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Health benefits of herbs and spices: the past, the present, the future



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Health benefits of herbs and spices: the past, the present, the future

The purpose of this supplement is to provide medical and health professionals with a review of the health benefits of herbs and spices.

The University of Wollongong, partner organisation of the National Centre of Excellence in Functional Foods, managed the development of the supplement through a committee comprising Professor Linda Tapsell, Dr Craig Patch and Ms Virginia Fazio.

Key academics and clinicians with expertise in health and nutrition were invited to review the health aspects of predominantly culinary herbs and spices, using scientific search strategies and National Health and Medical Research Council guidelines for assessing levels of evidence.

The resulting individual contributions were submitted to the management committee for the development of summary positions.

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HERBS & SPICES

Health benefits of herbs and spices: the past, the present, the future

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Summary

Linda C Tapsell

Herbs and spices have a traditional history of use, with strong roles in cultural heritage, and in the appreciation of food and its links to health. Demonstrating the benefits of foods by scientific means remains a challenge, particularly when compared with standards applied for assessing pharmaceutical agents. Pharmaceuticals are small-molecular-weight compounds consumed in a purified and concentrated form. Food is eaten in combinations, in relatively large, unmeasured quantities under highly socialised conditions. The real challenge lies not in proving whether foods, such as herbs and spices, have health benefits, but in defining what these benefits are and developing the methods to expose them by scientific means.

Cultural aspects

The place of herbs and spices in the diet needs to be considered in reviewing health benefits. This includes definitions of the food category and the way in which benefits might be viewed, and therefore researched. Research may focus on identifying bioactive substances in herbs and spices, or on their properties as a whole food, and/or be set in the context of a dietary cuisine.

The role of herbs and spices in health

The antioxidant properties of herbs and spices are of particular interest in view of the impact of oxidative modification of low-density lipoprotein cholesterol in the development of atherosclerosis. There is level III-3 evidence (National Health and Medical Research Council [NHMRC] levels of evidence¹) that consuming a half to one clove of garlic (or equivalent) daily may have a cholesterol-lowering effect of up to 9%. There is level III-1 evidence that 7.2 g of aged garlic extract has been associated with anticlotting (in-vivo studies), as well as modest reductions in blood pressure (an approximate 5.5% decrease in systolic blood pressure).

A range of bioactive compounds in herbs and spices have been studied for anticarcinogenic properties in animals, but the challenge lies in integrating this knowledge to ascertain whether any effects can be observed in humans, and within defined cuisines.

Research on the effects of herbs and spices on mental health should distinguish between cognitive decline associated with ageing and the acute effects of psychological and cognitive function. There is level I and II evidence for the effect of some herbal supplements on psychological and cognitive function.

There is very limited scientific evidence for the effects of herbs and spices on type 2 diabetes mellitus, with the best evidence being available for the effect of ginseng on glycaemia, albeit based

on four studies. More research is required, particularly examining the effects of chronic consumption patterns.

With increasing interest in alternatives to non-steroidal anti-inflammatory agents in the management of chronic inflammation, research is emerging on the use of food extracts. There is level II evidence for the use of ginger in ameliorating arthritic knee pain; however, the improvement is modest and the efficacy of ginger treatment is ranked below that of ibuprofen. More definitive research is required.

Public health and dietary implications

Recommendations for intakes of food in the *Australian guide to healthy eating*² do not yet include suggested intakes of herbs and spices. Future consideration should be given to including more explicit recommendations about their place in a healthy diet.

In addition to delivering antioxidant and other properties, herbs and spices can be used in recipes to partially or wholly replace less desirable ingredients such as salt, sugar and added saturated fat in, for example, marinades and dressings, stir-fry dishes, casseroles, soups, curries and Mediterranean-style cooking. Vegetable dishes and vegetarian options may be more appetising when prepared with herbs and spices.

Future directions

As several metabolic diseases and age-related degenerative disorders are closely associated with oxidative processes in the body, the use of herbs and spices as a source of antioxidants to combat oxidation warrants further attention. Immediate studies should focus on validating the antioxidant capacity of herbs and spices after harvest, as well as testing their effects on markers of oxidation. This will work in parallel with clinical trials that are aiming to establish antioxidants as mediators of disease prevention.

From a dietary perspective, the functionality of herbs and spices will be exposed through consideration of their properties as foods. As with most foods, the real benefits of including them in the diet are likely to emerge with a better understanding of the attributes of health that are best supported by food, and in methodological developments addressing the evidence base for their effects.^{3,4} These developments are well underway through evidence-based frameworks for substantiating health claims related to foods.⁵ At present, recommendations are warranted to support the consumption of foods rich in bioactive components,⁶ such as herbs and spices. With time, we can expect to see a greater body of scientific evidence supporting the benefits of herbs and spices in the overall maintenance of health and protection from disease.

Background

The historical and cultural use of herbs and spices

Ian Hemphill and Lynne Cobiac

Generally, the leaf of a plant used in cooking may be referred to as a culinary herb, and any other part of the plant, often dried, as a spice. Spices can be the buds (cloves), bark (cinnamon), roots (ginger), berries (peppercorns), aromatic seeds (cumin), and even the stigma of a flower (saffron). Many of the aromatic seeds known as spices are actually gathered from plants when they have finished flowering. A familiar example would be coriander, with the leaves being referred to as a herb, and the dried seeds as a spice. When referring to the stem and roots of coriander, which are used in cooking, and to onions, garlic and the bulb of fennel, these parts of these plants tend to be classified along with herbs, as they are often used fresh and applied in a similar way to cooking.

Herbs and spices have a long history of both culinary use and of providing health benefits, as well as acting as preservatives. Ancient Egyptian papyri from 1555 BCE record the use of coriander, fennel, juniper, cumin, garlic and thyme.⁷ It is reported that the Sumerians were using thyme for its health properties as early as 5000 BCE, and the farmers of Mesopotamia were growing garlic as early as 3000 BCE. An international trade in spices dates back to 4500–1900 BCE, mainly with Ethiopia. The ancient Egyptians worshipped garlic, and garlic cloves were found in the tomb of King Tutankhamen. Other Egyptians had wooden cloves of garlic in their tombs to keep the future meals of the afterlife tasty, wholesome and long-lasting.⁸ Dried mint leaves have been found in Egyptian pyramids dating around 1000 BCE.⁹ The Egyptians reportedly fed large amounts of radishes, onions and garlic to their slaves, ostensibly to keep them healthy.⁷ Cardamom and cinnamon (traded from Ethiopia) were also used extensively in ancient Egypt as spices, but less so for medicinal purposes. The Assyrians in Mesopotamia (a country now incorporated by modern day Iraq and Iran) also developed knowledge around the health benefits of herbs, and refer to juniper, saffron, and thyme around this time.⁷

In ancient Greece and Rome, herbs appear to have been used more than spices. Hippocrates (460–377 BCE) had a repertoire of 300 remedies that included garlic, cinnamon and rosemary, all of which were locally available.⁷ He reportedly used garlic to treat uterine cancer. Mint was highly valued for its positive effects on the digestive system, and liquorice was used as a sweet, but also as a herb for its anti-inflammatory actions and for asthma, chest problems and mouth ulcers. Rosemary was used to improve and strengthen memory — and is sometimes still burnt in the homes of Greek students taking exams. Around the first century CE, Pedanius Dioscorides — Greek physician, botanist, pharmacologist and surgeon — published the first plant monograph that included 600 herbs, describing how to choose, store and apply plants for a range of health benefits. Another Greek physician, Galen (131–200 CE), who lived in Rome from 162 CE, had a strong influence on the development of herbal remedies, but used complicated mixtures, containing up to 100 ingredients.⁷ Dioscorides' monograph was used as a principal reference in Europe until the 17th century.⁹

In China, the use of plants for health benefits is shrouded in legend. Two legendary Chinese emperors are credited with discovering and recording the medicinal properties of herbs — Sheng

Nong, the Divine Husbandman (2838–2698 BCE), and Huang Di, the Yellow Emperor (2698–2598 BCE).⁷ Traditionally, the Chinese have integrated food, nutrition and health, and will often include herbs and spices in specially prepared soups, dishes or beverages for both sustenance and for purported health benefits. Ginseng and *Ginkgo biloba* are reportedly used to improve stamina and cognitive performance, respectively. Other examples include the use of galangal for abdominal pain, nutmeg for diarrhoea, and cinnamon for colds and flu.⁷

In India, the traditional medicine, Ayurveda, evolved more than 5000 years ago in the Himalayas, with knowledge transmitted orally until it was written down in Sanskrit poetry — the Vedas — around 1500 BCE. It flourished in the 7th century. Ayurveda focuses on disease prevention and health promotion, with an emphasis on diet.^{10,11} Examples of Ayurvedic use of herbs and spices for health effects include turmeric for jaundice, basil to protect the heart, mace for stomach infections, cinnamon to stimulate circulation, and ginger as the universal medicine, in particular for relieving nausea and indigestion. Many of these herbs and spices are used in Indian cooking to impart flavour, and significant quantities can be consumed in one meal. It has been reported that such herbs and spices can supply reasonable quantities of nutrients as well, such as iron. It has been estimated that an adult in India can eat as much as 4 g of turmeric daily, which could provide 80–200 mg/day of the bioactive component curcumin. Some Indians have been reported to eat as much as 50 g of garlic in a week.¹²

With the decline of the Roman Empire around 476 CE, the development of Arabic medicine in 500–1300 CE preserved some of the knowledge surrounding the health benefits of herbs and spices, and built on the knowledge of Galen.⁷ The spread of Islamic culture into north Africa had profound effects in the region, blending their knowledge with that from China and India.

