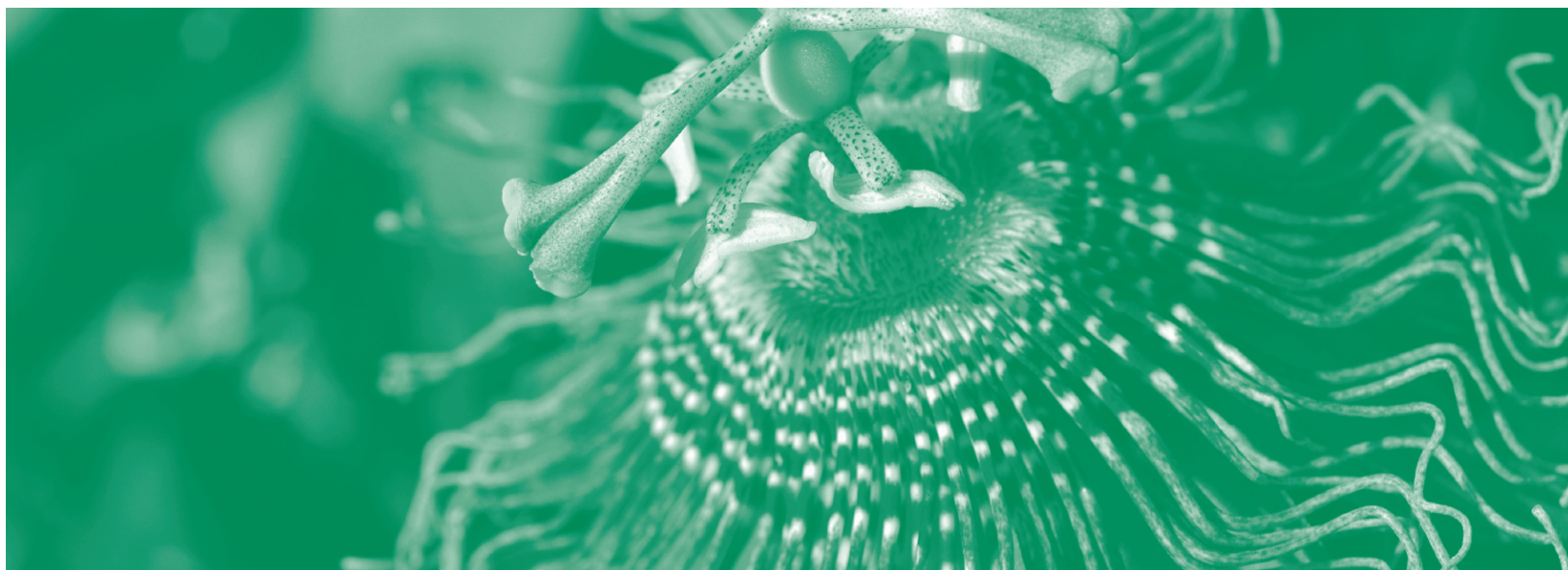


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Passionflower reduces pre-operative anxiety

Patient anxiety prior to surgery is a common scenario, and up to 80% of outpatients select a combination of anxiety-reducing (anxiolytic) as well as hypnotic premedication before hospital operations⁽¹⁾. Conventional management often involves benzodiazepine anxiolytic drugs, but these are not without adverse effects, the most common of which is psychomotor impairment and post-surgery drowsiness.

Aerial parts of the South American herb Passionflower (*Passiflora incarnata*), have traditionally been used as an anxiolytic and sedative in many countries. In Germany, the Commission E has approved its use for nervous

restlessness, and the British Herbal Compendium indicates its use for sleep disorders, restlessness, nervous stress, and anxiety^(2,3).

The benzoflavone moiety as well as other flavonoid compounds including chrysin, seem to be contributory to anxiolytic effects of *Passiflora*^(4,5). Beneficial effects during nicotine and alcohol withdrawal, have also been reported for a *Passiflora* benzoflavone moiety given subcutaneously to mice^(6,7). A greater lessening in opiate withdrawal symptoms in addicts when *Passiflora* was combined with the drug clonidine, has also been reported⁽⁸⁾.

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Passionflower reduces pre-operative anxiety - Continued

Anticonvulsant effects have been shown for injections of the hydroethanolic extract in mice, and these effects related to involvement of benzodiazepine and opioid receptors^(9,10).

However, while efficacy has been shown using rats in an animal model of anxiety^(11,12), evaluation of anxiolytic properties in human clinical trials has been limited to two robust trials to date^(13,14).

The first such trial, involved 162 subjects with neurosis/anxiety who were treated with either 90mg of a *Passiflora* tablet or mexazolam 1.5mg/day⁽¹³⁾. Improvement occurred in 37% of the *Passiflora* group and 44% of the mexazolam group. While a slightly lower incidence of adverse effects including drowsiness, was reported in the *Passiflora* group, these differences failed to reach statistical significance.

More recently, comparable anxiolytic effects to those of 30mg per day of the benzodiazepine oxazepam, were reported for *Passiflora* in an Iranian outpatient trial involving 36 outpatients with generalised anxiety disorder⁽¹⁴⁾. While oxazepam had a more rapid onset of action, its use was also associated with a greater level of impairment of job performance.

A Cochrane Review on *Passiflora* for anxiety disorder published in 2007, pooled results from the above two studies⁽¹⁵⁾. The authors concluded that these studies were too few in number to permit any conclusions to be drawn, but called for further trials involving larger numbers of participants, to evaluate the possible anxiolytic effects of *Passiflora*.

A team of researchers from the Department of Anaesthesiology and Critical Care at Tehran Amir Alam Hospital in Iran, have recently undertaken a clinical trial to evaluate the effects of *Passiflora* in patients with pre-operative anxiety⁽¹⁶⁾. This followed a pilot study involving ten patients by the same team.

Sixty patients aged from 25 to 45, who were about to undergo inguinal herniorrhaphy, were enrolled in the randomised, double-blind and placebo-controlled study. Patients with a history of anxiety disorders, or those consuming sedative, analgesic,

antidepressant or antiepileptic drugs, and patients with low levels of verbal anxiety, were excluded from the trial. Each participant received an oral premedication dose of placebo or *Passiflora incarnata* tablets (*Passipy*[™], IranDarouk, standardised to contain 1.01mg benzoflavone), at a dose of 500mg, 90 minutes prior to surgery.

