Phytonews

ISSN 1175-0251

Ginger for weight loss

Ginger root (*Zingiber officinale*) has been a popular culinary and medicinal herb for centuries, and a wide array of therapeutic properties have been validated by research over the past 20 years. These include its activities as a circulatory tonic and antioxidant[1,2,3,4] , an anti-emetic during nausea and vomiting[5,6], and as a spasmolytic and broad spectrum digestive tonic (see *Phytonews 16*[7]). Regular ingestion of ginger has also been shown to produce stimulant effects on pancreatic and small intestine digestive enzyme secretions[8,9] and bile secretion[10].

Other research during the past few years has revealed evidence of large doses of ginger being protective against atherosclerosis and hyperlipidaemia[11,12], an activity associated with inhibition of lipid peroxidation and enhancement of fibrinolytic activity. A study by Japanese workers which has evaluated these properties further, has now found evidence of antiobesity effects for this common medicinal herb[13].

Preliminary experiments in mice found an aqueous extract of ginger to reduce the elevation of plasma triacylglycerol levels after oral administration of a lipid emulsion containing corn oil, suggesting possible inhibition of hydrolysis and thus absorption of dietary fat. This lead to an investigation involving feeding a high fat diet to mice for 8 weeks, with and without concurrent ginger administration.

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Issue 22, July 2005

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Two doses of ginger were used, with the diet of one group of mice containing 1% aqueous extract of ginger, and another a higher dose of 3% ginger. Controls involving administration of a high fat diet only were used in both cases.

In the higher dose group, body weights at two to eight weeks after commencement of the study were significantly lower in mice fed the high-fat diet containing ginger than in controls fed the high-fat diet only. While body weights were not significantly reduced in mice fed the high-fat diet containing 1% extract of ginger, after eight weeks a favourable reduction in the parametrial adipose tissue weights was measured.

These findings suggest an antiobesity effect of an aqueous extract of ginger, due in part to inhibition of intestinal absorption of dietary fat by this phytomedicine.

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Antidiabetic effects of Sage

Traditional therapeutic uses of Sage *(Salvia officinalis)* are many and varied, utilising the antimicrobial, astringent, antioxidant and anti-hydrotic properties of this popular phytomedicine. Native to the Mediterranean region, Sage leaves have been an important part of Iranian folk medicine for the management of diabetes mellitus[1,2], and this has lead researchers in Tehran to evaluate it for possible hypoglycaemic activity[3].

Both the essential oil of Sage as well as a methanolic extract were given as single intraperitoneal injections to diabetic rats, and blood glucose and insulin levels were measured at 1, 3 and 5 hours after administration. Doses of 100 to 500mg per kg of a sage extract of unspecified strength, and 0.042 to 0.2ml per kg of sage essential oil were used.

A statistically significant decrease in serum glucose levels were measured in diabetic but not healthy rats following administration of the methanolic extract of sage, but not sage essential oil. No effects on serum insulin levels were seen.

Similar evidence of hypoglycaemic effects for sage has previously been reported by Mexican workers[4]. These preliminary studies in animals signify potential efficacy of this well-known plant in the treatment of diabetes, and indicates that human studies to further evaluate such activity may be warranted.

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Antithrombotic effects of Thyme and Rosemary

Myocardial infarction and stroke are cardiovascular diseases whose incidence in developed countries has risen considerably in recent decades, a trend linked to a large degree with changing dietary habits. Regular intake of foods such as red wine, olive oil, and the garlic and onion family vegetables has been widely associated with a preventative effect against these lifestyle-related atherothrombotic diseases.

Apart from these foods, evidence is emerging that several other fruits and vegetables with experimentally proven antithrombotic or antiplatelet effects, may also be effective in preventing coronary events and stroke[1,2,3] . While the platelet aggregation inhibitor drug aspirin is widely prescribed for this purpose, specific foods such as kiwifruit[4] (see *Phytonews 20*[5]) and onions[6], exhibit *in vitro* antithrombotic effects that are likely to contribute to a preventative effect against cardiovascular diseases.

A study by Japanese workers published in the May issue of *Nutrition*, used a primary *in vitro* platelet function test and a secondary laser-induced *in vivo* carotid artery thrombosis test in rats, to screen around 20 different herbs for potential antithrombotic effects[7]. This involved an *in vitro* test using herb filtrates mixed with blood drawn from rats to determine the rate of platelet aggregation and coagulation, followed by the same measurements on blood taken from animals soon after they had ingested particular herb filtrates (*in vivo* study).

