Herbal bitters:
For Cardiovascular disease and diabetes

PRACTITIONERS CALL

JANUARY 19TH 2019

GLEN NAGEL, ND

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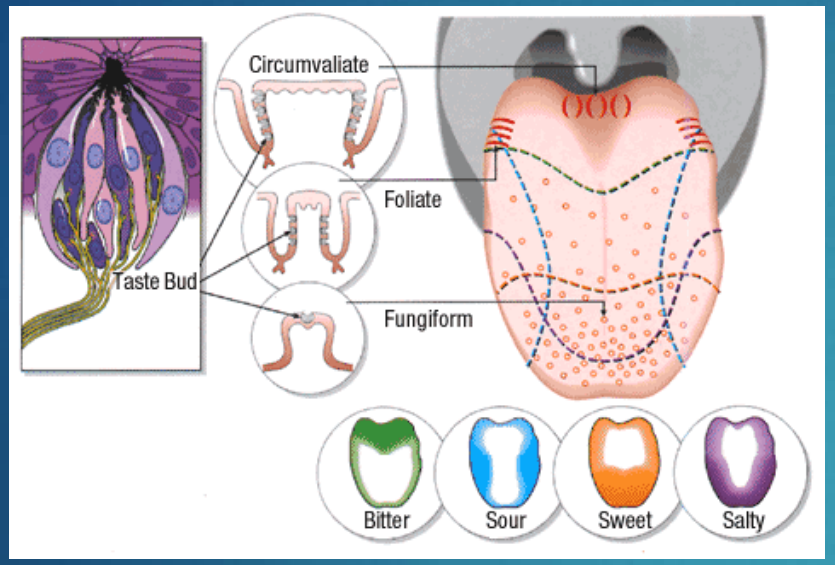
Glen Nagel, ND, RH (AHG)

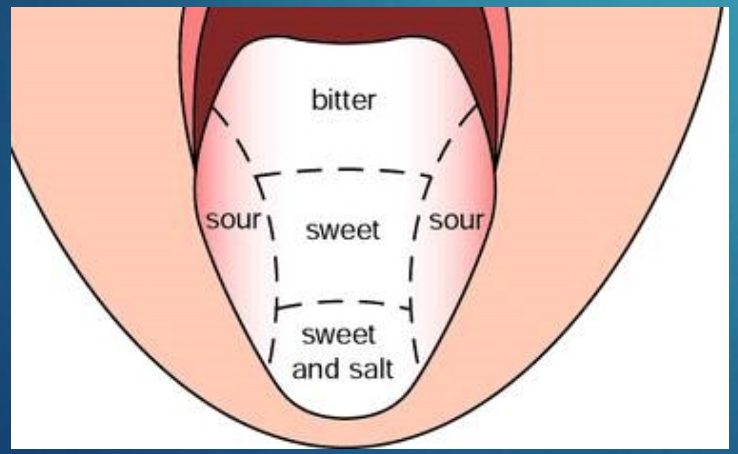
- Herbalist since 1984, Registered Herbalist with American Herbalist Guild.
- Former Associate Professor of Botanical Medicine with National College of Natural Medicine in Portland, Oregon.
- Former Assistant Professor at Bastyr University, in Kenmore Washington
- Consultant to the herbal industry and adjunct professor at NUNM in Portland, Oregon.

Is there a bitter deficiency syndrome?

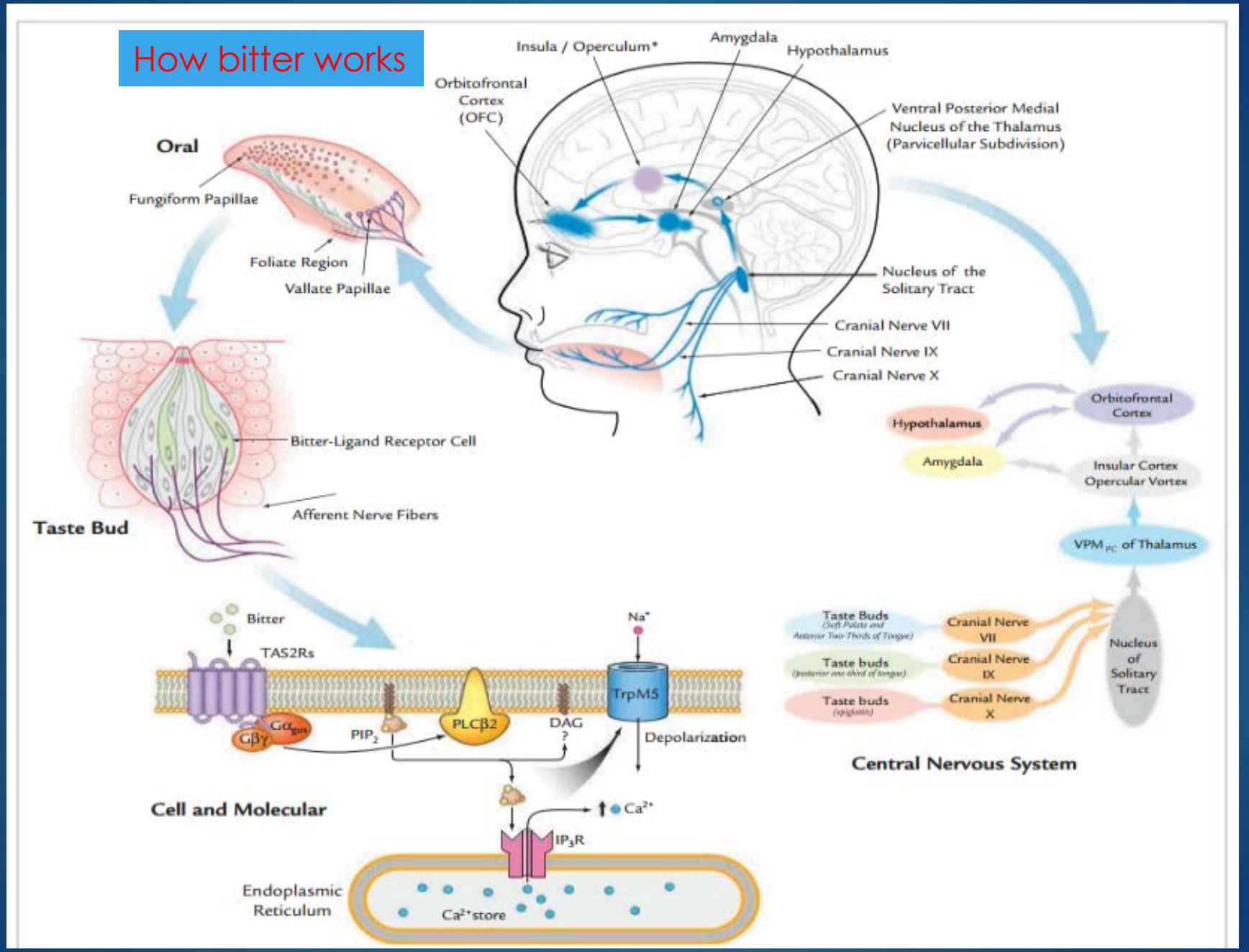
- Loss of bitter foods in modern diet
- Aversion to bitter with increasing obesity
- Increase in metabolic syndrome
- Increase in alcoholism
- Increase in type 2 diabetes
- Increase in food consumption
- Increase in thyroid dysfunction
- How do bitters effect health ?
- Is there a wider role for bitters in supporting health ?

