

Researchers link liver disease and drug metabolism

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Researchers at the University of Arizona College of Pharmacy have discovered that nonalcoholic steatohepatitis (NASH), an increasingly common but often undiagnosed liver disease, could have significant medical implications for people with type 2 diabetes.

People develop NASH when early [liver disease](#), characterized by too much fat in the [liver](#), is exacerbated by inflammation. Obesity, which is on the rise, is thought to contribute to the development of NASH. The disease has no symptoms that most people notice, and testing for it requires a [needle biopsy](#) of the liver, so it often goes undetected. Current estimates indicate that between 6 and 17 percent of Americans have NASH.

John Clarke, research associate, and Nathan Cherrington, professor, both of the college's Department of Pharmacology and Toxicology, recently published a study in the journal *Diabetes* showing that a mouse model of obesity, diabetes and NASH retained the anti-diabetic drug metformin longer than a control group of healthy mice. The study, "Mechanism of Altered Metformin Distribution in Nonalcoholic Steatohepatitis," found that NASH can change the way that drugs are eliminated from the body, potentially leading to toxic levels of metformin being retained in the body.

"This study, in addition to several of our other recent studies," Clarke says, "shows that NASH, either alone or in combination with genetic differences in drug transporters, can have a profound effect on drug

exposure."

Cherrington notes that this study is about the mechanism explaining how NASH changes the body's ability to get rid of metformin. The next step is to continue this investigation in the clinic to demonstrate the metformin-retention phenomenon in human patients with [type 2 diabetes](#). "If any clinician is going to provide precision medicine, they'll need to know the ability of the liver and kidneys to metabolize and eliminate drugs," he emphasizes.

More than 110,000 people are estimated to die each year from [adverse drug reactions](#), which is when the correct drug is given in an appropriate dose, but the patient experiences an unexpected serious adverse event. Metformin is still a relatively safe drug and effective therapy; more than 48 million prescriptions were filled for metformin in the United States in 2010. Because the study showed that patients with NASH retain metformin longer and at higher levels, leading to potential toxicity, NASH could explain some of these adverse drug reactions. This study may lead to individual treatment strategies where patients get the appropriate dose of metformin based on their ability to metabolize and eliminate the [drug](#).

More information: [diabetes.diabetesjournals.org/ ...
6/db14-1947.abstract](https://diabetes.diabetesjournals.org/.../db14-1947.abstract)

Provided by University of Arizona

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