Anxiety was evaluated by a numeric rating scale, and sedation scores were measured before, then 10, 30, 60 and 90 minutes after administration of premedication. Psychomotor function was assessed with the Trieger Dot Test and the Digit-Symbol Substitution Test upon arrival in the operating room, then 30 and 90 minutes after tracheal extubation. These involved the patient being asked to connect a series of dots arranged in a specific pattern, and a timed pen-and-paper test in which they were required to appropriately match numbers and symbols.

Various anaesthetic and other drugs were used during the surgery, and tramadol and ondansetron used to treat postoperative pain and nausea respectively. The time interval between arrival in the postanesthetic care unit and discharge, was also recorded for each patient.

The results showed that anxiety scores over time were significantly lower in the group of patients given *Passiflora* than in the control group ($p < 0.001$). The onset of *Passiflora*'s anxiolytic activity was apparent at 10 minutes following oral administration, and its effect seemed to peak at 30 minutes.

Levels of sedation, measured psychological variables, and recovery of psychomotor function, were however comparable in both groups.

While placebo controlled, little detail is provided concerning the methodology or post-treatment validation of blinding (effective concealment of which treatment was given). Nevertheless, as a well-designed clinical trial involving humans about to undergo a procedure that is intrinsically anxiety-inducing, its positive findings provide further convincing evidence of the anxiolytic effects of *Passiflora incarnata*. Furthermore, these results suggest that contrary to the generally

negative picture painted concerning the use of herbal medicines prior to surgery, administration of optimal doses of appropriate such agents can in fact, be a safe and useful adjunctive therapy during such procedures.

Refs:

1. Raeder JC, Breivik H. *Acta Anaesthesiol Scand* 31:509-514, 1987.
2. Blumenthal M. *The Complete Commission E Monographs*. Austin: American Botanical Council, 1998.
3. Bradley PR ed. *British Herbal Compendium*, Vol 1. Bournemouth: BHMA, 1992.
4. Dhawan K et al, *Fitoterapia* 72:922-926, 2001.
5. Wolfman C et al, *Pharmacol Biochem Behav* 47(1):1-4, Jan 1994.
6. Dhawan K et al, *Addict Biol* 7(4):435-441, Oct 2002. (2002a)
7. Dhawan K et al, *J Ethnopharmacol* 81(2):239-244, Jul 2002 (2002b)
8. Akhondzadeh S et al, *J Clin Pharm Ther* 26(5):369-373, Oct 2001a.
9. Nassiri-Asi M et al, *BMC Complement Altern Med* 7:26, Aug 8, 2007
10. Rad SS et al, *Annals Gen Psych*. 7(Suppl 1):S222, 17 April, 2008.
11. Dhawan K et al, *J Ethnopharmacol* 78(2-3):165-170, Dec 2001.
12. Dhawan K et al, *J Altern Complement Med* 8:283-291, 2002.
13. Mori A et al, *Clinical Evaluation* 21:383-440, 1993.
14. Akhondzadeh S et al, *J Clin Pharm Ther* 26(5):363-367, Oct 2001.
15. Miyasaka LS et al, *Cochrane Database Syst Rev*. CD004518. Jan 24, 2007.
16. Movafegh A et al, *Anesth Analg* 106(6):1728-1732, Jun 2008.

Anti-allergy properties of Burdock

In European herbal medicine, Burdock is mostly known for its depurative actions and used for the treatment of inflammatory and allergic skin conditions, including eczema and psoriasis. It is also an ingredient of Essiac, a herbal formulation popular for its alleged benefits in the treatment of cancer⁽¹⁾.

As is so often the case with western herbal medicines, pharmacological or clinical research to explore these traditional uses further, has been relatively limited to date. Interest in burdock by researchers is clearly increasing, however, with results from a number of studies on this plant recently reaching publication.

Inhibitory effects on platelet activating factor (PAF) binding were reported by Japanese researchers in 1992, using a hot aqueous extract of burdock⁽²⁾. As PAF is released from activated basophils and is involved in various inflammatory responses seen during allergies, possible anti-allergy effects by burdock were therefore implicated. Anti-inflammatory and antioxidant effects using a range of test systems were also reported by a Taiwanese team in 1996⁽³⁾.

When considered alongside the traditional use of burdock, these earlier studies suggested possible benefits of burdock as an intervention in the cascade of inflammatory events occurring during allergies. Current drug treatment of allergies consists of antihistamines, leukotriene receptor antagonists, mast-cell stabilisers, and corticosteroids, but side effects are relatively common⁽⁴⁻⁷⁾.

Researchers based at the University of Utrecht in the Netherlands, recently tested 10,000 different herbal extracts using a screen for inhibitory effects on basophil degranulation and leukotriene formation⁽⁸⁾. In these tests, one of the several different extracts of burdock screened, a 20% ethanolic extract made using roots and leaves, was found to have particular strength as an inhibitor of beta-hexosaminidase release from RBL-2H3 and RBL-hE1a-2B12 mast cells. It was therefore selected for more in depth studies using both *in vitro* and *in vivo* methods, to further evaluate

possible anti-allergic properties.

In subsequent experiments involving activated basophils in human Peripheral Blood Mononuclear Cells (PBMC's), both degranulation of mast cells and cys-leukotriene production were significantly inhibited by burdock extracts. These effects were seen at relatively low concentrations (IC₅₀ 8.3 and 11.4 microgram/ml, respectively). Burdock had no effects, however, on cell viability and metabolic activity of the PBMC's, suggesting an absence of toxicity as a result of these effects.

Biologically active components isolated from burdock include arctiin and its metabolite arctigenin and diartigenin, pectin, fructooligosaccharides, inulin and fructofuranan⁽⁹⁻¹¹⁾. Fractionation of the active burdock extract into 13 different fractions found that only one fraction showed inhibitory effects on mast cell degranulation, although attempts to identify the active component were unsuccessful.

