Reviews of articles on medicinal herbs

Jodie Tester

These abstracts are brief summaries of articles which have appeared in recent issues of herbal medicine journals, some of which may be held in the NHAA library.

Artichoke extract protects against alcohol-induced liver injury in mice


Alcoholic liver disease (ALD) is the leading cause of cirrhosis and liver-related death worldwide and is estimated to be responsible for 4% of global mortality. ALD encompasses a histological spectrum of liver injury from steatosis to alcoholic steatohepatitis (ASH) to fibrosis, cirrhosis and ultimately hepatocellular carcinoma. Potential mechanisms of acute alcohol-induced liver injury include oxidative stress, steatosis, endotoxin, immunity, and inflammatory mechanisms. Control of ALD at an early stage, such as prior to the occurrence of ASH, may play a role in preventing the development of ALD. Artichoke (*Cynara scolymus*) is an edible herbal medicine, previously studied for its possible antioxidative and hepatoprotective effects. Authors of the current study aimed to assess the preventive effects of ethanolic extract from artichoke on acute alcohol-induced injury in mice.

Male Institute of Cancer Research (ICR) mice were randomly divided into 6 groups of 10: Control; EtOH group (model group); Positive control (EtOH + bifendate); Low-dose artichoke group (EtOH + artichoke 0.4g/kg BW); Middle-dose artichoke group (EtOH + artichoke 0.8g/kg BW); High-dose artichoke group (EtOH + artichoke 1.6g/kg BW). Alcohol administration was with 12mL/kg BW one hour after bifendate or artichoke pre-treatment each day. All groups were fed for 10 consecutive days.

For serum biochemical markers, experiments found that artichoke extract significantly prevented elevated levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglyceride (TG) and total cholesterol (TC), in a dose-dependent manner compared with the EtOH group. ALT, AST, TG and TC are early biochemical and pathological markers of hepatocyte damage. Additionally, decreased levels of superoxide dismutase (SOD) and glutathione (GSH) were elevated by artichoke administration, both of which protect against reactive oxygen species caused by oxidative stress in alcoholic liver injury. In further experiments, it was found that compared to EtOH group, artichoke extract also significantly attenuated degeneration and necrosis of hepatic cells. It was noted that the dose of 1.6g/kg BW artichoke exhibited significant preventative potential for acute alcohol-induced liver injury, whereas the low-dose artichoke level of 0.4g/kg BW was not significant.

With alcoholic liver disease and alcohol-induced liver injury contributing to a significant health burden, the findings of a potential protective benefit of artichoke supplementation warrant further investigation. Future research to better understand and demonstrate efficacy, safety, optimal dosing, and outcome measures in humans is required.

Zizyphus complex not found to improve sleep quality in insomnia


Insomnia, defined by disturbances in sleep quality together with impairment of daytime functioning, is estimated to effect between 13-33% of Australians. Insomnia can range from acute and non-clinical to chronic and long-term. Whilst acute episodes will often resolve once the trigger is eliminated, many people will use short-term use of pharmaceutical medications such as benzodiazepine, or herbal supplements during these episodes.

Numerous herbal supplements have been studied with respect to their effect on sleep. The current study reports the results of a clinical trial which was designed to investigate the short-term effect of a combination formulation, LZComplex3 on sleep quality, mood and cognitive function in individuals with sleeping difficulties not caused by a primary sleeping disorder or other diagnosed conditions. The intervention contained Lactium™ (hydrolysed milk protein; alpha casozepine enriched), *Zizyphus jujube var. spinosa*, *Humulus lupulus*, magnesium oxide and vitamin B6. Participants were randomly allocated to receive the active intervention or a matched placebo. After a one week placebo run-in, patients completed a two-week course of either placebo or LZComplex3 and were instructed to take two tablets daily, 30 minutes before retiring for sleep.

Participants eligible for study included were healthy adults aged 18–65 years with no significant diagnosed disease, who had self-reported sleeping difficulties.
over the previous one month. Those with primary sleep disorders including sleep apnoea-hypopnea, narcolepsy, restless leg syndrome and Kleine-Levin syndrome were excluded. Assessments of sleep quality, daytime functioning and physical fatigue, mood and anxiety, stress reactivity, and cognitive function were completed by participants during the baseline and end of treatment visits. Participants also complete all subjective sleep, daytime functioning, physical fatigue, mood and anxiety assessments at home on days 1, 3 and 7 after baseline.

