



Clinical Monitor

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by Kerry Bone

Korean Ginseng Clinical Trial Finds Reduced Cancer Incidence

A randomised, double blind, placebo-controlled trial was conducted in China over 11 years to assess the impact of a period of regular Korean red ginseng (*Panax ginseng*) intake on the development of primary cancers.¹ The trial was a collaboration between several research centres in Korea and China. In all, 643 patients with chronic atrophic gastritis were enrolled in the trial, because this condition is associated with an elevated risk of stomach cancer. About 60% of the participants were men, more than half were smokers and their average age at the beginning of the trial was around 47 years. The dose of Korean ginseng extract was 1 g/week (taken as 4 discrete doses containing ginsenosides, 38 mg/week) and its ginsenoside profile suggests that this would correspond to around 5 g of root. This dose, or the matching placebo, was consumed for 3 years and the trial participants were followed-up 8 years later.

During the 11 years of the study, 16 cancer cases confirmed by pathological examination occurred in the placebo group versus 8 from the ginseng group. The relative risk (RR) for development of cancer in the ginseng group was 0.54, but this failed to reach statistical significance ($p = 0.13$), presumably because of the relatively low numbers in the trial. Of the 24 cancer patients, 21 were male and the RR for all cancers in the men was found to be statistically significant ($p = 0.03$) at 0.35. There were no differences in side effects between the two groups and the incidence of increasing blood pressure was higher in the placebo group. The authors concluded that Korean red ginseng exerted a non-organ-specific cancer preventative effect, consistent with previous epidemiological studies.

Comment

It should not be concluded from the study that Korean ginseng benefits only men in terms of cancer prevention. The likely reasons for the statistically significant protective effect in the men are their higher number in the trial and the greater incidence of cancers. The intervention dose was relatively low and is readily achievable (for example 10 mL/week of a 1:2

liquid extract). Also the intervention time of just 3 years suggests that Korean ginseng used for longer periods might confer greater protection against cancer, as has been suggested by earlier epidemiological studies from the same authors.²⁻⁴

This is the first prospective, randomised, controlled clinical trial of the effect of a medicinal plant on cancer incidence. Despite the relatively small number of participants, a protective effect was seen (in men). Hopefully, this research will open up a new chapter for herbal studies in preventative medicine.

REFERENCES

- 1 Yun TK, Zheng S, Choi SY et al. *J Med Food* 2010; **13**(3): 489-494
- 2 Yun TK, Choi SY. *Cancer Epidemiol Biomarkers Prev* 1995; **4**(4): 401-408
- 3 Yun TK. *Nutr Rev* 1996; **54**(11 Pt2): S71-S81
- 4 Yun TK, Choi SY. *Int J Epidemiol* 1998; **27**(3): 359-364

Studies Provide Insights into Effective Clinical Dose of Resveratrol

Currently resveratrol is probably the most actively researched phytochemical and a wide variety of properties have been demonstrated in pharmacological models. However, the paucity of clinic research raises questions about the effective and safe human dose, especially for health maintenance. A landmark animal experiment and subsequent discussions over dosage, together with two recent human trials, provide some insights into the appropriate human dosage of resveratrol.

An important pharmacological study was published in the eminent journal *Nature* in 2006. Rather than giving resveratrol to normal mice to see if it simulated calorie restriction, the effect of resveratrol on a high calorie diet was studied. Middle-aged (one-year-old) male mice on a high calorie diet were given resveratrol and compared to untreated mice on the same diet or a standard diet.¹ The administered doses of resveratrol were either 5.2 or 22.4 mg/kg/day for 6 months, but only results for the higher dose were reported.

