Complementary and alternative therapies in liver and gut disorders

Only a few of the many herbal remedies now popular as alternative therapies for various disorders have been subjected to clinical trials. Dietary interventions are also discussed.

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Interest in and use of complementary and alternative therapies for a wide range of illnesses has increased greatly in the past decade. Several studies document this trend in Western countries and some seek to identify reasons for the change in attitude to the use of these therapeutic approaches. Gastrointestinal diseases are no exception to the experience, and many patients presenting to gastroenterologists are taking or have taken alternative treatments for chronic disorders such as reflux disease, chronic hepatitis and chronic constipation or diarrhoea.

Alternative medicines and therapies are those usually taken instead of a standard Western medicine or treatment; complementary medicine therapies are those that would normally be taken in addition to a Western medicine or treatment. As in most parts of medical practice, there are overlaps between alternative and complementary therapies, with some patients taking a 'complementary' medicine as their only medication and others taking Western medicine and an alternative medicine. The key message for Western practitioners in relation to these therapies is to always ask about all possible additional treatments that a patient may be using.

The various complementary and alternative therapies available and commonly used in Australia are briefly defined in the box on page 60. This article discusses the toxicity of herbal remedies, particularly hepatotoxicity, and then examines the evidence for the usefulness of herbal remedies

IN SUMMARY

- **Toxicity and injury from herbal medications are well recorded.**
- **Herbal medications used inappropriately (for example, excessive doses and mixing herbal compounds without taking advice) can damage multiple organ systems.**
- **Anyone considering the use of a herbal remedy should be aware of the claims made for the product and its potential side effects.**
- **Patients should be monitored regularly to ensure that the use of a product is associated with benefit and not with harm.**
- **Alternative therapies tried by patients with chronic liver disease include dietary therapy and modification, homeopathic treatments and herbal medications, as well as exercise and meditation.**
- **Preparations that have been studied in trials and found to be candidates for liver disease therapy are *Silybum marianum* (milk thistle), Chinese herbal medicine CH-100, TJ-9 (sho-saiko-to, xiao-chai-hu-tang, minor bupleurum formula), phyllanthus extract and stronger neo-minophagen.**
- **Approval of a complementary medicine by the Therapeutic Goods Administration does not guarantee its efficacy in any particular disease state.**

Table 1. Medicinal plants frequently associated with allergic reactions[1]

Angelica	Holy thistle
Aniseed	Parsley
Cassia	Rosemary
Celery	Royal jelly
Dandelion	Wild carrot
Feverfew	Yarrow

Table 2. Common toxic chemical contaminants of herbal remedies

Aluminium	Diazepam
Aminopyrine	Ephedrine
Arsenic	Lead
Aspirin	Mercury
Betamethasone	Thallium
Bromhexine	Tin
Cadmium	Zinc
Caffeine	

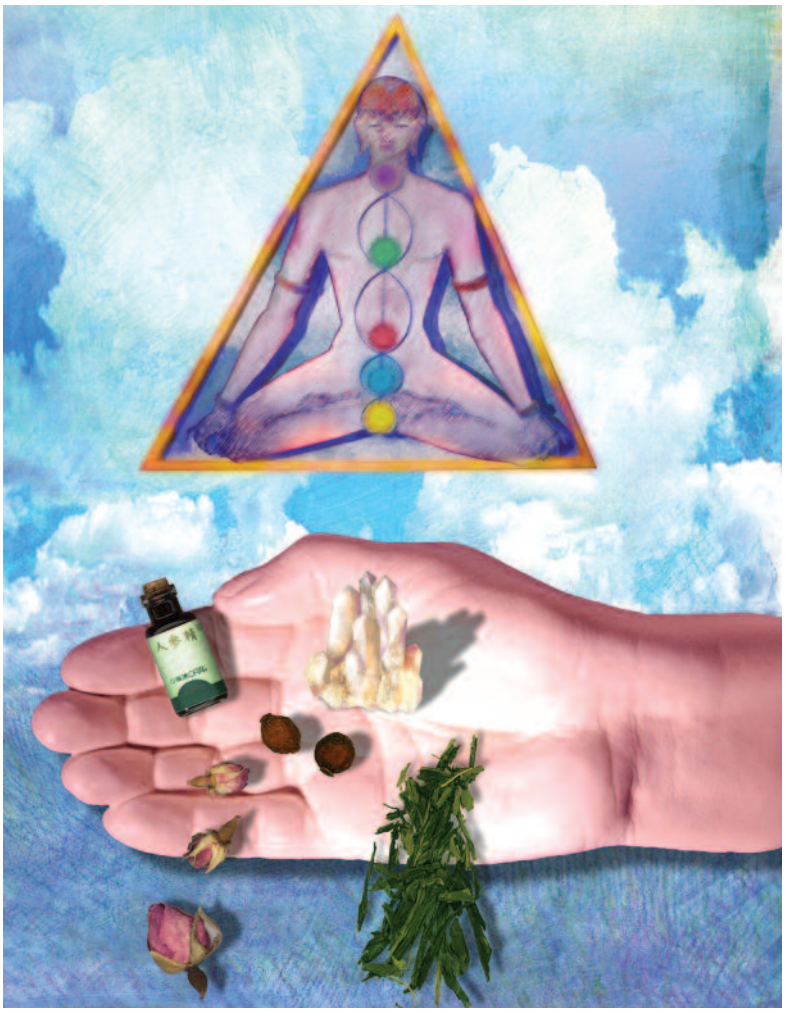
in gastrointestinal disorders. It is important to stress that there is no research evidence for the efficacy of many of these therapies in gastroenterological practice.

