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Herbal medicine and anaesthesia

草藥與麻醉

Herbal medicines are increasingly used in both western and Chinese societies. This is partly attributed to the alleged limitations of scientific medicine in the cure and control of chronic diseases. Many patients do not disclose that they have used herbs before surgery and hence their physicians remain unaware of the potential herb-drug interactions. With respect to anaesthesia, herbs can cause coagulation disorders, cardiovascular side-effects, water and electrolyte disturbances, endocrine effects, hepatotoxicity, and prolongation of the effects of anaesthetic agents. Anaesthesiologists should obtain a history of herbal medicine use from patients and work out the adverse perioperative herb-drug interactions in advance of the actual operation. If in doubt, the herbal medicine should be stopped for 2 weeks prior to anaesthesia and surgery.

草藥的使用在西方和華人社會日漸普遍。部份原因是由於西藥在治癒和控制慢性病方面的所謂局限性。許多患者在手術前並未透露曾服用草藥，因此他們的醫生沒有意識到草藥與其他藥物的潛在交互作用。對於麻醉，草藥可能會引起凝結物混亂、心血管副作用、水和電解液干擾，內分泌影響，肝細胞毒性，以及麻醉劑作用的延長。麻醉科醫生應了解患者服用草藥的既往史，在手術前解決不利的術前草藥與麻醉藥的交互作用。如有懷疑，應在麻醉和手術前停止服用草藥兩週。

Introduction

Herbs are annual, biennial, or perennial seed-producing soft-stem plants that exhibit medicinal or aromatic properties. For centuries before the advent of scientific medicine, traditional medicine of different cultures employed these medicinal plants as disease remedies. Written in approximately the second century BC, the classic Chinese Materia Medica, Shen Nong Bencao (神農本草), documents such use. Historically, herbs have also been used to produce anaesthesia. Dioscorides (AD 40-90), the Greek military physician, described the drinking of mandrake by patients to cause insensibility during surgery. He used the word *anaesthesia* for the first time. Hua Tao (AD 190-265), the Chinese physician and surgeon, prescribed the herbal anaesthetic mafesian with wine to render patients unconscious before performing operations. Some of these early herbal-healing arts were lost through time and many gave way to scientific medicine.

The surge in herbal medicine

The last few decades have witnessed a global resurgence of interest in herbal or alternative medicines. In China, this came as a result of a national policy to integrate scientific and traditional Chinese medicine (TCM) after the 1949 civil war, when scientific medicines and equipment were in short supply. In western affluent societies, some patients have become disillusioned about scientific medicine. They are dissatisfied with the unempathetic, complex, and expensive forms of treatment that often fail to cure chronic diseases, such as asthma and arthritis. Increasingly health-conscious, they turn to alternative medicine for natural substances that may promote health and treat or even prevent diseases, such as cancer and atherosclerosis. The overwhelmingly positive information in the media or obtainable via the internet, coupled with the easy access of herbal medicines, has boosted the growth of alternative medicine. However, the belief that herbal remedies are somehow 'gentler' and 'safer' than pharmaceutical drugs is definitely untrue.

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The increasing use of herbal medicines by the general public, amounting to US$3.24 billion in the United States in 1997, poses a concern for anaesthesiologists.[1,2] In a widely publicised study presented at the 1999 American Society of Anesthesiologists meeting, 17.4% of patients presenting for surgery used herbal remedies such as ginkgo biloba (32.4%), ginseng (26.5%), and garlic (26.5%).[3] Another study found that 22% of presurgical patients used herbs, such as echinacea and ginkgo.[4] Data on the use of herbal remedies in Hong Kong is not available. However, it may be even higher than that in the West, because herbs, such as ginkgo, ginger, and garlic, are fully integrated into the Chinese diet. Quantification of dosage consumed is also difficult.