The Five Basic Tastes





How bitter works



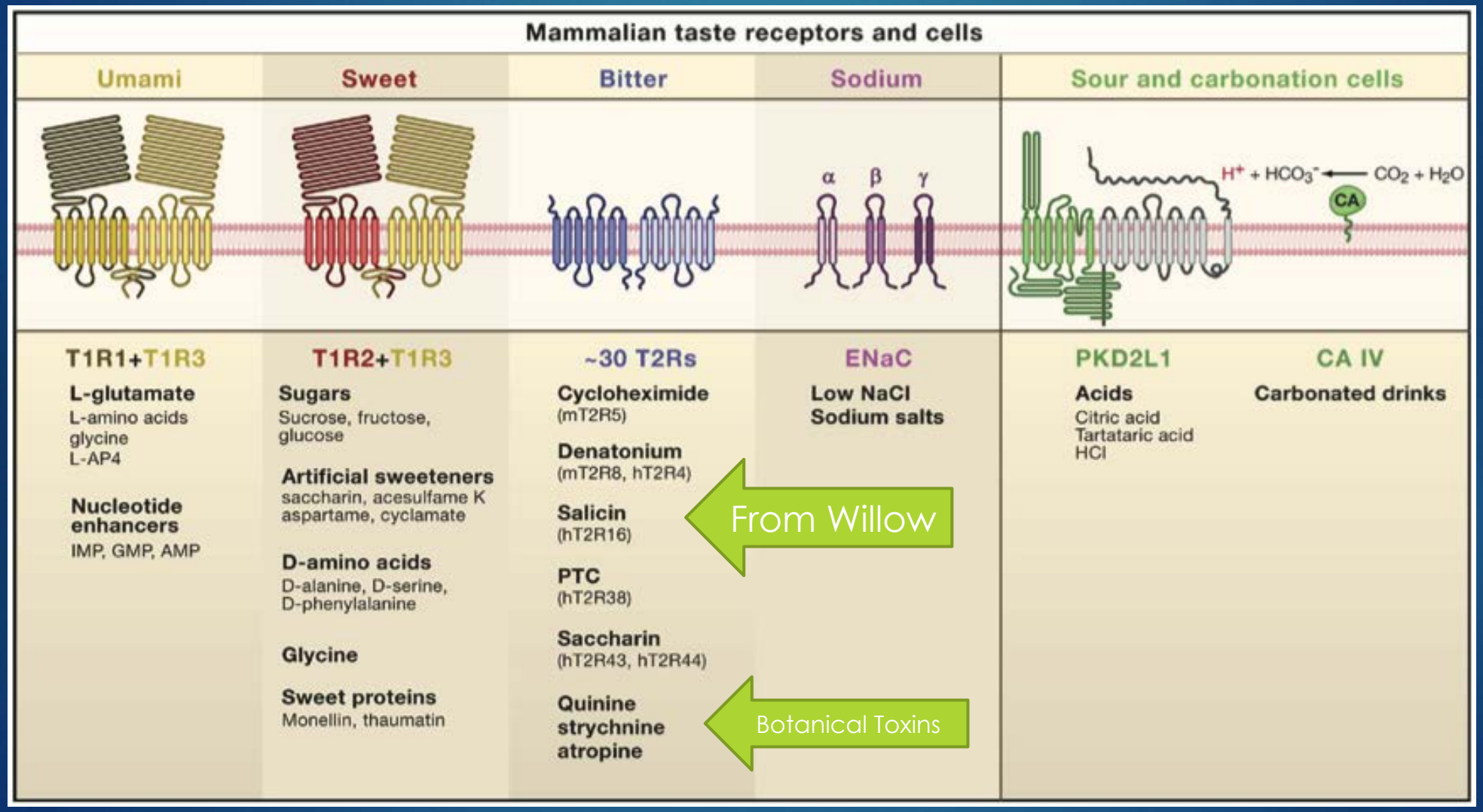
Clinical Therapeutics/Volume 35, Number 8, 2013

How bitter works?