Toxicity of herbal remedies

Many people regard herbal medications as 'safe' because they are natural. This is neither rational nor true. Toxicity and injury from herbal medications are well recorded, the toxicity usually being due to component(s) that are toxic (direct toxicity) or cause allergic or hypersensitivity reactions or to toxic contaminating organisms or chemical compounds (Tables 1 and 2). Western trained doctors generally express significant anxiety over the potential for herbal medications to cause toxic injury although the pharmaceuticals they prescribe also have potentially lethal side effects. Correctly used, however, complementary therapies may be less toxic than prescription agents.

There is evidence that herbal medications used inappropriately (for example, excessive doses and mixing herbal compounds without taking advice) can damage multiple organ systems.[1] Also, mild, moderate and life-threatening damage to liver, kidney, muscle and blood has been identified in patients who have reacted atypically to herbal medicines or who have taken inappropriate amounts. A further problem for patients these days relates to variable concentrations of products within commercial preparations of herbal medicine. Events with a major company in Australia have indicated that preparations are not always as pure or consistent as many would like to believe. Some herbal therapies that have been reported to cause liver damage are listed in Table 3.[2,3]

Anyone considering the use of a herbal remedy should be aware of the claims made for the product and its potential side effects. Patients should be monitored regularly to ensure that the



Complementary and alternative therapies

The following complementary and alternative medicine approaches are available and commonly used in Australia for various conditions. Exercise and meditation are also regarded as complementary approaches to the management of illnesses.

Acupuncture

Acupuncture is the stimulation of special points on the body, usually by the insertion of fine needles. Originating in the Far East some 4000 years ago, and first documented about 2000 years ago, it appears in Europe and North American medicine histories.

Aromatherapy

Aromatherapy is the use of volatile oils from plants. They are applied to the skin or inhaled in minute doses.

Ayurvedic therapies

Ayurveda is similar to traditional Chinese medicine in that it uses dietary alteration, yoga, exercise, herbal formulas and surgery to treat the whole person by addressing functional imbalances. The Ayurveda system of healing originated in India thousands of years ago.

Colonic irrigation

Colonic lavage or irrigation is an extended form of enema. The treatment is designed to cleanse the entire large bowel from rectum to caecum. The procedure involves the infusion of water at body temperature into the colon.

Dietary therapy

Comprehensive changes in eating patterns are involved in dietary therapy. Many diets, such as vegetarianism and veganism, originated as 'movements' characterised by political and ecological concerns; they were a moral stance towards food and a view of diet as inseparable from lifestyle.

Herbal medicine

Chinese, Japanese and Korean herbalism

The use of plants for healing purposes predates human history and forms the basis of much modern medicine. Herbalists generally use unpurified plant extracts, and claim that the several different constituents can work together synergistically so that the effect of the whole herb is greater than the summed effects of its components. They also claim that toxicity is reduced when whole herbs are used instead of isolated active ingredients ('buffering'). Often, several different herbs are used together. Herbal medicine is part of traditional Chinese medicine, the ancient holistic system of health and healing that focuses on stimulating the body's natural curative powers by the use of herbal medicine, acupuncture, dietary therapy, and massage and exercise.

Herbal remedies are available in a variety of forms, including tablets, powders and herbal teas.

Western herbalism

Modem Western herbalism emphasises the effects of herbs on individual body systems. For example, herbs may be used for their supposed anti-inflammatory, haemostatic, expectorant, antispasmodic or immunostimulatory properties.

