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Iberis: Important Herb for the Gut

Featured

Iberis

Actions

Bitter, increases intestinal tone.

Indicated for

As a simple (used on its own) for:

- poor appetite
- sluggish digestion
- as a digestive and tonic during convalescence.

As part of a formulation for:

- gastrointestinal discomfort
- dyspepsia

Highlights

- References to *Iberis amara* begin in classical Antiquity, with Galen and Pliny, first using the name "Iberis"
- Iberis is traditionally used as a bitter; most traditional applications are for the seed (and mostly as a homoeopathic remedy) but many plant parts used therapeutically
- The plant contains cucurbitacins, known for their bitter taste, as well as flavonoids
- Important component of a well-known 9-herb formula
- Iberis may provide an additional benefit over the other herbs [for functional dyspepsia]
  - one trial evaluated the 9-herb formula and the formula without Iberis: 9-herb formula tended to show stronger decrease in GI symptoms and the effect may be achieved earlier ›
  - although 6 symptoms improved with the use of both formulae, the Iberis-containing one improved another 2 symptoms: loss of appetite and early feeling of satiety ›

Iberis

Iberis amara is a member of the Brassicaceae (mustard) family. It is an annual, or rarely biennial, plant growing to about one foot (30 cm), with oblong toothed leaves and attractive flowers arranged in clusters. It is an important ornamental plant, as well as a medicinal plant. It originated in western Europe, however, it is cultivated widely. It is commonly referred to as a candytuft, such as bitter, annual, wild or rocket candytuft.

There are references to *Iberis amara* beginning in the classical Antiquity, with Galen and Pliny, who first used the name Iberis, meaning 'from Spain'.[1] It is said that the plant was named by a doctor who 'cured' his friend who was from this area.[2] The species, amara, means bitter in Latin.

The plant is used in two ways: the dried seeds in homoeopathy, and the whole fresh plant is an essential and major component of a well-known, 9-herb formula used to treat functional gastrointestinal complaints.[1] This herbal formula containing Iberis has been in use since the 1960s in Germany,[1,3] however, it is not clear how the use of Iberis was rediscovered. As it is the fresh plant that is used, the application may have derived from homoeopathy.[1]

All parts of the plant have been used: leaf, stem, root, but particularly the seed. Indications such as asthma, bronchitis, angina and heart conditions are cited, however, most often by the use of the seed as a homoeopathic remedy.[2,4,5]

The plant has been traditionally used as a bitter.[6,7] It has a strong, specific smell and a sharp taste, like cress.[8]

The bitter action is not surprising, as the plant contains cucurbitacins,[8] which are known for their bitter taste.[9]

Samples of plant (presumably whole plant) are found to contain cucurbitacin E, cucurbitacin I and flavonoids (particularly a kaempferol glycoside). The levels of these constituents vary by variety and growing conditions.[8] Glucoiberin, a glucosinolate (mustard oil glycoside), is also present in aerial parts.[10,11] This glucosinolate was so named because it was first isolated from the seeds of *Iberis amara*.[12]

As a bitter, Iberis may also have a choleretic effect. The bitter value of the fresh plant extract is very low.[13]

Clinical Trials: Functional Dyspepsia

Iberis has been almost exclusively evaluated in clinical trials as part of a herbal formula containing 8 other herbs. Iberis is considered the main component, and is combined with *Matricaria chamomilla* (chamomile) flower, *Carum carvi* (caraway) fruit, *Melissa officinalis* (lemon balm) leaf, *Silybum marianum* (St Mary's thistle) fruit, *Glycyrrhiza glabra* (licorice) root, *Chelidonium majus* (greater celandine) herb, *Angelica archangelica* (Angelica) root and *Mentha* x *piperita* (peppermint) herb. *Iberis amara* is present as an extract made from fresh whole, flowering and seeding plant. The daily dose of Iberis in this formula is equivalent to 225 mg of fresh plant. The other herbs are present as dried plant extracts.

It is noted that, except for Iberis, the doses of the herbs provided in the formula are very low in comparison to the usual therapeutic doses of the single herbs.[14] For example, based on proprietary information, the recommended dose of this 9-herb formula for adults and children over 12 years, provided chamomile equivalent to 200 mg/day of dried flower. The usual dose of dried chamomile (*Matricaria chamomilla*, previously *Matricaria recutita*) flower is 6–12 g/day when prepared as an infusion, or 1.5–3 g/day dried herb equivalent when administered as a liquid extract.

Given that the origin of the Iberis dose is not clear, and as it may have been derived from homoeopathy, it is possible that better clinical results may be achieved using higher doses of Iberis.

In four randomised, placebo-controlled trials (1994-2009), administration of the 9-herb formula was shown to provide significant benefit to patients with functional dyspepsia. The effect was superior to placebo.[15]

- For example, in the 2007 trial,[16] the Gastrointestinal Symptom (GIS) score improved for the herbal formula group by 6.9 points from baseline up to day 56, compared to an improvement of 5.9 points in the placebo group ($p < 0.05$; total of 308 patients). (The GIS, a validated questionnaire, comprises epigastric pain/upper abdominal pain, abdominal cramps, fullness, early satiety, loss of appetite, sickness, nausea, vomiting, retrosternal discomfort, and acid regurgitation/heartburn.)
- The beneficial effect can be anticipated in patients with symptoms related to gastric dysmotility, however, this effect is not based on the regulation of gastric emptying.
- In addition, two observational studies have also been published. These studies found that the time to onset of action (relief) is fast, and the beneficial effect is confirmed in children with functional gastrointestinal diseases, as seen by improvement of upper and lower gastrointestinal symptoms.

