**Bitters:**
- non-pharmacological classification
- based entirely on taste perception (for which we recognize a specialized receptor)
- consistent action from a diversity of molecules

**Mithridatum** (cure-all elixir): mixture of Egyptian kyphi and strongly bitter plants: parsley, wild carrot, gentian, poppy
Bitters are a traditional bitter-tasting aperitif / digestif used in all cultures


Much of the activity of bitters may result from **the physiologic response to poison – Alkaloids!** Psychoactive and maybe toxic. Recognizing them is advantageous, detoxification pathways are essential


Bitter taste is innate and triggers stereotypical behavioral outputs leading to rejection (**Steiner 1973; Chandrashekar et al. 2006; Beauchamp and Mennella 2009**). Although a clear correlation between bitterness and toxicity has not been established (**Glendinning 1994**), it is generally believed that this taste quality prevents mammals from intoxication by avoiding ingestion of potentially harmful food constituents (**Lindemann 1996; Drewnowski and Gomez-Carneros 2000**)

**Bitter T2R (TAS2R family) taste receptor**

On tongue, throat, along GI tract, pancreatic duct
On liver / gallbladder
In lungs!


Found in tongue, throat, GI tract and pancreatic duct.


Bitter T2R (TAS2R family) taste receptor

Respond to a variety of bitter molecules: iridoids, alkaloids, lactones; some volatile terpenoids, flavonoids, saponins


Pharmacology of T2R receptor stimulation:
- A little “stress” (alert) for the GI tract
- More stimulus, more receptors (unique). We must need it!
- reduce feeding behavior
- Immediate correlation to obesity: more T2R sensitivity, less obesity


Relatively unique: more bitter consumption leads to more T2R expression:

Stimulation of T2Rs decreases caloric ingestion:
Ongoing ingestive behavior is rapidly suppressed by a preabsorptive, intestinal “bitter taste” cue Lindsey A. Schier, Terry L. Davidson, Terry L. Powley AJP - Regu Physiol November 2011 vol. 301 no. 5 R1557-R1568


Boys highly sensitive to bitter are never obese, unlike their peers: Negri R, Di Feola M, Di Domenico S, Scala MG, Artesi G, Valente S, Smarrazzo A,
Rise in diabetes 2 rates in the US vs. Corn acres and yield the US

Not just the rise of sweet – but also removal of bitters (wild plants, coarse foods).

Profound implications – not just for individuals, but for culture, ecology too!


Hypothesis:

Human beings evolved in the context of a specific “chemosome” that was sourced from a very rich, biodiverse diet.

Non-toxic bitter tasting molecules (inherent parts of any whole food diet) provide the necessary information to the liver and GI tract to ensure optimal function.

Without non-toxic bitter tasting molecules, the chemosome is altered and GI fx atrophies, hepatic detox fx slows.
Pharmacology of bitters: AID DIGESTION
Improve endogenous production of digestive enzymes


The findings showed the saliva of hypersensitive subjects contained higher levels of amylase fragments, immunoglobulins, and serum albumin and/or serum albumin fragments. It also contained lower levels of cystatin SN, an inhibitor of protease.


Discussion of the use of Taraxacum for gas, spasm and bloating along with incomplete digestion


Pharmacology of bitters: AID DIGESTION
   Lower GI symptoms: bloating, cramping, spasm
   Constipation: relieves irregularity
   Loose stools: bitters slow transit

Delivered at the London School of Clinical Medicine
Discussion of the use of Taraxacum for gas, spasm and bloating along with incomplete digestion

Pharmacology of bitters: IMPROVE LIVER FUNCTION
   Heal and protect liver cells from damage, decreasing free radicals and oxidative stress
   Increase CCK / bile synthesis and excretion


Cholecystokinin (CCK) stimulated: [Am J Physiol Gastrointest Liver Physiol 292:G457-G461, 2007. First published 9 November 2006; Catia Sternini]

Pharmacology of bitters: IMPROVE LIVER FUNCTION
   Balance Phase I and Phase II metabolism, less toxic “spillover” into the bloodstream


Pharmacology of bitters: IMPROVE LIVER FUNCTION

Balance blood sugar:
Balance blood sugar through liver / pancreas activity – beginning with taste!
Reduce appetite and feeding behavior
Correct low blood sugar (hypoglycemia) in a fasted state.
Reduce hyperglycemia in a fed state


Amish family diabetes database, n>1300. Analysis of genetic variation of T2R expression and its correlation to insulin secretion and BG.

Bassoli et.al. 2007. Chlorogenic acid reduces the plasma glucose peak in an oral glucose tolerance test: effects on hepatic glucose release and glycemia. Cell Biochemistry and Function 26, 320-328

Peptide YY is a short (36-amino acid) protein released by cells in the ileum and colon in response to feeding. In humans it appears to reduce appetite. Release stimulated by bitters [Am J Physiol Gastrointest Liver Physiol 292:G457-G461, 2007. First published 9 November 2006; Catia Sternini]

Researchers noted that caloric intake during a buffet lunch offered two hours after the infusion of PYY was decreased by 30 percent in obese subjects (P<0.001) and 31 percent in lean subjects (P<0.001). [Batterham RL, Cohen MA, Ellis SM, Le Roux CW, Withers DJ, Frost GS, Ghaitei MA, Bloom SR (September 2003). "Inhibition of food intake in obese subjects by peptide YY3-36". The New England journal of medicine 349 (10): 941–8]


Pharmacology of bitters: DETOXIFY

Less systemic inflammation = Fewer allergies, asthma


Pharmacology of bitters: DETOXIFY

Less systemic inflammation = Improvement in chronic diseases (such as skin disease and many others)


Pharmacology of bitters:

Additional benefits: reflex activity on CNS (via vagus nerve, CCK)