Experiments were then conducted involving topical application of an aqueous extract of burdock to the ears of whey-sensitised mice, four hours prior to a challenge with this milk product antigen. Acute ear swelling was inhibited by 50% after application of a cream containing a 5mg dose of burdock extract.

A further experiment involving oral administration of burdock, however, found no influence on this acute mouse ear oedema. This suggests possible inactivation of active components and poor bioavailability from the gastrointestinal tract.

While it should be noted that only one dose (5mg) was evaluated in the oral study, these results support the use of topical rather than oral application of this plant for the acute inflammation experienced during an allergic skin condition. It is interesting in this respect, that such topical use of burdock was probably once more common than it is today^(12,13).

Other recent Korean investigations into the fruit of another plant, *Forsythiae suspensa*, have reported



Anti-allergy properties of Burdock - Continued

significant anti-inflammatory and antioxidant activities for arctigenin⁽¹⁴⁾. This compound is a main metabolite of the lignan arctiin found in burdock, and the inhibitory effects reported in this study on the release and production of several inflammatory mediators such as arachidonic acid metabolites and free radicals, are therefore of interest.

Korean researchers have also observed strong inhibition by another burdock constituent diartigenin, of macrophage nitric oxide (NO) production^(15,16). This molecule is involved in a number of inflammatory and pathological processes in mammals, and contributes to allergen-induced bronchial hyperresponsiveness⁽¹⁷⁾. Diartigenin has also been found to inhibit production of prostaglandin E2, tumor necrosis factor- α , interleukin (IL)-1 and IL-6, in zymosan- or lipopolysaccharide -activated macrophages^(16,18).

The significant reduction in release of inflammatory and allergy mediators reported for burdock extract by the Dutch researchers, along with its

ability to inhibit an acute allergic skin response in mice, suggest that this long-used phytomedicine could have useful indications as a treatment for allergies. This premise is supported by these other recent Korean studies, which validate and increase our knowledge of the range of anti-inflammatory effects shown by key lignan constituents of burdock.

Other recent research on burdock root has found evidence of gastroprotective⁽¹⁹⁾ and prebiotic⁽²⁰⁾ properties. Such additional actions could also be useful, as part of the dietary and herbal treatment of allergies.

Refs:

1. Zick SM et al, *J Altern Complement Med* 12(10):971-980, Dec 2006.
2. Iwakami S et al, *Chem Pharm Bull* 40:1196-1198, 1992.
3. Lin CC et al, *Am J Chin Med* 24:127-137, 1996.
4. Hindmarch I, Shamsi Z. *Clin Exp Allergy* 29 Suppl 3:133-142, 1999.
5. Ten Eick AP et al, *Drug Saf* 24:119-147, 2001.
6. Newnham DM, *Drug Saf* 24:1065-1080, 2001.
7. Marguet C et al, *Arch Pediatr* 11 Suppl 2:113s-119s, 2004.
8. Knipping K et al, *Exp Biol Med* (Maywood). Aug 14, 2008 (epub ahead of print)
9. Mkrtchian TA et al, *Ukr Biokhim Zh* 70:98-105, 1998.
10. Flickinger EA et al, *J Nutr* 132:2188-2194, 2002.
11. Wang HY, Yang JS, *Yao Xue Xue Bao* 28:911-917, 1993.
12. Grieve M. *A Modern Herbal*. Vol 1, New York. Dover Publications 1971 (reprint of 1931)
13. *Culpeper's Complete Herbal, and English Physician*. J Gleave & Son, Deansgate, Manchester, 1826.
14. Kang HS et al, *J Ethnopharmacol* 116, 205-312, 2008.
15. Park SY et al, *Chem Pharm Bull* 55(1):150-152, 2007.
16. Kim BH et al, *J Pharmacol Exp Ther* Aug 11, 2008 (epub ahead of print).
17. Eynott PR et al, *Eur J Pharmacol* 452(1):123-133, Sept 27, 2002.
18. Tian B, Brasier AR, *Recent Prog Horm Res*, 58: 95-130, 2003.
19. Dos Santos AC et al, *J Pharm Pharmacol* 60(6):795-801, Jun 2008.
20. Li D et al, *Anaerobe* 14(1):29-34, Feb 2008.



Gastroprotective properties of Burdock

Roots of Burdock (*Arctium lappa*) are commonly cooked then eaten as a vegetable in Japan and Portugal, a practice that was also popular in Europe during the Middle Ages.

Traditional use of Burdock in Asia include its use as a diuretic, and as part of the treatment of sore throats, tonsillitis, colds and measles, while in Brazil where it is known as 'bardana', it is used as a digestive stimulant, diuretic and depurative.

Seeds are also sometimes used in these traditional practices, including in China where they are used to help control diabetes⁽¹⁾, and in Russia where they are used to help alleviate peptic ulcers. Early research by Russian workers reported influences on gastric secretions in rats⁽²⁾.

Based upon some of these customary uses, a team of Brazilian researchers have recently evaluated the effects of a chloroform extract of burdock root on the digestive tracts of rats and mice⁽³⁾.

Oral administration of large doses (100mg/kg per day for 7 days) reduced acetic acid induced gastric ulceration in rats, in a similar manner to the drug omeprazole, used as a control. Omeprazole is a potent inhibitor of gastric acid secretion via irreversible inhibition of H⁺, K⁺-ATPase activity, and widely used as an anti-ulcer drug.