In the 9th century, the Emperor Charlemagne is quoted as saying, “a herb is a friend of physicians and the praise of cooks”, suggesting that the dual role of herbs and spices for flavouring and for health benefits was still recognised. During the 11th century, the knowledge of Arabic medicine filtered back to Europe, and by the 13th century, trade with Africa and Asia was bringing in new herbs and spices. Around this time, galangal was called the “spice of life”.⁷ Garlic was used by herbalists during the plague.⁷ Later, Louis Pasteur (1822–1895 CE) found that it killed bacteria, and it was even used on the battlefields to prevent gangrene.

Mediterranean diets have been associated with reduced incidence of some chronic diseases, such as heart disease and cancer.¹³ While dietary studies are complex, Mediterranean diets do include considerable amounts of garlic, rosemary, basil and thyme, among other herbs, which may help to explain some of the protective effects observed in populations following more traditional Mediterranean diets.

In Australia, the Indigenous population developed its own local herbal medicine based on the plants that were available. Their isolation meant that the Indigenous population did not encounter Western diseases, and so the use of herbs and plants was developed for less serious disorders. Examples include the use of river mint for coughs and colds, and wattle and eucalyptus for diarrhoea, fever, headache, and a range of other ailments.¹⁴

Given the long history of use of herbs and spices, they may be considered one of the first ever recorded functional foods.

Herbs and spices as functional foods

Linda C Tapsell

Examining herbs and spices from a functional food perspective might begin with how herbs and spices are used in the diet. There is no single definition of functional foods, but there are many contexts in which the concept is played out, including scientific endeavour, technological advancement, food marketing, and food standards regulation.¹⁵ From a scientific perspective, functional foods have been defined as “foods that provide benefit beyond basic nutrition”.¹⁶ This definition draws on notions of food (ie, a recognisable unit of consumption in contradistinction to drugs), notions of benefits (which implies the need for scientific evidence), and the notion of “basic nutrition” (a concept open to interpretation). In some ways, basic nutrition might actually reflect the current depth of nutrition knowledge and practice. Thus, meeting requirements for vitamins and minerals (which have recommended reference values)¹⁷ could be considered basic nutrition. The underlying view is that these nutrients are required to maintain normal bodily function. However, the way in which food components of today are studied is not limited to concepts of preventing clinical deficiency and maintaining homeostasis, but includes a growing recognition of the way in which food components actively interact with the body to support health and prevent abnormality and overt disease.¹⁸

Herbs and spices fit into this picture in a number of ways. In this supplement, the focus is on their role in the diet rather than their use as medicines. Establishing this role would involve identifying unique bioactive compounds to help identify target benefits. Research would then be conducted on the food itself (supplements), a meal based on the food (acute effects), or the food in a whole diet in which the observed benefits can be attributed to the specified combination. The traditional use of foods in various cultures provides many clues to this development. For example, certain meals in traditional Thai cuisine have a cultural history of supporting health based on their combination of herbs, spices and other foods,¹⁹ so that it might be better for dietary guidelines to reference dishes, rather than single foods as we do in Western societies (which tend to focus on targeted nutrients being delivered by core food groups). The real challenge then comes from defining benefits and providing the scientific evidence for these benefits.

In this supplement, the evidence for the benefits of herbs and spices is reviewed in the areas of cardiovascular and metabolic health, healthy ageing and cancer, and mental health and cognition. Applying nutrition knowledge about herbs and spices in public health guidelines and dietary practice is also considered. The supplement outlines the many ways in which the functionality of herbs and spices could be considered, providing direction for future research and developing an appreciation of the potential contributions of herbs and spices to health and wellbeing.

The health benefits of herbs and spices: how strong is the evidence?

Cardiovascular disease

Craig S Patch and David R Sullivan

Most evidence concerning the cardiovascular effects of culinary herbs and spices relates to the possible impact of garlic and garlic oil. Consumption of garlic or garlic oil has been associated with a reduction in total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels. Studies suggest that an intake of between half and one garlic clove per day can reduce cholesterol by 9%.^{20,21} This finding is consistent with a more recent meta-analysis of 13 placebo-controlled trials involving 781 patients taking garlic supplements. The authors concluded that intake of 600–900 mg of standardised garlic extract per day was associated with a modest 0.41 mmol/L decrease in serum cholesterol level.²² Although this was verified in the most current and comprehensive review,²³ the authors highlighted that the six most rigorous trials showed a non-significant trend (Box 1).^{24–29}

It has been suggested that this variation of effect may reflect a loss of active compounds during processing, or an inhibition in the enzymatic release of the active compounds from garlic.²⁵ Allicin has been proposed as the primary active compound, although the mechanism of action is still not well understood. Allicin is not present in fresh garlic and is converted from the precursor alliin within seconds of being crushed or chewed. Allicin is rapidly absorbed in the small intestine and converted to allyl mercaptan and allyl methyl sulfide soon after absorption.³⁰ In addition, factors related to food preparation, manufacturing, and in-vivo metabolism affect the bioactivity of allicin and may explain some of the heterogeneity of results found in these meta-analyses.^{21,22} With few exceptions, the more recent published trials have used dietary supplemental forms of garlic, rather than garlic as a food.³⁰ This has significant implications, as a study found that the allicin yield of 24 commercial brands of garlic tablets averaged 14% of the amount claimed on the label.^{21,31} Of the brands used in most of the clinical trials since 1995, the active ingredient was found to be only 2%–18% of that claimed on the label.³²

A number of clinical trials have examined the effect of garlic on cardiovascular risk factors other than lipoproteins and lipid levels. Garlic extracts have been associated with anticlotting effects,³³ as well as modest reductions in blood pressure (about a 5.5% decrease in systolic pressure).³⁴ However, of the 33 published studies with data on blood pressure, only four included patients with hypertension.⁶

Data on the effects of other herbs and spices are limited. In one trial, participants with hypercholesterolaemia who consumed 140 mg of lemon grass (*Cymbopogon citratus*) oil daily experienced a drop in cholesterol concentrations by up to 38 mg/dL, but this trial had no control group.³⁵ Spice components like ginger, capsaicin and curcumin have been associated with a decrease in LDL cholesterol and an increase in high-density lipoprotein cholesterol levels, but these results have been limited to rat studies.^{36,37}

The putative protective heart health benefits of antioxidants such as flavonoids have been extensively studied. A longitudinal study of 805 elderly men found that daily flavonoid intake from fruit, vegetables and tea of 25.9±14.5 mg (mean±SD) was inversely

associated with heart disease mortality.³⁸ Herbs and spices have an important role in dietary flavonoid intake. Chamomile, liquorice, onions, rosemary, sage and thyme have high flavonoid contents, but there is little evidence apart from epidemiological studies to support a direct cardiovascular health benefit from these herbs and spices.

In recent years, a substantial body of evidence has indicated that free radicals contribute to cardiovascular disease.³⁹ Oxidative modification of LDL is hypothesised to play a key role during the development of atherosclerosis. The use of antioxidants from dietary sources, including herbs and spices, is a promising alternative to the use of antioxidant supplements. In general, herbs and spices have high antioxidant concentrations that have the potential to inhibit the oxidation of LDL.^{40,41} Like fruits and vegetables, herbs and spices contain many different classes of antioxidants in varying amounts. It has been shown that the intake of herbs can contribute significantly to the total intake of plant antioxidants.⁴² A study found that the total phenolic content of culinary herbs ranged from 0.26 mg to 17.51 mg of gallic acid per gram fresh weight (Box 2).⁴³ These values were also found to be higher than traditional medicinal herbs.²⁵ At this stage, evidence of benefit from any form of antioxidant intake is restricted to surrogate markers of cardiovascular disease, such as oxidative damage, rather than clinical outcomes.

Obesity-related insulin resistance has emerged as a potent risk factor for cardiovascular disease. Dietary factors that affect satiety and thermogenesis could play an important role in determining the prevalence and severity of this problem. Herbs and spices may have a role to play in this regard. More data are also required on bioavailability, bioactivity, and efficacy of culinary herbs on outcomes.

Summary

- There is level III-3 evidence that a half to one clove of garlic (or equivalent) daily may have a cholesterol-lowering effect of up to 9%.
 - There is level III-1 evidence that 7.2 g of aged garlic extract has been associated with anticlotting (in-vivo studies), as well as modest reductions in blood pressure (about a 5.5% decrease in systolic pressure).
 - More evidence is required to determine any cardiovascular health effects attributable to herb and spice antioxidants.
-

Cancer

Michael Fenech

As yet, there are no data indicating that herbs and spices have an anticarcinogenic effect in humans, but there are several in-vitro studies and rodent in-vivo studies suggesting that certain herbs and spices may have a chemopreventive effect against the early initiating stages of cancer (Box 3).

