MedicineToday PEER REVIEWED

STW5 (Iberogast) herbal therapy and functional gastrointestinal symptoms

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Limited data suggest the herbal mixture STW5 (Iberogast) has some efficacy in patients with functional dyspepsia or irritable bowel syndrome. It may be worth considering if usual treatment is unsuccessful.

MedicineToday 2013; 14(6): 71-73

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Unexplained chronic gastrointestinal symptoms, including abdominal pain, diarrhoea, constipation, bloating and dyspepsia, are remarkably prevalent in Australia, affecting a third of people of all ages.[1] These symptoms have a major impact on health and wellbeing; they often impair quality of life and relationships and can reduce work productivity. Psychological comorbidity is common but is not considered a cause of the gastrointestinal symptoms. The costs of health-care seeking and medication use by those affected run into billions of dollars for the Australian economy.

Irritable bowel syndrome (IBS) is one of the best recognised functional gastrointestinal symptom complexes. Patients usually experience episodic abdominal pain, bloating and an irregular bowel habit. Another common syndrome is functional dyspepsia, characterised by epigastric pain or burning and early satiety or fullness after eating; these patients are often mislabelled as having gastro-oesophageal reflux disease (GORD) but respond relatively poorly to acid suppression therapy.

Treatment of both IBS and functional dyspepsia can be frustrating for both the patient and doctor. A combination of diet, exercise and a probiotic helps a proportion of people with IBS.[1] Little is available to treat patients with functional dyspepsia. Patients with functional gastrointestinal symptoms often try over-the-counter medications, including various herbal preparations of uncertain benefit.

WHAT IS STW5?

STW5 is a combination of nine herbs in a liquid form. It is a proprietary blend that was developed in Germany in 1961. The ingredients include *Iberis amara* (bitter candy tuft), from which is derived the trade name, Iberogast. The herbs included

HERBS INCLUDED IN STW5

STW5 (Iberogast) is a solution containing liquid extracts of nine herbs:[2]

- *Angelica archangelica* (angelica) root
- *Carum carvi* (caraway) fruit
- *Chelidonium majus* (celandine) dry herb
- *Glycyrrhiza glabra* (liquorice) root
- *Iberis amara* (bitter candy tuft) whole plant
- *Matricaria chamomilla* (chamomile; also known as *M. recutita*) flower head
- *Melissa officinalis* (lemon balm) leaf
- *Mentha* x *piperita* (peppermint) leaf
- *Silybum marianum* (St Mary's thistle) fruit

in STW5 are shown in the box on this page.[2]

STW5 was approved by the TGA in 2010 for the indication 'treatment of gastric and abdominal discomfort associated with functional and motility-conditioned gastrointestinal disturbances such as functional dyspepsia and irritable bowel syndrome'.[2] STW5 was registered via the TGA's new pathway for complementary medicines, the first herbal medicine to be registered after consideration of its efficacy as well as its safety.

EVIDENCE BASE FOR STW5

There are limited data from randomised controlled trials that support STW5 as efficacious. Only one four-week trial of STW5 in IBS has been published, in which 208 patients were randomly allocated to one of four arms.[3] Bitter candy tuft monotherapy, thought to relax smooth muscle, was equivalent to placebo (i.e. had no efficacy). The commercial STW5 preparation of nine herbs and a modified formula of six herbs including peppermint leaves were superior to placebo in terms of pain and overall symptom score. However, improvement in bowel disturbance was unimpressive.[3]

In functional dyspepsia, there is also limited evidence for efficacy of STW5.[4,5] A small meta-analysis of 273 patients randomised to STW5 or placebo, who were pooled from three trials, found a benefit but the main effect appeared to be on epigastric pain or reflux symptoms.[4] An eight-week trial showed a modest benefit not affected by *Helicobacter pylori* status.[5] The most recent data were presented at Digestive Disease Week in Orlando, Florida, in May, 2013. My colleagues and I reported the results of a randomised, double-blind placebo-controlled trial in 124 Australian patients with functional dyspepsia; the study was funded by the NHMRC. Both STW5 and a proton pump inhibitor were significantly better than placebo and had a similar response rate over a four-week treatment period. Notably, relapse rates were significantly higher after discontinuation of the proton pump inhibitor compared with STW5.[6]

HOW DOES STW5 POTENTIALLY WORK?

