



Clinical Research Review

e-Monitor No. 27 July 2009

by Michelle Morgan

Clinical Studies Evaluating Herbs

Silymarin in the treatment of patients with primary sclerosing cholangitis: an open-label pilot study.

Angulo P, Jorgensen RA, Kowdley KV et al. *Dig Dis Sci* 2008; **53**(6): 1716-1720

Primary sclerosing cholangitis is a chronic cholestatic liver disease that frequently leads to biliary cirrhosis. Treatment of thirty patients with primary sclerosing cholangitis using silymarin was investigated in a pilot trial. Participants received silymarin (420 mg/day) for one year. Those patients also taking cholestyramine were asked to take the drug at least 2 hours before or after silymarin. Twenty-three patients completed the treatment.

The results found that silymarin treatment:

- significantly reduced serum alkaline phosphatase and aspartate aminotransferase (AST)
- did not alter serum bilirubin levels or serum albumin
- did not alter the Mayo risk score (assesses the best time for a liver transplant and predicts survival in non-transplanted patients)

A positive response to treatment was defined as a decrease in serum alkaline phosphatase, total bilirubin or AST by greater than or equal to 50%, or a return to normal status without an increase of greater than or equal to 25% in other values. Treatment success in the total group of patients occurred if greater than or equal to 30% had responded to silymarin as defined above. Overall, 34% of patients had a positive response to silymarin.

Key Finding: Preliminary results suggest that silymarin may provide benefit in patients with primary sclerosing cholangitis.

Effect of Ginkgo Leaf Extract on Vascular Endothelial Function in Patients with Early Stage Diabetic Nephropathy.

Li XS, Zheng WY, Lou SX et al. *Chin J Integr Med* 2009; **15**(1): 26-29

A randomised trial conducted in China found that treatment with Ginkgo improved vascular endothelial function in patients with early stage diabetic nephropathy. All patients received 8 weeks' treatment with conventional therapy for diabetes. One group also received standardised Ginkgo extract (providing 57.6 mg/day of flavone glycosides and 14.4 mg/day of terpene lactones). Compared to baseline, there was significant improvement in dilation of the brachial artery in response to experimentally-induced congestion in those treated with Ginkgo. No change was observed in the control group. However, treatment with Ginkgo did not change the vascular dilation when nitroglycerin was administered. This suggests that treatment with Ginkgo may improve endothelial-dependent vascular function, but had no direct effect on the vascular function related to smooth muscle. In addition, the reduction in urinary albumin excretion rates was significantly greater under Ginkgo than that experienced in the control group.

Key Finding: Standardised Ginkgo extract may protect vascular endothelial function potentially assisting patients with early stage diabetic nephropathy.

Regression of follicular lymphoma with alternative therapy using Devil's Claw (DC); Coincidence or causation?

Wilson KS. *J Clin Oncol* 2009; **27**(Suppl): Abstr e19560

At the American Society of Clinical Oncology Annual Meeting 2009, clinical details of two patients with follicular lymphoma who self-treated with devil's claw (*Harpagophytum procumbens*, dosage undefined) were presented. One patient was also taking Essiac. CT scan images at baseline and follow-up (10 and 11 months later) provided objective evidence of regression of the tumours. Spontaneous regression in low grade lymphoma has been reported in 7 of 44 patients not taking herbal medicines or COX-2 inhibitors. However, the timing of the response in these two patients suggested a possible therapeutic benefit.

Key Finding: Tumour regression has been documented in two patients with follicular lymphoma who were taking devil's claw.

Safety, Adverse Reactions, Herb-Drug Interactions

Efficacy and tolerability of *Hypericum perforatum* in major depressive disorder in comparison with selective serotonin reuptake inhibitors: a meta-analysis.