In the *in vitro* experiments, thrombolytic, antiplatelet and anticoagulant activities were measured for various herb extracts, including common thyme, lemon balm, wasabi root, peppermint, lemon verbena, chervil, and rocket. The two most promising antiplatelet agents, thyme (*Thymus vulgaris*) and rosemary (*Rosmarinus officinalis*) were subsequently shown to produce significant inhibition of thrombus formation *in vivo*. These effects were shown to be preserved following heat treatment of these two herbs, indicating that the active antiplatelet components have low molecular weight and are probably not affected by cooking.

These relatively simple tests have produced evidence that these two popular culinary and antioxidant herbs may have protective effects against platelet aggregation and thus, against arterial thrombosis and cardiovascular disease.

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Anti-pruritic effects of Chamomile

Chamomile tea is widely consumed for its carminative and relaxant effects, and is reported as being effective in spasmodic and inflammatory conditions affecting the gastrointestinal tract. Topical preparations are also used for inflammatory conditions of the skin and mucous membranes, such as eczema, nappy rash and cracked nipples in breastfeeding mothers.

While histamine production by skin mast cells is considered to be an important mediator of pruritis (itchiness), antihistamine drugs are often ineffective in the treatment of this aspect of atopic dermatitis.

Studies by a team of Japanese researchers, have now shown that both long term[1] as well as acute[2] administration of Chamomile (*Matricaria recutita*) flowers produces a significant reduction in pruritis produced by a histamine releasing agent in mice. Thus oral administration of chamomile extract 2 hours before injection with a pruritis-inducing compound (compound 48/80), had a suppressive effect on scratching behaviour in mice.

This effect was shown to be dose dependent, with larger doses of Chamomile producing the best results. As well as the whole flower extract used, a single oral dose of the essential oil of chamomile, was also effective as an anti-pruritic agent.

Further experiments were carried out involving oral administration of two different antihistamine drugs (oxatomide and fexofenadine), which by themselves had limited efficacy in inhibiting scratching. When chamomile extract was administered one hour prior to these antihistamine drugs however, a synergistic effect became evident whereby inhibition of scratching occurred to a greater level than that seen following administration of chamomile or antihistamine alone. Antipruritic effects of oxatomide were increased from 18% to 60% when chamomile pre-treatment occurred, and those for fexofenadine improved from 16% to 55%.

This study shows a potential role for chamomile taken orally not only as a single treatment to help reduce skin scratching in atopic or allergic skin conditions, but also possible uses as an adjunctive treatment together with antihistamine drugs.

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Synergistic anticancer properties of Dan Shen and baicalin

As reported in issue 17 of *Phytonews*[1], the Chinese herb Baical Skullcap (*Scutellaria baicalensis*) has shown evidence of beneficial effects both in the chemoprevention and treatment of various cancers during recent years. Possible efficacy to reduce chemotherapy-induced nausea[2] as well as synergistic antioxidant properties when combined with grapeseed extract[3], have also been reported.

Researchers based at Clemson University and Oncology Research Institute in Greenville in the U.S., have now found evidence of a synergistic anticancer effect for two key compounds found in baical skullcap (scutellarin and baicalin), with an extract of another Chinese herb known to exhibit anticancer effects, Dan Shen (*Salvia miltiorrhiza*)[4].

Anti-proliferation effects on two human breast cancer cell lines (MCF-7 and T-47D), were measured for both scutellarin and baicalin, as well as for extracts of *Salvia miltiorrhiza* and *Camellia sinensis*. Inhibitory effects were seen for all four compounds, and when various combinations of these were used, *Salvia miltiorrhiza* together with either scutellarin or baicalin showed a synergistic effect on MCF-F cell proliferation. Anti-proliferative effects were also shown for all four compounds on other cancer cell types, including the human head and neck cancer (epithelial) cell lines CAL-27 and FaDu.

This preliminary *in vitro* study provides some validation for the practice of combining these two phytomedicines in Traditional Chinese Medicine formulations for various cancers. As with various drug combinations used in conventional drug-based chemotherapy, it also suggests that selected combinations of particular phytomedicines have the potential to produce synergistic or additive effects in the treatment of human malignancies.

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Black cohosh for Prostate Cancer?