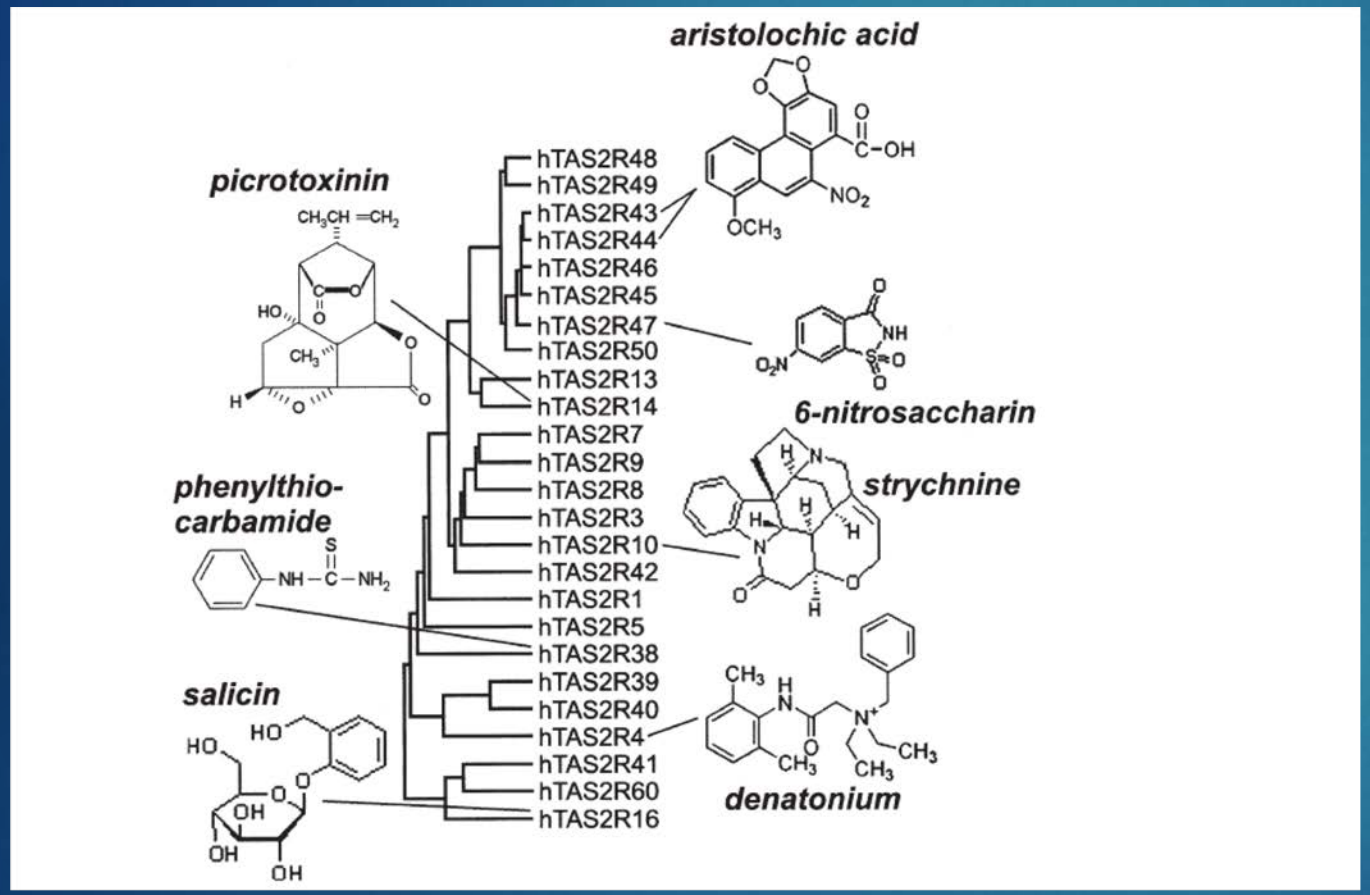
- The bitter taste starts when a bitter compound enters the oral cavity, where the ligand binds to a T2R G protein–coupled receptor (TAS2R) expressed in the apical membrane of receptor cells found in taste buds, triggering a cascade of signaling events, leading to the release of neurotransmitter that activates an afferent nerve fiber that transmits the signal via the cranial nerve to the brain.
- Taste buds are distributed in distinct fields in the oral, pharyngeal, and laryngeal epithelia, with each field innervated by a different cranial nerve branch.
- Taste receptors have also been identified in a variety of non gustatory tissues, such as the gut, where they have been proposed to play a role in nutrient and toxin sensing.
- The taste signals course through the brain and provide input to circuits that sub serve various functions, such as motor and physiological reflexes, discriminative perception, and affective processing.

