



Antioxidant nutrients

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SYNOPSIS

Ageing and a variety of age-related conditions such as heart disease and cancer may be linked to oxidation processes resulting from an excess of reactive molecules. Many compounds in food have antioxidant properties by interacting with the reactive molecules. Antioxidants from food include not only vitamins C and E and beta carotene, but also some elements such as selenium and copper (which form antioxidant metallo-enzymes), and other compounds found in plant foods such as flavonoids and polyphenols. A diet with a high content and wide variety of antioxidant nutrients appears to offer some health advantage. Taking a narrow range of antioxidant supplements may be ill-advised when they are of unproven efficacy and of possible harm. Regularly eating a wide variety of plant food is better than relying on a few antioxidant supplements.

Index words: food, phytochemicals, vitamin supplements.

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What are antioxidant nutrients?

In the body, certain molecules called reactive oxygen species (ROS) and reactive nitrogen species (RNS) are normally produced as part of the defence system and as the by-products of cellular metabolic processes utilising oxygen.¹ These reactive

species include free radicals or certain molecules which may be oxidising agents or convertible to free radicals.

Many factors can cause the body to produce more reactive species than are needed. These include smoking, drinking alcohol, too much fat in the diet, too much sun exposure, too many pollutants in the air and even too much exercise. Antioxidants are substances that reduce oxidation and so counteract the reactive species. If ROS or RNS outnumber the antioxidant stores in the body, they can inactivate enzymes, oxidise lipids and damage genetic materials (DNA). These processes have been linked to ageing and a variety of age-related conditions, including heart disease and cancer.

There are many compounds with so-called antioxidant properties that are derived from food (Table 1). However, a food, or foods, with antioxidant potential may or may not realise that potential *in vivo* for various reasons.

Naturally-occurring antioxidant vitamins include carotenoids (which may also be pro-vitamin A), the vitamin E family of compounds (tocopherols and tocotrienols) and vitamin C. Some elements found in the diet exert their *in vivo* antioxidant effects as metallo-enzymes such as selenium (as part of glutathione peroxidase) and copper (as part of superoxide dismutases). Some compounds found in fruits and vegetables that may promote health (phytochemicals) are powerful antioxidants.

Table 1

Antioxidant components in food

Components	Compounds	Food sources
Vitamins	Vitamin C (ascorbic acid) Vitamin E (tocopherols and tocotrienols) Beta carotene and other carotenoids	Citrus fruit, berries, papaya Seed-like cereal grains, nuts and oils derived from plants Orange pigmented, and green leafy vegetables
Elements	Copper (as part of superoxide dismutases) Selenium (as part of glutathione peroxidase)	Cocoa, wheat bran, yeast Grains, meats
Macronutrient-derived	Peptides e.g. glutathione	Whey protein
Phytochemicals (food components of plant origin)	Isoflavones e.g. genistein and daidzein Flavonols e.g. quercetin and kaempferol Polyphenols e.g. rosmarinic acid Catechins e.g. epigallocatechin gallate (EGCG)	Soy Tea, red wine, onions, apples Herbs - oregano, thyme Green tea
Zoochemicals (food components of animal origin)	Glutathione Ubiquinone (coenzyme Q ₁₀)	Meats Meats, especially meat organs, fish

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Do antioxidants delay ageing or prevent age-related diseases?

One of the major theories about biological ageing is that it depends on oxidation processes. For this reason, there is great interest in the antioxidant capacity of the human diet and of nutrient supplements. So far, most evidence suggests that plant-derived food is protective against age-related diseases, like cardiovascular disease and cancer, rather than ageing itself.

Many epidemiological studies have linked diets containing moderate to high proportions of fruit and vegetables to lower mortality and to a reduced risk of developing cardiovascular disease, cancers, cataracts and macular degeneration, cognitive impairment and Alzheimer's disease.²⁻⁵ Although clear cause and effect relationships are difficult to establish, these protective effects are probably due to combinations of nutrients and also to the non-nutritive substances found in these foods. In cohort studies, a survival advantage can be predicted if the diet contains a variety of food, principally from plant sources.⁶

Can we get enough antioxidant nutrients from food?

Any factors such as excessive dietary fat intake, smoking or alcohol consumption, leading to an increase in oxidation, could increase the requirement for antioxidant nutrients above that usually obtainable from food.

An advantage in getting antioxidants from food is that there are literally thousands of different antioxidants in the human diet⁷ and they are numerous in chemical types (Table 1). They may therefore act in integrated systems or cascades in which antioxidants may ferry free radicals within the biological system to safer destinations. For example, ROS or RNS may be dissipated from a lipid soluble environment, without lipid peroxide formation, to a water soluble environment through the availability of, in sequence, ubiquinone (coenzyme Q₁₀), vitamin E and vitamin C. Upon oxidation, these micronutrients need to be regenerated in the biological setting, hence the need for further coupling to other reducing systems such as glutathione/glutathione disulfide, dihydrolipoate/lipoate, or NADPH/NADP⁺ and NADH/NAD⁺. No one antioxidant can achieve this outcome alone.