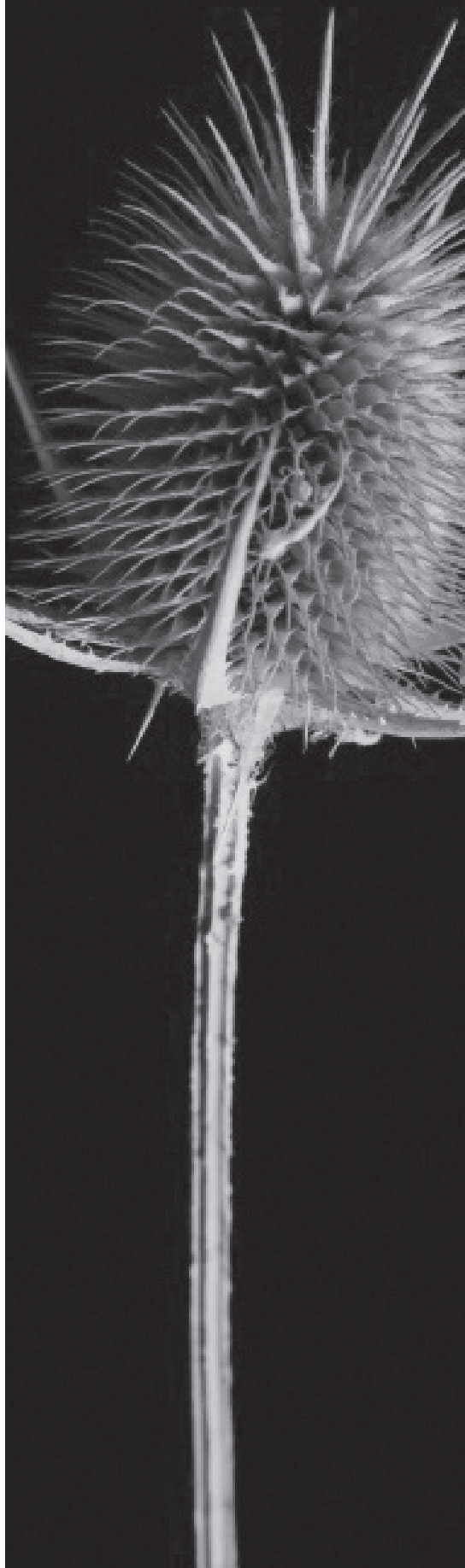
After investigating several possible mechanisms of this gastroprotective effect, the authors concluded that inhibition of gastric acid secretion, and possibly the antioxidant effects of burdock extract, were contributory to its gastroprotective properties. Several antioxidant compounds such as chlorogenic and caffeic acids, were identified in the burdock extract.

It should be noted that burdock root contains up to 45% of inulin, a common compound found also in roots of plants such as chicory and dandelion. This is an indigestible and somewhat mucilaginous compound which upon fermentation by bowel bacteria can result in flatulence, but also may encourage beneficial bowel flora and have a soothing and protective effect on the

gastrointestinal tract. Inulin has been researched extensively during recent years for its prebiotic properties, and shown to promote growth particularly of bifidobacteria within the human colon^(4,5). It is, however, unlikely that significant levels of inulin would have occurred in this particular burdock extract, as it is water soluble and would have been poorly extracted by the chloroform solvent used.

Refs:

1. Xu Z et al, *Phytother Res* 22(1):97-101, Jan 2008.
2. Os'kina OA et al, *Eksp Klin Farmakol* 62(4):37-39, Jul-Aug 1999
3. Dos Santos AC et al, *J Pharm Pharmacol* 60(6):795-801, Jun 2008.
4. Kolida S, Gibson GR *J Nutr* 137(11 Suppl):2503S-2506S, Nov 2007
5. Li D et al, *Anaerobe* 14(1):29-34, Feb 2008.





Favourable results from recent clinical trial on Ginkgo in prevention of dementia

It is currently estimated that 18 million people throughout the world have dementia, with Alzheimer's disease accounting for the majority of cases. With the aging population this figure has been forecast to increase 400% in incidence, rising to 29 million by 2020 and 34 million by 2025^(1,2,3). As no cure for this distressing disease has yet been identified, and health costs associated with its increasing prevalence are rising, ways to help prevent or delay it have become a major focus of research.

Extracts of the leaf of *Ginkgo biloba* have been widely taken by elderly people in developed countries for many years, for alleged anti-aging properties. Clinical trials have suggested efficacy to enhance or maintain cognition, treat peripheral vascular disease, alleviate tinnitus, and enhance coronary blood flow⁽⁴⁻⁸⁾. Mechanisms of action seem to relate to the powerful antioxidant effects of the flavone glycosides and terpene lactones found in concentrated ginkgo extracts, as well as possible effects on amyloid metabolism^(9,10).

The most intensive area of research involving ginkgo has been its effects on cognitive impairment. While one study indicated that it slowed the progression of symptomatic Alzheimer's disease, the dropout rate of trial participants was greater than 50%⁽¹¹⁾. A more recent placebo-controlled trial involving 500 individuals, however, failed to reveal any significant beneficial effect on cognition or significant adverse events⁽¹²⁾.

The journal *Neurology*, has recently published results from a randomised, placebo-controlled, double-blind study involving 118 cognitively intact subjects who took a standardised ginkgo preparation or placebo for three and a half years. Supported by the National Center for Complementary and Alternative Medicine in the USA, this pilot study has provided some interesting findings⁽¹³⁾.

Participants were men and women aged 85 years or older, recruited through mailings in the Portland,

Oregon area. Each had to have no subjective memory complaint or memory impairment as measured in a recognised memory scale test, and no clinical features of dementia or depression, before being accepted into the trial. An MRI scan of the brain of each participant was also undertaken, and medical records reviewed for inclusion and exclusion criteria.

Subjects were then randomly assigned to a group who were treated with a dose of 80mg standardised ginkgo extract three times daily, and another who received placebo three times daily. All participants also received a standard multivitamin containing 40 IU of vitamin E.

Annual face-to-face interviews with 6 month follow-up visits took place to assess health status changes, Mini-Mental State Examination Scores, depressive symptoms, activities of daily living, medication review, pill count, and health history review. Extensive cognitive testing of major cognitive domains and clinical examinations also took place at the annual visits.

Measured outcomes included the onset of mild cognitive decline (Clinical Dementia Rating or CDR progressing from 0 to 0.5), decline in memory function over time, and adverse events. Medication adherence or compliance, was also examined.

Fourteen of the 58 placebo group participants progressed to a CDR of 0.5 during the 42 month period, whereas only 7 cases occurred among the 60 participants in the ginkgo-treated group. The ginkgo-treated group also showed a tendency of less decline in memory over time. Both effects, however, fell just short of reaching statistical significance.