1 Summary of evidence for health effects of garlic and garlic extracts on lowering cholesterol levels

Study	Design	Studies/participants	Source	Dose	Measurement	Outcome
Warshafsky et al ²¹	Meta-analysis	5 homogenous studies	Garlic	Various doses	Cholesterol level	Patients treated with garlic showed a greater decrease in total cholesterol levels compared with those receiving placebo. Net cholesterol decrease attributable to garlic was estimated to be 0.59 mmol/L.
Stevinson et al ²²	Meta-analysis	13 trials	Garlic	Various, from 0.25 mg/kg to 900 mg daily	Total cholesterol level	Garlic reduced total cholesterol level from baseline significantly more than placebo, but the size of effect was modest and the robustness of the effect is debatable.
Ackermann et al ²³	Review article	45 randomised controlled trials lasting at least 4 weeks	Garlic preparation	Various	Total cholesterol, LDL, HDL and triglyceride levels, and platelet aggregation and blood pressure	Garlic may lead to small reductions in total cholesterol levels at 1 month and 3 months, but not at 6 months. Changes in LDL and triglyceride levels paralleled total cholesterol results. No significant changes in HDL levels were observed. Reduction in platelet aggregation was observed and effects on blood pressure were mixed.
Simons et al ²⁴	Randomised, double-blind, placebo-controlled, crossover trial	28 participants with mild to moderate hypercholesterolaemia	Garlic powder tablets	300 mg three times daily	Plasma lipid levels and blood pressure	No significant differences in plasma cholesterol, LDL, HDL, plasma triglycerides, lipoprotein (a) concentrations or blood pressure. There was no demonstrable effect of garlic on oxidisability of LDL.
Isaacsohn et al ²⁵	Randomised, double-blind, placebo-controlled, 12-week, parallel treatment trial	50 participants	Garlic powder	300 mg three times daily (equivalent to 2.7 g garlic or 1 clove of garlic per day)	Plasma lipid and lipoprotein levels	No significant lipid or lipoprotein changes in either the garlic-treated or placebo groups, and no significant difference between changes in the placebo-treated group compared with changes in the garlic-treated participants were observed.
Superko and Krauss ²⁶	Randomised, double-blind placebo-controlled trial	50 participants with moderate hypercholesterolaemia	Garlic	300 mg three times daily	Total cholesterol, LDL, HDL and triglyceride levels	No significant changes in plasma lipid levels after intervention were observed. Garlic therapy had no effect on major plasma lipoproteins.
Gardner et al ²⁷	Randomised, double-blind, placebo-controlled, parallel treatment trial	51 participants	Garlic powder	500 mg and 1000 mg	Plasma lipid levels	Reduction of LDL cholesterol level in full dose group was not significantly different from the other groups. No significant differences in total cholesterol, HDL and triglyceride levels were observed.
Gore and Dalen ²⁰	Review paper	GUSTO angiographic trial	Garlic	One-half to one clove per day	Cholesterol level	Cholesterol levels can be reduced by up to 9% by the consumption of one-half to one clove of garlic per day.
Berthold et al ²⁸	Randomised, double-blind, placebo-controlled trial	25 participants with moderate hypercholesterolaemia	Garlic oil preparation	5 mg twice daily	Serum lipoprotein levels, cholesterol absorption, cholesterol synthesis	Lipoprotein levels were virtually unchanged at the end of both treatment periods. Cholesterol absorption, cholesterol synthesis, mevalonic acid secretion, and changes in the ratio of lathosterol to cholesterol in serum were not different in garlic and placebo treatment.

LDL = low-density lipoprotein. HDL = high-density lipoprotein. GUSTO = Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. ♦

2 Total phenolic content of common herbs and spices⁴³

Herb or spice	Botanical name	Total phenolic content (mg of gallic acid/ g fresh weight) (Mean±SEM)
Basil (Sweet)	<i>Ocimum basilicum L.</i>	2.23±0.15
Coriander (Vietnamese)	<i>Polygonum odoratum</i>	3.09±0.12
Chives	<i>Allium schoenoprasum</i>	1.05±0.05
Dill	<i>Anethum graveolens</i>	3.12±0.06
Marjoram (hard sweet)	<i>Origanum x majoricum</i>	11.65±0.29
Oregano (Cuban)	<i>Plectranthus amboinicus</i>	0.34±0.00
Oregano (Mexican)	<i>Poliomintha longiflora</i>	17.51±0.22
Parsley	<i>Petroselinum crispum</i>	1.12±0.01
Rosemary	<i>Rosmarinus officinalis L.</i>	2.19±0.15
Spearmint	<i>Mentha spicata</i>	0.94±0.15
Thyme (Lemon)	<i>Thymus x citriodorus</i>	1.78±0.03
Garlic	<i>Allium sativum L.</i>	1.03±0.10

SEM = standard error of the mean. ◆

Herbs may act through several mechanisms to provide protection against cancer. Certain phytochemicals from herbs or herb extracts have been shown to inhibit one or more of the stages of the cancer process (ie, initiation, promotion, growth and metastases).⁶²⁻⁶⁵ Inhibition of phase I (procarcinogen activation) and induction of phase II (carcinogen deactivation) metabolic enzymes by herbal products may account for some of the preventive effects against the induction of gene or chromosomal mutations that may initiate cancer.^{62,63} For example, diallyl sulfide, a compound in garlic, is an efficient inhibitor of the phase I enzyme cytochrome P450 (CYP)3 IIE1 and significantly increases a variety of phase II enzymes, including glutathione S-transferase, quinone reductase and uridine diphosphate-glucuronosyltransferase, which are responsible for the detoxification of carcinogens.⁶³

Herbs may also protect against oxidative stress and inflammation, both of which are risk factors for cancer initiation and promotion as well as other pathological conditions.⁶⁴⁻⁶⁷ An imbalance between the generation of reactive oxygen species (eg, hydroxyl radical and superoxide radical anion) and cellular antioxidant capacity leads to a state of oxidative stress. Herbs and spices contain several natural water-soluble phenolic acids and flavonoids, such as caffeic acid and quercetin, that can scavenge reactive oxygen species, as well as containing lipid-soluble compounds such as tocopherols, carotenoids and sterols that may protect against the generation of genotoxic lipid peroxidation products, such as trans-4-hydroxy-2-nonenal.

Pro-oxidant and pro-inflammatory stimuli induce the mitogen-activated protein and nuclear factor κ B inhibitory protein (I κ B) kinases that activate nuclear factor κ B (NF κ B), enabling its translocation into the nucleus where it causes activation of cyclooxygenase-2 (COX-2) expression, subsequent prostaglandin pro-

duction, and excessive stimulation of cell division that can lead to growth of adenomas.⁶⁴⁻⁶⁷ The pro-inflammatory and pro-oxidant effect on increased cell proliferation, combined with oxidative-stress-induced chromosomal instability, increases risk for carcinogenesis (Box 4). The number of herbs with potential anti-inflammatory activity is impressive. Natural anti-inflammatory compounds found in herbs and spices (such as curcumin, gingerol and capsaicin) appear to operate by inhibiting one or more of the steps linking pro-inflammatory stimuli with COX activation, such as the blocking by curcumin of NF κ B translocation into the nucleus. It has been shown recently that the natural anti-inflammatory compounds quercetin, curcumin and silymarin were as effective as indomethacin (a non-steroidal anti-inflammatory drug) in inhibiting aberrant crypt foci in the rat.⁴⁴

Herbs and spices (or their fractions and constituents) with known anticarcinogenic effects in animal models of cancer include turmeric, basil, rosemary, mint and lemon grass, but there are no published reports on potential chemopreventive effects against cancer for other common spices such as thyme, coriander and dill. Turmeric has been widely used as a spice and colouring agent in foods. Recently, turmeric was found to have chemopreventive effects against cancers of the skin, forestomach, liver and colon, and oral cancer in mice.⁴⁴⁻⁴⁶

Oral treatment with basil-leaf extract significantly elevated the activities of cytochrome P450, aryl hydrocarbon hydroxylase, and glutathione S-transferase, all of which are important in the detoxification of carcinogens as well as mutagens. Moreover, basil-leaf extract was effective in inhibiting carcinogen-induced early-stage cancers in the skin and forestomach of mice.^{47,68} Orientin and vicenin, two water-soluble flavonoids isolated from the leaves of Indian holy basil (*Ocimum sanctum*), have shown significant protection against radiation-induced lethality and chromosomal aberrations in vivo.⁴⁸

A methanol extract of the leaves of the plant *Rosmarinus officinalis L.* (rosemary) and its constituent carnosol (a phenolic diterpene) inhibited 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced ornithine decarboxylase activity (a promoter of cell division via polyamine synthesis), TPA-induced inflammation, arachidonic acid-induced inflammation, TPA-induced hyperplasia, and TPA-induced tumour promotion in mouse skin.⁴⁹ Commercially available ground rosemary powder was shown to inhibit in vivo binding of 7,12-dimethylbenz[a]anthracene (DMBA) metabolites to mammary cell DNA in rats,⁵⁰ suggesting that components of rosemary may inhibit breast cancer. In fact, dietary rosemary and carnosol were both shown to inhibit rat mammary carcinogenesis when DMBA was used as the carcinogen.⁵¹ Using the C57BL/6J/Min/+ (Min/+) mouse, a model of colonic tumorigenesis, it was found that dietary administration of 0.1% carnosol decreased intestinal tumour multiplicity by 46%, potentially via its ability to enhance E-cadherin-mediated adhesion and suppress β -catenin tyrosine phosphorylation.⁶⁹ Carnosol has been shown to inhibit the invasion of highly metastatic mouse melanoma B 16/F10 cells in vitro.⁵² Furthermore, it has been shown to have antioxidant activity and suppresses nitric oxide production and iNOS gene expression by inhibiting NF κ B activation, which suggests possible mechanisms for its anti-inflammatory and chemopreventive action.⁵³

Geraniol, an acyclic monoterpene alcohol found in lemon grass (*Cymbopogon citratus*), was shown to inhibit growth and polyamine biosynthesis in human colon cancer cells.⁵⁴ Citral (3,7-dimethyl-

