



Managing Upper Digestive Problems with Herbs: Recent Developments and New Insights

Kerry Bone

Co-Founder and Director R & D, MediHerb

Adjunct Associate Professor, University of New England

Topics Covered

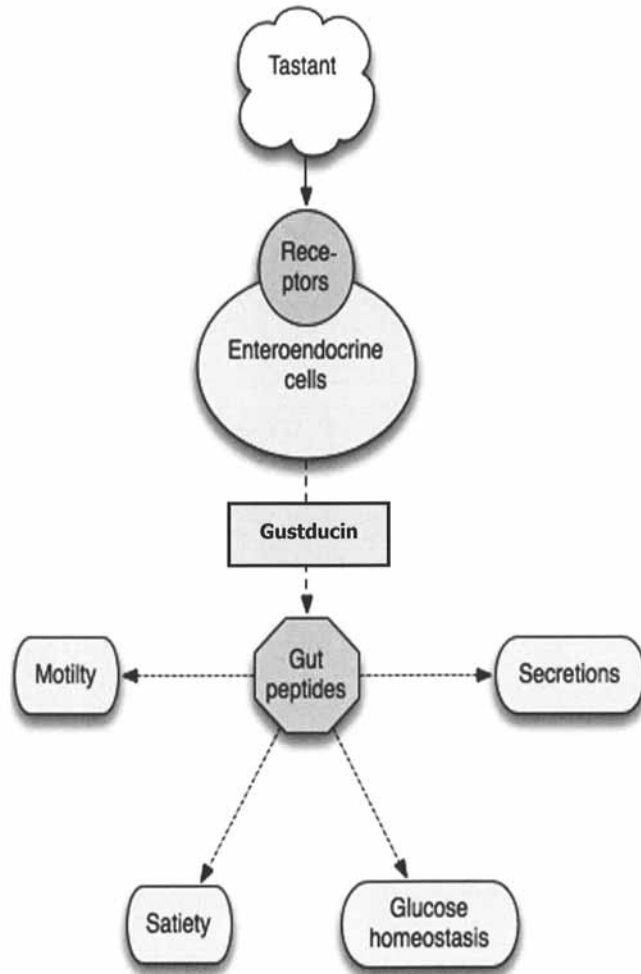
- The upper digestive tract is a tasting organ
- Key herbal actions, evidence and new insights:
 - bitter
 - demulcent and mucoprotective
 - cholaretic/cholagogue
 - carminative
 - pungent
- The importance of the gastric acid barrier
- Important health issues including gastroparesis and dyspepsia

The Five Tastes

- The five tastes are bitter, sweet, salty, sour and umami
- Umami, the Japanese word for “savoury” or “good taste” is generally now recognised as a basic taste
- Salty and sour are tasted through ion channels
- Taste receptors for bitter, sweet and umami are G protein-coupled receptors
- The key G protein involved with these receptors is gustducin¹