When the researchers subsequently limited the results to subjects who reported taking their medication, a significant outcome emerged in favour of ginkgo exhibiting a protective effect against cognitive decline. The authors noted that

Favourable results from recent clinical trial on Ginkgo in prevention of dementia - Continued

medication non-compliance and incident dementia might be confounded, and suggested that inclusion of noncompliant subjects in the analysis might bias results against ginkgo.

No difference in overall adverse events, dropout rates or deaths occurred between the two groups. However, more stroke or TIA episodes (7 cases) occurred in the ginkgo-treated group compared with the placebo group. All stroke cases except one were non-haemorrhagic, were generally not severe, and did not result in deaths.

In conclusion, while a protective effect of ginkgo against progression to clinical dementia was not clearly shown in this trial, the limited number of participants and relatively short duration, are likely to be contributory. This is an important point and the statistical power of these parameters is a probable constraint, proof of significant adverse effects from hormone replacement therapy for example, only being obtained from the U.S. Women's Health Initiative study which involved more than fifteen thousand patients. In their discussion, the authors estimate a need for over 2,800 subjects to attain

80% power to detect a significant effect of ginkgo being associated with a 20% reduction in risk of progression to a CDR of 0.5. They therefore call for a larger trial to confirm or refute these findings.

As an answer to this call, the editorial in the same issue of *Neurology* describes a similar but larger trial also underway in the U.S.⁽¹⁴⁾ This study, the Ginkgo in Evaluation of Memory (GEM) study, is a double-blind, placebo-controlled trial involving administration of 120mg of Ginkgo twice daily, to more than 3,000 people at four clinical sites around the United States⁽¹⁵⁾. This is the largest trial to evaluate potential preventative effects of ginkgo against dementia, and is assessing the incidence of dementia as well as overall rate of cognitive decline, functional status, cerebrovascular and cardiovascular disease incidence, and all-cause mortality, in participants all of whom were aged 75 at trial commencement, for a 5 to 7 year period. Results from this trial will also shortly be forthcoming, and will be of great interest.

Refs:

1. Brookmeyer R, Gray S. *Stat Med* 19: 1481-1493, 2000.
2. Haan MN, Wallace R. *Annu Rev Public Health*. 25:1-24, 2004.
3. Borenstein Amy et al, paper presented at Alzheimer's Association International Conference on Prevention of Dementia, Washington, June 2005.
4. Van Dongen MC et al. *J Am Geriatr Soc* 48(10): 1183-1194, 2000.
5. Wettstein A. *Phytomedicine* 6(6): 393-401, 2000.
6. Morgenstern C, Biermann E, *Int J Clin Pharmacol Ther* 40(5):188-197, May 2002.
7. Wu Y et al, *Phytomedicine* 15, 164-169, 2008.
8. Wu Y et al, *Phytother Res* 22, 734-739, 2008.
9. Luo Y. *Life Sci* 78:2066-2072, 2006.
10. Luo Y et al, *Proc Natl Acad Sci USA* 99:12197-12202, 2002.
11. Le Bars PL et al, *JAMA* 278:1327-1332, 1997.
12. Schneider LS et al, *Curr Alzheimer Res* 2:541-551, 2005.
13. Dodge HH et al, *Neurology* 70(19 Pt 2):1809-1817, 6 May, 2008.
14. DeKosky ST, Furberg CD, Editorial, *Neurology* 70(19 Pt 2):1730-1731, 6 May, 2008.
15. DeKosky ST et al, *Contemp Clin Trials* 27:238-253, 2006.





Cholesterol lowering effects of Globe Artichoke

Cholesterol and lipid lowering effects for the leaves of Globe Artichoke (*Cynara scolymus*) were first reported in rats in 1977⁽¹⁾. Early clinical studies in Poland and Germany also implicated possible hypocholesterolaemic and hypolipidaemic effects, although these were either uncontrolled or involved small numbers of patients⁽²⁻⁴⁾.

A larger study involving 557 patients and an average treatment duration of 43 days reported a significant fall in serum cholesterol and triglyceride levels in patients being treated for dyspeptic symptoms⁽⁵⁾. A further trial involving 143 patients with a high average baseline total cholesterol of 7.70mmol/l, reported an 18.5% reduction in total cholesterol, and a 22.9% reduction in LDL-cholesterol, as compared to 8.6% and 6.3% reductions respectively in the placebo group, following 6 weeks artichoke treatment⁽⁶⁾. The extract used in this study, was equivalent to a high 45grams of artichoke leaf per day.

A further clinical trial conducted by researchers based at the University of Reading in the UK, has recently evaluated the effects of lower doses of artichoke leaf extract, in a group of 131 adults with mild to moderate hypercholesterolaemia⁽⁷⁾.

All volunteers had recently measured plasma total cholesterol values in the range of 6.0 to 8.0mmol/l, and were randomised to receive either four capsules of artichoke leaf extract or matched placebo daily for 12 weeks. Each capsule contained 320mg of a standardised broad-spectrum aqueous extract (4-6:1) of artichoke leaf, containing at least 2.5% total caffeoyl-quinic acids and at least 0.1% luteolin-7-O-glucuronide. Apart from plasma lipid measurements at baseline and after 12 weeks, a questionnaire to assess general well-being was also completed by study participants at commencement and completion.

