Complementary medicines for intestinal parasites

By Liza Oates

Introduction
Intestinal parasites are most commonly caused by protozoa (single-celled organisms) or by helminths which include nematodes (roundworms), cestodes (tapeworms) and trematodes (flukes). Protozoa can multiply within the body but helminths cannot and are thus easier to eradicate with treatment without reinfection occurring. Herbal medicines have been traditionally used in the treatment of intestinal parasites for both humans and animals. For instance in South Africa herbal medicines are commonly used to treat both internal and external parasites in chickens.

In vitro studies have demonstrated antiparasitic effects of allicin against *Schistosoma mansoni* but most effects appear to occur at concentrations...
greater than that normally indicated for treatment. In vitro studies have also demonstrated an irreversible paralytic effect of garlic essential oil against *Fasciola gigantica* (liver fluke).10

**Adverse reactions**

Garlic may cause body and breath odour. It has also been associated with heartburn, nausea, flatulence, abdominal discomfort and diarrhoea. Adverse reactions are more common when taken on an empty stomach or at high doses.11

**Interactions**

Garlic may reduce the efficacy of antiretroviral medications such as saquinavir so concurrent use should be avoided. Theoretically garlic may interact with other blood thinning medications. However clinical studies have failed to confirm these effects. Additive effects are also theoretically possible with antihyperlipidaemic and *Helicobacter pylori* therapy, however these effects may be used for clinical benefit.11

**Use in pregnancy and lactation**

Doses in excess of usual dietary intake are not recommended.11

**Contraindications/cautions**

Patients with bleeding disorders or those within a week of elective surgery should avoid high intake of garlic.11

**Cautions and counselling points**

- A therapeutic trial of garlic may be warranted for those unable (or reluctant) to take, or who are resistant to standard antiparasitic treatments, especially for those with confirmed infection with *Giardia lamblia*, *Entamoeba histolytica* or *Hymenolepis nana*.11
- While effective therapeutic doses have yet to be established, recommendations of 3–4 cloves of fresh garlic/day (crushed, bruised or chewed to release the active compounds) are not uncommon.
- Those at risk of bleeding should use with caution.

**Chinese wormwood**

**Evidence for use**

Archaeological findings suggest that *Artemisia annua* (Chinese wormwood, sweet Annie, qinghao) has been used as a traditional remedy in China for more than 2,000 years. Much of the current research focusses on the use of its sesquiterpene lactone constituent, artemisinin, in the treatment of malaria, including the multi-drug-resistant protozoa *Plasmodium falciparum*. However, the efficacy of artemisinin also extends to other phylogenetically unrelated parasitic infections such as *Schistosoma japonicum* (blood fluke), *Toxoplasma gondii* (protozoa) and *Clonorchis sinensis* (Chinese liver fluke).13,15 While evidence of direct effects against parasites that reside in the gastrointestinal tract is limited, many human parasites enter the body via this route and may also reproduce there, so eggs can often been identified in stool cultures.

Artemisinin is a good example of an isolated constituent derived from a traditional herbal medicine which has been developed into a potent pharmaceutical compound. From this semi-synthetic analogue has been created which have improved bioavailability.16

In addition to the effects of artemisinin, crude extracts of the whole herb have also been tested in vitro for antiparasitic activity. An infusion of Chinese wormwood has been shown to control *Toxoplasma gondii*,17 and ethanolic extracts have been shown to kill flukes such as *Echinostoma caproni* which resides in the intestines, as well as *Schistosoma mansoni* and *Fasciola hepatica*.18 These results contribute to recent evidence that there may be a synergistic effect of multiple bioactive compounds in Chinese wormwood that require further exploration. For instance, flavonoids present in the leaf, may improve the bioavailability of artemisinin, and have shown a variety of biological activities including immunomodulatory activity in subjects afflicted with parasitic diseases.18 Antiparasitic properties have also been noted for *Artemisia absinthium* (wormwood), a close relative of Chinese wormwood, in animal experiments.19

**Adverse reactions**

Very little safety data is reported in the scientific literature, and whatever there is generally relates to the pharmacological analogues of artemisinin, such as artesunate, rather than the herb *A. annua* itself.

Alternatively, adverse reports may relate to its cousin *A. absinthium*, which contains thujone and absinthin, and should be used with caution in patients with compromised heart or brain function.20

A case report exists of possible temporary hepatitis, resulting in elevated liver enzymes, induced by a herbal preparation containing high doses of artemisinin (600 mg/day).21 Liver function should be monitored when taking high doses.

**Interactions**

May have additive effects with antimalarial and other antimicrobial drugs. Caution is advised in patients taking agents that affect angiogenesis.20

**Use in pregnancy and lactation**

Chinese wormwood may inhibit angiogenesis and is not recommended in pregnant or breastfeeding women due to a lack of available scientific evidence to confirm safety.20

**Cautions and counselling points**

- Antiparasitic effects have been described for Chinese wormwood but direct evidence for its use in the treatment of intestinal parasites is limited and dose recommendations are unclear.
- Caution is advised in patients taking agents that affect angiogenesis and liver function should be monitored especially at high doses.