1 Scott K. Taste Recognition: Food for Thought. *Neuron* 2005; **48**(3): 455-464

The Upper GIT is a Tasting Organ

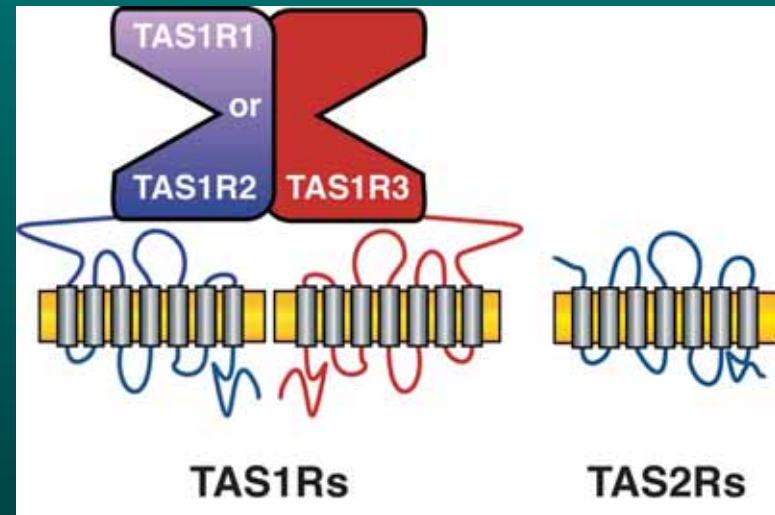


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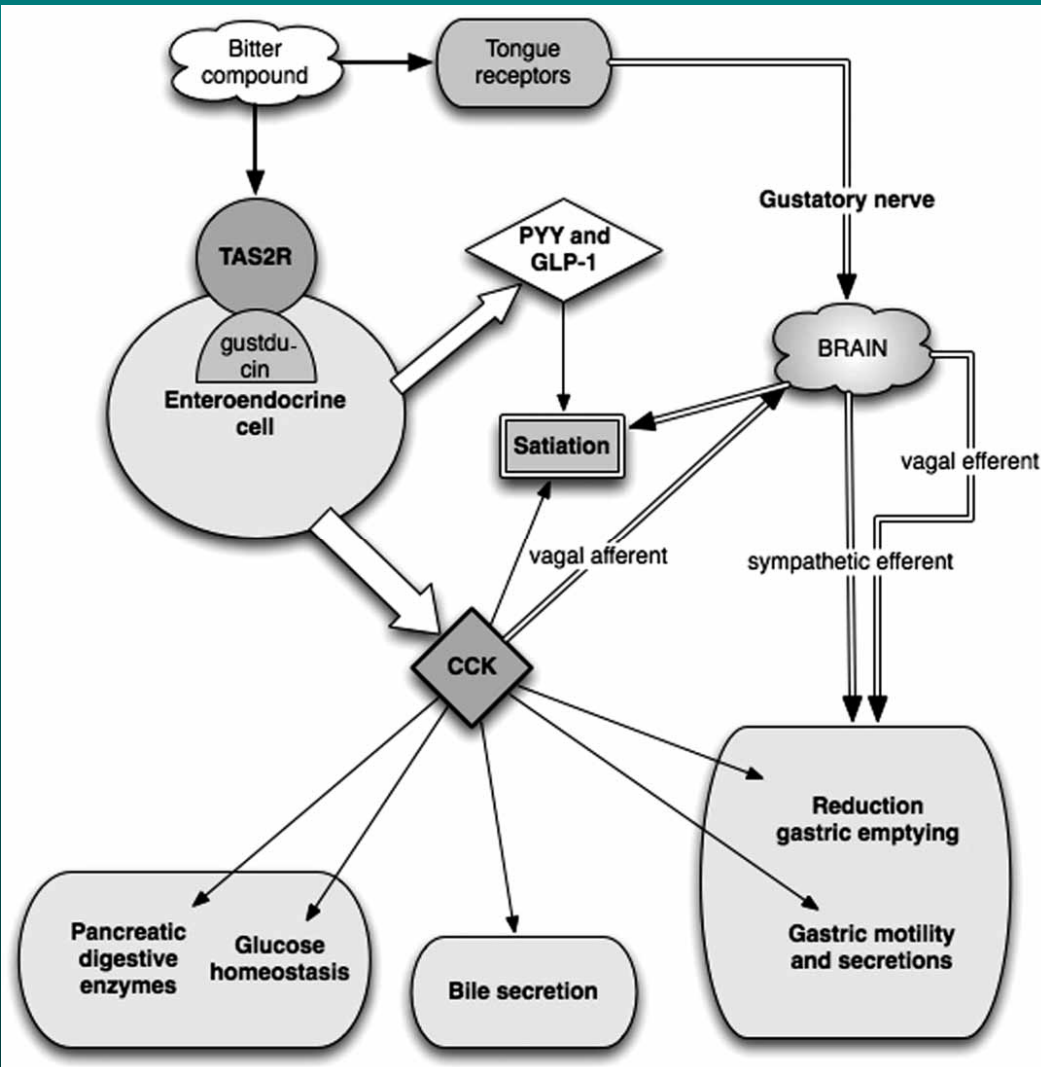
Valussi M. Functional foods with digestion-enhancing properties. *Int J Food Sci Nutr* 2011: [Epub ahead of print]