Pooled data from three randomised trials found the 9-herb formula was more effective than placebo regarding the severity of the most bothersome gastrointestinal symptom as rated by the patient ($p < 0.001$): at the end of treatment, the most bothersome symptom remained severe and very severe in 26% of patients in the placebo group but only in 7% of those taking the herbal formula. Stepwise regression analysis with the data at admission as independent variables and an individual symptom score at the final visit as a dependent variable, showed that treatment was significantly related to the outcome for 6 of 10 symptoms (abdominal cramps, epigastric pain, nausea, acid regurgitation, retrosternal discomfort, vomiting). The results are based on a total of 273 patients. Two of the trials were also discussed above, and the third trial was an unpublished report.[14] The unpublished report describes a trial that evaluated the 9-herb formula and Iberis extract alone in comparison to placebo. Neither the 9-herb formula nor Iberis had a significant effect over placebo.[14,17,18] The fresh plant dose of Iberis was the same in both herb groups, as the volume of the Iberis single liquid preparation was made up with alcohol to match the volume of the 9-herb formula.[17,18]

The 9-herb formula has been identified from clinical studies as having similar efficacy as the prokinetic/propulsive drugs metoclopramide and cisapride for the treatment of functional dyspepsia. (These drugs tend not to be used for this condition now, as they have severe adverse effects in rare cases.) The studies were randomised controlled trials (one each), and one retrospective cohort study (metoclopramide).[3]

A 2017 uncontrolled study was conducted in Russia with an unspecified number of outpatients. In most cases, treatment with the 9-herb formula for 4 weeks, resulted in a decrease in the total score for GSRS (Gastrointestinal Symptom Rating Scale) and a decrease in the subdimension scores. (The GSRS questionnaire measures 15 items in the following 5 subdimensions: abdominal pain, reflux, diarrhoea, constipation and indigestion. Indigestion included abdominal distension, eructation and flatulence.)

The most interesting observation was the relief of reflux symptoms in patients with concomitant gastroesophageal reflux disease by treatment with either the herb formula alone or in combination with maintenance doses of proton pump inhibitors.[19]

One of the trials,[20] discussed in the reviews above,[14,15] also evaluated the combination of the 8 other herbs in the 9-herb formula.[20]

- Both the 9-herb formula and the formula not containing Iberis (8-herb formula) significantly improved gastrointestinal symptoms compared to placebo. There was no statistically-significant difference between the two herb formulations, however, the 9-herb formula tended to show a larger decrease in GIS score. For example, from baseline over the 4 weeks, the score decreased by 71.1%, 61.7% and 14.4%, for the 9-herb, 8-herb and placebo groups respectively. Sixty patients completed the study.
- In addition, the improvement could be achieved earlier with the 9-herb formula: within the first 2 weeks, 84.2% of patients in the 9-herb formula group experienced stable improvement of at least two symptoms, compared to 47.4% of those taking the 8-herb formula (p = 0.023). (Stable improvement was defined as improvement by at least 2 scale points from baseline and no later deterioration.)
- Nausea, sickness, fullness, abdominal cramps, retrosternal discomfort and especially epigastric pain improved under the action of both formulations. However, in comparison to placebo, the formula containing Iberis also significantly improved symptoms of loss of appetite and early feeling of satiety. (Note: Sickness in this validated test refers to discomfort combined with the impression for the need to vomit.) The authors suggested that Iberis provided an additional benefit to patients with functional dyspepsia.

Possible Mechanism

The actions of the 9-herb formula and its individual herbal components have been investigated, in mostly only *in vitro* models. The main actions of Iberis are listed.

- Iberis had a tonic effect on relaxed, or only slightly contracted, intestinal muscle. Caraway also exhibited this action. In contrast, several herbs exerted a spasmolytic effect (decreased acetylcholine- and histamine-induced contractions).[21,22]
- Iberis increased the amplitude of electrically-induced contractions in isolated intestinal muscle. The other herbs in the formula either had no activity or decreased the contractions.[21,23]
- Iberis reduced visceral hypersensitivity (*in vitro*).[21]
- Iberis may also have some anti-inflammatory activity on intestinal tissue. The *in vitro* test results suggest a modest effect as not all the results were positive.[21] In addition, Iberis strongly increased IL-8 release (which is pro-inflammatory) in oesophageal epithelial cells.[24]
- Iberis reduced stomach acid content and output *in vivo*,[21,25] although the doses were high (in terms of human equivalency).

Safety

There is little information available about the safety of Iberis. The safety of the 9-herb formula has been extensively evaluated with animal and *in vitro* research, with the results not showing any significant toxicity. The 9-herb formula has recorded an extremely low number of adverse effects (21/50009) in clinical and observational studies.[26]

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