3 Summary of evidence for health effects of herbs and spices on cancer

Study	Design	Tissue/organism	Bioactive agent/ source	Dose	Measurement	Outcome
Volate et al ⁴⁴	In-vitro animal study	Colon of 235 male F344 rats	Quercetin, curcumin, rutin, silymarin, whole ginseng mixture	50–15000 ppm	Aberrant crypt foci suppression and effects of test compounds on evoking apoptosis.	Test compounds significantly suppressed aberrant crypt foci at different most effective concentrations. All test compounds except silymarin induced apoptosis, with quercetin being the most potent.
Chuang et al ⁴⁵	In-vitro animal study	Diethylnitrosamine (DEN)-induced liver inflammation and hyperplasia in rats	Curcumin (turmeric)	200 mg/kg or 600 mg/kg	Oncogenic activity by immunoblotting analysis	Curcumin strongly inhibited DEN-mediated increased expression of oncogenic p21 ^{ras} and p53 proteins in liver tissues of rats, the expression of proliferating cell nuclear antigen, cyclin E and p34 ^{cdc2} , but not Cdk2 or cyclin D1 and DEN-induced increase of transcriptional factor NFκB. However, curcumin did not affect DEN-induced c-Jun and c-Fos expression.
Chuang et al ⁴⁶	In-vivo animal study	C3H/HeN mice injected with N-diethylnitrosamine (DEN)	Curcumin (turmeric)	0.2% curcumin-containing diets	Intermediate biological markers by western blot, and incidence of hepatocellular carcinoma	81% reduction multiplicity and 62% reduction in incidence of hepatocellular carcinoma were observed. Curcumin-containing diet also reversed the increase in levels of p21 ^{ras} , PCNA and CDC2 proteins.
Dasgupta et al ⁴⁷	In-vivo animal study	Liver of Swiss albino mice	Basil-leaf extract	200 and 400 mg/kg body weight	Enzyme activities, lipid peroxidation	Basil-leaf extract was very effective in elevating antioxidant enzyme response by increasing significantly hepatic enzyme activities. Lipid peroxidation and lactate dehydrogenase activity were significantly decreased.
Vrinda and Uma Devi ⁴⁸	In-vitro animal study	Human peripheral lymphocytes	Orientin and vicenin (Indian holy basil leaf)	6.25–20 μmoles/L	Micronucleus count	Both compounds showed significant antioxidant activity in vitro, and therefore give significant protection to human lymphocytes against the clastogenic effect of radiation at low, non-toxic concentrations.
Huang et al ⁴⁹	In-vivo animal study	Mouse skin	Rosemary	1.2 or 3.6 mg	Number of tumours per mouse	Number of tumours reduced by at least 50% in the treatment group. Rosemary also inhibited carcinogenic enzyme activity, inflammation, hyperplasia and tumour promotion.
Amagase et al ⁵⁰	In-vivo animal study	Mammary cell of 55-day-old rats	Rosemary extract	0.5% and 1% in diet	DNA adducts	Rosemary is effective in reducing the binding of 7,12-dimethylbenz[<i>a</i>]anthracene (DMBA) metabolites to rat mammary cell DNA.
Singletary et al ⁵¹	In-vivo animal study	Mammary cell of female rats	Rosemary extract and carnosol and ursolic acid	0.5% in diet or 200 mg/kg	DNA adducts	Rosemary extract and carnosol groups exhibited significant decrease in the in-vivo formation of rat mammary DMBA-DNA adducts compared with controls. Carnosol is one constituent of rosemary that can prevent DMBA-induced DNA damage and tumour formation in rat mammary gland.
Huang et al ⁵²	In-vitro study	B16/F10 rat melanoma cells	Carnosol (rosemary)	Various concentrations	Antimetastatic potentials by soft agar assay, B16/F10 rat cell migration, metalloproteinase activity	Carnosol exhibited antimetastatic potential, dose independently inhibited B16/F10 cell migration and decreased activity of metalloproteinase. Inhibition of activation of transcription factors NFκB and c-Jun were also observed.

Lo et al ⁵³	In-vitro study	Mouse macrophages	Carnosol (rosemary)	Various concentrations	Antioxidant and enzyme activities	Carnosol suppressed the nitric oxide production and iNOS gene expression by inhibiting NFκB activation, and provided possible mechanisms for its anti-inflammatory and chemopreventive action.
Carneseccchi et al ⁵⁴	In-vitro study	Human colon cancer cell line	Geraniol and other monoterpenes	400 moles/L	Cancer cell growth, apoptosis and enzyme activities	Geraniol caused a 70% inhibition of cell growth and concomitant inhibition of DNA synthesis. No signs of cytotoxicity or apoptosis were detected. A 50% decrease in enzymes which enhance cancer growth was also observed.
Nakamura et al ⁵⁵	In-vitro study	Normal rat liver epithelial cell line, RL34 cells	Citral (lemon grass)	Various concentrations	GST (glutathione S-transferase) activity	Electrophilic property characterised by the reactivity with intracellular nucleophiles including protein thiol or glutathione plays an important role in the induction of GST.
Puatanachokchai et al ⁵⁶	In-vivo and in-vitro study	Male F344 rats	Lemon grass extract	Dietary concentrations of 0, 0.2%, 0.6% or 1.8%	8-hydroxydeoxyguanosine production	Inhibitory effects of lemon grass extract happened on the early phase hepatocarcinogenesis in rats.
Suaeyun et al ⁵⁷	In-vivo animal study	F344 rats	Ethanol extract of lemon grass	0.5 or 5g/kg body weight	DNA adducts and aberrant crypt foci analysis	Lemon grass treatment significantly inhibited DNA adduct formation in both the colonic mucosa and muscular layer, but not in the liver. Lemon grass extract also exhibited antioxidant activity.
Lantry et al ⁵⁸	In-vivo animal study	(C3H/HeJ X A/J) F1 hybrid mice	Perillyl alcohol	Various doses	Maximum tolerated dose of perillyl alcohol, tumour incidence, tumour multiplicity	Maximum tolerated dose was 75 mg/kg body weight; 22% reduction in tumour incidence and 58% reduction in tumour multiplicity were demonstrated.
Yu et al ⁵⁹	In-vitro bacterial mutagenicity study	Salmonella typhimurium strain TA98	Water extract of spearmint	5% (weight/volume)	Activity against mutagens NPD (4-nitro-1,2-phenylenediamine) and N-OH-IQ (2-hydroxyamino-3-methyl-3H-imidazo[4,5-f]quinoline)	Non-toxic concentrations inhibited mutagenic activity of N-OH-IQ in a concentration-dependent fashion but had no effect against NPD. Chloroform and methanol extracts of spearmint also possessed antimutagenic activity against N-OH-IQ.
Yu et al ⁵⁹	In-vivo animal study	F344 rats	Water extract of spearmint	2% (weight/volume) as the sole source of drinking fluid before, during, and after 2-week treatment with IQ (2-amino-3-methylimidazo[4,5-f]quinoline, a carcinogen in cooked meat).	Reduction in aberrant crypt foci in colon (a colon adenoma model)	Colonic aberrant crypt foci in the rats given spearmint water extract and IQ were inhibited significantly at 8 weeks ($P < 0.05$) compared with rats given IQ alone.
Zheng et al ⁶⁰	In-vivo animal study	Mouse target tissue	Myristicin (parsley, nutmeg)	2.5–20 mg	Ability to induce increased activity of the detoxifying enzyme system.	Myristicin showed high activity as a glutathione S-transferase inducer in the liver and small intestinal mucosa.
Ahmad et al ⁶¹	In-vivo animal study	Mouse liver	Myristicin (parsley, nutmeg)	5–50 mg	Mechanism of induction of GST	Myristicin increased GST activity by 4–14-fold over control tissue. Treatment caused a slight change in the GST- π levels while the levels of GST- α showed a modest increase.

ability and bioefficacy of herbs and spices and their components as chemopreventive agents against the various stages of cancer directly in humans.

Summary

- There is potential for herbs and spices in chemoprevention of cancer *in vitro* and in rodent cancer models.
- There is as yet no reliable evidence for beneficial effects in humans *in vivo* at customary intake levels.

Mental health and cognition

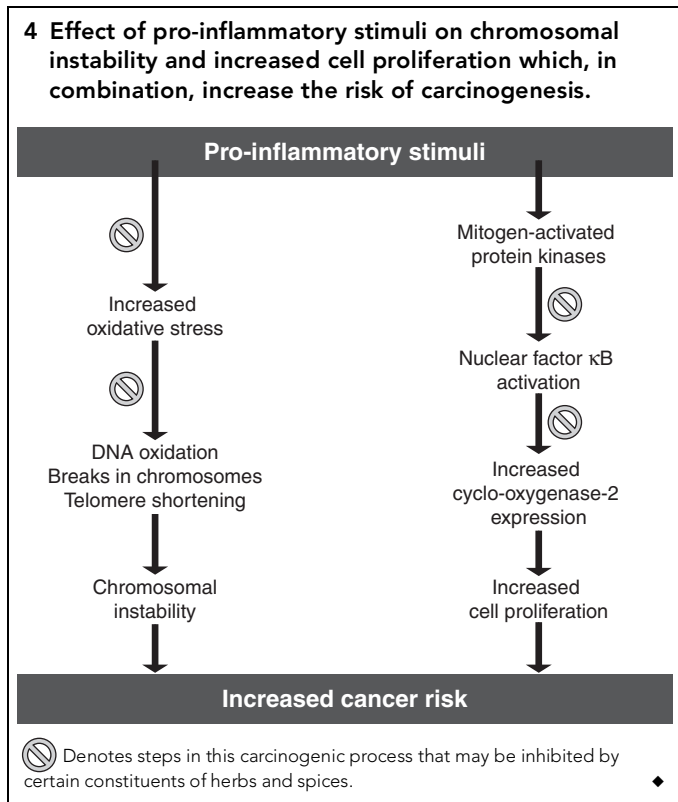
Steven Roodenrys

There is a very long history in traditional medicine of the use of plants to influence psychological states and processes as well as physical health. In particular, the traditional practices of Ayurvedic medicine in India and Chinese medicine have included treatments for psychological conditions such as anxiety, and preparations to enhance cognitive processes such as memory and attention. Recent decades have seen an increased use of herbal preparations for both of these purposes in Western society despite relatively little scientific research having been conducted to investigate their efficacy.