The Bitter Receptor

- Recent research has made considerable advances in our understanding of the bitter taste receptors. A family of approximately 30 such receptors (denoted TAS2R, previously T2R) has been identified in mammals¹
- The TAS2Rs are broadly tuned to each detect multiple bitter substances, explaining how humans can recognise numerous bitter compounds with only a limited set of receptors



Upper Gastrointestinal Effects of Bitters



Valussi M. Functional foods with digestion-enhancing properties. *Int J Food Sci Nutr* 2011: [Epub ahead of print]

A New Insight into the Bitter Action

- Bitter herbs do NOT need to be tasted to favourably influence digestive function
- In fact, clinical research on Gentian dating from 1998¹ supports this concept but now we understand why
- This means that tablets or capsules containing bitter herbs are clinically active, although higher doses are probably necessary



1 Wegener T. *Z Phytother* 1998; **19**: 163-164

Bitters Can Help Regulate Metabolic Function

- In epidemiological studies, functional variants in bitter taste receptors have been linked to alcohol dependency,¹ adiposity,² eating behaviour disinhibition³ and body-mass index⁴
- Generally, people with lower bitter tasting sensitivity exhibited the poorer health measure
- The presence of bitter receptors on enteroendocrine cells suggests the mechanism behind these effects

1 Wang JC, Hinrichs AL, Bertelsen S et al. *Alcohol Clin Exp Res* 2007; **31**(2): 209-215

2 Tepper BJ, Koelliker Y, Zhao L et al. *Obesity (Silver Spring)* 2008; **16**(10): 2289-2295

3 Dotson CD, Shaw HL, Mitchell BD et al. *Appetite* 2010; **54**(1): 93-99

4 Feeney E, O'Brien S, Scannell A et al. *Proc Nutr Soc* 2011; **70**(1): 135-143

Bitters Can Help Regulate Metabolic Function

Insulin resistance

- It also suggests a role for bitter herbs in glucose homeostasis and insulin resistance
- In support of this 94 patients with prediabetes exhibited improvements in BMI, glycaemic control and body fat when given just 16 to 48 mg/day of isohumulones (hop bitter acids) as capsules in a double blind placebo-controlled clinical trial¹



Demulcency and Mucoprotection

- Mucilaginous remedies are used for their topical emollient and internal demulcent properties and their direct, if temporary, benefits in the management of inflammatory conditions of the digestive tract
- This anti-inflammatory effect is probably more than just mechanical, although the protective benefits of a layer of mucilage on the digestive mucosa are obvious, especially as an extra barrier to gastric acid



Demulcency and Mucoprotection

- In experimental models the protective effect of mucilage isolated from *Plantago major* leaves against gastric ulcer has been demonstrated¹
- It has also been shown that guar gum forms a layer closely associated with the intestinal mucosal surface providing a protective barrier²



- 1 Obolentseva GV, Khadzhai YaI, Vidyukova AI et al. Effect of some natural substances on ulceration of the rat stomach caused by acetylsalicylic acid. *Bull Exp Biol Med* 1974; **77**: 256-257
- 2 Blackburn NA, Johnson IT. The influence of guar gum on the movements of insulin, glucose and fluid in rat intestine during perfusion in vivo. *Pflügers Archiv* 1983; **397**: 144-148, 1983.

Demulcency and Mucoprotection

- In contrast to previous views, gastric ageing is not associated with reduced acid production
- It is however linked to impaired gastric mucosal defence and increased susceptibility to chronic injury from *H. pylori* and NSAIDs
- Impaired healing capacity is also a key feature that delays ulcer healing in the elderly
- This all suggests a key role for healing herbs like Gotu Kola and enhancing mucoprotection

Choleretics and Cholagogues

- Clinically-proven choleretic and cholagogue herbs (which will help with fat digestion, cholesterol and toxin excretion and exert a laxative activity) are relatively few
- Best data exist for *Cynara* (Globe Artichoke) and *Chelidonium*
- For example, in an early, open clinical study involving 198 patients with biliary fistula, *Cynara* extract demonstrated choleretic and cholagogue effects and clinical improvement¹