Clinical Therapeutics/Volume 35, Number 8, 2013

Many types of Mammalian Taste Receptors



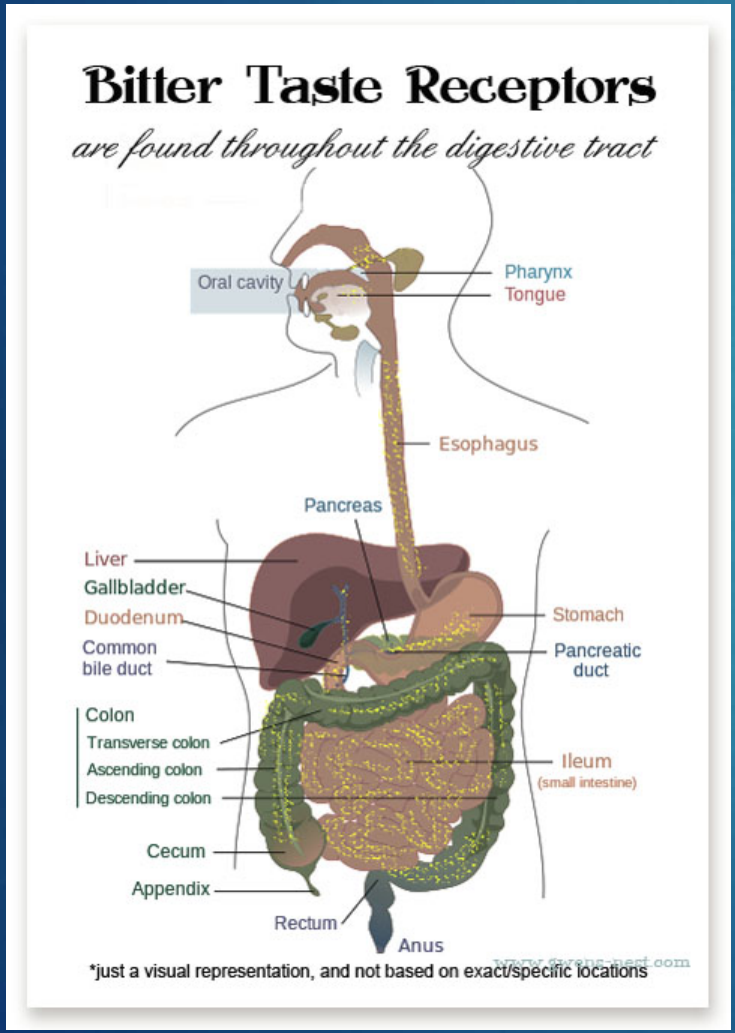
Bitter receptors



- Agonist for human bitter taste receptors are structurally diverse
- Individual bitter agents stimulate specific bitter receptors.

Cellular and Molecular Life Sciences 63: 1501-1509, 2006

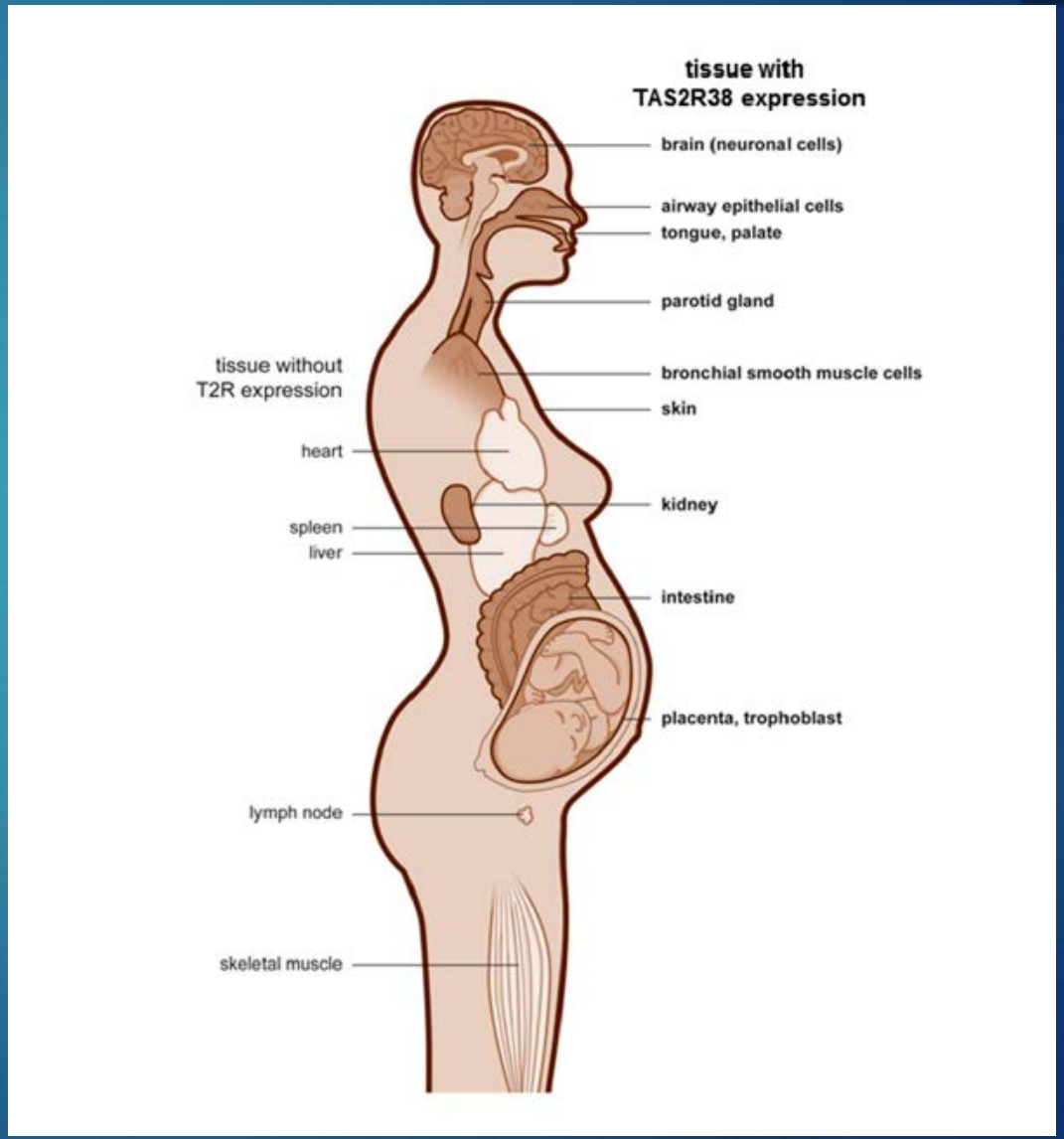
Bitter receptors are found all over the body



- Old thought was that bitter receptors were on the back of the tongue only
- Now we know bitter receptors are found all over the digestive tract and beyond
- Recent research has found them in the lungs, bronchi and in the placenta and thyroid gland
- Bitters receptors seem to be important to humans!

HUMAN TISSUE EXPRESSING TAS2R38 RECEPTORS

Conclusion: We could show for the first time that the taste receptor TAS2R38 is expressed and functionally active in placental tissues, namely in the syncytiotrophoblast and in the amnion both of which protect the embryo. Therefore, apart from the prevention of toxic food intake, TAS2Rs might play a general role in the communication with environmental factors and the protection of the body against the environment.