As discussed in *Phytonews 21*[1], various studies have reported an anti-proliferative action in human breast cancer cell cultures for extracts of black cohosh (*Cimicifuga racemosa*)[2,3,4,5]. Encouraged by the favourable results from these studies, two separate groups of researchers in Switzerland and Germany have now investigated the effects of this phytomedicine on human prostate cancer, also known to be hormone dependent[6,7].

An *in vitro* study was conducted using three types of different prostate cancer cells, one androgen-sensitive and the other androgen insensitive, to determine possible growth inhibitory effects of an extract of black cohosh[6]. A significant and dose dependent inhibition of cancer cell growth occurred in all cell lines used, with concentrations of the black cohosh extract required to produce 50% growth inhibition (IC50) after 72 hours ranging between 37.1 and 62.7 micrograms per ml. These effects were shown to be due to activation of caspase enzymes responsible for cell destruction, and the subsequent induction of apoptosis (cell death) .

Similar antiproliferative effects against hormone dependent human prostate cells using a different experimental method, were reported by German researchers, shortly after this Swiss study[7]. Significant inhibition in the growth of prostate cancer cells was observed using concentrations of a black cohosh extract as low as 50 nanograms per ml. This effect was observed under normal basal conditions, as well as under oestradiol and dihydrotestosterone-stimulated conditions.

The researchers speculated that this anti-cancer effect could be mediated through activation of the aryl hydrocarbon receptor (AhR) by black cohosh compounds, as a receptor binding study showed interaction of black cohosh with these receptors. AhR is widely expressed in mammalian tissues and tumours, and activation of AhR receptors has previously been shown to cause inhibition of prostate cancer cell growth[8,9].

An additional study by the same group of German researchers which evaluated the effects of black cohosh on the prostate and bones of rats, has implicated other potential benefits of this phytomedicine in the management of male cancers[10]. Although osteoporosis is most seen as a problem in women associated with oestrogen loss during menopause, orchidectomy (testicle excision), is a procedure undertaken in the management of both testicular as well as sometimes prostate cancer. This as well as certain hormonal drug treatments such as luteinising hormone releasing agonists used in prostate cancer, can lead to osteoporosis in men[11].

The German study reported that black cohosh treatment had a preventative effect against osteoporosis of the tibia in orchidectomised rats, yet unlike testosterone, no adverse stimulation of prostate cell growth occured. The authors concluded that black cohosh may be useful to prevent osteoporosis in aged male patients with reduced testosterone production.

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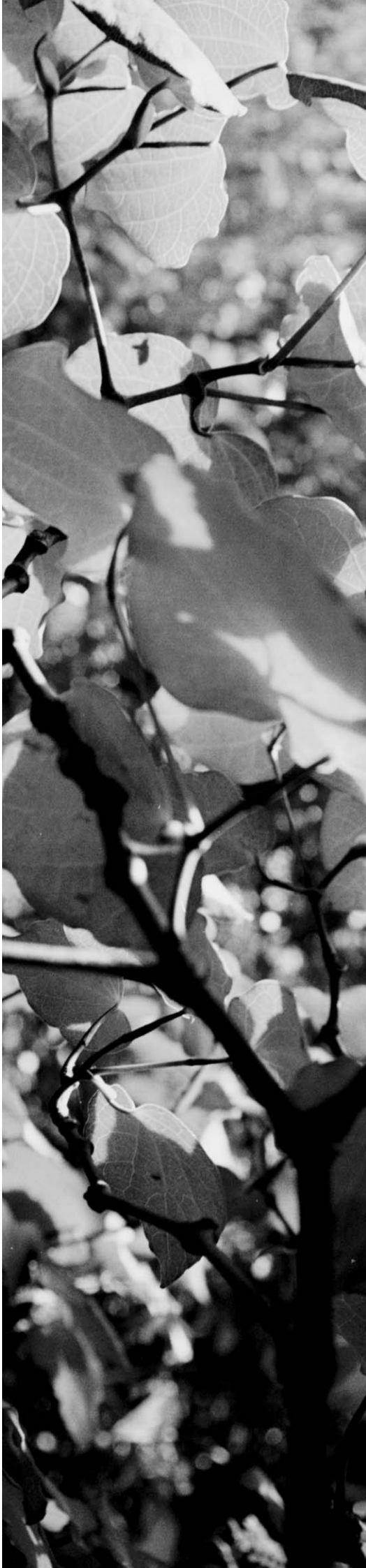

Bupleurum inhibits Human Lung Cancer cells in vitro

Bupleurum root is a major ingredient of various traditional Chinese herbal mixtures widely used to treat chronic immunological, liver and lung diseases. Antitumour effects and inhibition of metastasis during liver and ovarian cancer as well as melanoma have been reported for several of these bupleurum-containing formulations[1,2,3,4,5].