Nobody really knows which component or components are useful and which have no value. The available physiological data are not very informative, although the herbal combination may have some visceral analgesic properties as well as effects on serotonin receptors. There may be an anti-inflammatory action (subtle mucosal inflammation with immune activation characterises a subset of patients with IBS and functional dyspepsia).[7-10]

Other data suggest that peppermint oil may reduce abdominal pain in IBS, so perhaps this explains any benefit of STW5.[1] Liquorice was prescribed in the past for ulcer dyspepsia with benefit.[1] In functional dyspepsia, STW5 has been shown in a study from Adelaide to relax the proximal stomach after a meal (this relaxation is impaired in a subset with functional dyspepsia), but again which components of STW5 promote this relaxation is unknown.[10]

SAFETY OF STW5

STW5 appears to be relatively safe based on the available data, but caution is needed. STW5 is a drug and like any other drug will likely have potential toxicities, albeit rare. Hypersensitivity reactions have been reported. More serious toxicity might occur. For example, celandine herbs in high doses produce alkaloids that are potentially hepatotoxic.[3]

MANAGEMENT OF FUNCTIONAL DYSPEPSIA AND PLACE OF STW5

For patients with documented functional dyspepsia (predominant meal-related epigastric pain that is mild to moderate, or frequent early satiety or postprandial fullness, with normal results on endoscopy), I recommend the following management. This includes STW5 as second-line symptomatic therapy if usual medical treatment is unsuccessful.[11]

- Provide reassurance and explanation. Note that functional dyspepsia has no associated mortality.
- Identify medications (e.g. NSAIDs or aspirin) or life stressors that may contribute to dyspepsia and can be mitigated. Reduce anxiety and treat underlying depression.
- Advise patients to stop smoking and to minimise alcohol use. Only very limited data suggest functional dyspepsia may be linked to smoking, and alcohol is not a recognised risk factor, but this advice still seems sensible.
- Test for current *H. pylori* infection (e.g. with a ^{13}C urease breath test). If results are positive, try to eradicate the infection as this provides a substantial benefit in a minority of patients.
- Prescribe a trial of acid suppression therapy (proton pump inhibitor or H_2 blocker) for eight weeks; stop acid suppression if symptoms do not improve and switching between drug classes fails.
- Consider prescribing a prokinetic agent (e.g. domperidone), especially if

the patient has moderate to severe symptoms after most meals.
- Consider STW5 if usual medical treatment is unsuccessful. A four-week trial seems reasonable, then stop and observe whether a response is maintained.
- If all these steps fail, consider a trial of a low-dose tricyclic antidepressant (as a 'visceral analgesic'); if beneficial at eight to 12 weeks then continue for up to six months and then stop. There is no evidence that selective serotonin receptor inhibitors (SSRIs) are beneficial.
- For patients who fail to respond to any of these management steps, reconsider the diagnosis carefully. Occasionally biliary or pancreatic pathology or other unusual diseases can masquerade with the symptoms of functional dyspepsia.

A 2007 study implicating excess duodenal eosinophils in a subset of people with functional dyspepsia and early satiety may lead to new therapies.[12]

CONCLUSION

STW5 may help some patients with IBS and functional dyspepsia but data are limited, particularly in IBS. I have prescribed STW5 in my practice with mixed results, but some people claim to feel better. It probably is most useful for abdominal pain. How long STW5 should be taken is undefined. I currently use it as second-line symptomatic therapy in functional dyspepsia and await better long-term data to guide my practice. MT

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COMPETING INTERESTS: Professor Talley has received NHMRC funding to investigate Iberogast and has consulted for the German manufacturers of Iberogast in the past.