The mice receiving the high-calorie diet (HCD) become overweight, whether they were receiving resveratrol or not. However, a clear survival benefit from resveratrol

was evident: survival rates for mice on the HCD plus resveratrol were the same as those for the mice on the standard diet (SD). Although resveratrol increased survival, it was also important to ascertain whether quality of life was maintained. This was determined by the rotarod test, which measures balance and coordination. Surprisingly, the resveratrol-fed mice on the HCD steadily improved their motor skills as they aged, to the point where they were indistinguishable from the SD group. Resveratrol also corrected the following parameters in the overfed mice to levels similar to those observed in the SD mice: plasma insulin, fasting glucose, plasma albumin, plasma amylase, liver weight, aortic elastic lamina morphology and mitochondria levels in liver tissue. Furthermore, resveratrol opposed the effects of the HCD on 144 out of 153 significantly altered metabolic pathways.

These dramatic results provoked worldwide attention and the observation that with resveratrol “you can eat your cake and not have it”. However, they also led to considerable discussion as to whether the amount of resveratrol given to the mice was realistically achievable in humans. Many media sources at the time stressed that the doses used could be interpreted to mean several hundred or even thousands of litres of wine per day in human equivalent doses (HEDs).² A 2007 paper pointed out that this was a serious misinterpretation of the results leading to unnecessary scepticism of this important research.² It reflected a general ignorance of the scientific community and public regarding appropriate methods of dose extrapolation between species, which should be based on surface area rather than body weight.² In other words, the HED for a 60 kg human adult from a mouse dose of 22.4 mg/kg is not 60 times 22.4 mg (1344 mg), but instead just 109 mg. While not reasonably achievable through the consumption of wine (which typically contains 2 to 3 mg resveratrol per litre), this dose of resveratrol is readily reached by the use of an extract of the herb *Polygonum cuspidatum* (giant knotweed).

Information about the appropriate human dose of resveratrol comes also from recent clinical trials. Nineteen overweight/obese men or post-menopausal women (BMI 25-35 kg/m²) with untreated borderline hypertension consumed three different single doses of resveratrol (30, 90 or 270 mg) or a placebo at weekly intervals in a double blind, randomised, crossover comparison.³ One hour after the resveratrol consumption, its level in plasma and its impact on flow-mediated dilatation (FMD) of the brachial artery were assessed. Impaired FMD is associated with several cardiovascular risk factors, including hypertension and obesity. With increasing doses of resveratrol there were proportional increases in plasma resveratrol concentrations. FMD was significantly increased by

resveratrol at all doses compared to placebo ($p < 0.05$), but the higher doses had only a marginally greater impact than the 30 mg dose.

Two groups (10 in each) of normal-weight healthy participants were randomised to placebo or a *Polygonum cuspidatum* extract containing 40 mg/day resveratrol for 6 weeks.⁴ In mononuclear cells taken from participants after 6 weeks the extract had induced significant antioxidant and anti-inflammatory effects ($p < 0.05$). Also it significantly reduced plasma concentrations of TNF-alpha (tumor necrosis factor-alpha), IL-6 (interleukin-6) and C-reactive protein ($p < 0.05$).

Comment

Based on these studies, an effective long-term human dose for resveratrol probably ranges from 30 to 110 mg/day. While higher doses up to 200 mg/day could be considered where the need exists, doses beyond this limit might not only be unnecessary, they could also prove to be unsafe. There are still many uncertainties in the resveratrol research and it would be wise to exercise caution at this stage. A daily dose of resveratrol of 100 mg from *Polygonum cuspidatum* is certainly within the realms of traditional doses used for Chinese herbs.

REFERENCES

- 1 Baur JA, Pearson KJ, Price NL et al. *Nature* 2006; **444**(7117): 337-342
- 2 Reagan-Shaw S, Nihal M, Ahmad N. *FASEB J* 2007; **22**(3): 659-661
- 3 Wong RH, Howe PR, Buckley JD et al. *Nutr Metab Cardiovasc Dis*. 2010 Jul 29. [Epub ahead of print]
- 4 Ghanim H, Sia CL, Abuaysheh S et al. *J Clin Endocrinol Metab* 2010; **95**(9): E1-E8

How Willow Bark Works on Inflammation Provides Clue to Cancer-Preventative Role

The protective effect of regular aspirin use against a range of cancers, but especially colorectal cancer, has been suggested by several epidemiological studies.¹ But the use of even low doses of aspirin is linked to at least twice the risk of gastric bleeding, and possibly also doubles the risk of a cerebral bleed.¹ Hence, there is considerable controversy around the promotion of aspirin for cancer prevention.