As part of their work to try and identify active anticancer compounds in traditional herbal formulations, Taiwanese researchers have found that an acetone extract of *Bupleurum scorzonerifolium* reduces the proliferation of human lung cancer cells *in vitro*[6] . This species of bupleurum, common in the south of China, is phytochemically very similar to *Bupleurum chinense* or *B. falcatum*, and is regarded as having the same actions.

Anticancer activity for bupleurum was previously shown to occur probably through activation of apoptosis, a complex process involving cell death characterised by DNA fragmentation, chromatin condensation, cell shrinkage and formation of membrane-enclosed vesicles[6]. These effects were associated with inhibition of telomerase, an enzyme involved in chromosome separation during mitosis and tumour cell growth, whose inhibition has been shown to cause highly specific cancer cell death[7]. Anti-angiogenic activity *in vitro* has also been reported for another related species *Bupleurum longiradiatum*, but not *in vivo*[8].

The anticancer properties of bupleurum were recently investigated further in a Taiwanese study using five common human cancer cell lines (lung, breast, colon, hepatocellular and ovarian), and in an *in vivo* study involving mice with A549 lung cancer[9]. Cells were treated using different concentrations of an acetone extract of bupleurum for 24 hours, and IC50 (50% inhibitory concentration) values determined. All cancer cell types had their growth inhibited by bupleurum incubation, with hepatoma cells being most susceptible, and breast cancer cell lines least sensitive.

Additional possible mechanisms for these anticancer activities were then further explored by measuring antiproliferative effects and the activity of bupleurum extract on various other enzymes and biochemical pathways involved in tumour cell growth. These further *in vitro* studies revealed evidence of a range of relevant activities involving several such pathways and processes. Activation of caspases (protease enzymes involved in apoptosis) as well as induction of G2/M cell cycle arrest and polymerisation of tubulin, were all implicated as possible mechanisms of bupleurum-mediated anticancer effects[9].

Saikosaponins are prominent ingredients of bupleurum species, and the anti-inflammatory, antibacterial, antiviral and antihepatotoxic properties of bupleurum have been largely associated with these[10, 11]. However, while *in vitro* cytotoxic actions against hepatoma for various saikosaponins has been reported[12, 13,14], extraction using different solvents indicated that non-saikosaponin and non-polar constituents of bupleurum root appeared be the most likely active anticancer components in these latest studies[9].

In an additional study involving mice, A549 lung cancer tumour sizes following daily intraperitoneal injection of bupleurum for 4 days were shown to be suppressed in a dose-dependent manner at doses of 300 or 500mg/kg. While adequate bioavailability of the non-polar active components of bupleurum following oral administration remains unknown, these studies provide interesting findings in support of further work to evaluate the potential application of bupleurum in the treatment or prevention of lung cancer.

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Anticancer properties of Chaste Tree

While the ripe fruits of *Vitex agnus-castus* (Chaste Tree) are used almost exclusively for the treatment of various gynaecological conditions such as premenstrual tension, amenorrhoea and hyperprolactinaemia, screening tests undertaken in the search for potential anticancer agents have revealed evidence of cytotoxic activities for this popular phytomedicine.

The first report of a cytotoxic effect for Vitex was made by Israeli researchers using an ethanol extract in 1994, using a Chinese hamster lung cancer cell line[1]. Various flavonoid constituents also exhibited cytotoxic activities against mouse lymphocytic leukaemia cells[1]. These findings were subsequently extended by Japanese and American researchers who reported cytotoxic effects on six human cancer cell lines, including uterine, cervical, ovarian, breast, colon, small cell lung, and gastric signet ring carcinoma[2,3,4]. Vitex-induced DNA fragmentation was shown to induce these effects, which appeared to be due to apoptosis and was selective against cancerous cells only.