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F1000Reports
BIOLOGY

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Taste isn't just for taste buds anymore

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Taken together, the findings suggest that the taste transduction cascade is not restricted to taste per se or even to systems regulating food intake. The receptors mediating taste transduction evolved early in the vertebrate lineage, and were adopted widely as a **chemodetection system** in a variety of organ systems. Questions still remain as to what the natural ligands are for many of the nongustatory functions of the "taste" transduction system

Herbal bitters: A long history of Use

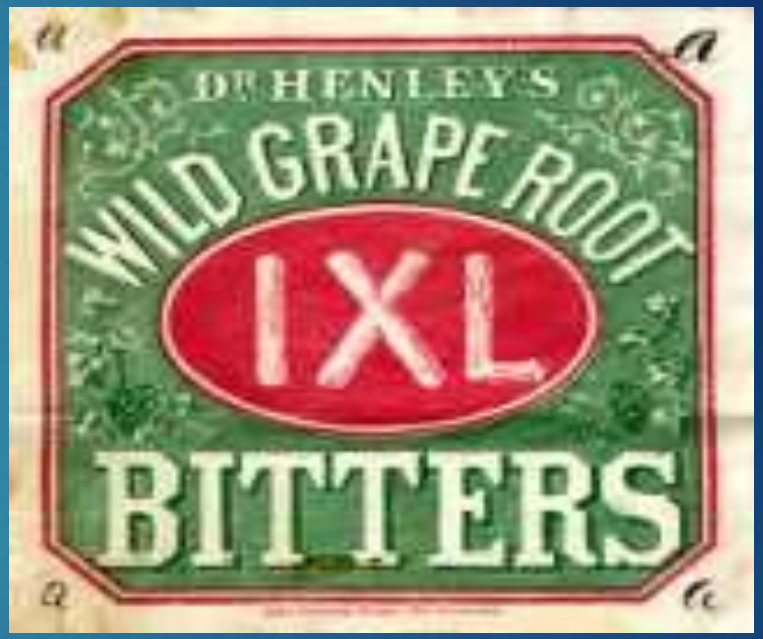
- Has a long historical use as medicine and drinks
- Any plant that tastes bitter is bitter
- Many herbal drinks are bitter
- Many bitters are also classified as a tonic.
- You know when it is bitter !
- Rediscovered recently in food and medicine.
- Many new studies on the action of bitters and effects on physiology.

Aperitif , digestif and bitters

- **Apéritifs** and **digestifs** are drinks, typically alcoholic, that are normally served before (apéritif) or after (digestif) a meal.
- Apéritif may also refer to a snack that precedes a meal. This includes, chocolate, crackers, cheese, pâté or olives.
- "Apéritif" is a French word derived from the Latin verb *aperire*, which means "to open." The French slang word for aperitif is "apro."
- Bitters are botanical drinks that are bitter and are often used as Aperitifs or Digestifs to support digestion.

Historical Sayings about bitters

- Sweet to the taste buds, bitter to the stomach
- Bitter to the tongue, then sweet to the stomach
- The bitters are a tonic for all digestion and especially promote acid secretion



Traditional indications for bitters

- Loss of appetite, low HCL
- Indigestion, bloating, gas
- Nausea, diarrhea, constipation
- Abdominal distention
- Malnutrition, malabsorption
- Weakness, pale skin with edema
- Yellow or white tongue coating
- Atonic digestion and elimination
- Depression and or mood disorders
- Digestive issues that come with aging.

Traditional contra-indications of bitters

CONTRA-INDICATIONS

- Avoid in cases of acute GI inflammation, irritation
- Avoid in pregnancy
- Avoid in children under 5