Carminative Herbs

- Carminative herbs relieve gas and soothe intestinal spasm and pain by relaxing intestinal smooth muscle and especially sphincters
- Hence high doses of carminatives can aggravate gastro-oesophageal reflux, but in lower doses they can help this problem by better co-ordinating gastric contractions
- The best-known carminative is *Mentha piperita* (Peppermint) and it has been proven to relax sphincters in the gut

Spasmolytic Herbs

- Spasmolytic herbs relax the smooth muscle of the digestive tract and again the best proven clinical activity is for *Mentha piperita* (Peppermint), especially as the essential oil, although Matricaria (Chamomile) has good activity as well
- The spasmolytic activity of Peppermint has led to some novel applications in the upper GIT



Spasmolytic Herbs

- For example:
 - Diffuse oesophageal spasm (DOS) is a rare condition that results in simultaneous oesophageal contractions leading to symptoms of chest pain and dysphagia. Diagnosis can be controversial. In an open-label pilot study in 8 patients with DOS, 5 drops of peppermint oil in 10 mL of water completely eliminated simultaneous oesophageal contractions in all patients ($p < 0.01$)

Pungent Herbs

- Like bitters, pungency is a physiological (sensor activated) classification rather than a phytochemical one
- The three most commonly used hot spices are the cayenne pepper (*Capsicum species*), the black pepper and Ginger
- While their pungent components (respectively capsaicin, piperine and the gingerols and shogaols) are chemically distinct, it is now known that they act upon a common group of nerve cell receptors: the vanilloid receptors, especially TRPV1¹

Ginger

- Pharmacological studies indicate that Ginger and/or the gingerols promote gastric acid, are mucoprotective, promote bile flow and enhance gastrointestinal motility (as do some antinausea drugs)
- Human clinical studies demonstrate marked antinausea activity, carminative effects, and substantially increased rates of gastric emptying
- Clinical activity has been demonstrated in patients suffering from gastroparesis/functional dyspepsia

The Gastric Acid Barrier

- A poor gastric acid barrier is a relatively neglected issue in intestinal dysbiosis management
- A number of studies highlight some alarming concerns over the long-term safety and appropriate use of the most commonly prescribed antacid drugs, namely the proton pump inhibitors (PPIs)
- One editorial entitled “Failing the Acid Test” concludes that the benefits of PPIs probably do not justify the risks for many users¹



The Gastric Acid Barrier

- One study retrospectively examined the relationship between PPIs and *Clostridium difficile* infection (CDI) in elderly patients.¹ The incidence of this disease has nearly tripled in the US in the past decade and the lower gastric acid resulting from PPI use might facilitate the growth of potentially pathogenic gastrointestinal organisms such as this
- An association between PPI use and CDI was found, with a hazard ratio (HR) of 1.42
- The US FDA is now issuing drug warnings about this risk

1 Linsky A, Gupta K, Lawler EV et al. *Arch Intern Med* 2010; **170**(9): 772-778

Gastroparesis

- Gastroparesis is a non-obstructive condition that results in delayed gastric emptying
- Symptoms include abdominal distention, nausea, abdominal fullness (discomfort) after eating, vomiting, heartburn and abdominal bloating
- While damage to the vagus nerve (as in diabetes) or surgery can be causes, in many cases the cause is unknown (idiopathic)
- Gastroparesis can be one of the issues underlying the vague syndrome known as “functional dyspepsia”

Gastroparesis: Case History

- A female patient aged 56 presented with the main symptoms of nausea, occasional heartburn and premature fullness, with a medical diagnosis of idiopathic gastroparesis
- Conventional drug treatments had been unsatisfactory
- She was prescribed Ginger 1:2 extract at 1 to 2 mL with water before each meal and also digestion-promoting tablets (1 before each meal, sucked for 60 seconds and then swallowed)