The molecular mechanisms of this Vitex-induced apoptosis were recently investigated further, using a human gastric signet ring carcinoma cell line (KATO-3)[5]. Measurements of the effect of Vitex incubation on various biochemical pathways were undertaken, and in all cases, the results suggested that Vitex-induced apoptosis in these gastric cancer cell lines was caused by intracellular oxidative stress. Vitex-mediated activation of the caspase cascade pathway resulting in cytotoxicity to cancer cell lines was shown, and these effects were accompanied by an increased intracellular oxidised state and a diminution in intracellular glutathione. Cytotoxicity was blocked when the anti-oxidant substances N-acetyl-L-cysteine or glutathione were added, suggesting that intracellular oxidative stress and mitochondrial membrane damage within the tumour cells was responsible for Vitex-induced apoptosis.

A number of other Vitex species have also shown evidence of anticancer properties, including *Vitex rotundifolia*[6,7,8], *Vitex trifolia*[9], and *Vitex negundo*[10]. As with these recent studies on *Vitex agnus-castus*, flavone compounds found in these species appear to contribute significantly to their in vitro cytotoxic effects. Vitexicarpin (casticin) is one such flavone found in all four of these Vitex species, and has been found to exhibit broad and potent cytotoxicity in a range of human cancer cell lines, including human myeloid leukaemia[7,10,11]. Cell-cycle arrest and antimitotic activity by vitexicarpin has also been reported[11] . Results from both this recent Japanese study and the Israeli one however, suggest that the combined cytotoxic effects of both flavonoids and other constituents in Vitex are greater than those of individual components.

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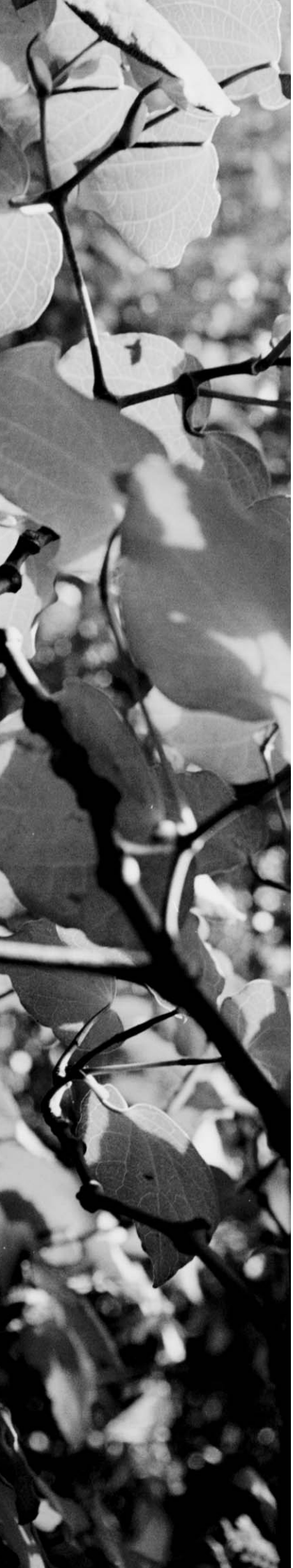

Red meat increases risk of bowel cancer

Dietary factors have been estimated from epidemiological studies to contribute to around 80% of cases of cancer of the colon[1]. In particular, a significant connection between the dietary intake of red meat and risk of colon cancer has been suggested by epidemiological studies in many countries[2,3,4,5,6,7].

In most westernised countries colorectal cancer is a leading cause of cancer death after lung, breast and prostate cancer. New Zealand has the world's highest rate of death from colon cancer in females, and the third highest for men[8]. New Zealanders also have one of the world's highest intakes of red meat, with an average consumption of 48kg per year of lamb and beef alone in 1998[9]. This is substantially higher than official recommended intake levels[10]

Despite convincing international evidence showing a clear association between high levels of red meat consumption and colorectal cancer however, consumer awareness of this issue remains low. Publication of the first reports of such a link eight years ago triggered much controversy and strong media campaigns sponsored by the meat industry[11]. A study published last year reported that 72% of Americans still centred their meals around animal fats[12], leaving little room for vegetables and other food groups rich in antioxidants and fibre that not only help prevent cancer, but also heart disease and probably various other diseases[13]. Intake of fruit and vegetables by New Zealanders also continues to be low[14]. The popularity of the Atkins diet, which recommends unlimited consumption of animal fats and protein as a means of weight loss, has also undoubtedly contributed to an ongoing high meat intake in recent years, despite the lack of studies investigating the long term risks of such eating patterns[15].

Findings from the European Prospective Investigation into Cancer and Nutrition, the largest study yet to research this subject, were published in the June 15th issue of the J*ournal of the National Cancer Institute(16).* This pan-European study not only confirmed a link between red meat intake and bowel cancer, but achieved a reasonable amount of coverage in the popular press.