The underlying assumption often made is that the cancer-preventative activity of aspirin hinges on its ability to inhibit cyclo-oxygenase (COX), especially its inducible form COX-2. COX-2 is an obvious molecular target for cancer prevention, since this enzyme is strongly and rapidly induced in response to mediators of inflammation such as NF-kappa-B, as well as growth

factors, cytokines and endotoxin.¹ COX-2 is involved in cell proliferation and tumour promotion.

Aspirin is made by adding an acetyl group to salicylic acid. The well-described therapeutic effect of aspirin in preventing heart attacks is attributed to the inhibition of COX-1 in platelets. This occurs by the irreversible attachment of the aspirin acetyl group to the amino acid serine located within the COX-1 enzyme active site. As a result access of arachidonic acid, the COX-1 substrate, is hindered resulting in inhibition of thromboxane synthesis. In contrast, the inhibition of COX-2 effects by aspirin might not be due to acetylation of the COX-2 active site, but rather to the salicylate part of the molecule. Supporting this is the finding that aspirin is about 160 times more specific to COX-1 than COX-2. Furthermore, the active site of COX-2 is larger than for COX-1 and so it can accept arachidonic acid even when acetylated.¹ In addition, aspirin has a relatively short half-life in circulating blood (around 20 minutes) and is rapidly deacetylated to yield salicylate. Hence any long-term anti-inflammatory effect of aspirin must be derived from salicylate.²

Recent research suggests that salicylate does not so much inhibit COX-2 activity, but rather acts upstream to inhibit COX-2 expression (production). Based on their *in vitro* experiments, Wu and team have proposed that salicylate does indeed act by inhibiting the COX-2 production that would normally follow from pro-inflammatory signals to the cell and in response to NF-kappa-B. The specific mechanism is suggested to be the inhibition of RSK1/2 (ribosomal S6 kinase 1/2), which is a key factor in mediating COX-2 transcription.³ In other words, the cancer-preventative activity of aspirin is possibly mediated by the reduced COX-2 production induced by salicylate.

If aspirin is active at reducing COX-2 via the salicylate it delivers into the bloodstream, this suggests that natural salicylates, and specifically salicin in willow bark, will also act in a similar way. The research not only provides a credible explanation for the anti-inflammatory mechanism of willow bark, it also suggests that the cancer-preventative benefits of aspirin might also apply to natural salicylates. The distinct advantage of natural salicylates, and specifically willow bark, is their lack of activity on COX-1 and hence much safer long-term therapeutic profile in terms of bleeding risk.

Comment

Salicylic acid was prepared from isolated plant constituents in the 1830s and in 1874 a factory was set up for its large-scale production. The activity of salicylic acid was confirmed clinically for the treatment of rheumatic disorders in 1876. In the same year, successful treatment with salicin (from willow bark)

was described for 8 patients with acute and subacute rheumatism. Unfortunately salicin (which is stomach-friendly) was largely overlooked and the cheaper salicylic acid remained the focus of pharmaceutical attention. As the use of salicylic acid or its salicylate salts increased, the problem of severe gastric side effects became more evident. The German pharmaceutical company Bayer began looking for a version of salicylic acid with a better side effect profile and between 1893 and 1897 Felix Hoffman developed an improved way of producing acetylsalicylic acid. He tested it on his father, whose chronic arthritis improved markedly.⁴ In 1899 acetylsalicylic acid was commercially released with the name aspirin, apparently from the former botanical name for meadowsweet.