The herbs that have received the most scientific attention in regard to influencing psychological processes have been drawn from the traditional medicines rather than the culinary herbs. A search of MEDLINE and PsycINFO using the various herb names (eg, basil, coriander) and the terms cognition, memory, attention, dementia and anxiety found only one study of the effect of any of these herbs on psychological processes — it investigated the hypnotic and anxiolytic effects of lemon grass. In this placebo-controlled, double-blind study, lemon grass was taken as a herbal tea for 2 weeks; no effects were found.⁷¹

The use of herbal treatments for anxiety is probably the most common example of a herbal influence on mental health. *Passiflora incarnata*, or passionflower, is approved for use as a sedative by the German Commission E (an expert committee commissioned by the German Government in 1978 to evaluate herbal drugs and preparations from medicinal plants). *Valeriana officinalis*, or valerian, is probably one of the most widely available herbal treatments, and has been shown to have sedative effects in humans. A review of evidence for behavioural effects and possible chemical pathways for their action concludes that compounds in valerian interact with GABA systems (widespread systems affected by γ -amino butyric acid) in the brain; however, despite identifying flavonoids in passionflower as the likely agent, they do not appear to act on GABA receptors.⁷²

More recently, herbs drawn from traditional Chinese medicine, such as *Ginkgo biloba* and ginseng, have been advocated for a reputed beneficial effect on cognitive processes.⁷³ There is level I evidence to support the claim that ginkgo can ameliorate cognitive decline in dementia^{1,74} and level II evidence that it can improve some aspects of memory function in healthy adults.^{1,75} Further, an extract from ginkgo has been shown to affect cerebral circulation, activity in the cholinergic system, and to have antioxidant properties, all of which may contribute to effects on cognitive function (Box 5).⁸¹ However, a population-based study



2,6-octadienal), isolated from the methanol extract of lemon grass, was identified as a novel inducer of the phase-2 enzyme glutathione S-transferase.⁵⁵ Lemon grass extract reduced the number of putatively preneoplastic lesions and the level of oxidative hepatocyte nuclear DNA injury, as assessed in terms of 8-hydroxydeoxyguanosine production in the liver of male Fischer 344 rats.⁵⁶ Inhibitory effects of lemon grass extract on the formation of azoxymethane-induced DNA adducts and aberrant crypt foci (a preneoplastic lesion) were recently demonstrated in the rat colon.⁵⁷

Perillyl alcohol, a naturally occurring monoterpene found in lavender, cherries and mint, caused a 22% reduction in tumour incidence and a 58% reduction in tumour multiplicity in a mouse lung tumour bioassay.⁵⁸ Rats given spearmint water extract (2% weight/volume) as the sole source of drinking fluid before, during, and after 2-week treatment with a colon carcinogen derived from cooked meat, showed significant reductions in colonic aberrant crypt foci compared with rats given water only.⁵⁹

As a culinary herb, parsley is regularly consumed and parsley-leaf oil is also used extensively for garnishing and seasoning. Myristicin, a major volatile aroma constituent of parsley, showed high activity as an inducer of the phase 2 enzyme glutathione S-transferase in the liver and small intestinal mucosa of strain A/J albino mice,^{60,61,70} and a 65% inhibition of tumour multiplicity in a rodent lung cancer model.⁷⁰

The results of studies cited above indicate the potential for herbs and spices in chemoprevention of cancer *in vitro* and in rodent cancer models. However, there is as yet no reliable evidence for beneficial effects in humans *in vivo* at customary intake levels. There is clearly a need for placebo-controlled clinical trials to determine safety and optimal dosage, bioavail-

5 Summary of evidence for health effects of herbs and spices on cognitive function and mental health

Study	Design	Tissue/organism/ participants	Bioactive agent/ source	Dose	Measurement	Outcome
Carlini ⁷²	Review article	In-vitro study	<i>Passiflora incarnata</i> (passionflower) extract	Not mentioned	Sedative and anxiolytic effects	Flavonoids appeared to be responsible for the anxiolytic and sedative effects. Findings on the mechanisms of action were mixed.
Frank and Gupta ⁷⁶	Review article	Mouse hippocampal cell model of oxidative stress Rat model of acute and chronic stress	Aged garlic extract	Not mentioned	Antioxidative and stress level effects	Flavonoids in aged garlic extract protected primary neurons from glutamate toxicity and oxidative injuries.
		Animal model of Alzheimer's disease	Curcumin from ginger or turmeric	Not mentioned	Protection against damage induced by amyloid β -protein	Superior results were obtained with curcumin (compared with ibuprofen).
		In-vitro study	Ferulic acid	Not mentioned	Antioxidative effects	Ferulic acid, being a potent antioxidant, inhibited lipid peroxidation.
		In-vitro study	Polyphenolic compounds	Not mentioned	Cytotoxicity, apoptotic features and anti-oxidative activity	Formation of fAbeta (β -amyloid fibrils) was inhibited and preformed fAbeta was destabilised in a dose-dependent manner.
Eidi et al ⁷⁷	Animal study	190 male Wistar rats	Ethanollic sage-leaf extract	3.5 g single dose	Long-term memory retention test	Ethanollic extract increased memory retention.
Akhondzadeh et al ⁷⁸	4-week double-blind, randomised trial	36 outpatients with generalised anxiety disorder	Passionflower extract	45 drops per day	Hamilton Anxiety Rating Scale	Passionflower extract is effective for managing generalised anxiety disorder.
Akhondzadeh et al ⁷⁹	4-month double- blind, randomised, placebo- controlled trial	42 patients with mild to moderate Alzheimer's disease	Sage extract	60 drops per day	Changes in the Alzheimer's Disease Assessment Scale and Clinical Dementia Rating	Sage extract produced a significantly better cognitive function outcome than placebo.
Rahman ⁸⁰	Review article	Not revealed	Various compounds derived from garlic	Not mentioned	Cerebral function	The role of garlic in preventing cerebral ageing through its antioxidant properties is supported by a few studies.

failed to find an effect on the recall of newly learned information after a short delay and the efficiency of working memory processes after a 30-day intervention.⁷⁵

Consuming herbs can be expected to benefit cognitive function to the extent that they benefit cerebral circulation. For example, it has been shown that people with hypertension perform more poorly on a range of cognitive tasks,⁸² and cardiovascular disease is associated with impaired cognition.⁸³ Dietary factors that promote cardiovascular health will therefore also maintain cognitive function, although the effect of any single foodstuff is likely to be small.

Perhaps more importantly, antioxidant intake is related to cognitive function because it protects against neuronal degeneration. A review of studies of the effects of antioxidants on Alzheimer's disease shows quite mixed results; this is attributed to the fact that most studies involve participants who have already been diagnosed with dementia, while epidemiological studies suggest that the most likely benefit of antioxidants is in preventing dementia.⁷⁶ Some epidemiological studies have shown a relationship between plasma levels of antioxidants and dementia and cognitive impairment.⁸⁴ At this point in time, the evidence suggests that total antioxidant intake may influence cognitive decline with age through the neuroprotective action of antioxidants.

Summary

- There is little evidence that culinary herbs and spices directly influence cognition.
- There is level I and II evidence for the effect of some herbal supplements on psychological and cognitive function.
- Total antioxidant intake (to which herbs and spices contribute) may influence cognitive decline with age through the neuroprotective action of antioxidants.
- Randomised, placebo-controlled intervention studies of the effects of culinary herbs and herbal supplements are required.

6 Summary of evidence for health effects of herbs and spices on type 2 diabetes

Study	Design	Participants	Bioactive agent/ source	Dose	Measurement	Outcome
Vuksan et al ⁸⁴	Randomised, placebo-controlled, crossover trial	19; 10 without diabetes and 9 with type 2 diabetes	Ginseng or placebo	3 g	Area under curve of blood samples before and at 15, 30, 45, 60, 90 and 120 minutes after glucose challenge	Area under curve reduced by 18%±31% (mean±SD) in those without diabetes when ginseng was taken 40 minutes before glucose. Area under curve reduced by 19%±22% and 22%±17% in those with type 2 diabetes when taken with or before glucose, respectively.
Vuksan et al ⁸⁵	Multiple occasions, randomised, placebo-controlled trial	10 without diabetes	American ginseng or placebo	3, 6 or 9 g of ground ginseng root powder	Area under curve of capillary blood glucose levels before and at 0, 15, 30, 45, 60 and 90 minutes after glucose challenge	All three doses of American ginseng reduced glucose levels at 30, 45 and 60 minutes; 3 and 9 g reduced glucose levels at 90 minutes ($P < 0.05$). At 60 minutes, 9 g of American ginseng reduced glucose levels more than 3 g ($P < 0.05$). All doses reduced area under curve (3 g, 26.6%; 6 g, 29.3%; 9 g, 38.5%; $P < 0.05$).
Sotaniemi et al ⁸⁶	Double-blind, placebo-controlled trial	36 with type 2 diabetes	Ginseng	100 mg and 200 mg	Fasting blood glucose level, glycated haemoglobin (HbA _{1c}) level, body weight	Ginseng reduced fasting blood glucose and HbA _{1c} levels and body weight. Placebo also reduced body weight, but did not alter fasting blood glucose levels.
Vuksan et al ⁸⁷	Randomised, placebo-controlled, crossover trial	12 without diabetes	American ginseng	0, 1, 2 and 3 g	Area under curve of capillary blood glucose levels before and at 0, 15, 30, 45, 60 and 90 minutes after glucose challenge	Glucose levels reduced over the last 45 minutes of the test after 1, 2 and 3 g of ginseng compared with placebo ($P < 0.05$); no differences were found between doses. In the last 60 minutes, glucose and area under curve were lower when ginseng was taken 40 minutes before glucose challenge than when taken at 20, 10 or 0 minutes before ($P < 0.05$).