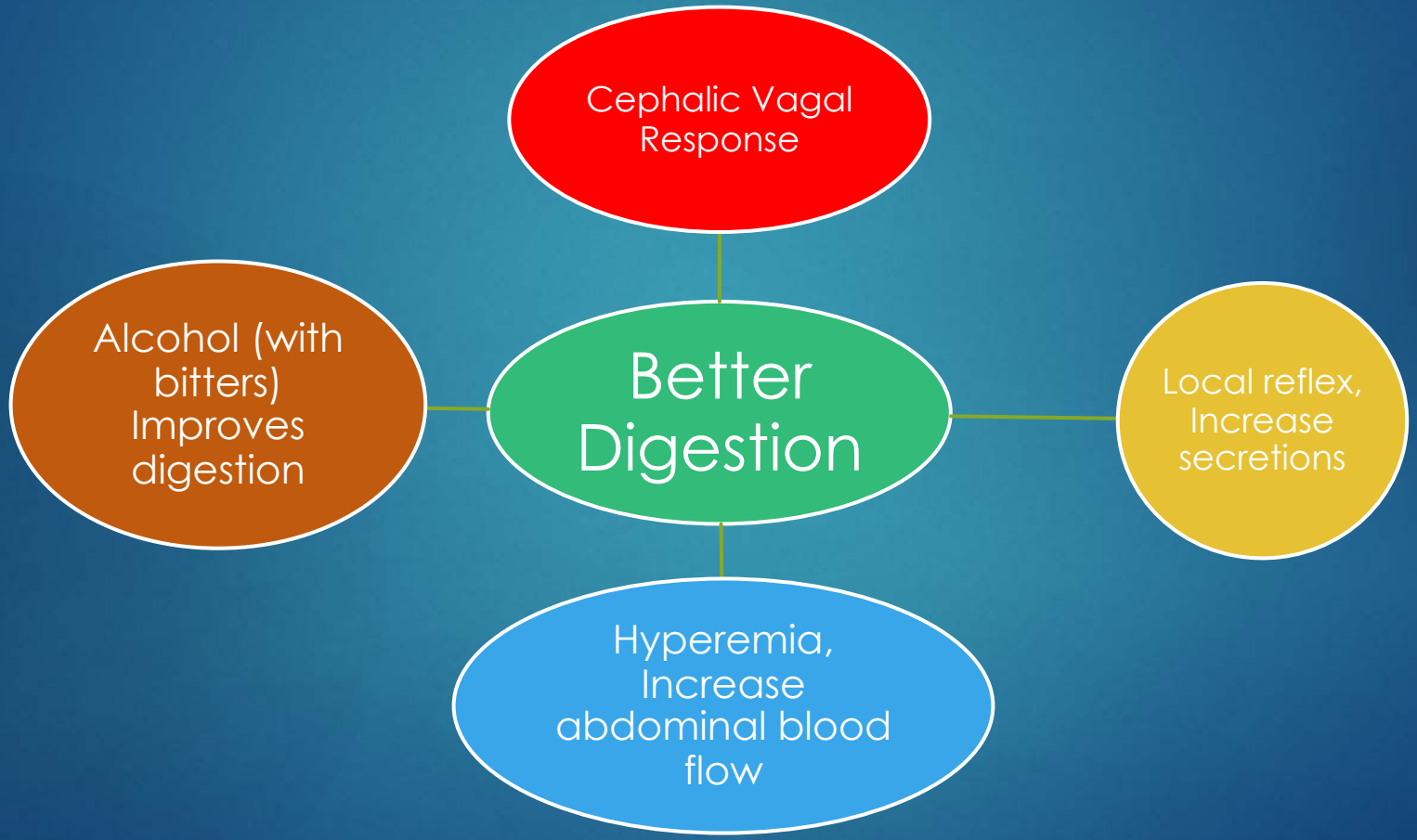
Types of Herbal bitters

- *True bitters: Only bitter*
- *Centaurium umbellatum*
- *Gentiana lutea*
- *Hydrastis canadensis*
- *Mahonia aquifolium*
- *Aloe spp. Bitter Aloe*
- *Eupatorium perfoliatum*
- *Menyanthes trifoliata*
- *Cinchona bark*
- *Quassia bark*

- Aromatic bitters: bitter with flavor
- *Artemisia absinthium*
- *Achillea millefolium*
- *Humulus lupulus*

- Nutritional bitters with Prebiotics
- *Taraxacum*
- *Articum*
- *Inula*
- *Angelica*
- *Cynara*

Current summary of how bitters Improve digestion



New bitter concepts

- The bitter receptors TR2 a family of G protein coupled receptors
- Can sense over 100 types of bitters based on testing
- Can have effects without tasting the bitterness
- Chronic inflammation can over express TR2 receptors leading to adverse response to bitters
- The bitters stimulate natural incretins and hence stimulate insulin and lower glucose
- The bitters may act directly as endocrine triggers, by passing the CNS
- Stimulate Hyperemia increasing GI blood flow
- The bitter may lead to less obesity and improve metabolic syndrome via increase fullness, and hormone stimulation
- Lack of bitter sensitivity may contribute to alcoholism

New actions for bitters

- Blood Sugar Support
  - Incretin effect
  - Probiotics from bitter herbs
- Cardiovascular effects
  - Lipid Moderating
  - Metabolic syndrome
- Supports decrease craving for alcohol
- Thyroid Balance
  - The bitter receptors found in thyrocytes
  - Can block or enhance TSH production
- Vascular effect Increase gut circulation, increase BP
- Neuronal effects
  - Stimulate endocrine hormones via gut
  - Improved digestion , absorption
  - Appetite stimulant , but increase satiety and weight loss
- Chronic Inflammation
  - Pro inflammatory compounds serve to over express T2Rs, Leading to adverse bitter response
  - The bitters can down regulate Tumor Necrosis factor receptors

Research on bitters

OPEN ACCESS Freely available online

PLoS one

Bitter Taste Receptors Influence Glucose Homeostasis

Cedrick D. Dotson[1], Lan Zhang[2], Hong Xu[2], Yu-Kyong Shin[3], Stephan Vigues[1], Sandra H. Ott[4], Amanda E. T. Elson[1], Hyun Jin Choi[1], Hillary Shaw[4], Josephine M. Egan[3], Braxton D. Mitchell[4], Xiaodong Li[2], Nanette I. Steinle[4], Steven D. Munger[1]*

1 Department of Anatomy & Neurobiology, University of Maryland School of Medicine, Baltimore, Maryland, United States of America, **2** Senomyx, Inc., San Diego, California

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receptor negatively impacts glucose homeostasis, providing an important link between alimentary chemosensation and metabolic disease.

TAS1R- and TAS2R-type taste receptors are expressed in the gustatory system, where they detect sweet- and bitter-tasting stimuli, respectively. These receptors are also expressed in subsets of cells within the mammalian gastrointestinal tract, where they mediate nutrient assimilation and endocrine responses. These findings suggest that a functionally compromised TAS2R receptor negatively impacts glucose homeostasis, providing an important link between alimentary chemosensation and metabolic imbalance.

Gut microbiota fermentation of prebiotics increases satietogenic and incretin gut peptide production with consequences for appetite sensation and glucose response after a meal[1–3]

Patrice D Cani, Elodie Lecourt, Evelyne M Dewulf, Florence M Sohet, Barbara D Pachikian, Damien Naslain, Fabienne De Backer, Audrey M Neyrinck, and Nathalie M Delzenne

ABSTRACT

Background: We have previously shown that gut microbial fermentation of prebiotics promotes satiety and lowers hunger and energy intake in humans. In rodents, these effects are associated with an increase in plasma g
appetite regulation a
Objective: Our aim
mentation on satiety
human volunteers b
sampling to measure
Design: This study w
controlled trial. A to
were randomly assi
biotics/d or 16 g dext
performed in the mo
test, satiety, glucose homeostasis, and related hormone response.
Results: We show that the prebiotic treatment increased breath-hydrogen excretion (a marker of gut microbiota fermentation) by ≈3-fold and lowered hunger rates. Prebiotics increased plasma glucagon-like peptide 1 and peptide YY concentrations, whereas postprandial plasma glucose responses decreased after the standardized meal. The areas under the curve for plasma glucagon-like