The irony of this story is that research is beginning to suggest nature was indeed the best chemist: salicin might have a better safety-activity profile for pain management and cancer prevention than aspirin (but not, of course, for antiplatelet activity). While it is too soon to be suggesting willow bark for cancer prevention, it is reassuring to know that patients taking the herb long-term might be safely benefiting their health in ways other than pain relief.

REFERENCES

- 1 Elwood PC, Gallagher AM, Duthie GG et al. *Lancet* 2009; **373**(9671): 1301-1309
- 2 Wu KK. *Circulation* 2000; **102**(17): 2022-2023
- 3 Wu KK. *Thromb Haemost* 2006; **96**(4): 417-422
- 4 Vane JR, Botting RM. *Thromb Res* 2003; **110**(5-6): 255-258



Clinical Research Review

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by Michelle Morgan

Clinical Studies Evaluating Herbs

The iron-chelating potential of silybin in patients with hereditary haemochromatosis.

Hutchinson C, Bomford A, Geissler CA. *Eur J Clin Nutr* 2010; **64**(10): 1239-1241

There have been a few anecdotal reports of reduced requirements for maintenance phlebotomy in hereditary haemochromatosis patients taking St Mary's thistle (*Silybum marianum*) extract. It is thought that the extract may be binding iron and thereby reducing non-haem iron absorption. In a pilot, crossover study conducted in the United Kingdom, 10 hereditary haemochromatosis patients consumed 13.9 mg of iron via a vegetarian meal with either 200 mL of water, 200 mL of water and concentrated standardised extract of St Mary's thistle (140 mg of flavanolignans calculated as silybin*), or 200 mL of black tea (containing 170 mg of polyphenols as gallic acid equivalents) on 3 separate occasions. Patients received phlebotomy to maintain their serum ferritin within the normal range, but were not phlebotomised during the study. Consumption of extract resulted in a significant reduction in the postprandial increase in serum iron compared with water and tea.

* **Reviewer's Note:** Extract composition verified from product information.

Key Finding: In a pilot study, concentrated standardised extract of St Mary's thistle reduced iron absorption in haemochromatosis patients.

Silexan, an orally administered Lavandula oil preparation, is effective in the treatment of 'subsyndromal' anxiety disorder: a randomized, double-blind, placebo controlled trial.

Kasper S, Gastpar M, Muller WE et al. *Int Clin Psychopharmacol* 2010; **225**(5): 277-287

Oral administration of a lavender essential oil preparation has previously shown benefit in patients with generalised anxiety disorder (*Phytomedicine* 2010; **17**(2): 94-99). The anxiolytic efficacy of a lavender essential oil preparation was recently investigated in a double-blind trial of patients with anxiety disorder not otherwise specified (according to accepted diagnostic references). (This category generally includes disorders with prominent anxiety or phobic avoidance that do not meet criteria for any specific anxiety disorder, adjustment disorder with anxiety or adjustment disorder with mixed anxiety and depressed mood. It is also known as 'subsyndromal' anxiety disorder.) Two hundred and sixteen patients were randomised to receive capsules containing 80 mg of essential oil of *Lavandula angustifolia* or placebo with 0.08 mg of lavender essential oil (to match the smell). One capsule per day was ingested for a period of 10 weeks. Primary outcome measures were changes in the Hamilton Anxiety Scale (HAMA) total score and the Pittsburgh Sleep Quality Index (PSQI). Patients had initial scores of greater than or equal to 18 points for HAMA, and greater than 5 for PSQI. Those with a decrease in HAMA or PSQI total scores of greater than or equal to 50% by the end of treatment were assessed to be responders. Those who had a HAMA total score of less than 10 points or a PSQI total score of less than 6 points at the end of the trial were classified as being in remission. Secondary measures included the Clinical Global Impressions (CGI) scale, the Zung Self-rating Anxiety Scale (SAS), and the SF-36 Health Survey Questionnaire.

