Clinical Summary

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Lu P, Zhang CH, Lifshitz LM, ZhuGe R. Extraoral bitter taste receptors in health and disease. J Gen Physiol 2017;149(2):181-197.

Bitter Taste Signaling is a Whole Body Health Event

For centuries, bitter foods have been considered beneficial to health. Only recently was it discovered that bitter 'taste' receptors are present not only on the tongue but also in organs throughout the body. This review summarizes research on the immunometabolic impacts of bitter principles and how genetic polymorphisms in bitter receptors may influence health.

For sweet, salty, sour, and umami flavors, the tongue has only one type of receptor. For bitter compounds, the human tongue possesses at least 25 different chemoreceptors—and most of these bitter receptor types have multiple genetic variants, resulting in considerable individuality in responsivity to bitter substances. Though our understanding of bitter receptor function is limited, bitter receptors may have evolved as a means of discouraging the ingestion of toxins. However, their presence in many non-oral tissues and functional variability suggests that their significance to health goes far beyond taste perception.

Bitter 'taste' receptors have been found in immune cells, the brain, airways, skin, liver, kidneys, testes, ovaries, nasal sinuses, heart, thyroid gland, bones, breasts, pancreatic beta cells, and intestines. For this reason, bitter receptors may be useful molecular targets in immune, metabolic, and endocrine conditions.

In this review, the authors detail mechanisms through which bitter receptor ligands may impact innate immunity, digestive secretion, thyroid hormone production, smooth muscle contraction, the glycemic response, and other diverse functions. They also describe genetic polymorphisms in bitter receptors and their health effects in humans and animals.

T2Rs are type II taste receptor cells, or bitter taste receptors, and they are a member of the G protein-coupled receptor family known to modulate biological responses.

According to the authors, "T2R agonists can inhibit the release of proinflammatory cytokines and eicosanoid release from blood leukocytes."

Review Highlights

Among many bitter receptor activities noted in this review, we highlight the following:

- Bitter receptors are G protein-coupled receptors, a family of receptors that are the target of many medications. Though bitter receptor function is only now being elucidated, many pharmacologic actions may take place through interacting with these chemosensors.
- The authors cite research suggesting that bitter receptor signaling contributes to the innate immune barrier function of the skin, airways, and digestive epithelium.
- Neutrophils appear to express several bitter receptors, and in concert with other signaling inputs, these interactions can result in increased or decreased neutrophil migration.
- Body mass index has been found to correlate significantly with immune reactivity in colonic mucosal cells expressing the T2R38 receptor, as yet the most widely researched bitter receptor.
- Bitter receptors may be involved in clearing surface microorganisms and limiting bacterial biofilm formation. In human sinus epithelium, activation of the T2R38 bitter receptor generates nitric oxide as a local bactericide.
- Bitter receptors have been discovered in multiple brain structures, and some bitter molecules are able to cross the blood-brain barrier.
- Genetic expression of particular bitter receptors has been linked to risk for Parkinson's disease, schizophrenia, and possibly also for breast cancer.
- Bitter receptor polymorphisms have been found to modify risk for altered glucose and insulin metabolism, cardiovascular disease, colorectal cancer, rhinosinusitis, infection with gram-negative bacteria, gingivitis, and dental caries.
- Gut protection from parasitic infection may be partly orchestrated by bitter receptor responses.
- Bitter herbal constituents can trigger secretion of glucagon-like peptide-1 (GLP-1), with potential beneficial implications for glycemic response, fat metabolism, and appetite.
- In preclinical experiments, bitter compounds have been seen to dose-dependently relaxed contracted airways and to influence ciliary motion along airways.
- In severe asthma, leukocyte bitter receptors have been found to be upregulated, and bitter receptor ligands may help limit their cytokine release.
- In aortic and pulmonary muscle, bitter receptor ligands have shown relaxant effects. Cardiac muscle cells express at least five bitter receptors, and bitter compounds have been found to influence aortic, systolic, and ventricular blood pressures.

- In small intestinal enteroendocrine cells, bitter receptor activation can stimulate multidrug resistance proteins (phase III detoxification enzymes) to actively pump out bitter toxins.
- In human and animal thyroid cells expressing bitter receptors, their activation can alter thyroid hormone secretion.
- In preclinical studies, various bitter receptor ligands have been seen to relax or contract urinary smooth muscle, with implications for functional bladder conditions.
- Genetic variants in bitter receptors may possibly even influence lifespan, though early study results need confirmation in larger populations.

NUTRITION CONCLUSION

Bitter is more than just a taste. Bitter 'taste' signaling is a crucial body-wide messaging system that may affect immune balance and metabolic regulation as well as organ function and disease risk. Bitter compounds from foods and other sources hold significant therapeutic potential, and regular consumption of bitter plants may be an important nutritional consideration.