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Medicinal Mints

The medicinal properties of the humble mint family (Labiatae or Lamiaceae) are often underestimated or ignored by the scientific community. But a few recent studies support the contention that they might have a more important role to play in natural therapies, including the care of conditions such as hyperthyroidism, stress and Alzheimer's disease.

Either *Lycopus virginicus* (Bugleweed) or *Lycopus europaeus* (Gypsywort) is traditionally used for the management of the symptoms of hyperthyroidism, especially Grave's disease.¹ While there were some uncontrolled clinical trials conducted in the 1950s, modern evidence for this use was lacking.¹ Hence it is encouraging to find the recent publication of a controlled open study which examined the effect of *Lycopus europaeus* on thyroid function and associated symptoms in 62 patients with hyperthyroidism of unspecified causes.² The study population consisted of patients with a TSH <1.0 mU/L and hyperthyroidism-associated symptoms. The main clinical outcome measured was 24-hour urinary T₃ and T₄ excretion after around 12 days of therapy and the study found that T₄ excretion was significantly increased by *Lycopus* (p=0.032). There was also a trend to increased T₃ excretion that did not achieve clinical significance. This occurred in conjunction with a reduction of some symptoms, specifically increased heart rate in the morning. However, TSH and serum T₃ and T₄ levels were not changed. It was proposed by the authors that a renal mechanism was responsible for the increased T₄ clearance.

There have been several clinical studies on lemon balm (*Melissa officinalis*) that have demonstrated sleep-promoting and spasmolytic effects, often in conjunction with other herbs.³ While recent studies have maintained the focus on the nervous system, different applications have been investigated. A systematic review of the potential of herbs for Alzheimer's disease identified two members of the Labiatae, namely lemon balm and sage (*Salvia officinalis*).⁴ Both herbs have yielded promising results in small controlled trials, which were assessed by the reviewers as having been adequately reported according to the Jadad scale.⁴ In particular the lemon balm, which was given at a dose

equivalent to around 3 g per day, produced a significantly better outcome on cognitive function than placebo in patients with mild to moderate Alzheimer's disease and had a positive effect on agitation in such patients.^{4,5}

Another study conducted in the UK used a double blind, placebo-controlled crossover design to examine the impact of a single dose of lemon balm on laboratory-induced psychological stress.⁶ At a single dose of 600 mg of extract (around 3 g of dried herb), the lemon balm reduced the negative mood effects of the laboratory stress simulator and significantly increased self-rated calmness and reduced self-rated alertness in healthy volunteers. The authors suggested that their findings support the traditional use of lemon balm as a calming agent and mild sedative and proposed that lemon balm possibly has an inhibitory action on the neurotransmitter gamma-aminobutyric acid (GABA) within the central nervous system.

Comment

This mode of action on the kidney is a new and interesting finding for *Lycopus* in hyperthyroidism. Previous pharmacological studies suggested that the herb inhibited the binding of TSH to its receptor on the thyroid gland.¹ However, this mechanism implies a clinical reduction in T₃ and T₄, which was not observed in the current study. One possible reason for this discrepancy was that the dose of *Lycopus* used in the study featured above was relatively low, being around 40 mg per day (presumably of dried extract which would equate to around 200 mg of dried herb, or around 3 mL of 1:2 per week).² Higher doses, as are more commonly used by herbal clinicians, might indeed have seen a reduction in T₃ and T₄. Clinical experience suggests that such higher doses of *Lycopus* can also elevate TSH in patients with Grave's disease. Another weakness of the study was that the entry point of TSH <1.0 mU/L means that patients with both clinical and sub-clinical hyperthyroidism were included in the study. Also the cause of the hyperthyroidism was not differentiated.