The following results were obtained:

- The mean HAMA total scores decreased by 16.0 points (59.3% decrease) from baseline in the lavender group, compared to 9.5 (35.4% decrease) in the placebo group ($p < 0.001$). PSQI total scores decreased by 5.5 points (44.7% decrease) in the lavender group, compared to 3.8 points (30.9% decrease) for placebo ($p = 0.002$).
- Analysis of individual items of the HAMA found that efficacy was demonstrated for the Psychic Anxiety and Somatic Anxiety subscales. Among the 7 components of the PSQI, lavender oil preparation was particularly effective in

improving the subjective quality of sleep, sleep latency, daytime tiredness and subjectively perceived sleep duration.

- There were significantly more responders in the lavender oil group (76.9%) compared to the placebo group (49.1%, $p < 0.001$). Similarly for remitters: 60.6% versus 42.6% ($p = 0.009$).
- For anxiety, the data obtained in the SAS confirmed the results of the HAMA. Compared to the placebo group, patients treated with the lavender oil preparation showed greater improvements in mental and physical health (SF-36). In terms of severity of illness and clinical improvement at the end of treatment (as per CGI), lavender oil was superior to placebo.
- There was no significant difference between the groups regarding the number of patients experiencing adverse events.

Key Finding: Oral administration of essential oil of lavender provided an anxiolytic effect and improved sleep in patients with anxiety disorder not otherwise specified.

St. John's wort extract LI160 for the treatment of depression with atypical features - a double-blind, randomized, and placebo-controlled trial.

Mannel M, Kuhn U, Schmidt U et al. *J Psychiatr Res* 2010; **44**(12): 760-767

A double-blind, placebo-controlled trial conducted in Germany investigated the efficacy of St John's wort extract for the treatment of atypical depression. Atypical depression requires the presence of atypical vegetative features such as hypersomnia (excessive sleepiness) or increased appetite and weight gain (hyperphagia). One hundred patients with mild and 100 patients with moderate depression were randomised to receive St John's wort extract (equivalent to about 2.7 g/day of dried herb) or placebo for 8 weeks. The primary outcome measure was the change of the 17-item Hamilton depression scale (HAM-D₁₇) from baseline. Secondary outcomes were measured using the depression sub-score of the Patient Health Questionnaire (PHQ-9), the Clinical Global Impression (CGI), a patient's satisfaction scale, the Hamilton Anxiety Scale (HAMA) and the sum score of atypical vegetative symptoms of the HAM-D₂₈ (items 22-26).

The following results were obtained:

- HAM-D₁₇ scores decreased by 6.7 points from baseline in the St John's wort group, compared to 5.1 for placebo ($p < 0.05$). The percentage reduction of the HAM-D₁₇ for St John's wort extract (52.3%) compared to placebo (41.9%) approached statistical significance ($p = 0.051$). This was interpreted as a moderate effect size, and for patients with moderate depression the effect is in line with that observed in patients with atypical depression treated with monoamine oxidase inhibitors.
- No significant benefit could be observed for the sum score of the atypical vegetative items of the HAM-D₂₈ (items 22-26), however, the sum score of the hypersomnia items (items 22-24) showed a significant superiority for St John's wort extract over placebo ($p < 0.01$).
- The HAMA, PHQ-9, CGI-I and patient's satisfaction scales demonstrated superiority of St John's wort extract over placebo ($p < 0.01$).
- Improvement was seen as early as week 4 (HAM-D₁₇, HAMA, PHQ-9, HAM-D₂₈ (items 22-24)).
- Confining the analysis to moderately depressed patients, a highly significant benefit for HAM-D₁₇ scores was found ($p = 0.02$). Patients suffering from moderate depression improved better with St John's wort treatment compared to placebo (odds ratio: 1.78) than patients with mild depression (odds ratio: 1.21).
- More adverse events were reported for those taking St John's wort than for placebo (15 versus 8, reported in 13% and 7% of patients, respectively). Adverse events were mild or moderate in severity, and no reactions beyond those well known for St John's wort were observed. Sixteen of the 23 adverse events cleared by the end of the study.

