

Beer's bitter delight is tasted in the gut

September 26 2018, by Bradley J. Fikes, The San Diego Union-Tribune



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Hoppy beers are famous as a driver of craft brewing. But the challenging taste of hops goes far beyond the palate. According to a new study from Scripps Research scientists, the bitter flavor literally reaches into your gut.

Moreover, chemicals in hops called isohumulones may help control



obesity, type 2 diabetes and other diseases.

Intestinal taste receptors detect isohumulones, according to the study. While the work was performed in mice and needs to be confirmed in humans, it's already known that people also have taste receptors in their gut.

Previous research indicates that intestinal taste receptors influence the production of hormones as well as appetite, said Enrique Saez, a Scripps Research associate professor. And hops extracts have been shown to reduce weight gain and decrease insulin resistance.

So the study fills a gap in research between the observed effects of <u>hops</u> extracts and the chemicals and molecular mechanism causing the effects, Saez said.

The study was recently published in the journal Molecular Metabolism.

Isohumulones are being studied by Seattle's KinDex Pharmaceuticals as therapy for metabolic diseases such as Type 2 diabetes and <u>polycystic</u> <u>ovary syndrome</u>. The company is studying the compounds in people under the name KDT501.

KinDex asked Saez and associates to study isohumulones to better characterize what they do. With that knowledge, KinDex could optimize the drugs, said Saez. He is on the KinDex advisory board with colleagues Paul Schimmel and Ben Cravatt.

"We were quite surprised when reviewing the literature," Saez said. "It turned out that these <u>taste</u> receptors are expressed not only in the mouth, but also in the gut, the airway epithelia, the liver, and some other organs."



These <u>receptors</u> appeared to have evolved as protection against eating bitter substances, which are often poisonous, Saez said.

Isohumulones work indirectly. They stimulate release of a hormone called glucagon-like peptide-1, or GLP-1, that works with insulin to decrease <u>blood sugar levels</u>, he said. The chemicals also promotes satiety.

"It makes you feel fuller, and other hormones that this <u>bitter taste</u> <u>receptor</u> also regulates limit the absorption of nutrients in the gut," he said. "So in effect it probably limits absorbing these potentially poisonous compounds."

A mimic of GLP-1 was developed by San Diego's Amylin Pharmaceuticals as a diabetes medication, exenatide. It was discovered in an unlikely place, the saliva of the Gila monster.

The drug is sold as Byetta and in extended release form as Bydureon. It was attractive enough that Amylin was purchased for \$7 billion by Bristol-Myers Squibb in 2012.

However, exenatide must be injected, limiting its usefulness, Saez said.

"Isohumulones are small molecules that you can eat," he said.

More information: Bernard P. Kok et al. Intestinal bitter taste receptor activation alters hormone secretion and imparts metabolic benefits, *Molecular Metabolism* (2018). DOI: 10.1016/j.molmet.2018.07.013

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Citation: Beer's bitter delight is tasted in the gut (2018, September 26) retrieved 8 May 2024 from <u>https://medicalxpress.com/news/2018-09-beer-bitter-gut.html</u>

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