Of the 241 people screened for eligibility and the placebo run-in period, 171 participants were randomised to treatment, of which the modified intention to treat population included 160 participants (placebo n=82, LZComplex3 n=78). After two weeks supplementation, there were no differences between groups in the primary outcome of change in overall sleep quality from baseline despite observed improvements in sleep quality. Furthermore, the secondary outcomes measured including daytime functioning and physical fatigue, mood and anxiety, cognitive performance and stress reactivity did not support a benefit of LZComplex3 over placebo.

Strengths of the study include its use of the placebo run-in period designated to identify and exclude placebo responders. It is noted by authors that the two-week treatment duration may not have been sufficient to observe a treatment effect. Furthermore methodological limitations including sleep disorder allocation and misclassification of acute and chronic conditions may have impacted results. The importance of studies reporting negative efficacy results is essential to ensure quality of prescribing and to better understand the ideal patient population, and optimal durations of treatment.

**Peppermint and caraway oil in functional dyspepsia**


Functional dyspepsia (FD) is a common condition thought to affect more than 10% of the population. FD is defined by symptoms of the upper gut such as epigastric pain or burning, early satiation, and postprandial epigastric fullness. Complementary or herbal treatments are widely used in FD. The current study investigated the symptomatic relief and impact on quality of life (QOL) of a peppermint and caraway oil combination in patients with FD.

The study was a prospective, double-blind, multicentre trial conducted in an outpatient setting of general practitioners and physicians in Germany. Adult subjects of either sex with chronic or recurrent FD, persisting for at least 6 months with the current episode lasting for at least 1 week, were eligible for study inclusion. Patients were not eligible for the study if they had gastroesophageal reflux disease (GERD) or predominantly symptoms of GERD, functional dyspepsia of reflux type, or predominantly symptoms of IBS. Exclusion criteria also included concomitant medication with potential influence on outcome measures including prokinetics, agonists and antagonists of GI hormones, acid-reducing drugs, sedatives, laxatives, non-steroidal antiinflammatories, opioids, calcium antagonists and any other herbal preparations. All patients had a one-week placebo run-in period. Eligible patients were then randomised to receive either 2x1 capsules per day of the active intervention or matching placebo, with treatments to be taken at morning and noon, before meals. The active intervention was a fixed peppermint (90mg)/caraway(50mg) oil combination (Menthacarin). Active intervention lasted for 4 weeks with post baseline assessments performed after two weeks and at the end of treatment.

Of the 128 patients included in the run-in phase, 114 were randomised (1:1) to active treatment or placebo. After two weeks of therapy, the active intervention showed significant improvement of FD symptoms from baseline, compared to placebo. From baseline to end of treatment at 4 weeks, the average symptom score decreased by 62.3% and 26.0% for the active and placebo groups, respectively. Furthermore, the peppermint/caraway combination had a significant effect on disease-specific QOL. The interventions were well tolerated.

With a prevalence of dyspepsia estimated to range between 20-30% in the Western world, a significant number of whom may be suffering from FD. Accordingly, FD remains a significant burden to the healthcare system. Safe and effect treatments that not only provide symptomatic relief, but further improve quality of life are of great interest. The current study provides evidence to support a beneficial role of peppermint oil and caraway oil in providing relief from gastrointestinal symptoms of functional dyspepsia.

**Anti-obesity effect of Panax ginseng in obese rats**


Obesity is a major public health issue worldwide, with concurrent increase in incidence of metabolic diseases. Whilst many studies have investigated potential treatments for obesity, pharmacological agents for long-term obesity treatment are limited. Strategies for the prevention of obesity, including functional foods and plants, are therefore of great importance.
The root of ginseng has been used traditionally for the treatment and prevention of a variety of conditions. Roots of *Panax ginseng* (Korean ginseng) have previously demonstrated to exhibit anti-adipogenic activity in *in vitro* research. The aerial parts of Korean ginseng are less well understood in terms of pharmacological and anti-obesity effects. The current study examined the anti-obesity effect of leaf extracts of Korean ginseng in high-fat diet (HFD)-induced obese rats.