The evidence for the clinical activity of lemon balm is currently more robust than for *Lycopus*. In particular the reduced agitation observed in Alzheimer patients and the calming effects seen in simulated stress suggest

that this plant is indeed a significant herbal sedative. The proposed mechanism of action via GABA implies that lemon balm might combine well with valerian, which is also thought to influence GABA. As noted previously, there are in fact several clinical studies from Germany where this herb combination has improved sleep quality.³

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Useful Clinical Effects from Chinese Herbs

Clinical research on traditional Chinese herbs continues unabated, with many of these trials being published in mainstream western medical journals. Some recent trials or case reports have revealed novel and useful applications, three of these are discussed below.

The antipsychotic drug risperidone, used in the management of schizophrenia, often causes raised prolactin (defined as >20 mg/mL for men and >25 mg/mL for women). This elevation of prolactin results from the dopamine-blocking effect of the drug on the hypothalamus and can cause distressing symptoms, such as disrupted menstrual cycles, galactorrhoea and sexual impairment. The drug bromocriptine is often prescribed to relieve this side effect, but often aggravates the psychosis and abnormal involuntary movements.

Since the combination of licorice (*Glycyrrhiza species*) and Paeonia (*Paeonia lactiflora*) has been used in traditional Chinese and Japanese medicine for the treatment of hyperprolactinaemia, its effect on this risperidone-induced side effect was compared against bromocriptine in a recent clinical trial.¹ Twenty women with schizophrenia receiving risperidone maintenance treatment who were diagnosed with hyperprolactinaemia received either a decoction of the herbal combination (from 15 g licorice and 30 g Paeonia per day) or bromocriptine (5 mg per day) in a crossover design. The treatment period was 4 weeks. Severity of psychotic symptoms, adverse events, serum prolactin, oestradiol, testosterone and progesterone levels were examined at baseline and end point. The

herbal decoction produced a significant decrease in serum prolactin levels, without exacerbating psychosis or changing other hormones, and the decreased amplitudes were similar to those of bromocriptine (24% vs 21%-28%). Moreover, there was a significantly greater proportion of patients during the herbal treatment than bromocriptine treatment showing improvements of the adverse effects associated with hyperprolactinaemia (56% vs 17%, $p=0.037$). These results suggest that the herbal therapy can yield additional benefits while having comparable efficacy in treating antipsychotic-induced hyperprolactinaemia in individuals with schizophrenia.

The effect of rhubarb root (*Rheum officinalis*) on plasma lipids and vascular endothelial function was investigated in 103 patients with diseased arteries (atherosclerosis) in a randomised, controlled clinical trial.² Over 6 months patients received a placebo or dried rhubarb decoction (50 mg/kg), which corresponds to about 13 g/day of dried root for a 70 kg adult. At the end of the trial period there was a modest but significant reduction in total and LDL cholesterol in the patients receiving rhubarb. Flow-mediated dilation (FMD) was also substantially and significantly improved in the herbal group. Impaired functioning of the lining of arteries, especially reduced endothelium-dependent dilation and hence flow, is associated with coronary atherosclerosis and coronary risk factors. The effect of rhubarb on FMD might mean that it could reduce angina symptoms, restore the arterial lining towards better health and improve arterial circulation. Despite the high dose of rhubarb used in the trial, only around 10% of patients experienced diarrhoea, which was mild and resolved without symptomatic therapy. (*R. palmatum* is also acceptable as medicinal rhubarb in traditional Chinese medicine).

Finally, an interesting case report described the use of a formulation containing Astragalus (*Astragalus membranaceus*) by a patient with idiopathic membranous nephropathy, which is autoimmune in origin.³ Effective conventional treatment for this disorder is lacking because immunosuppressive drugs have not demonstrated clear efficacy. Also the variability of the clinical severity and the tendency to spontaneous remission in some patients further complicate any assessment of proposed treatments.³

The report describes an elderly woman with nephrotic syndrome and confirmed primary (idiopathic) membranous nephropathy. After failure of conventional therapy, she began using a herbal formulation prescribed by a traditional Chinese physician at 15 g/day for 3 months. The paper incorrectly describes Astragalus as the "active ingredient" in the treatment, when it in fact was the formulation *Four Ingredient Tablet for Nephritis* containing Astragalus, Baical

skullcap, Gardenia and Pyrrosia. Her urine protein:creatinine ratio decreased from 9.5 to 1.65, the serum albumin level increased from 24 to 28 g/L and her oedema was resolved. After cessation of the herbal treatment for 6 weeks her condition deteriorated, only to be improved again after reinstatement of the therapy. Complete remission of the proteinuria occurred 9 months later and it did not return after the cessation of the herbs. The authors proposed that although causality is suggested by both the temporal association and the remission of proteinuria with exposure and re-exposure, it is not proven by this case report. Additional studies of this treatment in immune-mediated glomerular diseases are warranted.

