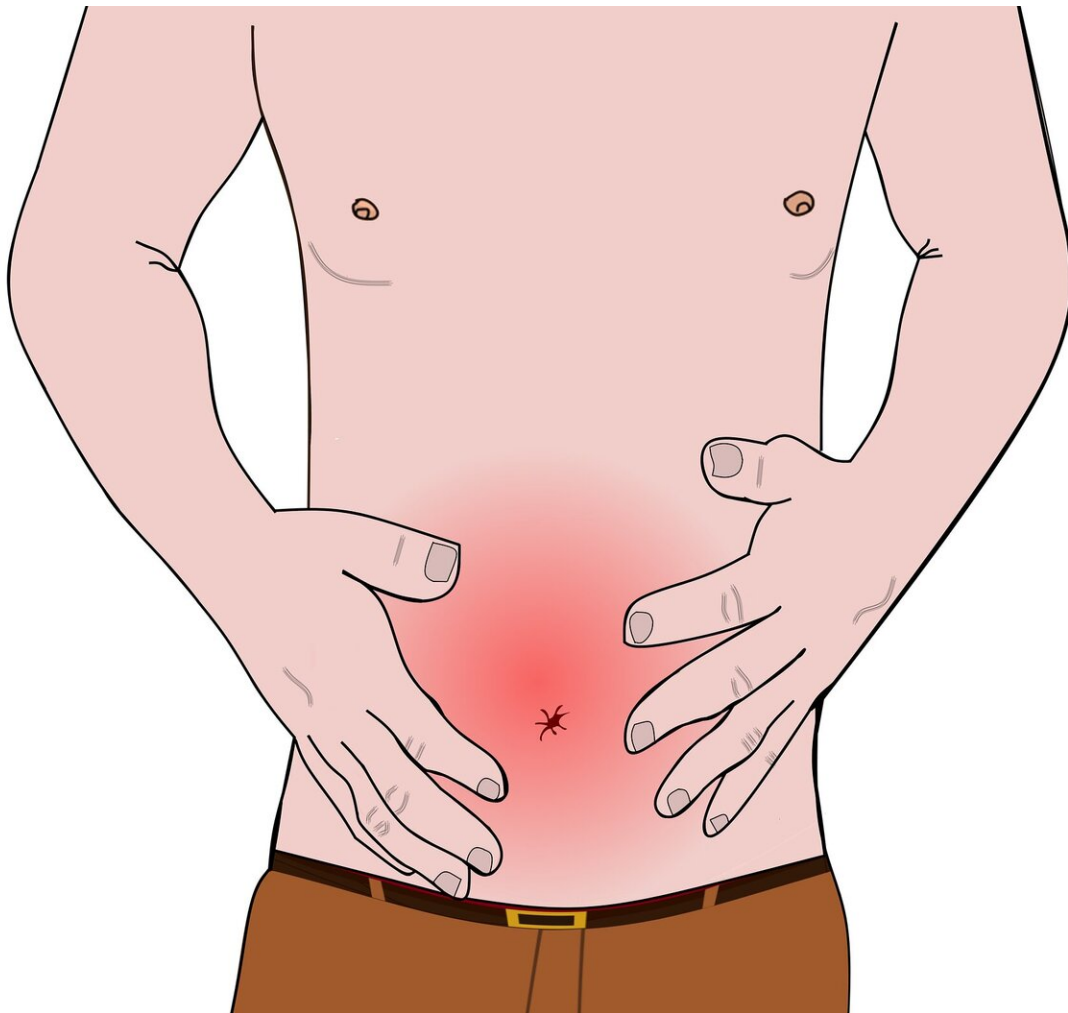


# CFTR inhibition: The key to treating bile acid diarrhea?

July 3 2019

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Estimates are that roughly 1 percent of people in Western countries may have bile acid diarrhea, including patients with Crohn's disease, ileal resection, diarrhea-predominant irritable bowel syndrome (IBS-D), and chronic functional diarrhea. Current management for bile acid diarrhea has demonstrated limited efficacy, with some therapies producing significant side effects. A recent study published in *The FASEB Journal* explored the efficacy of CFTR (cystic fibrosis transmembrane conductance regulator) inhibition to reduce excessive secretion in the colon due to bile acids.

Researchers studied cell culture models of human intestinal cells. Based on prior studies showing that chenodeoxycholic acid (CDCA) increases secretion in the colon and is linked to CFTR activation, researchers added CDCA to the cultures, which caused an increase in CFTR activity. They then added CFTR inhibitors to the cultures and used short-circuit current measurement to measure CFTR activity. Researchers found that CFTR inhibitors including investigational drug (R)-BPO-27 were able to fully block the increased CFTR activity.

"Bile acid diarrhea is a common problem for which therapeutic options are limited and often ineffective," said Alan S. Verkman, MD, Ph.D., a researcher within the Departments of Medicine and Physiology at the University of California, San Francisco. "Inhibition of chloride and fluid secretion in the intestine by a CFTR inhibitor offers a new therapeutic option to reduce diarrhea associated with excess bile acids."

Motivated by data implicating CFTR as a major determinant of bile acid secretion, the research team also tested the CFTR inhibitor in a rat model of bile acid diarrhea involving direct infusion of [bile acids](#) into the colon. Once again, (R)-BPO-27 was effective; this time, in reducing the increased stool water content.

"To see a physiologist as talented as Alan Verkman, and his colleagues,

enter this field and offer such insights is a significant advance," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*.

Provided by Federation of American Societies for Experimental Biology

Citation: CFTR inhibition: The key to treating bile acid diarrhea? (2019, July 3) retrieved 5 May 2024 from <https://medicalxpress.com/news/2019-07-cftr-inhibition-key-bile-acid.html>

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