Key Finding: St John's wort extract was beneficial for the treatment of atypical depression, particularly for hypersomnia.

Safety, Adverse Reactions, Herb-Drug Interactions

Effects of *Ginkgo biloba* extracts on diazepam metabolism: a pharmacokinetic study in healthy Chinese male subjects.

Zuo XC, Zhang BK, Jia SJ et al. *Eur J Clin Pharmacol* 2010; **66**(5): 503-509

A study with 12 healthy volunteers found that standardised Ginkgo extract did not affect the pharmacokinetics of diazepam. Standardised Ginkgo extract (240 mg/day) was taken for 28 days. The daily dose of ginkgo flavone glycosides was 57.6 mg/day, and 14.4 mg/day for terpene lactones (ginkgolides and bilobalide). The combination was also well tolerated, and no drug-related serious adverse events were reported.

Key Finding: Standardised Ginkgo extract did not affect the pharmacokinetics of diazepam in healthy volunteers.

Disease Understanding, Diet, Lifestyle

Lowering midlife levels of systolic blood pressure as a public health strategy to reduce late-life dementia: perspective from the Honolulu Heart Program/Honolulu Asia Aging Study.

Launer LJ, Hughes T, Yu B et al. *Hypertension* 2010; **55**(6): 1352-1359

Analysis suggests that 17% of late-life dementia cases are attributable to midlife systolic blood pressure (SBP) levels between 120 and 140 mm Hg. Among those who did not report taking antihypertensive medication in midlife, 27% of dementia cases could be attributed to SBP levels of greater than or equal to 120 mm Hg. These estimates are based on more than 25 years of follow-up in a Japanese-American population, and take into account the presence of other factors suspected to increase the risk for dementia (such as age, smoking history, diabetes, body mass index) and account for the competing risk of mortality associated with high blood pressure.

Sodium restriction as initial conservative treatment for urinary stone disease.

Yun SJ, Ha YS, Kim WT et al. *J Urol* 2010; **184**(4): 1372-1376

A South Korean retrospective study investigated the relationship between urinary sodium, urinary metabolite excretion and the risk of recurrence in 798 urinary stone formers. Urinary sodium was found to significantly influence volume, pH, and calcium, uric acid, oxalate and citrate in urine of men; and volume, pH, and calcium, uric acid and citrate in urine of women. Of the 798 stone formers, 191 were included in recurrent stone analysis. At a median follow up of 56.1 months, 46 of 98 stone formers (46.9%) with normal natriuresis (sodium excretion via urine, 220 mEq or less per day) experienced stone recurrence, compared to 60 of 93 (64.5%) with hypernatriuresis (urinary sodium greater than 220 mEq/day). Patients with hypernatriuresis also had significantly decreased time to stone recurrence than those with normal urinary sodium excretion. The authors suggest that restriction of sodium in the diet should be the first step in preventive therapy for urinary stone disease.

Olive oil during pregnancy is associated with reduced wheezing during the first year of life of the offspring.

Castro-Rodriguez JA, Garcia-Marcos L, Sanchez-Solis M et al. *Pediatr Pulmonol* 2010; **45**(4): 395-402

A cross-sectional study investigated 1409 infants attending clinics in Spain. Information on wheezing during the first year of life and mothers' diet during pregnancy was collected. The following results were found:

- Adherence to a Mediterranean diet and using olive oil for cooking/dressing salads during pregnancy were both significantly associated with less wheezing during the first year of the infant's life.
- After controlling for variables associated with wheezing, only olive oil consumption during pregnancy remained associated with less wheezing: olive oil use during pregnancy was associated with about 40% less wheezing of the infant during their first year of life.