Type 2 diabetes mellitus

Jennifer B Keogh and Peter M Clifton

The biguanide drug metformin, a popular first-line treatment for diabetes, was developed from French lilac (*Galega officinalis*). To date, this is the only plant-derived treatment for diabetes. At present, the best clinical evidence available for culinary herbs and spices in the treatment of diabetes is for cinnamon, and that is not very convincing. Early in-vitro studies of spices such as cinnamon, cloves, bay leaves and turmeric have shown that they display insulin-enhancing activity.^{85,86} Mechanistic studies suggest that extracts of cinnamon increase in-vitro glucose uptake and glycogen synthesis and increase insulin-receptor phosphorylation.⁸⁷⁻⁸⁹ A recent study tested the hypothesis that cinnamon would lead to improved glucose tolerance in people with type 2 diabetes mellitus.⁸⁹ Sixty men and women were randomly assigned to one of six groups. The first three groups were given 1, 3 or 6 g of cinnamon (*Cinnamomum cassia* extract in capsules) or placebo (same number of capsules). After 40 days, all three doses of cinnamon improved fasting glucose levels (by 18%–29%; $P < 0.05$).⁸⁹ However, 20 days later, glucose levels were still lower with the lowest dose only, so it is not clear if any of the effects were due to the spice. In addition, glycated haemoglobin (HbA_{1c}) levels were not measured. It is not clear from this study whether less than 1 g of cinnamon per day would also be beneficial, and this is an important question given that an intake of more than 1 g of cinnamon daily would require supplementation. Triglyceride and LDL cholesterol levels were also lowered by cinnamon, and this again persisted 20 days after cessation of the spice in the two lowest doses, suggesting that a reduction in energy and fat intake had occurred in this group, and this would account for the effects on glucose. A second, double-blind randomised crossover study of 29 postmenopausal women with type 2 diabetes published this year showed that 1.5 g of cinnamon daily had no effect on whole-body insulin sensitivity or oral glucose tolerance, and lipid levels were also unchanged. In conclusion, the effect of cinnamon is still unproven.⁹⁰

There are many examples of non-culinary herbs that have been tested for their effects on blood glucose, but many of the data are very poor. The 10 most popular plant preparations prescribed by herbalists in Italy for glucose control are gymnema, psyllium, fenugreek, bilberry, garlic, Chinese ginseng,

dandelion, burdock, prickly pear cactus and bitter melon.⁹¹ Although there is also some evidence for the clinical efficacy of ginseng in managing diabetes, there are concerns about the reproducibility of its effect based on batch, dose and time of taking the herb.⁹² A 2004 study reported differences in glycaemic effect according to the type of ginseng tested, suggesting that the antihyperglycaemic effect of ginseng can be highly variable.⁹³ A randomised clinical trial in 2000 evaluated ginseng in 19 lean people; 10 without, and 9 with diabetes (Box 6).⁹⁴ They received 3 g of ginseng or placebo 40 minutes before, or with, 25 g of glucose. Participants (both with and without diabetes) taking ginseng 40 minutes before the glucose showed a significant reduction in glucose level compared with those taking placebo ($P < 0.05$). There were also reductions in the area under the glycaemic curve for both those with and without diabetes mellitus. In a further study, 10 people without diabetes received, in random order on 12 occasions, 0, 3, 6 or 9 g of ginseng at 40, 80, or 120 minutes before 25 g of glucose. Ginseng reduced postprandial glucose levels ($P < 0.05$), and 9 g had a slightly greater effect than 3 g.⁹⁵

Only one study has reported the effect of ginseng ingestion on HbA_{1c}. A 1995 report investigated the effect of ginseng in people newly diagnosed with type 2 diabetes mellitus.⁹⁶ Over 8 weeks, 36 participants were randomly assigned to receive either ginseng (100 mg or 200 mg) or placebo. Overall, ginseng reduced fasting blood glucose levels and body weight, and the group taking 200 mg of ginseng also showed reduced HbA_{1c} levels. These results suggest that ginseng may have a delaying effect on gastric emptying, although a sulfonylurea-like activity may also play a part.⁹⁶ In conclusion, evidence supporting the efficacy of non-culinary herbal treatments is limited and, at present, the best evidence for clinical efficacy is for ginseng.

Summary

- Studies of herbal treatments in diabetes are often very small, and extrapolating the results to the general population of people with diabetes is not appropriate.
 - The best evidence for effect on glycaemia is for ginseng (four studies, with one reasonable sized study showing a reduced HbA_{1c} level with 200 mg of ginseng).
 - Longer, larger randomised trials with acceptable clinical endpoints are needed to clarify the chronic effects of these herbs.
-

Osteoarthritis and inflammatory response

Craig S Patch

The role that diet plays in minimising the negative effects of ageing has been extensively investigated. Target health issues related to the ageing process include the process of oxidation, the promotion of bone health, memory retention and cognition. With respect to culinary herbs and spices, the best evidence is associated with anti-inflammatory effect, particularly in mediating osteoarthritic pain reduction.

Therapy for osteoarthritis is directed at symptoms, as there is no established disease-altering treatment. Currently, treatment

options are confined to pharmacological interventions such as analgesia, anti-inflammatory and intra-articular regimens.⁹⁸ However, the recent withdrawal of cyclo-oxygenase inhibitors has led many consumers to herbal remedies such as ginger. What follows is a review of the evidence for efficacy of ginger in treating symptomatic osteoarthritis.

Ginger (family Zingiberaceae) is a mixture of over several hundred known constituents, including gingerols, β -carotene, capsaicin, caffeic acid, curcumin and salicylate.⁹⁹ Animal models have been used for in-vitro and in-vivo testing of formulations and powders of ginger, and have shown that it acts as a dual inhibitor of both cyclo-oxygenase and lipo-oxygenase,¹⁰⁰ as well as being an inhibitor of leukotriene synthesis.¹⁰¹ Three trials have tested the effects of ginger extract on pain. A randomised, placebo-controlled crossover study of 46 patients with knee pain showed that ginger had no effect. It was suggested that there may have been a carry-over effect of the ginger extract which blurred the results, as explorative statistics before the crossover suggested a positive effect.¹⁰² However, in subsequent studies, ginger extract was found to have a statistically significant effect in reducing knee pain, but the effect was only moderate.¹⁰³⁻¹⁰⁵ An interesting recent trial of a proprietary combination of iso- α -acids from hops, rosemary extract and oleanolic acid (440 mg/day for 8 weeks) suggested a beneficial effect on pain in patients with arthritis.¹⁰⁶ Although these findings seem promising, there is much more to be done in this area. The relative effectiveness of different extracts is unknown, and there are methodological limitations in measuring this. More clinical studies are needed to confirm these results, considering the confounding effects of the total diet.

A few studies, mostly randomised controlled trials, investigating the effect of ginger on osteoarthritis and rheumatoid arthritis have been identified (Box 7).^{102-104,107,109} Various doses of ginger extract, ranging from 510 mg to 1 g per day, were tested. Pain level was assessed by various validated measures of pain, such as visual analogue scales, Western Ontario and McMaster Universities (WOMAC) osteoarthritis index total score, and SF-12 Health Survey. These trials found that the pain level of the participants in the intervention group was significantly lower than that in the placebo group, and suggests level II evidence¹ for the efficacy of ginger in this setting ($P < 0.05$). In addition, decreased use of non-steroidal anti-inflammatory drugs and analgesics was also observed. However, this improvement was modest¹⁰³ and the efficacy of ginger treatment was ranked below that of ibuprofen.¹⁰²

Experimental studies have shown that ginger inhibits the inflammation process. Ginger constituents are dual inhibitors of arachidonic-acid metabolism (a key pathway in inflammation).¹¹⁰ Similar anti-inflammatory activity shown with turmeric (a member of the ginger family) is also suggestive of a potential health benefit.¹¹¹ In addition, epidemiological studies have indicated that populations that consume foods rich in specific polyphenols (such as ginger) have lower incidences of inflammatory disease.¹¹²

Many questions remain to be answered about the effects of antioxidants and the inflammatory process. Future intervention studies should include a detailed assessment of the bioavailability of antioxidants in addition to polyphenols. Beyond clinical trials carried out with antioxidant-rich foods such as ginger, more studies with pure, isolated compounds will also be needed to establish their role in inflammatory diseases.