**Other options**

**Black walnut**

*Juglans nigra* (black walnut) has been used to treat intestinal parasites in animals22 and has played a role in the treatment of intestinal conditions in humans since ancient Greek and Roman times. More recently it was made popular by Dr Hulda Clark who claimed that the green hull surrounding the nut of the black walnut tree could eradicate intestinal parasites and in the process cure cancer.23 Despite these elaborate claims there is little experimental evidence24 to confirm the antiparasitic effects and no clinical trials have been conducted in humans.
Black walnuts differ from their close relative the English walnut (*Juglans regia*) and can contain high levels of serotonin which may affect the results of urinary 5-hydroxyindoleacetic acid analysis (black walnuts [304 μg/g +/- 46] vs. English walnuts [87 μg/g +/- 20]). Although the black walnut extract (BWE) model is used to induce laminitis in horses it is only the heartwood of the tree that exerts this effect. Given the prevalence of treenut allergies those at risk should also avoid black walnut.

**Papaya seeds**

In a randomised placebo-controlled trial in Nigeria, 20 mL of a liquid preparation made from the seeds of the tropical fruit *Carica papaya* (papaya, pawpaw) was given to children with stool microscopic evidence of intestinal parasites. Stool clearance rates after seven days were significantly higher in the papaya group (76.7% vs. 16.7%, p<.001). No harmful effects were reported.

**Myrrh**

*Mirazid* is a patented preparation of *Commiphora molmol* (myrrh) that appears to be effective against the intestinal fluke (a flat worm) known as *Heterophyes heterophyes*. It is also registered in Egypt for the treatment of other fluke related conditions, schistosomiasis and fascioliasis.

**Berberine containing herbs**

Berberine is a plant alkaloid present in medicinal herbs such as *Hydrastis canadensis* (goldenseal), *Berberis aquifolium* (Oregon grape), and *Berberis vulgaris* (barberry). Berberine extracts have demonstrated significant activity against a variety of organisms including protozoa and helminths. It is known to inhibit the growth of the intestinal protozoan parasites *Entamoeba histolytica*, and *Giardia lamblia* and is also effective against other protozoa including *Trichomonas vaginalis* and *Plasmodium falciparum*, one of the species of *Plasmodium* that causes malaria.

Berberine has also demonstrated strong nematocidal activities against *Toxocara canis* (dog roundworm).

**Conclusions**

While studies have been conducted on the use of herbal medicines in the treatment of parasites that affect other animal species, as well as parasites that affect sites other than the intestines in humans, clinical studies demonstrating direct effects against parasites that reside in the human gastrointestinal tract are extremely limited. Currently garlic and Chinese wormwood show some potential for use and, along with other herbs (such as black walnut, papaya seed, myrrh and berberine containing herbs), deserve further research into their efficacy and safety.

**Key learning points**

- There is preliminary evidence suggesting that garlic and Chinese wormwood may warrant a therapeutic trial in patients unable (or reluctant) to take, or who are resistant to standard antiparasitic treatments.
- Effective doses have yet to be established and safety data for herbs such as Chinese wormwood is limited.

**References**

Questions

1. Knowledge about the antiparasitic properties of traditional herbal medicines most likely developed from:
   a) Early humans observing the behaviour of other animals.
   b) Herbalists employing the ‘doctrine of signatures’ to assess plants for their medicinal potential.
   c) In vitro studies on isolated components such as artemisinin.
   d) Clinical use of analogs of herbal constituents such as artesunate.

2. Garlic is contraindicated for concurrent use with which of the following medications?
   a) Antihyperlipidaemic medications (e.g. atorvastatin).
   b) Antihypertensive medications (e.g. irbesartan).
   c) Antiretroviral medications (e.g. saquinavir).
   d) Helicobacter pylori triple therapy.

3. There is preliminary evidence for the use Chinese wormwood as an antiparasitic agent against which of the following organisms?
   a) Clonorchis sinensi, Entamoeba histolytica, Schistosoma japonicum/mansoni, Toxoplasma gondii.
   b) Clonorchis sinensi, Juglans nigra, Schistosoma japonicum, Toxoplasma gondii.
   c) Entamoeba histolytica, Juglans nigra, Schistosoma mansoni, Toxoplasma gondii.
   d) Clonorchis sinensi, Schistosoma japonicum/mansoni, Toxoplasma gondii.

4. Which of the following statements is TRUE regarding the bioactive constituents found in herbal medicines?
   a) Allicin is a thiosulfinate found in Commiphora molmol.
   b) Artemisinin is a sesquiterpene lactone found in Artemisia absinthium.
   c) Berberine is an alkaloid found in Hydrastis canadensis.
   d) Thujone is a flavonoid found in Allium sativum.