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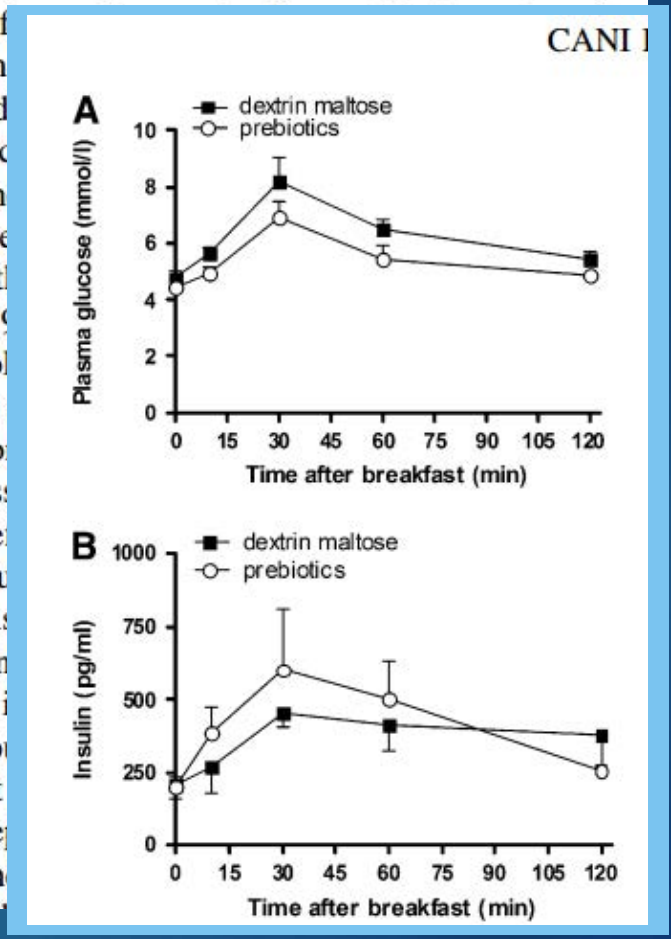
Together with recent findings by others provide evidence that prebiotics could be a useful tool for controlling food intake and glucose homeostasis and promising agents for maintaining or restoring both glucose and energy homeostasis.



Am J Clin Nutr 2009;90:1236–43

Published in final edited form as:

Curr Opin Investig Drugs. 2010 April ; 11(4): 447–454.

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Taste

Incretin hormones are released from the intestines upon nutrient ingestion and contribute to glucose homeostasis in part by promoting insulin secretion from the pancreas. Drugs that enhance the incretin response have emerged as effective treatments for T2DM. Several recent studies have revealed that incretin secretion from enteroendocrine cells in the intestines can be modulated by the T1R (sweet and umami)and T2R (Bitter) receptors, proteins that have been demonstrated to function as taste receptors.

Abstract

Type 2 diabetes mellitus (T2DM), which is characterized by insulin and glucose dysregulation, is a major contributor to the development of cardiovascular disease, renal failure and premature death. Incretin hormones are released from the intestines upon nutrient ingestion and contribute to glucose homeostasis in part by promoting insulin secretion from the pancreas. Drugs that enhance the incretin response have emerged as effective treatments for T2DM. Several recent studies have revealed that incretin secretion from enteroendocrine cells in the intestines can be modulated by T1R and T2R receptors, proteins that have been demonstrated to function as taste receptors. This review focuses on the intriguing finding that taste receptors may be involved in modulating the incretin response, and considers T1Rs and T2Rs as potential targets for new hypoglycemic drugs.

Nutrition, Metabolism & Cardiovascular Diseases (2016) **26**, 293–301

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Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

Gentiana lutea exerts anti-atherosclerotic effects by preventing endothelial inflammation and smooth muscle cell migration

R. Kesavan [a,1], S. Chandel [a,1], S. Upadhyay [a,1], R. Bendre [a], R. Ganugula [b], U.R. Potunuru [a], H. Giri [a], G. Sahu [a], P. Uday Kumar [b], G. Bhanuprakash Reddy [b], G. Joksic [c], A.K. Bera [a], Madhulika Dixit [a,*]

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KEYWORDS
Atherosclerosis;
Gentiana lutea;
Isovitexin;
Endothelial inflammation;
Smooth muscle cell;
PLC-γ;
ROS

Abstract *Background and aims:* Studies suggest that *Gentiana lutea* (GL), and its component isovitexin, may exhibit anti-atherosclerotic properties. In this study we sought to investigate the protective mechanism of GL aqueous root extract and isovitexin on endothelial inflammation, smooth muscle cell migation, and on the onset and progression of atherosclerosis in streptozotocin (STZ)-induced diabetic rats.
Methods and results: Our results show that both GL extract and isovitexin, block leukocyte adhesion and generation of reactive oxygen species in human umbilical vein endothelial cells (HUVECs) and rat aortic smooth muscle cells (RASMCs), following TNF-alpha and platelet derived growth factor-BB (PDGF-BB) challenges respectively. Both the extract and isovitexin blocked TNF-α induced expression of ICAM-1 and VCAM-1 in HUVECs. PDGF-BB induced migration of RASMCs and phospholipase C-γ activation, were also abrogated by GL extract and isovitexin. Fura-2 based ratiometric measurements demonstrated that, both the extact, and isovitexin, inhibit PDGF-BB mediated intracellular calcium rise in RASMCs. Supplementation of regular diet with 2% GL root powder for STZ rats, reduced total cholesterol in blood. Oil Red O staining demonstrated decreased lipid accumulation in aortic wall of diabetic animals upon treatment with GL. Medial thickness and deposition of collagen in the aortic segment of diabetic rats were also reduced upon supplementation. Immunohistochemistry demonstrated reduced expression of vascular cell adhesion molecule-1 (VCAM-1), inducible nitric oxide synthase (iNOS), and vascular endothelial cadherin (VE-cadherin) in aortic segments of diabetic rats following GL treatment.
Conclusions: Thus, our results support that GL root extract/powder and isovitexin exhibit anti-atherosclerotic activities.