7 Summary of evidence for health effects of herbs and spices on arthritis

Study	Design	Participants/organisms/ tissue	Bioactive agent/source	Dose	Measurement	Outcome
Wigler et al ¹⁰⁴	6-month randomised, double-blind, controlled, crossover study	29 patients with symptomatic gonarthrosis	Ginger extract v placebo	1 g/day (250 mg capsule four times daily)	Pain on movement and of handicap (VAS of pain)	Significantly lower pain level was found in the ginger group. No significant difference was found between groups at crossover.
Bliddal et al ¹⁰²	Randomised, placebo-controlled, crossover study	56 participants with osteoarthritis	Chinese ginger extract (EVEXT33) capsule v ibuprofen v placebo	170 mg ginger extract three times daily; 400 mg ibuprofen daily	Pain assessment (VAS of pain — Friedman test)	Efficacy of treatment ranked ibuprofen above ginger and ginger above placebo. No significant difference was found between ibuprofen and ginger during crossover.
Altman and Marcussen ¹⁰³	6-week randomised, double-blind, placebo-controlled, multicentre, parallel-group study	247 patients with osteoarthritis of the knee and moderate-to-severe pain	Ginger extract (EVEXT77) capsule	255 mg twice daily	Reduction in "knee pain on standing" (VAS of pain)	Significant but modest improvement was found in the ginger extract group.
Sohail et al ¹⁰⁷	8-week randomised, multicentre clinical trial	65 patients with osteoarthritis and rheumatoid arthritis	Stinging nettle extract Devil's claw extract Ginger root extract (as atrisin capsule)	300 mg 200 mg 20 mg (all twice daily)	Assessment of pain and functional disability (VAS of pain)	Improvements in all efficacy parameters were observed. Less NSAID and analgesic medications were used by participants.
Muhlbauer et al ¹⁰⁸	In-vivo animal study	11 Wistar Hanlbm rats	Powdered sage, rosemary and thyme Essential oil extracted from sage and rosemary Monoterpenes (borneol, thymol and camphor)	1 g Various 1.0 mmol/L	Urinary excretion of [³ H]-tetracycline Urinary excretion of [³ H]-tetracycline Bone resorptive activities	Bone resorption was significantly reduced/inhibited. Significant inhibition of bone resorption. Direct inhibition of the osteoclast resorption pit assay

EVEXT33 and EVEXT77 are patented standardised ginger extracts. VAS = visual analogue scale. NSAID = non-steroidal anti-inflammatory drug.

Summary

- Various doses of ginger extract, ranging from 510 mg to 1 g per day, reduce subjective arthritic knee pain measures compared with placebo ($P < 0.05$).
- Decreased use of non-steroidal anti-inflammatory drugs and analgesics has been observed in study participants taking ginger extract.
- There is level II evidence for the use of ginger in ameliorating arthritic knee pain; however, this improvement is modest, and the efficacy of ginger treatment is ranked below that of the ibuprofen prescribed to the participants.

Public health

Peter G Williams

It is difficult to estimate the current level of consumption of culinary herbs and spices by Australians. The Australian Bureau of Statistics trend data on apparent consumption of foods do not include herbs and spices,¹¹³ and results from the last National Nutrition Survey (NNS) in 1995 provide only limited information on consumption — that median daily intake of herbs, spices, seasonings and stock cubes combined was estimated to be 1.4 g per adult (declining with age from 4.2 g in 19–24-year-olds, to 0.7 g in those aged 65 years and older), with only 3.1% of people reported consuming this category of food items on the day of survey.¹¹⁴ The separate intakes of herbs and spices alone are not reported. Intake by males appeared to be higher than that by females, but the low values make it difficult to assess the significance of this difference. In New Zealand, the consumption of spices, estimated using import data, was 364 g per year, or around 1 g per day,¹¹⁵ a similar value to that reported in the NNS.

One comparison of spices used in representative vegetable-based and meat-based recipes from 36 different countries found Australia (with a mean of 3.4 spices per recipe) had a moderate level of use compared with the international mean of 3.9 (ranging from 1.6 in Norway to 6.9 in Indonesia).¹¹⁶ However, increased use of herbs and spices as flavourings in foods is a major trend worldwide,¹¹⁷ with sales growth of 20%–30% over the past 5 years in both the United Kingdom and the United States.¹¹⁸ It has been suggested that this trend is partly driven by demographics; as consumers age, their palates can become more adventurous. Promotion can also be important — a recent UK advertisement in which Jamie Oliver encouraged consumers to experiment with nutmeg boosted sales of that spice fourfold.¹¹⁹

Based on retail sales data, consumption of herbs and spices in Australia has increased in line with global trends, and this is expected to continue. The market for local fresh-cut culinary herbs was estimated to be worth over \$62 million per year in 2004 and continues to grow at 20% per annum.¹⁰⁵ Information from major supermarket sales in 2003 suggests that total retail sales of fresh herbs and spices were valued at \$54 million, and sales for dried products were valued at a further \$107 million. The sales volumes of fresh herbs are shown in Box 8.

Although there is increasing interest and research in the health-promoting and protective properties of herbs and spices,^{120–122} there are few authoritative recommendations about intake in existing national dietary guidelines. The first recommendation in the NHMRC dietary guidelines for Australian adults is “Enjoy a wide variety of nutritious foods”,¹²³ and in the NHMRC dietary guidelines for older Australians, a food variety checklist given in an appendix includes the recommendation to use herbs and spices regularly.¹²⁴ The same food variety checklist has also been used as the basis of a checklist to assess intakes of phytochemical-dense foods, and herbs and spices make up 11 out of the 64 foods in the checklist (basil, oregano, mint, dill/fennel, parsley, pepper, ginger, cumin, turmeric, coriander, rosemary/thyme).¹²⁵

The higher the score the more adequate the diet is suggested to be in phytochemicals. However, it is acknowledged that such

food scores need to be further developed, and are not backed by any health outcome studies at this stage.

The two NHMRC dietary guidelines each have another recommendation for using herbs and spices. In the dietary guidelines for adults, the background chapter on choosing foods low in salt states that among the recommended substitutes for salt are ingredients such as curry spices, garlic and onion, and herbs.¹²³ The guidelines for older Australians note particularly that age-related sensory loss of smell and taste is common in older people, especially those who take many medications, and can have adverse effects on overall nutrient intake. The guidelines recommend experimentation with new flavourings such as herbs and spices to stimulate appetite and support adequate overall intakes.¹²⁴

A few other countries have made similar recommendations about herbs and spices. In the 2005 revision of the *Dietary guidelines for Americans*, the chapter on choosing a diet moderate in salt and sodium recommends flavouring with herbs and spices.¹²⁶ Perhaps the country with the most direct recommendation about the health benefits of culinary herbs is Greece. Their dietary guidelines not only refer to the usefulness of herbs as salt substitutes, but also state: “oregano, basil, thyme and other herbs grown in Greece are good sources of antioxidant compounds”.¹²⁷ This emphasis on the health-promoting properties of herbs is of interest, given research in Australia that has found that first generation Greek migrants have 35% lower mortality from cardiovascular and overall mortality than Australian-born controls, despite high prevalence of risk factors such as obesity, smoking and sedentary lifestyles. It has been suggested that one of the dietary factors contributing to this lower mortality could be their high intake of antioxidant-rich plant foods, including garlic and herbs.¹²⁸

Despite the generally supportive statements in the dietary guidelines, the quantitative recommendations for intakes of food

8 Major supermarket sales of fresh herbs and spices in Australia 2003¹⁰⁵

Herb or spice	Amount sold (kg)	Retail sales value
Garlic	1 767 000	\$7 941 100
Ginger	592 900	\$7 259 900
Chilli	425 000	\$3 755 300
Basil	74 200	\$7 373 200
Coriander	73 900	\$8 860 600
Parsley	30 500	\$8 415 000
Mint	18 800	\$2 151 500
Chives	18 400	\$2 225 500
Lemon grass	17 400	\$950 300
Rosemary	15 200	\$1 169 700
Oregano	9 700	\$594 700
Dill	6 100	\$1 074 900
Thyme	3 600	\$693 300
Other	845 800	\$9 104 000

in the *Australian guide to healthy eating* do not yet include suggested intakes of herbs and spices.¹²⁹ Those recommendations aim primarily to ensure adequate intakes of nutrients for which recommended dietary intakes have already been established, and it is probably too early for there to be more definitive recommendations about foods based on their content of other phytochemicals. It should also be borne in mind that there are possible adverse effects of some spices (such as chilli and peppers) if consumed in large quantities,¹²¹ although this is unlikely to be a significant risk at normal levels of use. Thus, the apparent increasing consumption of culinary herbs and spices is certainly a welcome trend that is worthy of closer monitoring, and in future,

more explicit recommendations about their place in a healthy diet should be included.

Summary

- Recommendations for intakes of food in the *Australian guide to healthy eating* do not yet include suggested intakes of herbs and spices.
 - Future consideration should be given to including more explicit recommendations about the place of herbs and spices in a healthy diet.
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Dietary implications

Virginia A Fazio and Karen E Inge

Food variety and diversity

The use of herbs and spices can assist in increasing the consumption of vegetables and fruit. Many national nutrition guidelines stress the importance of consuming a wide variety of food, including the *Australian guide to healthy eating*,² *Eat well Australia*¹³⁰ and *Dietary guidelines for Americans*.¹²⁶ The healthy nutrition message is now one of increasing food variety and diversity to maximise the range of nutrients consumed on a regular basis. Internationally, there are programs such as the “Go for 2&5” campaign in Australia¹³¹ and “5 a day the color way” in the US.¹³² Herbs and spices naturally fit within such programs, as they encourage increased use of vegetables by adding flavour and interest to the diet.