Gastroparesis: Case History

- 4 weeks later she reported that her nausea and heartburn were gone, but the bloating was still there
- Over the ensuing months the patient reported her digestion as “good”, with minimal symptoms as long as she remembered her herbs



Dyspepsia

- Dyspepsia is a term commonly (and loosely) used to describe pain or discomfort in the upper abdomen
- It is reported by around 25% of adults in Western societies
- Heartburn alone is not considered to be true dyspepsia
- The most important causes are non-ulcer (functional) dyspepsia, peptic ulcer, gastro-oesophageal reflux (GOR) and (rarely) gastric cancer
- Endoscopy is the most reliable means of diagnosis

Helicobacter and Dyspepsia

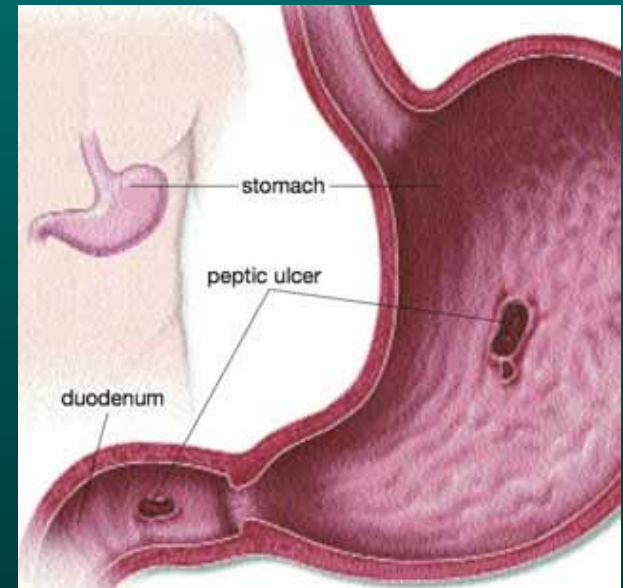
- Currently *Helicobacter pylori* is recognised as the most common cause of peptic ulcer¹
- The role of Helicobacter in non-ulcer dyspepsia is controversial¹
- Helicobacter is probably the most significant factor behind the development of gastric cancer
- In contrast, it had been speculated that eradicating *H. pylori* might worsen GOR
- However research shows that it has no impact either way²



1 Suzuki H, Nishizawa T, Hibi T. *J Gastroenterol Hepatol* 2011; **26**(Suppl 3): 42-45
2 Harvey RF, Lane JA, Murray LJ et al. *BMJ* 2004; **328**(7453): 1417

Peptic Ulcer Disease: Pathophysiology

- Both duodenal and gastric ulcers are essentially gastric ulcers
- They occur in gastric mucosa in the stomach or in gastric metaplasia mucosa in the duodenum
- The mucosa may be attacked by:
 - excess acid
 - bacteria (*H. pylori*)
 - drugs (NSAIDs)



Peptic Ulcer Disease: Pathophysiology

Main Causes

- *H. pylori*
- NSAIDs
- Idiopathic



Idiopathic peptic ulcer disease is increasing in occurrence

Calam J, Baron JH. *BMJ* 2001; **323**: 980-982

Chow DK, Sung JJ. *Nat Clin Pract Gastroenterol Hepatol* 2007; **4**(4):176-177

Peptic Ulcer Disease: The Forgotten Factors

- With the focus on *H. pylori* and NSAIDs as obvious causes of peptic ulcer disease a number of previously-recognised pathogenic factors are now largely overlooked
- Only a small percentage of patients positive for *H. pylori* develop peptic ulcer disease
- Similarly, not everyone who uses NSAIDs ends up with peptic ulcers
- These forgotten factors are likely to be particularly relevant for idiopathic peptic ulcers these are mainly diet, lifestyle and stress