Homeopathy

Homeopathy is the use of ultra low dose preparations administered according to the principle that 'like should be cured with like'. Practitioners select a chemical that would, if given to healthy volunteers, cause the presenting symptoms of the patients. This substance or combination of substances is then made up in a highly diluted solution and administered on a regular basis.

Massage

Therapeutic massage is the manipulation of the soft tissue of whole body areas to bring about generalised improvements in health, such as relaxation or improved sleep, or specific physical benefits, such as relief of muscular aches and pains.

Naturopathy

Naturopathy is a therapeutic system emphasising the philosophy of 'nature cure'. It incorporates Western herbal medicine, homoeopathy, dietary intervention and other practices such as hydrotherapy and exercise.

Nutritional supplements

The range of nutritional supplements includes many animal and plant products, as well as various vitamins and minerals. Some supplements have known active ingredients, such as linolenic acid in evening primrose oil, while others, such as blue-green algae and kelp, have not been fully characterised biochemically. Some are taken to improve general health and performance, and others for specific clinical indications. Most are taken in pill form. There are overlaps between herbal and nutritional supplements.

Osteopathy and chiropractic

Osteopathy and chiropractic are therapies of the musculoskeletal system. Practitioners work with bones, muscles and connective tissue, using their hands to diagnose and treat abnormalities of structure and function.

use of a product is associated with benefit and not with harm, as neither or both may occur in the same patient. Appropriate usage is more likely if a practitioner well trained in herbal medicine is consulted. Self-medication with any form of medicine, be it herbal or standard Western medicine, runs a risk of complications.

Alternative therapies and the liver

Patients with chronic liver disease have tried many alternative therapies over the years, including dietary therapy and modification, homeopathic treatments and herbal medications, as well as exercise and meditation. Evidence for the efficacy of many of these is lacking, and other than herbal therapy, they cannot be recommended.

Dietary therapies

The liver cleansing diet, a short term diet high in raw fruit and vegetable and low in fat, is probably the best known dietary therapy for patients with chronic liver disease.[4] While the theory underpinning the diet is unproven, many patients declare they feel better and have improved liver tests while on the diet. It is of interest that newer data show a link between body mass index, serum lipids and liver function in chronic hepatitis C virus infection. These findings may provide an explanation for the apparent benefit of the liver cleansing diet in many individuals. Data would now suggest that all patients with chronic liver disease should aim to maintain an ideal body weight and normal serum lipids and glucose levels.

The liver cleansing diet also recommends dietary changes that result in the consumption of probiotics (living microorganisms that on ingestion in adequate amounts exert health effects beyond inherent basic nutrition).

Herbal medications and the liver

Herbal remedies have been used in some parts of the world for centuries to treat liver conditions but have only recently become popular in Australia for this use. The increased interest in herbal therapies is part of a general trend towards using natural products and possibly relates to the perception that these 'medicines' are more patient-friendly than conventional therapies.

Of the thousands of herbal preparations that are claimed to have medicinal qualities, only a few have undergone proper scientific testing to determine their effectiveness in liver disease. Preparations that have been studied in trials and found to be candidates for liver disease therapy are *Silybum marianum* (milk thistle), Chinese herbal medicine CH-100, TJ-9 (sho-saiko-to, xiao-chai-hu-tang, minor bupleurum formula), phyllanthus extract and stronger neo-minophagen. Although these medications are popular remedies in use today, trials as to their effectiveness and side effects are ongoing.

In Australia, a number of complementary medicines have been approved by the Therapeutic Goods Administration but this does not guarantee efficacy in any particular disease state.

Silybum marianum (milk thistle)

Silybum marianum, also commonly known as milk thistle and St Mary's thistle, is a herb recorded in antiquity as a tonic for liver conditions. Silymarin (an extract from milk thistle seed) contains a mixture of silybinin, ellydianin and sillchristin. Silybinin, the most abundant of these, is the main active component. Many studies have suggested that silymarin has protective effects on the liver, reducing the toxicity of several drugs and toxins. The mechanism of liver protection is unknown but is likely to be linked to antioxidant and cell membrane stabilising properties.[5]

Clinical trials of silymarin in humans with liver disease have produced inconclusive results. The most consistent observation is that silymarin can reduce the levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase

