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Small intestine can sense and react to bitter toxins in food

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Toxins in food often have a bad, bitter taste that makes people want to spit them out. New UC Irvine research finds that bitterness also slows the digestive process, keeping bad food in the stomach longer and increasing the chances that it will be expelled.

This second line of defense in the gut against dietary toxins also triggers the production of a hormone that makes people feel full, presumably to keep them from eating more of the toxic food.

This discovery has the potential to help scientists develop better therapies for ailments ranging from cancer to diabetes, and it may explain why certain isolated populations around the world have adapted to eat and enjoy local foods that taste bad to outsiders and make them sick.

The study, appearing online Oct. 9 in the *Journal of Clinical Investigation,* was performed with mice, and the results probably translate to humans, said Timothy Osborne, molecular biology and biochemistry professor and study senior author.

"We have evolved mechanisms to combat the ingestion of toxins in our food," Osborne said. "This provides a framework for an entirely new area of research on how our bodies respond to what is present in our diets."

Mammals have evolved to dislike the bitter taste of toxins in food. This

response is particularly important when they eat a lot of plant material, which tends to contain more bitter-tasting, potentially toxic ingredients than meat.

Examples of bitter-tasting toxins include phenylthiourea, a compound that destroys the thyroid gland, and quinine, found in tonic water, which can be deadly in large doses.

If toxins are swallowed, bitter-taste receptors in the gut sense them and trigger the production of a hormone called cholecystokinin that both suppresses appetite and slows the movement of food from the stomach to the small intestine.

Interestingly, the UCI scientists found that cholesterol regulates the activity of bitter-taste receptors in the intestine, and diets high in plant material and potential toxins naturally are low in cholesterol, compared to low-toxin, high-cholesterol, meat-based diets.

In small intestine cell cultures, low levels of cholesterol triggered a stronger receptor response – meaning they worked better – while high levels caused a weaker response.

The same response was observed in mice that were given drugs to stop the production and absorption of cholesterol. Not only were their receptors more active, their small intestine cells produced two to three times the amount of the appetite-suppressing hormone in the presence of bitter food, compared to normal mice.

Scientists say that regulation of taste receptors by dietary constituents likely explains why groups of people taste certain foods differently.

"One group of people may think something tastes great and can metabolize it just fine, but a group from the outside may think it tastes

horrible and get sick," Osborne said. "The first group likely adapted to the food through a change in the expression and pattern of their dietary sensing molecules."

With this knowledge, scientists could make medicines less bitter, which in turn would allow for increased palatability and quicker absorption. Drugs used to treat cancer sometimes include molecules that taste bitter. Also, changing the patient's eating habits could improve the effectiveness of such drugs.

In addition to the appetite-suppressing hormone, bitter-taste receptors in the gut activate the production of glucagon-like peptide 1, a protein that stimulates insulin secretion in the pancreas. Drugs currently are on the market that attempt to stabilize this protein in people with diabetes, and therapies aimed at increased production are attractive therapeutic targets.

"Because bitter-taste receptors are expressed in the gut, a new avenue exists to identify ways to stimulate production of GLP-1," Osborne said. "It could be very beneficial for the treatment of diabetes and possibly other diseases."

Source: University of California - Irvine