Some actually work better when co-ingested in a group of antioxidants. The mix of antioxidants may also facilitate absorption. An example of this is the enhancement of lycopene absorption after taking a combination of beta carotene and lycopene.^{8,9}

According to the National Health and Medical Research Council, Australians have 'access to a nutritious and varied food supply, containing all the known nutrients in more than adequate amounts. People eating a good diet that included breads and cereals, vegetables and fruit, meat or meat substitutes and dairy products do not require vitamin and mineral supplements. These foods, whether fresh or processed, provide a balanced source of vitamins and minerals'.¹⁰ There is, however, a question as to whether this statement is valid. This

is not because the Australian diet cannot provide enough antioxidant nutrients, but rather whether or not it provides the range and amounts of these nutrients required for optimal health given the current food choices by some groups. For example, according to the 1995 National Nutrition Survey, young Australians do not eat enough fruit as a source of antioxidants; only 37% of those aged 19-24 years reported eating fruit the day before interview.

Are supplements beneficial and safe?

Many believe that if enough of an essential nutrient is good, then more is better. However, when large amounts of antioxidant nutrients are taken, they can also act as pro-oxidants by inducing oxidative stress.^{11,12} Furthermore, pro-oxidant activity can induce either beneficial or harmful effects in biologic systems.¹²

From available evidence, we cannot yet answer the question as to whether micronutrient supplements actually improve health or decrease risk of disease where food cannot.^{13,14} In addition, whilst there are areas of health promise for some antioxidants presently available, there are conflicting data in relation to their adverse effects. For example, favourable effects of vitamin E have been observed in relation to Alzheimer's disease and prostate cancer, but the use of high doses of vitamin E is also associated with increased risk of mortality from some cancers, possibly fatal as opposed to non-fatal myocardial infarction, and haemorrhagic stroke.¹⁵ Beta carotene supplements, whether on account of the isomers used or because they have been used in isolation, have increased the incidence of tumours; they should no longer be used.¹⁶ Another area of concern about supplements is how much suppression of oxidation may be compatible with good health, as toxic free radicals are required for defence mechanisms.

Antioxidants in clinical practice

High intakes of antioxidant nutrients from food sources appear to offer some health advantages. In addition, a diet high in fruit and vegetables often means a lower intake of fat and a higher intake of fibre, which may also protect against many diseases. Vitamin and mineral supplements do not necessarily make up for 'poor food habits' or 'unhealthy lifestyle practices'.¹⁰ It is advisable to eat a wide variety of cereals, fruit and vegetables in reasonable amounts rather than rely on supplementation with a few antioxidants.

Claims that antioxidant supplements have a therapeutic benefit are scientifically unjustified at present. Antioxidant activity determined *in vitro* may not be relevant *in vivo*; antioxidant nutrients have many functions, and may act through other mechanisms rather than as antioxidants. Prevention of disease through dietary supplementation may be a worthwhile objective, but dose response data are required to evaluate pharmacologic and toxicologic effects. The promotion of antioxidants as therapeutic agents is inappropriate when their efficacy is unproven and their toxicology uncertain. It is much more realistic to envisage claims that a wide variety of plant-

derived food might be protective against excess oxidant activity whilst retaining the required level of such activity for defence against infection.

Conclusion

Basic foods and condiments like herbs and spices are extensive sources of antioxidants. The benefits of antioxidants may depend on their variety and interactions. We know that we can optimise health by encouraging the consumption of a wide variety of nutritious foods, but we cannot, so far, be sure about the risks and benefits of taking antioxidant supplements.

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Self-test questions

The following statements are either true or false (answers on page 151)

7. Naturally-occurring antioxidants have no adverse effects.
8. A beneficial effect of an antioxidant found in food may not occur if the antioxidant is taken as a supplement.

Dental implications

Prepared by Associate Professor R.G. Woods of the Australian Dental Association

Digoxin in the 21st century (page 136)

The cardiac glycoside digoxin is taken by an increasing number of dental patients. The drugs used in dental treatment which may interact with digoxin include tetracyclines, erythromycin, catecholamines in local anaesthetic preparations (which may increase the risk of arrhythmia) and non-steroidal anti-inflammatory drugs such as diclofenac.

It is prudent to use an alternative to adrenaline or other catecholamine vasoconstrictors in local anaesthetics. Alternative vasoconstrictors available in dental preparations include felypressin with prilocaine hydrochloride.

Notwithstanding this comment, clinically there appears to be no reaction to up to 4 mL of local anaesthetics containing adrenaline in the low concentration of 1:200 000 (5 microgram/mL). Extra care should be taken to avoid intravascular injection.

Treatments should be carefully planned. Consultation with the patient's medical practitioner may be necessary. Appointments for patients taking digoxin should be kept as brief as practicable. If extensive treatment is planned it is often prudent to monitor the patient with an electrocardiograph and oximetry. Sometimes oxygen may be needed, so it should be available in the surgery.