Table 3. Hepatotoxic herbal therapies*

Herbal name	Common name	Toxicity
Gui-jiu	Podophyllum	Hepatic injury
Yan-hu-suo	Corydalis	Hepatitis
Ren-shen	Ginseng (*Panax ginseng*)	Hepatitis
Herbal teas	*Ephedra* spp.	Hepatitis
	Panax pseudo-ginseng root	Hepatorenal injury
	Comfrey†	Hepatic injury
Larrea	Chaparral†	Hepatic injury
Teucrium	Germander	Hepatic injury
Labiatae	Pennyroyal	Hepatic injury
Pyrrolizidine alkaloids	*Tussilago* (coltsfoot), *Borago* (borage), *Symphytum* spp. (comfrey)	Hepatic injury

*Preparations containing valerian, asafoetida, hops, skullcap and gentian have resulted in hepatitis.[2]
†Comfrey and chaparral are banned in Australia.

(AST), which are biochemical markers of liver inflammation, in a range of liver diseases including acute viral and alcoholic hepatitis, and chronic hepatitis.[6-8] Silymarin is also reported to reduce length of hospital stay in acute viral hepatitis, improve symptoms in chronic hepatitis subjects and even increase survival in patients with cirrhosis.[9-11] However, not all trials report positive outcomes,[11,12] and those that did recruited only small patient numbers and lacked uniformity in both diagnosis and the type and dose of silymarin preparation used.

Nevertheless, the compound is well tolerated and has few side effects, which is why it is one of the most popular herbal remedies for liver diseases in use today.

CH-100

The Chinese herbal medicine CH-100, a proprietary formulation of 19 herbs, was the subject of an Australian clinical trial.[13] This placebo-controlled double-blind study of 40 patients with chronic hepatitis C showed a significant reduction in ALT over six months in those receiving CH-100 ($p<0.03$), with 20% of treated patients normalising their ALT. Hepatitis C virus was not cleared in any patient. Previous uncontrolled trials reported in the Chinese literature further support a useful role for this medication. Side effects of CH-100 include gastrointestinal disturbance and potentially hypertension (due to the licorice root [*Glycyrrhiza*; active ingredient glycyrrhizin] contained in the formulation).

At present in Australia a number of patients are taking CH-100 for chronic hepatitis B or C. Two randomised placebo-controlled trials, involving more than 100 patients (randomised in the ratio of two on active therapy to one on placebo), have now been completed. They have shown that patients report an improvement in symptoms while on the therapy but were unable to confirm the originally reported fall in ALT levels.[14,15] Possible reasons for the different outcome include the fact that larger studies are harder to control and patients may have been less rigorous in their adherence to the medication schedule. Equally plausible is the suggestion that with smaller numbers and an original study, all patients looked after their health more actively and the benefit shown reflected this rather than any beneficial effect of the herbal medication.

Salvia miltiorrhiza, one of the components of CH-100, has been shown to decrease oxidative hepatic damage and fibrosis in a number of animal models, with activity being demonstrated to be due to several specific compounds.[16]

Evidence also supports a role for glycyrrhizin (see under 'Stronger neo-minophagen').

TJ-9, sho-saiko-to, xiano-chai-hu-tang or minor bupleurum formula

TJ-9 is a combination of seven herbs – bupleurum root, pinellia tuber, scutellaria root, jujube fruit, ginseng root, licorice root and ginger root (bupleurum is known in Japan as saiko and in China as chai hu) – and is the most commonly used compound for chronic liver diseases in Japan.[17] It appears to have a range of beneficial effects on the liver, including 'enhancement of the immune system'. One multicentre randomised placebo-controlled double-blind study showed liver enzymes were lowered in chronic hepatitis.[18] Studies have indicated specific benefits in hepatitis C and B (including HBeAg and HBsAg clearance), and a decreased risk of progression to liver cancer.[19] In a prospective study of 280 patients with cirrhosis, hepatoma was decreased over five years of observation. Subjective symptom improvement may be an additional benefit.

Unfortunately, serious side effects have been reported with this compound, including interstitial pneumonitis, which can be fatal. The incidence of this latter side effect appears higher when TJ-9 is given in conjunction with interferon (perhaps 4.0%, compared with 0.7% with the herb alone),[20,21] and the injury appears to be mediated by an alteration of the immune system, the pneumonitis occurring within days or up to six months later. Therapy includes cessation of herbs and, possibly, the use of corticosteroids.

