Ginkgo

Ginkgo biloba L., also known as fossil tree, kew tree, maidenhair tree, yin xing (whole plant), yin xing ye (leaves), bai guo (seeds)

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PREPARATIONS: The leaf is the part used medicinally; in Traditional Chinese Medicine and in Japan, the seed is also used, although it contains some toxic constituents. Extracts of ginkgo leaf are available in several dose forms, including capsules, tablets and tinctures. Chopped or powdered forms of the dried material are also available. Several products marketed as dietary supplements containing ginkgo are available on the New Zealand market.

ACTIVE CONSTITUENTS: Ginkgo has been described as having polyvalent action; that is, the combined activities of several constituents are responsible for its effects. Important constituents of the leaves include the ginkgo flavonoid glycosides (e.g. glycosides of quercetin and kaempferol) and the terpene lactones (e.g. ginkgolides A, B and C). Modes of action demonstrated in preclinical studies include cardiovascular and haemorheological effects, antagonism of platelet-activating factor, antioxidant activity and effects on concentrations of certain neurotransmitters. Seeds contain ginkgotoxin (4-O-methylpyridoxine) and ginkgolic acids.

MAIN USES: Ginkgo leaf and seed have a history of traditional use in China for asthma and the seed also as an antitussive and expectorant. Contemporary interest in ginkgo leaf is focussed on its use in cognitive deficiency and dementia, intermittent claudication (from peripheral arterial occlusive disease) and vertigo and tinnitus of vascular origin. It is also used and promoted for cognitive improvement in healthy individuals.

EVIDENCE FOR EFFICACY: Recent Cochrane systematic reviews are available of clinical trials that assessed the effects of standardised ginkgo leaf preparations in cognitive impairment and dementia, intermittent claudication, acute ischaemic stroke, tinnitus and age-related macular degeneration. These reviews conclude that there is no convincing evidence available to support the efficacy of the ginkgo preparations tested in cognitive impairment and dementia, intermittent claudication, recovery after ischaemic stroke and tinnitus; there was insufficient research to determine whether or not ginkgo is efficacious in age-related macular degeneration. Many trials, particularly older ones, have methodological limitations.

A Cochrane systematic review of trials of ginkgo for cognitive improvement in healthy individuals is in preparation.

ADVERSE EFFECTS: Typically, Cochrane systematic reviews of (usually small-scale) clinical trials have not shown any difference between ginkgo and placebo with respect to the frequency of adverse events, including bleeding episodes. However, spontaneous reports of adverse effects associated with the use of ginkgo preparations have raised concerns about the risk of haemorrhagic reactions, including intracranial and ocular bleeding. Many of these cases concern individuals who were also taking conventional antiplatelet and/or anticoagulant agents, although some concerned use of ginkgo only.

A small number of drug interaction studies have indicated that ginkgo leaf extracts generally had no

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Summary message

Evidence for the efficacy of ginkgo extracts for cognitive impairment and dementia, intermittent claudication, acute ischaemic stroke, tinnitus and age-related macular degeneration is unconvincing. Ginkgo preparations have been associated with haemorrhagic reactions. Health professionals should be aware of the possibility of (undisclosed) use of ginkgo; use of ginkgo should be avoided, or at least used only with caution, in patients with bleeding disorders and those taking conventional anti-platelet or anticoagulant agents. If using ginkgo, these patients should be advised to be vigilant for signs of bleeding and to seek professional help. Suspected adverse drug reactions should be reported to CARM. As with all herbal medicines, different ginkgo products vary in their pharmaceutical quality, and the implications of this for efficacy and safety should be considered.

statistically significant effects on antiplatelet effects and/or pharmacokinetics of clopidogrel or ticlopidine, or on the pharmacokinetics and pharmacodynamics (INR) of warfarin. However, these studies involved healthy volunteers and the relevance of these findings to the clinical setting is unclear.

It is prudent to advise that use of ginkgo should be avoided in patients with bleeding disorders, since it is unlikely that the benefit–harm balance is favourable on the basis of current evidence. Likewise, ginkgo should only be used with caution in patients taking anticoagulant and/or antiplatelet agents. Some authors advise that the evidence is insufficient to advise patients taking such medicines to avoid using ginkgo. If ginkgo is used, patients should be advised to monitor for bruising and other signs of bleeding, and to seek professional help if this occurs.

Contact with or ingestion of the fruit pulp can cause severe allergic reactions.

Health professionals are reminded to report suspected adverse reactions associated with all medicines, including vaccines and complementary medicines, to the Centre for Adverse Reactions Monitoring (http://carm.otago.ac.nz).

DRUG INTERACTIONS: See *Adverse effects* for information on interactions with antiplatelet/anticoagulant agents.

Drug interaction studies involving healthy volunteers who received ginkgo leaf extracts have indicated that ginkgo induces the metabolism and lowers concentrations of omeprazole; it is unlikely that the benefit–harm balance for using ginkgo in patients being treated with omeprazole would be favourable on the basis of current evidence. Similar studies have shown that ginkgo leaf extracts did not appear to have clinically relevant pharmacokinetic interactions with alprazolam, caffeine, chlorzoxazone, dextromethorphan, diclofenac, digoxin, donepezil, fexofenadine, flurbiprofen, midazolam, propranolol, ritonavir, theophylline or tolbutamide.

There is limited evidence from preclinical studies that the administration of ginkgo and amikacin may accelerate amikacin-induced ototoxicity, and that ginkgo may lead to raised concentrations of diltiazem and nifedipine and reduced concentrations of nicardipine. There is also some limited clinical evidence of an interaction with nifedipine.

There is a small number of isolated case reports of breakthrough seizures in patients taking sodium valproate, with or without phenytoin, in patients who began taking ginkgo leaf extract or were taking several products containing ginkgo. Until further information is available, patients should be made aware of this possible interaction.

Key references

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