Herbs and Helicobacter

- Current research suggests that herbs can have only a supportive role in the management of Helicobacter and they are most suitable for cases where antibiotic therapy is not fully successful
- Activity has been demonstrated *in vitro* for *Allium sativum* (Garlic), *Thymus vulgaris* (Thyme), *Salvia species* (Sage), *Cinnamomum species* (Cinnamon), Hydrastis (Golden Seal), Arctostaphylos (Bearberry) and *Camellia sinensis* (Green Tea), among others
- Moderate benefits have been shown in clinical trials for raw garlic, *Rheum species* (Rhubarb Root), *Vaccinium macrocarpon* (Cranberry), *Nigella sativa* (Black Cumin), broccoli sprouts

Peptic Ulcer Disease

Therapeutic Strategy: Goals, Actions and Herbs

- Licorice and mucilaginous demulcent herbs (Marshmallow Root, Slippery Elm) to enhance mucoprotection. These are best taken before meals, and in the case of duodenal ulceration should be taken at least half an hour before eating. Licorice also improves pancreatic bicarbonate secretion
- Whilst bitter herbs such as Gentian are contraindicated in duodenal ulcers, they may be valuable in gastric ulcers because of their trophic effect on the gastric mucous membrane

Peptic Ulcer Disease

Therapeutic Strategy: Goals, Actions and Herbs

- Golden Seal is restorative to mucous membranes and also antibacterial. However, because of its bitterness it is best given as a tablet
- Also other antimicrobial remedies such as Thyme herbal liquid and raw crushed Garlic will help to resolve *H. pylori* presence, although many ulcer patients find raw Garlic difficult to take. Astringent herbs such as Grape Seed extract, Rhubarb and Green Tea are also antimicrobial

Peptic Ulcer Disease

Therapeutic Strategy: Goals, Actions and Herbs

- Immune enhancing herbs such as Echinacea will also help resolve *H. pylori* presence and improve repair mechanisms. They have been traditionally used in peptic ulcer disease
- Gently astringent herbs will assist ulcer healing and boost mucoprotection in the vicinity of the ulcer. They are, in a sense, a natural analogue to the drug sulcrafate. A good example is Meadowsweet. Strongly astringent herbs such as Cranesbill can aggravate

Peptic Ulcer Disease

Therapeutic Strategy: Goals, Actions and Herbs

- Anti-inflammatory herbs such as bisabolol-type Chamomile and vulneraries such as Calendula will break the vicious cycle of ulceration and accelerate the healing process. Herbs which benefit the microcirculation (Bilberry, Ginkgo and Grape Seed extract) should also assist healing
- Herbs that decrease the negative effects of stress on the body are indicated and include nervine tonics such as Skullcap, mild sedatives such as Valerian and adaptogens like Siberian Ginseng

Peptic Ulcer Disease

Therapeutic Strategy: Goals, Actions and Herbs

- Meadowsweet is considered by some herbalists to be a normaliser of the acidity of the stomach.¹ It does appear to decrease the negative effects of acid and pepsin on the mucosa
- Some patients with peptic ulcer disease may experience irritation from liquid herbal therapies, and one approach is to start with a low dose and gradually increase it over several weeks or otherwise use tablets

1 Roberts F. *Modern Herbalism for Digestive Disorders*. Thomsons, Northamptonshire, 1981

Peptic Ulcer Disease

Example formulation

Meadowsweet	1:2	20 mL
Licorice	1:1	20 mL
Chamomile	1:2	20 mL
Gotu Kola	1:2	25 mL
Echinacea Root	1:2	<u>25 mL</u>
		110 mL

Dosage: 5 mL with water three times a day half hour before meals

In combination with Slippery Elm before meals plus additional treatments for Helicobacter if required

Gastro-oesophageal Reflux Disease (GORD)

- Most common gastrointestinal problem seen in primary care¹
- Main symptoms are typically heartburn and acid regurgitation¹
- People in eastern countries have a much lower incidence than in the west²



1 Fass R, Ofman JJ. *Am J Gastroenterol* 2002; **97**(8): 1901-1909

2 Shaheen N, Provenzale D. *Am J Med Sci* 2003; **326**(5): 264-273

GORD: Modern Classification

- Non-erosive or negative-endoscopy reflux disease (NERD) which may account for up to 70% of patients with GORD¹
- Erosive oesophagitis (EO)²
- More severe complications of EO such as oesophageal ulceration or stricture (rare)³
- Barrett's oesophagus: columnar tissue metaplasia (rare)³