Rahimi R, Nikfar S, Abdollahi M et al. *Prog Neuropsychopharmacol Biol Psychiatry* 2009; **33**(1): 118-127

This meta-analysis compared the efficacy and tolerability of St John's wort (*Hypericum perforatum*) with selective serotonin reuptake inhibitors (SSRIs) in the treatment of mild to moderate depression. Clinical trial data was collected from 1966 to June 2008. Thirteen randomised controlled trials met the criteria and were included for analysis. Patients received either St John's wort or an SSRI (fluoxetine, paroxetine, citalopram, sertraline), and in six trials a third group received placebo. For efficacy, information on clinical response, remission and effect size (reduction in Hamilton Rating Scale for Depression (HAMD) score) was obtained. Assessment of safety was determined from numbers of adverse events and withdrawal from the study due to adverse events. Duration of treatment ranged between 4 and 12 weeks.* Data for remission considered only the trials of 8 and 12 weeks' duration.

The results indicate:

- The rates of clinical response, remission and reduction of HAMD score were similar between St John's wort and SSRIs.
- The number of patients reporting adverse events was not different between St John's wort and SSRIs.
- Withdrawal due to adverse events caused by SSRIs was higher than for St John's wort.

* **Reviewer's Note:** At least eight different St John's wort extracts (one was undefined) were trialled. This included extracts that were high and low in hyperforin content.

Key Finding: St John's wort has similar efficacy and reports of adverse events as SSRIs for the treatment of mild to moderate depression. However, St John's wort exhibits lower withdrawal rates from treatment due to adverse events.

Reversible worsening of Parkinson disease motor symptoms after oral intake of *Uncaria tomentosa* (cat's claw).

Cosentino C, Torres L. *Clin Neuropharmacol* 2008; **31**(5): 293-294

A case was reported in Peru of the worsening of motor signs in a patient with Parkinson's disease after taking cat's claw. The man's condition had been well controlled, despite some mild to moderate dyskinesia, wearing-off phenomena and some "sudden off" episodes. He prepared "hot extracts of the bark of cat's claw that were served in a cup and orally taken 3 times daily during almost 3 weeks"*. A few days after commencing the cat's claw beverage, tremor and hypokinesia markedly increased, with the patient in off states most of the day. After withdrawal of cat's claw he remained markedly hypokinetic for another week. Motor symptoms then progressively improved to reach the state prior to intake of cat's claw. The dosage of his drug medications had remained unchanged.

* **Reviewer's Note:** Despite the information in the title of this case report, the botanical definition of the bark is not described. There are two chemotypes of *Uncaria tomentosa*: one contains predominantly pentacyclic oxindole alkaloids (POAs), the other contains predominantly tetracyclic oxindole alkaloids (TOAs). Another medicinal plant referred to as cat's claw is *Uncaria guianensis*, it contains predominantly TOAs. TOAs have known central nervous system activity.

Key Finding: A case of an adverse effect in Parkinson's disease, possibly caused by ingestion of cat's claw, has been reported. The botanical definition of the herb used is not certain.

Disease Understanding, Diet, Lifestyle

Musculoskeletal pain is associated with a long-term increased risk of cancer and cardiovascular-related mortality.

McBeth J, Symmons DP, Silman AJ et al. *Rheumatology* 2009; **48**(1): 74-77

A cross-sectional study conducted in the United Kingdom investigated whether those with regional and widespread pain disorders have an increased risk of mortality. People aged 16 years and over were recruited from three general practices. They were asked whether they had experienced any pain in the past month that lasted for one week or more, and if so, to indicate the site of their pain. A baseline survey was received from 4515 participants in 1996, and they were followed up until either death or 30th April 2005. Overall 4344 volunteers contributed, with a follow-up period ranging from 0.4 to 8.3 years.

A total of 35.2% reported regional pain and 16.9% reported widespread pain. In comparison with those without pain, there was a 20% and 30% increased risk of dying over the follow-up period among those with regional and widespread pain, respectively. Regional and widespread pain was associated with significantly elevated risk of death from cancer. The mortality risk from both cancer and cardiovascular deaths was found to increase with the number of pain sites that subjects reported. This study confirms previous epidemiological observations.

Duration of vasomotor symptoms in middle-aged women: a longitudinal study.