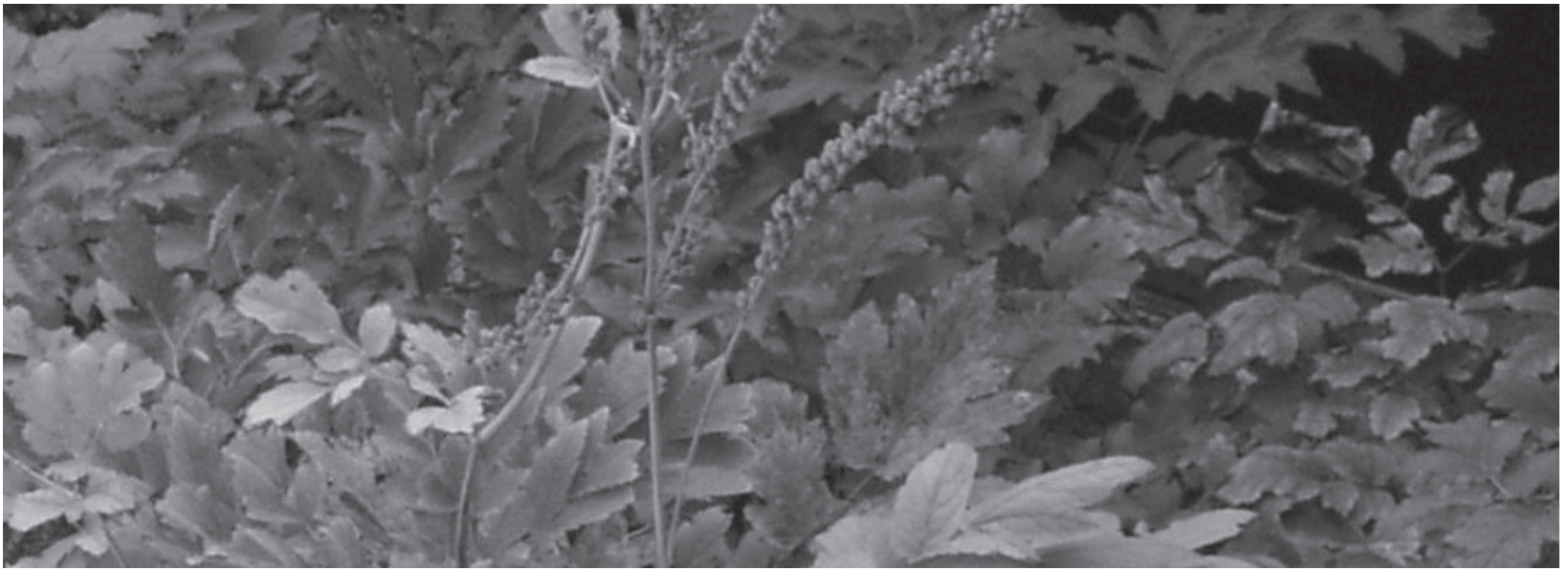
Artichoke treatment was associated with an average 4.2% decrease in plasma total cholesterol levels, while levels increased by an average of 1.9% in the control group. This difference of 6.1% between both

groups was statistically significant. No significant differences were observed between groups for LDL cholesterol, HDL cholesterol or triglyceride levels, or in general well-being.

This study provides further evidence that artichoke leaf extract may help reduce plasma total cholesterol in adults with mild to moderate hypercholesterolaemia. While the effects reported were mild, previous studies suggest that higher dosages of artichoke extract, may well have produced a greater response.

Refs:

1. Lietti A, *Fitoterapia* (48) 153-158, 1977
2. Wojcicki et al, *Herba Pol.* 27, 265, 1981.
3. Rasmussen PL, *Phytonews* 3, published by Phytomed Medicinal Herbs Ltd, Auckland, New Zealand, ISSN 1175-0251, May 1999.
4. Kraft K., *Phytomedicine* 4(4), 369-378, 1997.
5. Fintelmann V. & Menssen H.G., *Deutsch Apoth. Ztg.* 136, 1405, 1996.
6. Englisch W et al, *Arzneimittelforschung* 50, 260-265, 2000.
7. Bundy R et al, *Phytomedicine*, in press, 2008 doi:10.1016/j.phymed.2008.03.001



More evidence of Black cohosh's inhibitory effects on human breast cancer cells

Inhibitory effects of root extracts of the North American herb black cohosh (*Cimicifuga racemosa*) on human breast cancer cell growth have been reported in a number of studies published since 1999⁽¹⁻⁶⁾. Potentiation of the anticancer properties of the drugs tamoxifen⁽⁷⁾ and doxorubicin⁽⁸⁾ has also been reported, and the black cohosh triterpene glycoside actein enhances cytotoxic effects of several chemotherapy drugs on human breast cancer cells⁽⁹⁾. As outlined in the November 2007 issue of *PhytoNews*⁽¹⁰⁾, evidence of a possible protective effect against the risk of breast cancer and breast cancer recurrence, has also arisen through favourable results from two recent separate retrospective studies in humans⁽¹¹⁻¹²⁾.

Researchers based at the College of Physicians and Surgeons, Columbia University in New York, have recently undertaken more in depth studies to try and determine the nature of the compounds responsible for these activities in black cohosh⁽¹³⁾. Black cohosh fractions enriched with triterpene glycosides as well as purified components from black cohosh and related Asian species of *Cimicifuga*, were tested for their effects on growth of oestrogen receptor negative, Her2 overexpressing human breast cancer cell lines (MDA-MB-453). These types of cells had previously been shown to be most sensitive to the growth inhibitory effects of the ethyl acetate fraction and the purified triterpene glycoside actein (β -D-xylopyranoside) from black cohosh.

Breast cancer cells were exposed to increasing concentrations of black cohosh extracts containing 1%,

15% or 27% triterpene glycosides or purified triterpene glycosides from *Cimicifuga* species, for 96 hours, then the number of viable cells determined. Concentrations required to cause a 50% growth inhibition (IC_{50}) were calculated, as was the ability of MDA-MB-453 cells to form colonies. Another set of experiments involved exposure of actein to MCF7 and MCF7 Her-2 breast cancer cells, to determine whether sensitivity correlated with Her-2 expression.

The extract containing only 1% triterpene glycosides, produced no cell growth inhibition, and the extract with 27% triterpene glycosides, the strongest inhibition. Isoferulic acid, a polyphenol sometimes cited as a key active constituent of black cohosh, was found in lowest concentrations in the 27% triterpene glycoside extract, suggesting it has no contributory role to these anti-cancer effects. The triterpene glycoside with the strongest inhibitory effects on cancer cell proliferation had an IC_{50} of 3.2 μ g/ml, compared to 5.7 μ g/ml for actein. Several other black cohosh components also exhibited growth inhibitory effects, with IC_{50} values ranging from 6 μ g/ml to 72 μ g/ml.

Actein also reduced the ability of MDA-MB-453 cells to form colonies, with an IC_{50} of 10 μ g/ml after 96 hours exposure. MCF7 Her-2 human breast cancer cells were more sensitive to growth inhibition by actein than oestrogen receptor positive, low Her-2 cells.