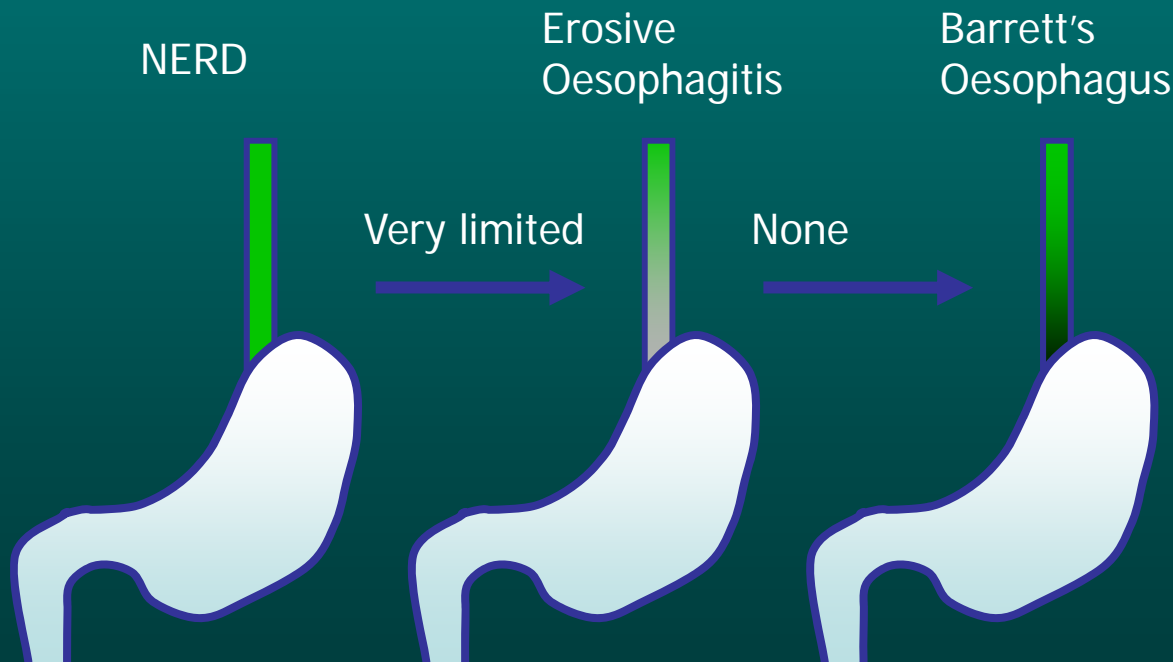
1 Quigley EM. *Aliment Pharmacol Ther* 2003; **17** (Suppl 2): 43-51

2 Fass R, Ofman JJ. *Am J Gastroenterol* 2002; **97**(8): 1901-1909

3 Shaheen N, Provenzale D. *Am J med Sci* 2003; **326**(5): 264-273

Is GORD a Disease Spectrum?

- Current thinking challenges that there is a progression of disease, in particular NERD may not progress to organic disease