- Other factors remained associated with wheezing: male gender, day care attendance, maternal asthma, maternal smoking during pregnancy, infant eczema and mould stains on the household walls. Industrial infant food consumption and overweight/obesity (of the infant) were not associated with wheezing.

Measurement of ultrafine particles and other air pollutants emitted by cooking activities.

Zhang Q, Gangupomu RH, Ramirez D et al. *Int J Environ Res Public Health* 2010; **7**(4): 1744-1759

Cooking can emit gaseous pollutants and particulate matter. Ultrafine particles (UFPs) which have a diameter of less than 100 nm, are major components of particulate matter. UFPs have been shown to be more toxic than larger particles due to their smaller size and larger surface area. A study conducted in the United States assessed the effects of a range of cooking styles and parameters on UFPs, particulate matter with an aerodynamic diameter less than 2.5 microns (PM_{2.5}) and black carbon emissions. In the first stage Indian, Chinese and Italian cooking styles were used at high temperature on an electric stove with exhaust fan turned on. In the second phase, one cooking activity (American cooking: frying chicken) was used to test different stove types, cooking temperatures and exhaust fan settings.

- Measurements of the average UFP concentration, PM_{2.5} and black carbon concentrations emitted by cooking activities ranged from 13400–604000 particles/cm³, 10.0–230.9 microg/m³ and 0.1–0.8 microg/m³, respectively.
- Lower UFP concentrations were observed during boiling, while higher levels were emitted during frying.
- The highest UFP concentrations were observed when using a gas stove at high temperature with the kitchen exhaust fan turned off.
- The lowest UFP concentrations were measured when using an electric stove at medium temperature with the exhaust fan turned on.
- The exposure to UFPs from cooking was not confined to the kitchen. With an open kitchen, UFPs were dispersed to other rooms.

Prospective associations between early childhood television exposure and academic, psychosocial, and physical well-being by middle childhood.

Pagani LS, Fitzpatrick C, Barnett TA et al. *Arch Pediatr Adolesc Med* 2010; **164**(5): 425-431

A longitudinal study conducted in Canada studied 5-month-old infants and their families with follow-up at 17, 29, 41 and 53 months, to estimate the influence of early childhood television exposure on academic, psychological and lifestyle characteristics in grade 4 (10 years of age). Complete parent reports on television viewing (time per day) were available for 1314 children. Television exposure at 29 months was a mean of 8.82 hours per week and rose to 14.85 hours per week by 53 months. Eleven percent of children at 29 months and 23.4% of children at 53 months viewed more than 2 hours of television daily.

Adjusting for preexisting individual and family factors, every additional hour of television exposure at 29 months corresponded to:

- 7% and 6% unit decreases in classroom engagement and achievement in mathematics, respectively;
- 10% unit increases in victimisation by classmates;
- 13% unit decreases in time spent doing weekend physical activity;
- 9% unit decreases in activities involving physical effort;
- higher consumption scores for soft drinks and snacks (9% and 10%, respectively); and 5% unit increases in body mass index.

Long term Tai Chi exercise improves physical performance among people with peripheral neuropathy.

Li L, Manor B. *Am J Chin Med* 2010; **38**(3): 449-459

A study conducted in the United States investigated the effect of 24 weeks of Tai Chi practice on physical function in individuals with peripheral neuropathy. Twenty-five women and men were recruited. Tai Chi practice included three, one-hour, instructor-led group sessions per week, starting with warm-up exercises and progressing to a modified form of Tai Chi. Participants began the practice from a seated position and progressed to standing with and without the

assistance of a chair. After 6 weeks of Tai Chi, significant increases were observed in functional gait (as assessed by the 6-minute walk and timed up-and-go tests) and in leg strength performance. Continued improvement was observed in the timed up-and-go test. Plantar pressure sensation also improved significantly. There was no significant change in eyes-closed standing balance.