The study used leaf extracts of ginseng (three years old) prepared from young, green leaf (GL) or old, dried leaf (DL), with leaf samples extracted with distilled water. Six week old male Sprague-Dawley rats were randomly assigned to the following groups: normal diet (ND); HFD; HFD + GL supplementation (3.3mg/kg); and HFD + DL supplementation (3.3mg/kg). Each group had seven rats. GL and DL were administered orally on each day of the experiment period. Blood was collected on the final day of experiments for measuring plasma marker levels of nephrotoxicity, hepatotoxicity, and lipid profiling.

At the end of the experiment, the final body weights of GL- and DL-supplemented rats were slightly lower than those of HFD; however, this did not reach statistical significance. The abdominal and epididymal adipose tissue mass was significantly decreased in the GL- and DL- rats compared to the HFD fed rats. Markers of renal and liver function were similar between HFD-fed rats and HFD-GL and HFD-DL rats. Plasma triglycerides and LDL-cholesterol levels were reduced in the GL- and DL- rats compared to control whilst HDL-cholesterol was also increased in the HFD-DL group.

Cell line testing examined the potential mechanisms of action of the herbs. The DL-leaf extracts of Korean ginseng were found to suppress the adipogenesis of the adipocytes through modulation of central transcription factors. The GL-extract, however, was thought to exert its effect through metabolic modulation or increased energy expenditure. Further research is required to establish the mechanism of action of ginseng in this therapeutic area, and to understand differences between the effect of old and young leaf. As obesity continues to be a significant health problem, advances in this area of research are greatly needed.

**Saffron extract in healthy adults with low mood**


Mental health disorders are a leading cause of disability and health and economic burden. Lifetime prevalence of anxiety, mood or substance use disorders is estimated to be at 45% in Australia. Low mood can be defined by many of the same symptoms as depression including sadness, fatigue, pessimism, changes in appetite, changes in sleep patterns, and anhedonia, yet prescription medications are not appropriate in these instances. Interest in alternative therapies has become a point of interest for management of low mood.

*Crocus sativus* L., commonly known as saffron, has been a focus of research over recent years for its potential as a treatment for mood disorders and depression. Proposed mechanisms of action for saffron include inhibiting re-uptake of dopamine, serotonin and noradrenaline, and as an antioxidant. The aim of the current research was to evaluate the effect of a standardised saffron extract on mood for four weeks in a healthy population reporting low mood in a randomised, double-blind, placebo-controlled trial.

The active treatment was a standardised saffron extract (affron® Pharmactive Biotech Products) derived from *C. sativus* L. stigmas which was standardised to contain >3.5% Lepticrosalides, a measure of the bioactive compounds present in saffron including safranal and crocin. The study was conducted in Brisbane, Australia, with participants recruited through public media and a subject database. Participants were eligible for inclusion if they were self-reporting low mood, were not diagnosed with depression or another mood disorder, and were otherwise healthy (BMI <30). Exclusion criteria included diagnosis with a mood disorder, or had tested positive for depression on the Beck Depression Inventory (BDI >20). In total 128 participants were enrolled and randomly allocated to receive saffron 28mg/day, saffron 22mg/day or placebo for four weeks. Mood was measured at baseline and at the end of study using Profile of Mood States (POMS), the Positive and Negative Affect Schedule (PANAS), and the Depression Anxiety Stress States (DASS-21 scale). Sleep was monitored using the Sleep Quality Index (PSQI).

Authors reported a significant decrease in negative mood and symptoms related to stress and anxiety at the 28mg/day dose compared to placebo. No significant between-group treatment effect was noted for positive effect in PANAS. No significant improvement was observed in sleep quality in any treatment group. No treatment effect was observed at the 22mg/day dose. The significance of changes from baseline to end of study within groups were not well reported.

Limitations of the study include its self-reporting nature, possible confounding effects, and the healthy population use. Additionally, the statistical reporting did not provide p values for all study parameters reported limiting interpretation of the reported findings. Whilst the study demonstrated effectiveness of the saffron extract in improving low mood and stress in an otherwise healthy population, more research is required to fully understand its potential for appropriate clinical use in this patient population.
References