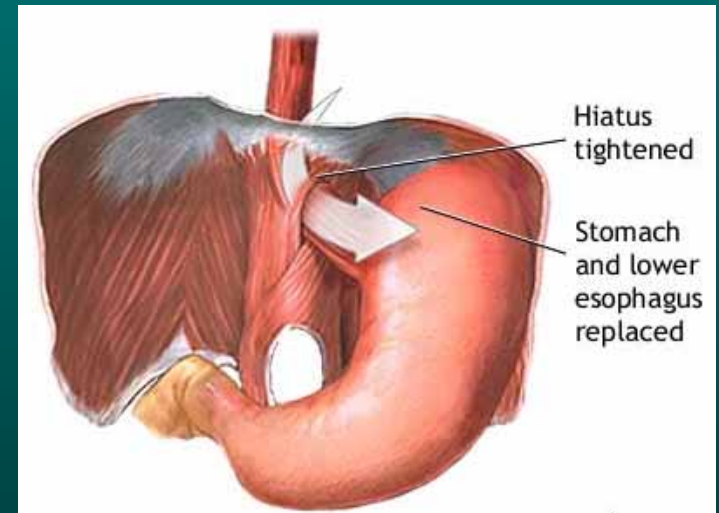


Features of NERD

- While patients do respond symptomatically to acid-inhibiting drugs, response rates are much lower than for EO
- NERD patients often experience hoarseness, chronic cough, asthma and other related symptoms as complications of reflux
- NERD patients have similar impairment of quality of life as those with EO
- Only around 50% of patients with NERD have excess acid reflux

The Pathophysiology of GORD

- Modern research highlights factors such as abnormal gastric motility and mixing, poor sphincter function and tone, hiatal hernias and obesity as key factors
- In addition poor acid clearance and low mucosal resistance are considered to be relevant



Bone K, Mills SY. *Principles and Practice of Phytotherapy. Modern Herbal Medicine*. 2nd ed. Elsevier, Edinburgh. In Press.

Gastro-oesophageal Reflux

Therapeutic Strategy: Goals, Actions and Herbs

- Improve mucosal resistance with demulcent herbs such as Licorice and Marshmallow Root. These are best taken after meals and before bed. Additional supplementation with Slippery Elm powder can be useful: the raft concept
- Spasmolytic herbs such as Cramp Bark and Corydalis to restore balance to smooth muscle function. Carminatives (low doses) may be of value, especially in NERD

Gastro-oesophageal Reflux

Therapeutic Strategy: Goals, Actions and Herbs

- Increase sphincter tone and improve gastric emptying and saliva output with bitter tonic herbs at low doses. However, they also increase gastric acid so should be used cautiously. Gentian and Wormwood are the strongest bitters. If their use aggravates then gentler bitters such as Dandelion Root, Globe Artichoke or Yarrow could be tried
- Reduce inappropriate levels of gastric acid using antacid herbs - the best is Meadowsweet, but other astringent herbs also have this property and so apparently does Chamomile

Gastro-oesophageal Reflux

Therapeutic Strategy: Goals, Actions and Herbs

- Improve healing and allay inflammation with vulnerary herbs (Chamomile, Gotu Kola) and anti-inflammatory herbs (particularly Chamomile). For best results use a Chamomile high in bisabolol
- Alleviate the effects of stress on the functioning of the autonomic nervous system with anxiolytic herbs (such as Passionflower and Valerian) and nervine tonics (especially Skullcap and St John's Wort)
- Treat any associated gastroparesis with Ginger

Gastro-oesophageal Reflux

Example Liquid Formula

Passionflower	1:2	20 mL
Chamomile	1:2	25 mL
Cramp Bark	1:2	20 mL
Licorice	1:1	20 mL
Meadowsweet	1:2	<u>20 mL</u>
		105 mL

Dosage: 5 mL with water three times a day **after** meals. An extra dose can be taken before retiring in the evening. Works best in combination with Slippery Elm powder **after** meals.

Case History: GORD

A Young Girl with Reflux and Vomiting

- A mother visited with her 11-year-old daughter seeking treatment for regurgitation and reflux
- The girl had suffered from this problem ever since being a baby and was small for her age: “failure to thrive”
- She was intolerant of dairy products and could not have large meals
- I gave advice that the vomiting back of food may be a habit and suggested she try to control it

Case History: GORD

Treatment consisted of the following:

Meadowsweet	1:2	25 mL
Chamomile	1:2	25 mL
Gentian	1:2	5 mL
Withania	1:2	<u>50 mL</u>
		105 mL

Dosage: 4 mL with water twice a day **after** meals, together with a liquid herbal iron tonic and Siberian Ginseng tablets at 2 per day

Case History: GORD

Treatment outcomes:

- The mother reported over the ensuing 4 to 6 months that the episodes of vomiting and reflux reduced in frequency and eventually stopped
- Although still small for her age, her appetite is better and she is eating more. As a result her growth rate had improved