A total of 478,040 men and women from ten European countries were enrolled into the study between 1992 and 1998, at which time they were all free of cancer. They were then prospectively followed and their dietary habits recorded and quantified. The mean follow-up time from baseline was 4.8 years, and over this period 1329 cases of colorectal cancer were documented.

A high (more than 160g/day) versus low (<20g/day) intake of red and processed meat was shown to increase the risk of colorectal cancer by 35%, while regular fish ingestion (more than 80g/day versus <10g/day) reduced the rate of colorectal cancer by 31%. An even stronger association between colorectal cancer and red and processed meat was found after correcting these results for measurement error, with processed meat in particular, increasing the risk of cancer development. The absolute risk of development of colorectal cancer within ten years for an individual aged 50 years, was calculated at 1.71% for those in the highest category of red and processed meat intake, and 1.28% for those in the lowest category of meat intake.

No relationship of colorectal cancer to poultry intake was revealed by this study. Those in the lowest category of fish intake had an even higher incidence of 1.86%, versus 1.28% for those who ate fish regularly. Frequent consumption of raw or cooked fish has previously been associated with a reduced rate of colon cancer in a Japanese study, an effect especially marked in males aged over 60 years, smokers and frequent meat eaters[17].

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A recent analysis of data from a Swedish study involving more than 61,000 women aged 40-75 years, has also found a significant association between consumption of red meat with colon cancers, but indicated that this association varies for different types of colorectal cancer. The risk of distal colon cancer was more than doubled in women who consumed 94 grams or more red meat per day compared to those who consumed less than 50 grams per day. Such women were only 28% more likely to develop rectal cancer, and little increase in the incidence of cancer of the proximal colon was observed[6].

Genetic factors are known to play a role in the aetiology of colon cancer, and certain types of this disease such as familial polyposis are strongly associated with the presence of particular inherited genes[18, 19]. The expression of other genes such as CD36, which seems to play important roles in the metabolism of oxidised low-density lipoprotein and long-chain fatty acids, also seems to be associated with an increased risk of developing colon cancer, particularly in large consumers of meat[20].

Folic acid has been associated with a protective effect against colon cancer particularly in women, an effect seen even more strongly in those with a family history of colon cancer [21,22]. A protective effect of beta-carotene has also been revealed by findings from a recent American population-based study[23]. Recent evidence also supports a protective effect of calcium and vitamin D in the aetiology of colorectal neoplasia[24].

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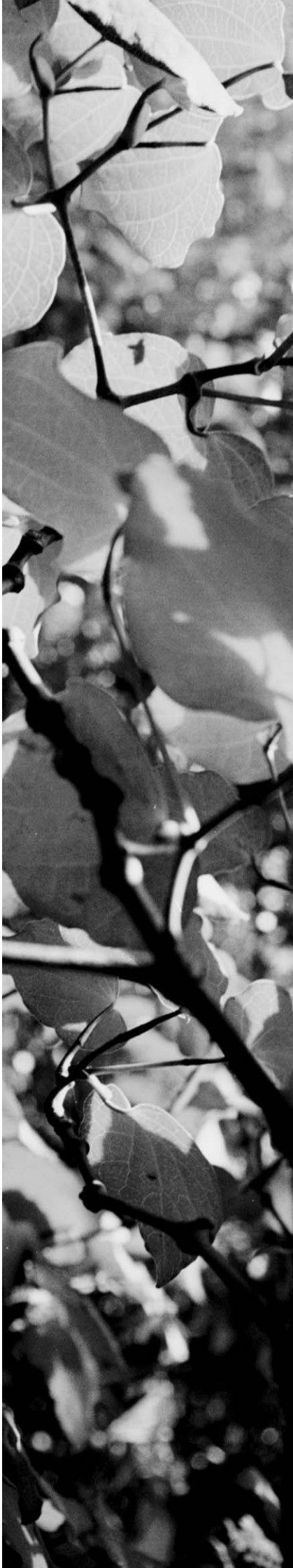

Dementia epidemic forecast

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 in incidence of 400%, rising to 29 million by 2020 and 34 million by 2025[1,2,3]. An estimated 71% of these will be in developing countries. With no cure for this distressing disease yet identified, and the rising health costs associated with its increasing prevalence, ways to help prevent it are becoming a major public health concern.