Abstract: Our results support that GL root extract / powder and isovitexin exhibit anti atherosclerotic activities.

Dosing bitters

- Generally small doses , repeated frequently
- 15-30 drops of extract, or 0.5-1.0 ml
- Larger doses may improve action , but increase slowly
- Before meals or after
- Present to the taste buds as tea or extract
- Capsule and tablet of bitters have been found to be useful for GI tract bitter receptors and general systemic effects

Take the 30 day bitter Challenge !

- To improve your digestion and overall health take the 30 day bitter challenge.
- Find a bitter formula, herb or combination that has one of the true bitters or Eupeptic Bitters.
- Take 10-30 drops of the bitter before meals, ideally 10 minutes, or after meals
- Take enough to get strong bitter sensation and " bitter shudder"
- Continue for 30 days, moving the dose up or down depending on reaction
- Assess your health before or after.

Summary: New herbal bitter

Bitter Tonic

Promotes normal healthy appetite and digestion

- **<u>Ingredients:</u>**
- *Gentiana lutea* (gentian)
- *Pimpinella anisum* (anise)
- *Zingiber officinale* (ginger)
- Anise essential oil

Bittersweet Elixir

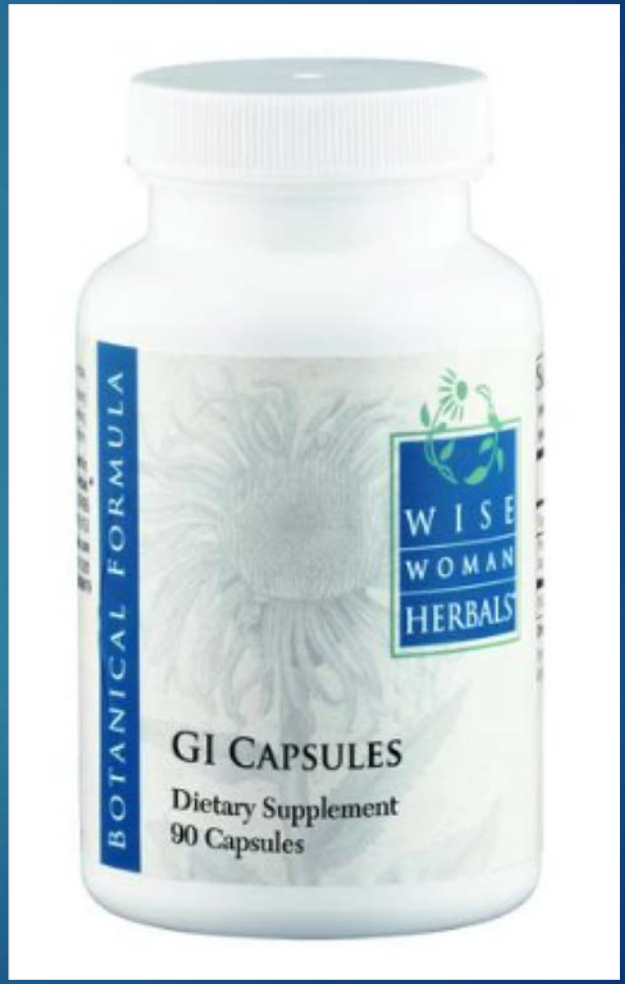
Promotes normal healthy appetite and digestion without a strong bitter taste

- **Ingredients**:
- *Taraxacum officinale* (dandelion root)
- *Gentiana lutea* (gentian)
- *Inula helenium* (elecampane)
- *Foeniculum vulgare* (bitter fennel)
- *Zingiber officinale* (ginger)
- *Curcuma spp.* (turmeric)
- *Ulmus spp.* (slippery elm)
- Fennel essential oil
- Base:
  - Mountain spring water
  - Honey
  - 20% organic alcohol

GI Capsules

Promotes normal healthy integrity and function of the gastrointestinal tract.

- ** Based on Robert's Formula from the 19th century.*
- **Ingredients:**
- *Althaea officinalis* (marshmallow)
- *Geranium maculatum* (cranesbill)
- *Echinacea purpurea* (echinacea)
- *Ulmus spp.* (slippery elm)
- *Curcuma spp.* (turmeric)
- *Hydrastis canadensis* (goldenseal)
- 100% vegetarian capsules



Digest Tea

Refreshing beverage that soothes and supports normal healthy digestive function.

- **Ingredients:**
- *Glycyrrhiza gabra* (licorice)
- *Foeniculum vulgare* (fennel)
- *Mentha piperita* (peppermint)
- *Mentha spicata* (spearmint)
- *Citrus sinesis* (orange peel)

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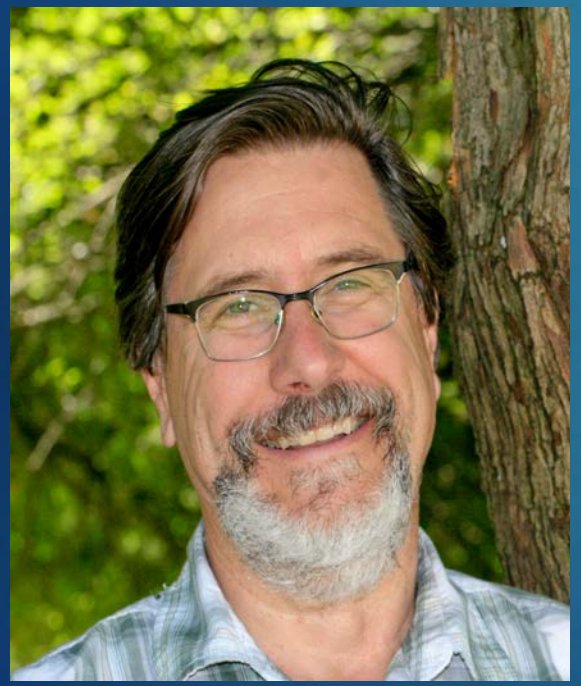

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