These experiments provide further evidence of the triterpene glycoside fraction of black cohosh including actein, being contributory to the *in vitro*

inhibitory effects of this phytomedicine against human breast cancer cells. They also corroborate results of previous studies by the same researchers⁽¹⁴⁾.

While human pharmacokinetic studies to ascertain levels of these particular constituents reached in breast tissue following oral administration are needed, this latest study provides further support for a possible effect of black cohosh in the prevention and treatment of human breast cancer.

Refs:

1. Dixon-Shanies D, Shaikh N. *Oncol Rep*;6(6):1383-7. 1999 Nov-Dec
2. Watanabe K et al. *Chem Pharm Bull* (Tokyo) 50, 121-125, 2002.
3. Bodinet C, Freudenstein J. *Breast Cancer Res Treat*;76(1):1-10. 2002
4. Einbond LS et al. *Breast Cancer Res Treat* 83(3):221-231, Feb 2004.
5. Hostanska K et al. *Biol Pharm Bull* 27(12):1970-5; Dec 2004.
6. Hostanska K et al. *Breast Cancer Treat*. 84(2):151-60; Mar 2004.
7. Burdette JE et al. *J Agric Food Chem*. 20;50(24):7022-8. 2002 Nov
8. Rockwell S et al. *Breast Cancer Res Treat* 90(3):233-239, Apr 2005.
9. Einbond LS et al. *Planta Med* 72(13):1200-1206, Oct 2006.
10. Rasmussen PL, *PhytoNews* published by Phytomed Medicinal Herbs Ltd, New Zealand, ISSN 1175-0251, November 2007
11. Zepelin HH et al. *Int J Clin Pharmacol Ther* 45(3):143-154, Mar 2007.
12. Rebeck TR et al. *Int J Cancer* 120(7):1523-1528, Apr 1, 2007.
13. Einbond LS et al. *PhytoMedicine* 15, 504-511, 2008.
14. Einbond LS et al. *Anticancer Res* 27(2):697-712, Mar-Apr 2007.



New Zealand studies on use, understanding and attitudes towards CAM

The widespread use of complementary medicines or therapies (CAM) by populations of developed countries, is now well established. This usage obviously varies between different population and ethnic groups, although these aspects have been less researched or discussed to date.

A 1994 study reported that 25% of the UK population, and 50-70% of the populations of France and Germany, were using CAM at that time⁽¹⁾. Overall use of CAM in Australia was reported to be 48.5% in 1993⁽²⁾, while in the U.S., a usage rate of around 36% was reported in 2000^(3,4).

The design and methodology of such surveys, including what types of therapies are defined as 'complementary and alternative', and the population or participant demographics, clearly influence their findings. What is known, is that women, those from higher socio-economic and educational backgrounds, and those with serious or chronic illnesses, generally tend to be high users^(4, 5, 6, 7, 8).

In the 2002 U.S. National Health Interview Survey, higher usage rates of herbs and supplements were revealed for people with multiple racial backgrounds, with 21.9% of American Indians or Alaskan natives, versus only 19.1% of whites and 14.3% of blacks, being users⁽⁴⁾. Regional differences were also shown, with residents of California being higher users than the rest of the U.S. population.

Findings from three separate New Zealand studies published over recent years, would seem to highlight the relevance of such demographic factors^(6,9,10).

A 2001 study involving 200 cancer patients attending clinics at two separate provincial cities, found that 49% of these were using CAM⁽⁶⁾. A larger study involving 1043 patients and relatives presenting at an Emergency Department at Waikato Hospital in Hamilton in late 2004 and early 2005, found that 38% of participants had used CAM, although this excluded massage⁽⁹⁾. Publication of this study in the New Zealand Medical Journal at the time, was accompanied by an editorial written by a British academic, which discussed why New Zealanders' "love affair with alternative medicine" was cause for concern⁽¹¹⁾.

In the cancer patient study, only 41% of CAM users had discussed this usage with their oncologist, while in the Waikato study only 37.3% had told their medical practitioner about such usage. This situation is however a regular finding from similar international studies, and failure of doctors to ask their patients about CAM usage, seems to be a widespread deficiency.

Results from a recent small study involving inpatients at Gisborne Hospital, further explored the level of traditional and complementary medicine use⁽¹⁰⁾. This provincial hospital services a largely rural population in an area where 47% of

people identify as Maori, which is significantly greater than the 14% of Maori in the general New Zealand population.

A comprehensive questionnaire into basic demographic, disease and treatment-related data that listed a total of 25 different traditional and complementary (TCAM) therapies was used to interview a total of 92 patients between January and February 2006. Patients were asked about their knowledge and use of each modality, and related information obtained by the interviewer over a period of at least half an hour per participant. The average age of the patients interviewed was 54 years, 50% were female, and 44% Maori.

Of the patients interviewed, 91% had used TCAM at some stage during their life, and most had used more than one modality. The average number of modalities used by all patients was 6.4, and women were more frequent users than men.

The most popular modality was massage, having been used by 73% of the 88 respondents, while chiropractic was used by 54% of respondents. The use of most modalities was fairly equal among different ethnic groups, although a higher usage of Rongoa Maori/traditional Maori medicine, hypnotherapy, spiritual healing, and imagery/visualisation was used by Maori. Non-Maori participants reported higher rates of usage of yoga, chiropractic, homoeopathy,

osteopathy and acupuncture.

Of the biologically based therapies enquired about, usage of vitamins was most popular (65% of the 88 respondents), with herbal therapies being the next most used modality (49% of respondents).

Symptom relief and improved quality of life were specified as the most common reasons for using TCAM (98% and 95% of cases respectively), with 83% listing hope of a cure, and 73% listing prevention of disease recurrence, as being their reasons for use. While 70% thought that TCAM was not at all helpful for their present condition, 64% reported it had been helpful in the past, and 86% would use it in the future.