Col NF, Guthrie JR, Politi M et al. *Menopause* 2009; **16**(3): 453-457

Current medical education materials and clinical guidelines report that most women experience vasomotor symptoms for 6 months to 2 years during the menopausal transition. One frequently cited report states that hot flushes resolve in 85–90% of women within 4 to 5 years. However, the evidence underpinning these statements and the data obtained from cross-sectional studies have been questioned. Well-designed longitudinal studies are likely to provide the most reliable information.

The study began in 1991 with interviews of Australian-born women aged between 45 and 55 years and residing in Melbourne. Of those who were eligible, 438 agreed to participate. Women were interviewed annually. The data for 205 women at end of 13 years of follow-up was analysed. All of the participants were white, which may limit the generalisability of the results to other racial or ethnic groups.

The study found:

- The mean duration of *bothersome* menopausal symptoms was estimated to be 5.2 years in those who never used hormone replacement therapy (HRT). (The analyses relate to hot flushes that were perceived as bothersome.)
- If women who used HRT were included, the mean duration was 5.5 years. (During the observation period, there was a high usage of HRT – 47% in the 13-year follow-up cohort.)
- In the 13th year of follow-up, 23% of women still reported flushing.
- The only factor associated with duration of hot flushes was regular exercise. More exercise was associated with shorter symptom duration.

Perceptions of individual and community environmental influences on fruit and vegetable intake, North Carolina, 2004.

Boyington JE, Schoster B, Remmes Martin K et al. *Prev Chronic Dis* 2009; **6**(1): A04

A study investigated the perceptions of environment on intake of fruit and vegetables in a cohort of 2479 people recruited from 22 family practices in North Carolina. The study consisted of two phases: a telephone survey followed by an assessment phase for a subsample of 32 participants which involved for example, focus groups, individual interviews and use of photographs. The telephone survey assessed participants' perception of the quality, variety and affordability of the fruit and vegetables they purchase. The assessment phase looked at behavioural issues. The 2479 participants involved in the telephone survey had a mean age of 52.8 years, mean body mass index (BMI) of 29.4, and were predominantly female, white, married and high school graduates. Many of this group were affected by chronic disease, for example, high blood pressure (45.3%), depression (30.8%), diabetes (18.7%). Some participants had more than one condition. The 32 subsample participants were older, heavier and less educated. The following results were obtained.

<p>Telephone Survey</p> <ul style="list-style-type: none"> • A greater percentage of people with high BMI perceived the quality of the fruit and vegetables at their grocery store to be excellent compared to people with low BMI. (The authors speculated that those with higher BMI may be less discriminating.) • People without a comorbid condition were less likely to rate the variety and quality of their food as excellent and were somewhat less likely to rate the affordability as excellent.
<p>Assessment</p> <p>Perceptions related to reduced or limited dietary intake of fruit and vegetables:</p> <ul style="list-style-type: none"> • taste-bud fatigue (boredom with commonly eaten foods) • work-related stress, inflexible work schedules, food options at workplace, long work hours, variability in shift work schedules • lack of forethought in meal planning and preparation • easy access to fast food restaurants • economic status • concerns about food safety e.g. presence of antibiotics and pesticides • contradictory nutrition messages from the media and health professionals <p>Perceptions related to beneficial effect on dietary intake of fruit and vegetables:</p> <ul style="list-style-type: none"> • spouses e.g. 'my wife likes to eat healthy' • the personal value of cooking at home • purchasing at farmer's markets (lower cost) • early childhood dietary exposure e.g. 'a well-balanced diet was something I grew up with'

Note: Current health status and the ability to garden had both a beneficial and detrimental effect on dietary intake of fruit and vegetables (depending on the individual circumstances).

Sugar-sweetened beverages, serum uric acid, and blood pressure in adolescents.

Nguyen S, Choi HK, Lustig RH et al. *J Pediatr* 2009; **154**(6): 807-813

Cross-sectional data from 4867 adolescents aged 12 to 18 years in the National Health and Nutrition Examination Survey (NHANES), 1999-2004 was analysed. NHANES collected information on the health and nutrition from a representative household population in the United States. Certain populations, such as adolescents and racial/ethnic minorities were oversampled to improve estimates in these groups. Dietary details were assessed from 24-hour recall interviews. Sugar-sweetened beverages included fruit drinks, sports drinks, soft drinks and soda, sweet drinks reconstituted from powders and sweetened tea or coffee.