Campaigns throughout the world encouraging an increase in the consumption of fruits and vegetables are consistent with the dietary guidelines promoted by the World Health Organization.¹³³ There are multiple factors that influence the quantity and variety of vegetables consumed. Research from the US suggests that factors such as age, education, and percentage of income spent on food at home are all positive influences on the amount and variety of vegetables consumed. This research also shows that the number of children in large households reduces the variety of vegetables consumed.¹³⁴ In addition, an analysis by the Australian Institute of Health and Welfare of the 2001 National Health Survey found that the percentage of people who consumed fewer than four serves of vegetables a day decreased with age. In addition, 76.8% of those aged 19–34 years were low vegetable consumers, as were 62.4% of those aged 75 years and over.¹³⁵ One of the barriers to increasing consumption is the limited range of preparation techniques (including interesting flavours) that people feel confident in using with fruit and vegetables.¹³⁵

Herbs and spices increase bioavailability of other nutrients

The nutrients and other biologically active components (such as antioxidants) in food do not always show the same health benefits when the active substance is isolated from food and ingested as a pure compound.¹³⁶ There are synergistic effects between nutrients that affect absorption and bioavailability.¹³⁶ Salad dressings containing herbs and spices can increase the antioxidant capacity of the salad.¹³⁷ Marjoram, for example, has been shown to increase the antioxidant capacity by 200%¹³⁷ (ie, a 200 g portion of a salad enriched with 3 g of marjoram equated to an intake of 4000 oxygen radical absorbance capacity units).¹³⁷ On the other hand, the presence of herbs and spices will not always result in improved absorption of nutrients. Just as some vegetables can limit the absorption of calcium, zinc and iron, research has shown, for example, that a reduction in non-haem iron absorption can be seen in the presence of rosemary oil.¹³⁸

Practical application

The use of herbs and spices may help to lower salt, fat and sugar intake. Some practical advice includes:

- Stir fries can have meat or chicken or fish marinated before cooking in minimal oil. These dishes often include the addition of garlic, ginger and chilli.
- Curries can be based on either meat or vegetables. Low-fat curries rely on minimal use of coconut milk or cream, but many traditional curries and their accompaniments are low in fat. Herbs and spices are integral to the seasoning of these dishes.
- There is an enormous variety of Mediterranean dishes. Many of the recipes have high proportions of vegetables and rice, pasta or couscous. The oils used are generally heart-friendly.
- Fresh herbs are usually better added towards the end of cooking or just before serving to preserve their flavour. Parsley can be added at any time.
- Amounts of fresh herbs used are usually 2–4 times more than dried herbs. Some herbs like basil darken when bruised but this does not change the flavour. All fresh herbs should be prepared just before using.
- Dried herbs can be added at any stage of cooking, but use should be guided by recipes as some herbs, such as bay leaves, are added very early in cooking. Some dried spices are heated at the beginning of cooking to release their flavours. More flavour is released by grinding with a mortar and pestle.
- Garlic releases more flavour when it has been chopped or mashed. It should not be overheated as it may burn and become bitter.
- The hottest parts of chillies are the seeds and white internal membranes. Removing them will result in a milder flavour.

Understanding food combinations is important in cooking with herbs and spices. Traditional use matches them with certain foods, but this is not meant to be restrictive. Herbs are clustered into families, so the traditional combinations can be exchanged with others from the same family for variety or personal taste preferences.

Parsley family

- Parsley — in multiple forms, used raw and in cooking with meat, fish, chicken and vegetables.
- Dill — used in salads, sauces and with fish, sour cream, and in cheese and potato dishes.
- Coriander (cilantro) — popular in Mexican cooking and many Asian and Middle Eastern cuisines. Useful in marinades, dressings, salsas and in cooked dishes. Leaves, roots and seeds are used.

Mint family

- Mint — many forms with slightly different tastes are used raw and in cooking, dressings, marinades, drinks, yoghurt, desserts, sauces, vegetable dishes and salads.
- Basil — used with tomatoes (fresh and in sauces) and in soups and casseroles with tomato. Also used in salad dressings, pesto, and with pasta, rice, vegetables, meat, chicken and seafood, and in South-East Asian cooking in curries, soups and noodle dishes.
- Marjoram — used in meat, fish, egg, and cheese dishes, and in pizza.
- Oregano — essential for Italian and Greek dishes, but also used in cheese and egg dishes.
- Sage — used with veal, and in stuffing and cheese dishes.

SUPPLEMENT

- Thyme — used in casseroles, soups, and poultry stuffing.
- Rosemary — used in marinades, sauces and stuffing, and with fish, poultry and soups.

Allium family

- Chives — used in salad dressings, soups, light sauces, and with egg, cheese, fish and chicken.
- Garlic — included in almost every cuisine from Asian to Mediterranean. Used in marinades, dressings, sauces, and in stir-fried and slow-cooked dishes.

Other

- Bayleaves — generally used in slow-cooked meat and soup dishes.
- Chilli — used with meat, chicken and poultry, shellfish, tomato dishes, and curries. Popular in Asian, Mexican, African and Caribbean cooking.

- Ginger — used in many Asian dishes, but also in cakes, biscuits, desserts and with fruit and juices.
- Lemon grass — can be used as a tea or beverage and is included in many Asian dishes.
- Tarragon — used with chicken and fish and in salad dressings and egg dishes.

Summary

- The use of herbs and spices may encourage variety in food intake. Herbs and spices support nutrient diversity by encouraging new food choices.
 - Higher vegetable intakes are linked with improved health. Vegetarian options and vegetable dishes may be more appetising when prepared with herbs and spices.
 - Many low-fat cooking methods are improved by using herbs and spices in soups, casseroles, marinades and dressings.
 - Herbs and spices are a healthy alternative to salt as a seasoning.
-

Moving forward

Linda C Tapsell

Herbs and spices have only recently captured the attention of the scientific community as providing potential health benefits. As a result, there needs to be a significant investment in human clinical trials to substantiate many of the hypothesised health benefits. Nevertheless, this review provides encouragement for further scientific inquiry. The evidence presented in this review suggests that most of the health effects of herbs and spices on cancer, cardiovascular disease, arthritis and mental health protection may be mediated through their potent antioxidant effects, given the range of activity across the group as a whole (Box 9).⁴² As science uncovers the role of antioxidants in many degenerative diseases associated with ageing, herbs and spices may have a place as an important source of antioxidants in the diet.

While the bioactivity of individual antioxidants may be known, their effects on health may not be as significant as the combination of the whole class of bioactives working through multiple mechanisms of action. This may well be the case in nutrition generally, where, for example, it is now being argued that the health benefits of n-3 fatty acids are attributed to moderate health effects mediated through multiple pathways rather than a single significant mechanism.¹³⁹ Like the work undertaken with these essential fatty acids, research is required to uncover the mechanisms by which antioxidants deliver health benefits, and then the impact of exogenous antioxidants in this context. A deeper understanding of this role will help to establish recommended intakes, as has been the case for vitamins and minerals. Finally, an understanding of how antioxidant-rich foods (such as herbs and spices) fit within the context of the whole diet, in balance with all other requirements, will enable research at the clinical level to establish the evidence for their putative place in health promotion and disease prevention.

In summary, as several metabolic diseases and ageing-related degenerative disorders are closely associated with oxidative processes in the body, the use of herbs and spices as a source of

9 Antioxidant activity of common dried herbs and spices.⁴²

Common name	Botanical name	Antioxidant activity*
Clove	<i>Syzygium aromaticum</i>	465.3 mmol/100 g
Oregano	<i>Origanum vulgare</i>	137.5 mmol/100 g
Cinnamon	<i>Cinnamomum zeylanicum</i>	98.4 mmol/100 g
Peppermint	<i>Mentha piperita</i>	78.5 mmol/100 g
Thyme	<i>Thymus vulgaris</i> L.	74.6 mmol/100 g
Rosemary	<i>Rosmarinus officinalis</i> L.	66.9 mmol/100 g
Marjoram (sweet)	<i>Origanum majorana</i>	55.8 mmol/100 g
Basil	<i>Ocimum basilicum</i> L.	30.9 mmol/100 g
Ginger	<i>Zingiber officinale</i>	22.5 mmol/100 g
Dill	<i>Anethum graveolens</i>	15.9 mmol/100 g
Curry	<i>Murraya koenigii</i> L.	13.0 mmol/100 g
Chives	<i>Allium schoenoprasum</i>	7.1 mmol/100 g
Parsley	<i>Petroselinum crispum</i>	3.6 mmol/100 g
Coriander	<i>Coriandrum sativum</i> L.	3.3 mmol/100 g
Vanilla seeds	<i>Vanilla planifolia</i>	2.6 mmol/100 g
Garlic	<i>Allium sativum</i> L.	2.1 mmol/100 g

* Mean total antioxidant activity per 100 g. ◆

antioxidants to combat oxidation warrants further attention. Immediate studies should focus on validating the antioxidant capacity of herbs and spices after harvest, as well as testing their effects on markers of oxidation. This will work in parallel with clinical trials that are aiming to establish antioxidants as mediators of disease prevention.

Competing interests

Gourmet Garden (manufacturer of fresh herb products) has provided finance for the cost of the review and honoraria (\$800 per section) to the contributing authors. Gourmet Garden has paid the University of Wollongong, partner in the National Centre of Excellence in Functional Foods, a consultancy fee to develop further materials including consumer education that may reference this publication. Ian Hemphill owns Herbie's Spices, which is a retail outlet selling herbs and spices in Sydney, mainly to the food service industry. He is a recognised expert in this area and has written books on the subject. Peter Clifton recently completed a consultancy with Gourmet Garden, analysing the antioxidant content of its major herbs. Virginia Fazio and Karen Inge consult to Gourmet Garden on the communication of the application of herbs and spices. Gourmet Garden did not influence the authorship nor comment on any draft of the manuscript.

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