Comment

The use of the licorice and Paeonia combination for the treatment of risperidone-induced side effects is not new. Several case observation studies were published in 1999.⁴ In these cases an equal parts combination of the two herbs was used. The findings of the controlled trial above suggest that the combination could also be of value in primary hyperprolactinaemia in both men and women. This would be a very useful clinical application, as hyperprolactinaemia is a cause of infertility.

The Astragalus-related case report is yet another example of how herbs regarded as immunostimulants can exert an immune-modulating role in autoimmune disease. As the authors suggest, a controlled clinical trial would help to further establish the value in nephropathy of the Chinese herbal treatment used.

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Marshmallow Root and ACE Inhibitor Cough

According to the Therapeutic Guidelines website, at least 15% of patients receiving angiotensin converting enzyme (ACE) inhibitors (prescribed usually for hypertension or congestive heart failure) develop a persistent dry cough.¹ This is thought to be due to a lowering of the cough reflex threshold and it occurs more commonly in women. There is no advantage in changing from one ACE inhibitor drug to another.

A randomised, double blind, placebo-controlled trial was conducted to evaluate the effect of marshmallow root (*Althaea officinalis*) on ACE inhibitor cough.² Sixty patients completed the trial and took either a placebo or a marshmallow root liquid (1 mL 3 times daily, product information not specified) for 4 weeks. Mean cough score improved significantly in the herbal group, falling from 2.66 at baseline to 1.23 ($p < 0.05$).

Comment

The above trial is a novel clinical verification of the traditional assertion that marshmallow exerts a reflex demulcent activity. The theory is that the soothing effect of the abundant mucilage in the root on the upper digestive tract effects an elevation of the cough threshold (among other things). This is possibly initiated by a reflex activity mediated by the vagus nerve.³

The demulcent mucilage-containing medicinal plants also have other therapeutic uses, including a soothing and protective effect on the lining of the digestive tract. In particular they can act as raft-forming agents in anti-reflux preparations. The properties of such agents were recently reviewed, where it was proposed that they are an ideal therapy for gastro-oesophageal reflux.⁴ This is because they can protect the oesophageal mucosa by providing a physical barrier between the corrosive gastric fluid and the oesophageal lining. They thereby act locally by reducing the contact time of refluxate with the oesophageal mucosa and so do not interfere with normal digestive processes, unlike the antacid drugs.⁴

Raft-forming anti-reflux agents form a viscous, gelatinous barrier at the top of the stomach contents that prevents the acidic gastric contents from being refluxed into the lower oesophagus. This barrier floats on the stomach contents like a raft. It acts as a moveable sealant that precedes the gastric acid into the oesophagus during reflux, protecting and coating the mucosa. Apart from this barrier function, these preparations also help in maintaining the pH of the lower oesophagus more towards neutral.⁴

Successful raft formation requires sufficient gastric contents to position the treatment in the fundus, where it can prevent reflux of acid or be refluxed preferentially to the gastric contents. In order to achieve this the treatment must be taken after meals. Furthermore, body position can play an important role in establishing a successful raft. Lying on the right side allows the raft to float into the greater curvature of the stomach, sit on top of the stomach contents and to empty after the meal.⁴

Raft-forming agents used in conventional medications include the alginates, pectin and xanthan gum.

However, the traditional mucilaginous herbs, especially slippery elm (best taken as the powder or the capsules) and marshmallow root, are likely to offer a distinct therapeutic advantage, as confirmed by the experience of herbal clinicians.

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