma glucose levels over 12 weeks compared to placebo. Treatment was generally well tolerated, with adverse events consistent with those for currently available metformin products.

The phase 2 randomized trial included 240 patients with type 2 [diabetes](#) at multiple study centers. Patients received either 600, 800 or 1,000 mg of Metformin DR once daily, blinded placebo, or unblinded Metformin XR at 1,000 or 2,000 mg per day. Patients previously on metformin (88 percent of subjects) had their metformin therapy withheld for two weeks prior to randomization.

More information: The published paper is titled "The Primary Glucose-Lowering Effect of Metformin Resides in the Gut, Not the Circulation. Results From Short-term Pharmacokinetic and 12-Week Dose-Ranging Studies," and is available at care.diabetesjournals.org/content/early/recent.

Provided by University of North Carolina Health Care

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