Stronger neo-minophagen

The Japanese medicine stronger neo-minophagen is often used for chronic hepatitis. Its principle active component is glycyrrhizin, which is also found in CH-100 and TJ-9. A retrospective cohort study in hepatitis C found a 7% or 12% cumulative incidence of hepatoma at 10 or 15 years in 84 patients who received the preparation for a median of 10.1 years, compared with incidences of 12% or 25%, respectively, in 108 patients who did not receive it.[22]

Phyllanthus extract

Extracts of several *Phyllanthus* species have been used in a variety of liver disorders for centuries. Practitioners on the Indian subcontinent have the greatest experience of the use of these agents, but literature demonstrating the efficacy of any of the products remains sparse.[23-27]

Alternative therapies in other gut disorders

Irritable bowel syndrome

Patients use a variety of approaches to assist in the management of irritable bowel syndrome (IBS), including drugs, dietary modifications, counselling and, more recently, Chinese herbal medicine. The research literature lends some support to two complementary interventions – peppermint oil (Mintec) and Chinese herbs. A review of eight controlled trials of the use of peppermint oil in IBS indicated that peppermint oil could be efficacious for symptomatic relief of IBS.[28] In addition, two recent controlled clinical trials of the use of Chinese herbs for IBS provide evidence that Chinese herbs may bring symptomatic

relief to patients with IBS.[29,30] Further studies are under way in this condition.

Homeopathy in postoperative ileus

There is some preliminary evidence that homeopathy can reduce the duration of ileus after abdominal or gynaecological surgery. A systematic review of six clinical trials revealed homeopathy helped shorten the postoperative time to normal small bowel function by around seven hours.[31,32]

Gut function and dietary intake

There is much less research evidence to support the use of nutritional components in the prevention of gut disorders or in the maintenance of gut health than there is for other forms of intervention. There are few intervention trials with foods or food ingredients that meet the very high standards used for adequately controlled randomised double-blinded pharmaceutical trials. With foods, it is often impossible to blind the recipients to the changes being made, so studies are more difficult to carry out. Consequently, dietary interventions rely on an evidence base compiled from epidemiological associations drawn from cohort and case–control studies or from ecological studies of populations.

The task for the biochemist is to establish a plausible biochemical pathway that might explain the association. The task for the epidemiologist to establish that the food ingredient is indeed on the causal pathway to the disease being studied.

What can be said is that diets of certain foods can decrease or increase the risk of development of gut disorders:

- there is convincing evidence that diets high in fruits and vegetables decrease the risk of developing stomach and colorectal cancer[33,34]
- there is probable evidence that high intakes of alcohol increase the risk of developing colorectal cancer[35-37]
- there is probable evidence that salted food and high salt intake increase the risk of developing stomach cancer.[35,37]

Probably the best overall dietary advice for attaining and maintaining gut health is to follow the Australian dietary guidelines and consume a diet that is high in cereals, fruits and vegetables while maintaining physical activity and moderating fat and alcohol intake.

Micronutrients

There has been considerable research in the field of micronutrients and gut health (in particular, the antioxidant vitamins and more recently flavinoids such as lycopene found in tomatoes). Some cohort and case–control studies have shown higher risks of developing stomach and colorectal cancers with lower intakes of these micronutrients. Intervention trials using supplements have produced mixed results and further work is needed before any conclusions can be drawn. The Australian dietary guidelines emphasise high cereal, fruit and vegetable intake, which leads to high intakes of these important micronutrients.

Maintenance of healthy gut structure and function

Preserving the appropriate micro-organism population in the large bowel and supplying appropriate fuels for maintaining normal cellular metabolism in the gut will enable a healthy gut structure and function. Glutamine, short chain fatty acids and soluble dietary fibre rich in beta glucan are the components most often recommended by dietary therapists.

The consumption of foods containing soluble fibre and fructo-oligosaccharides promotes the growth of those micro-organisms that are beneficial to health (probiotics). These micro-organisms (most commonly lactobacilli, bifidobacteria and streptococci) utilise the fibre and produce short chain fatty acids for use by the gut cells.[38] Maintenance of a healthy gut micro-organism population is also aided by consumption of these foods. All of these food ingredients can be obtained by consuming a diet high in cereal, fruit and vegetables and following the Australian Dietary Guidelines.

Conclusion

While many people in Australia are using alternative medicines and therapies in the strong belief that they are benefiting from them, it is clear that very few of these treatments have been subjected to rigorous clinical trials. Events in Australia have highlighted difficulties in ensuring products are safe and dependable. It is suggested that information be sought as to the evidence for any particular product having benefit in the disease in question before embarking on any alternative or complementary treatment. MT

A list of references is available on request to the editorial office.

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