Only 3% of respondents reported experiencing side effects from TCAM therapies, but when asked, 78% felt that TCAM should be regulated, this being defined by the interviewer as "for example like pharmaceuticals drugs, you have to have a consultation with a qualified person first before purchasing any TCAM medicines". Consultations with TCAM practitioners had been pursued by 43% of patients prior to medical evaluation in the past. Despite this,

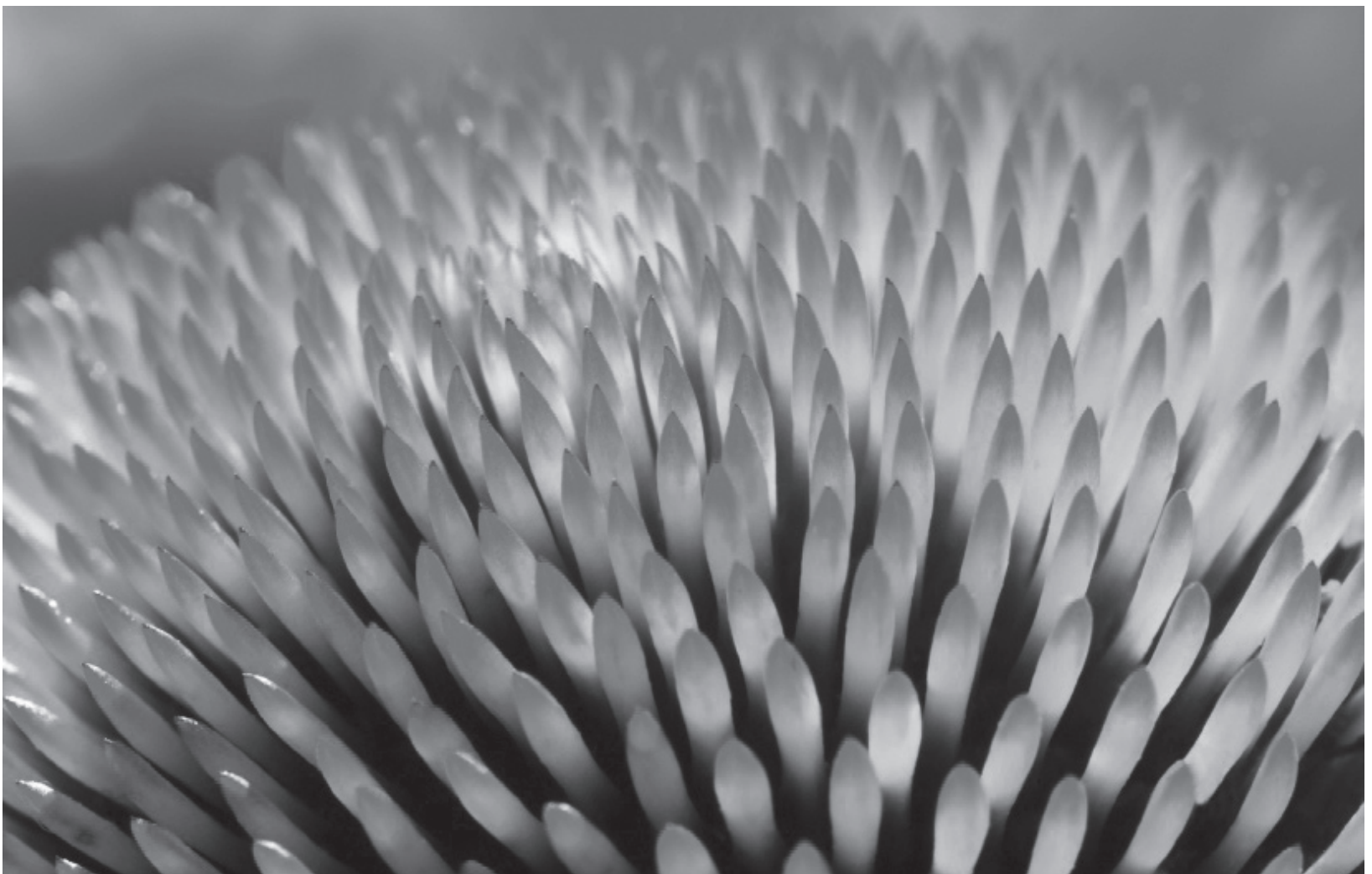
only 11% of patients reported being questioned by their doctor on their use of TCAM.

Of interest also, was that virtually all respondents (97%) stated they would use TCAM therapies in the hospital itself if these were available. Of the different therapies listed, massage, Rongoa Maori and herbal medicines were the most popular suggestions.

The higher level of overall usage identified in this study compared to that in the two earlier but still recent studies^(6,9), almost certainly relates in part to methodological and demographic differences. The intentional inclusion of 'traditional' as well as 'complementary and alternative' medicine in this survey, undertaken in a region where Maori culture has significant influence, could also be relevant. It seems likely, however, that in New Zealand at least, significant regional differences in the popularity and awareness of CAM exist, and furthermore, that TCAM is being increasingly used by the New Zealand population. The latter is consistent with findings from the U.S., Australia and the UK, which show increasing usage of CAM in each country over recent years^(3,12,13).

Refs:

1. Fisher P & Ward A. *BMJ* 309, 107-111, 1994.
2. MacLennan AH et al, *Lancet* 347:569-573, 1996
3. Barnes PM *Adv Data* 27(343):1-19, May 2004.
4. Kennedy J. *Clin Ther* 27(11):1847-1858, Nov 2005.
5. Von Gruenigen VE et al, *Int J Gynaecol Cancer* 11:205-209, 2001.
6. Chrystal K et al, *NZ Med J* 116(1168):u296, Jan 24, 2003.
7. Vapiwala N et al, *Cancer J* 12(6):467-474, Nov-Dec 2006.
8. Upchurch DM. *J Womens Health (Larchmt)* 16(11):102-113, Jan-Feb 2007
9. Nicolson T, *NZ Med J* 119(1233): 1-13, May 5, 2006
10. Evans A et al, *NZ Med J* 121(1278):21-34, Jul 25, 2008.
11. Ernst E. New Zealanders' love affair with "alternative" medicine: reason for concern? *NZ Med J* 119(1233), 5 May 2006.
12. Ritchie MR. *Proc Nutr Soc* 66, 479-482, 2007.
13. Zhang AL *Ann NY Acad Sci* 1114:204-215, Oct 2007



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