

## New bitter blocker discovered

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Although bitterness can sometimes be desirable – such as in the taste of coffee or chocolate – more often bitter taste causes rejection that can interfere with food selection, nutrition and therapeutic compliance. This is especially true for children. Now, scientists from the Monell Center and Integral Molecular describe the discovery of a compound that inhibits bitterness by acting directly on a subset of bitter taste receptors.

"Bitter taste is a major problem for pediatric drug compliance and also for proper nutrition, such as eating those healthy but bitter green vegetables," said Monell senior author Paul Breslin, Ph.D., a sensory biologist. "But we currently have very limited ways to effectively control bitter taste."

Bitterness is detected by a family of approximately 25 different taste receptors called TAS2Rs. Together, the TAS2Rs respond to a broad array of structurally different compounds, many of which are found in nature and can be toxic.

Discovery of bitter blockers would help scientists understand the signaling mechanisms of these receptors and promote the design of novel and more effective blockers.

Monell and Integral Molecular are collaborating on a large project to understand the structure and function of TAS2Rs. In a serendipitous discovery, the researchers found that probenecid, a molecule frequently used in receptor assays, is an inhibitor of a subset of bitter taste receptors. Probenecid also is an FDA-approved therapeutic for gout.



In the study, published in *PLoS ONE*, a series of in vitro studies revealed that probenecid does not physically block interaction of bitter molecules with the receptor's primary binding site. Rather, it appears to bind elsewhere on the receptor to modulate the receptor's ability to interact with the bitter molecule.

"Probenecid's mechanism of action makes it a useful tool for understanding how bitter receptors function," said Integral Molecular senior author Joseph B. Rucker, Ph.D. "This knowledge will help us develop more potent bitter taste inhibitors."

A series of human sensory studies established that probenecid robustly inhibited the bitter taste of salicin, a compound that stimulates one of the target receptors.

"This demonstrates how we can take in vitro experiments and go on to show how they make a difference functionally and perceptually," said Breslin.

Additional studies will continue to explore the structure and function of TAS2Rs. The overall goal is to identify the regions of the receptors that contribute to bitter molecule binding and how binding events lead to signaling events within the cell.

Understanding modulation of bitter receptor function may have additional implications for the respiratory and gastrointestinal systems, as bitter taste receptors also are expressed in the nose, the lungs and the intestines.

Provided by Monell Chemical Senses Center

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