The contribution of obesity to this likely future epidemic, is becoming increasingly clear, as indicated by findings from a recent longitudinal population-based study recently published in the *British Medical Journal*[4]. This well-designed study involved 10,276 men and women enrolled in a Californian healthcare system who had undergone detailed health evaluations from 1964 to 1973 when they were aged 40-45. They were then followed from 1994 to 2003, during which their incidence of dementia and other illnesses was monitored.

During the mid-life examination, height and weights were measured, and body mass index calculated (weight/height^2, or BMI). Patients were then categorised as obese (BMI $\geq$ 30), overweight (BMI 25.0-29.9), normal (18.6-24.9), or underweight ($\leq$ 18.5). The predictive value of mid-life adiposity, including this body mass index as well as tricep and subscapular skinfold thickness, was determined as a risk factor for developing dementia at a later age. Outcome measurements were adjusted to exclude contributions from age, sex, race, education, smoking, alcohol use, marital status, diabetes, hypertension, hyperlipidaemia, stroke, and ischaemic heart disease.

During the average 27 year follow-up period, dementia was diagnosed in 713 (6.9%) of participants. The risk of dementia for those who had been obese at age 40-45 was 74% higher than those with normal body weights at this age, while those classified as overweight during middle age had a 35% higher risk of dementia. The link between obesity and dementia was highest for women, with obese women being twice as likely to develop dementia as normal women, although the same association was evident also for men.

Similar findings have been obtained from two other studies in recent years. The first of these was a Swedish study involving 392 nondemented adults who were followed from age 70 to 88[5]. A total of 93 participants developed dementia over this 18 year period, with an association between being overweight (higher body mass indices at ages 70, 75 and 79) and dementia development being revealed for women but not men. For every 1.0 increase in BMO at age 70 years, the risk of Alzheimers disease increased by 36%.

Data from a recent Korean study involving 467 individuals aged 65 years or older, have also revealed a strong association between poor cognitive performance and general obesity[6].

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Fruit and vegetable juices reduce risk of Alzheimers

Increased susceptibility to the long term effects of oxidative stress and inflammatory mediators are widely thought to contribute to the aetiology of age-related neurological diseases such as Alzheimer's and Parkinsons[1]. Accumulation of reactive oxygen species in the brain are thought to exhaust antioxidants, subsequently leading to the onset or progression of Alzheimers disease in particular.

Phytochemicals found in fruits and vegetables show a multiplicity of beneficial effects in ameliorating age-related deficits in brain performance[1,2,3]. Supplementation with blueberry, spinach or strawberry has been reported as reversing the negative effects of aging on motor behaviour and neuronal signalling, and blueberry protects against ischaemia-induced brain damage in rodents[4,5,6,7]. Protective effects against the adverse influence of neurotoxins on calcium recovery, as well as oxidative stress to muscarinic receptor subtypes implicated in Alzheimers, have also been shown for a range of antioxidant-rich fruit extracts[6,8].

A protective effect of vegetables against dementia was first reported by the Adventist Health Study in 1993, in which American subjects who ate meat were reported as being much more likely to develop dementia than their matched vegetarian counterparts[9]. However assessing diet is difficult in Alzheimer's disease patients, and a study based upon measurement of isotopic ratios (delta 15 N) in hair samples as a measure of long term dietary habits, did not confirm these findings[10].

Findings from a study conducted by a team at the University of South Florida which looked at dietary factors in the frequency of this disease, were presented at the U.S.-based Alzheimer's Association's first conference on prevention of dementia, held in Washington in June[11]. More than 1800 older Japanese American men and women in Seattle who were free of dementia at the onset were followed for periods up to nine years, and dietary consumption measured.

Elderly people who drank fruit or vegetable juices at least three times per week, were found to have a 75% less risk of developing Alzheimer's than those who drank these juices less than once a week. This signifies that something as simple as incorporating more fruit and vegetables into the diet, may have a significant protective effect against Alzheimer's, as well as cardiovascular and other age-related diseases.

Other studies in recent years have also implicated a role for dietary fish intake[10,12,13] as well as folic acid[14] , in reducing the incidence of declining cognitive function and dementia.

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Written by Phil Rasmussen. Edited by Noeline Jonkers

Published 4 times a year for customers of Phytomed Medicinal Herbs Ltd
P.O. Box 83068, Te Atatu South, Auckland 1008, New Zealand.

Subscriptions for non-customers: $28 per year for 4 issues