Pill for skin disease also curbs excessive drinking, new study shows

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Researchers from Oregon Health & Science University and institutions across the country have identified a pill used to treat a common skin disease as an "incredibly promising" treatment for alcohol use disorder.

Their study was recently published in the *Journal of Clinical Investigation*.

On average, the people who received the medication, called apremilast, reduced their alcohol intake by more than half—from five drinks per day to two.

"I've never seen anything like that before," said co-senior author Angela Ozburn, Ph.D., associate professor of behavioral neuroscience in the OHSU School of Medicine and a research biologist with the Portland VA Health Care System.

The lead author is Kolter Grigsby, Ph.D., a postdoctoral fellow in the Ozburn laboratory at OHSU.

Beginning in 2015, Ozburn and collaborators searched a genetic database looking for compounds likely to counteract the expression of genes known to be linked to heavy alcohol use. Apremilast, an FDA-approved anti-inflammatory medication used to treat psoriasis and psoriatic arthritis, appeared to be a promising candidate.

They then tested it in two unique animal models that had a genetic of risk for excessive drinking, as well as in other strains of mice at laboratories across the country. In each case, apremilast reduced drinking among a variety of models predisposed to mild to heavy alcohol use. The researchers found that apremilast triggered an increase in activity in the nucleus accumbens, the region of the brain involved in controlling alcohol intake.

Researchers at the Scripps Research Institute in La Jolla, California, then tested apremilast in people.

The Scripps team conducted a double-blind, placebo-controlled clinical

proof-of-concept study involving 51 people who were assessed over 11 days of treatment.

"Apremilast's large effect size on reducing drinking, combined with its good tolerability in our participants, suggests it is an excellent candidate for further evaluation as a novel treatment for people with alcohol use disorder," said co-senior author Barbara Mason, Ph.D., Pearson Family professor in the Department of Molecular Medicine at Scripps.

The clinical study involved people with alcohol use disorder who weren't seeking any form of treatment, and Mason predicts that apremilast may be even more effective among people who are motivated to reduce their alcohol consumption.

"It's imperative for more clinical trials to be done on people seeking treatment," Ozburn said. "In this study, we saw that apremilast worked in mice. It worked in different labs, and it worked in people. This is incredibly promising for treatment of addiction in general."

An estimated 95,000 people in the United States die every year from alcohol-related deaths, according to the National Institute on Alcohol Abuse and Alcoholism.

Currently, there are three medications approved for alcohol use disorder in the United States: Antabuse, which produces an acute sensitivity akin to a hangover when alcohol is consumed; acamprosate, a medication thought to stabilize chemical signaling in the brain that is associated with relapse; and naltrexone, a medication that blocks the euphoric effects of both alcohol and opioids.

More information: Kolter B. Grigsby et al, Pre-clinical and clinical evidence for suppression of alcohol intake by apremilast, *Journal of Clinical Investigation* (2023). DOI: 10.1172/JCI159103