Sugar-sweetened beverages, particularly in the United States, are primarily sweetened with high fructose corn syrup, a mixture of fructose and glucose. Fructose is metabolised in the liver and increases uric acid levels. Serum uric acid levels and blood pressure were measured. Serum uric acid level (even within normal range) is associated with cardiovascular risk factors such as hypertension and metabolic syndrome.

The study found:

- Drinking any amount of sugar-sweetened beverages in a day was reported by 82.5% of adolescents.
- Adolescents who drank more sugar-sweetened beverages tended to be older and male.
- Sugar-sweetened beverage consumption was associated with higher intake of total calories, sodium and caffeine.

After adjusting for a number of possible confounding factors (including body mass index, smoking, alcohol and caffeine intake, other dietary factors):

- serum uric acid increased by 0.18 mg/dL in adolescents in the highest category of sugar-sweetened beverage consumption (> 36 oz/day) compared with those in the lowest category (1-12 oz/day). (One can of soda contains about 12 ounces (oz), approximately 350 mL.)
- systolic blood pressure z-score increased by 0.17 from the lowest to the highest category of sugar-sweetened beverage consumption. This represented an increase of 2 mm Hg.

These results were statistically significant.

Sleep hygiene practices of good and poor sleepers in the United States: an internet-based study.

Gellis LA, Lichstein KL. *Behav Ther* 2009; **40**(1): 1-9

An Internet-based survey assessed the sleep hygiene practices of 128 good sleepers and 92 poor sleepers who were residents of the United States. Sleep hygiene broadly refers to a set of behaviours that influence the quality of one's sleep. The formal category, inadequate sleep hygiene is defined as engaging in one or more of the following behaviours: improper sleep scheduling, the use of sleep-disturbing products, engaging in activating or arousing activities close to bedtime, the use of the bed for activities other than sleep (e.g. for reading, eating, watching television or paying bills) and maintaining an uncomfortable sleeping environment. Participants admitted into the study were classified as good or poor sleepers based on scores from the Pittsburgh Sleep Quality Index. Comparison with United States demographics found the sample had an overrepresentation of college graduates and Caucasian individuals.

The survey found:

- Although sleep hygiene practices were generally good, poor sleepers showed increased cognitive activity in the bed, even after controlling for depression and anxiety.
- Poor sleepers also reported statistically significant increases in excessive noise in the bedroom, uncomfortable nighttime temperature and activities that were exciting, emotional or demanded high concentration near bedtime.

Increased television viewing is associated with elevated body fatness but not with lower total energy expenditure in children.

Jackson DM, Djafarian K, Stewart J et al. *Am J Clin Nutr* 2009; **89**(4): 1031-1036

Increased television (TV) viewing has been consistently found to be associated with increased body mass index (BMI) in both children and adults. Changes in both food intake and physical activity have been implicated in the association between TV viewing and body fatness. In this cross-sectional study conducted in the United Kingdom, 89 children aged 2-6 years from mainly middle- to upper-class white families were recruited. Body composition was determined by dual energy X-ray absorptiometry (DXA, a more objective direct method than BMI). Total daily energy expenditure for a period of 14 days was measured directly using the doubly labelled water method. Physical activity was measured using a wrist monitor for 7 consecutive days.

The following results were found:

- The children watched an average of 1.87 hours/day of TV.
- There was a significant positive association between fat mass (corrected for fat-free body mass) and TV viewing.
- Each extra hour of watching TV was associated with an extra 1 kg of body fat.
- Children who watched more TV were also significantly less physically active.
- Despite TV viewing being linked to lower physical activity, the relationship between TV viewing and fatness is not mediated by physical activity.
- The results suggest that the association between TV viewing and fatness is more likely to be due to an effect on food intake.