Since herbal products are classified as dietary supplements by the Food and Drug Administration (FDA) in the United States, they do not need to go through rigorous testing to demonstrate safety and efficacy, unlike scientific medicines. Quality control in the production and labelling of herbal medicines or pills thus becomes a concern. Similarly, the Hong Kong Pharmacy and Poisons Ordinance only provides control on adulteration with western drugs. As 70% of patients do not volunteer information on the use of alternative medicines to their doctors, clinicians should always be alert to this possibility.

In the perioperative period, anaesthesiologists should be aware of the effect of herbs on bodily functions and the possible herb-drug interactions, as these might affect the choice of the safest anaesthetic technique.

Potential hazards of herbal medicine

The efficacy and side-effects of herbal medicines have only been assessed in a few randomised, double-blind, controlled studies. There are logistical problems, such as specifying the active ingredient and standardising the dose. Using ginseng as an example, ginsenosides belong to a group of diverse steroidal saponins found in ginseng. Different ginsenosides may have opposing effects. The profiles of ginsenosides isolated from American and Asian ginseng,[5] or wild and cultivated ginseng,[6] may be very different. Hence, much of the available literature on the side-effects of herbal remedies is based on case reports, where temporal relations and other concomitant drug uses are not often mentioned.[7]

The adverse effects of herbal medicines include: toxicity due to overdose; contamination by other medicinal plants, such as digitalis[8]; mistaken plants, especially in Chinese herbal tea mixtures; physiological changes on bodily systems; and adverse drug interactions. The problems relevant to anaesthetic practice can be broadly classified into: coagulation disorders, cardiovascular side-effects, water and electrolyte disturbances, endocrine effects, hepatotoxicity, and prolongation of the effects of anaesthetic agents (Table 1). Some of the commonly used herbs will be discussed in relation to their general indications and herb-drug interactions (Table 2). Since terms used in TCM and western medicine may carry a different meaning, those terms appearing in quotation marks in the tables and text refer to the TCM context.

Table 1. Summary of the potential effects and toxicity of some common herbal medicines in anaesthetic practice

Potential problems	Related herbs
Coagulation disorders	• Potential bleeding risk [contain coumarin derivative(s)], antiplatelet effect: angelica root, arnica flower, anise, asafoetida, celery, chamomile, fenugreek, horse chestnut, licorice root, lovage root, parsley, passionflower herb, quassia, red clover, goat's rue, meadowsweet, willow bark, onion, borage seed oil, bogbean • Documented bleeding risk: danshen, dong quai, ginseng, ginkgo, garlic • Others: evening primrose oil, feverfew, ginger, guarana, kava kava, mate, vitamin E • Potential anticoagulation: chamomile, chondroitin, garlic, ginger, ginseng, goldenseal, kelp, vitamin E, capsicum
Cardiovascular side-effects	• Hypertension, hypokalaemia, oedema: licorice root • Interaction with central nervous system medications, hypertension, tachycardia: St John's wort • Disturbances of cardiac rhythm: ma huang • Others: chan su, chaste tea, garlic, ginkgo, ginseng, goldenseal, green tea, guarana, hawthorn berries, kava kava, mate, yohimbe, foxglove
Water and electrolyte disturbances	• Reduced effect of antihypertensives: goldenseal • Sodium retention, hypokalaemia: licorice root • Others: ginseng, green tea, kelp, mate, saw palmetto
Endocrine effects	• Postmenopausal bleeding: ginseng • Hyperglycaemia: ginseng, garlic, ginger, glucosamine, chromium, fenugreek, nettle, sage • Hypoglycaemia: garlic, ginseng, angel pearl, bitter melon, devil's claw, ma huang, tongyi, zhen qi, karela • Benign prostatic hypertrophy: saw palmetto • Oestrogen effects: dong quai
Potential for hepatotoxicity	• Hepatitis: valerian, skullcap, chaparral, certain Chinese herbal preparations • Potentiation of hepatotoxic drugs: echinacea • Hepatotoxicity: red yeast rice, skullcap, willow bark (in children), borage seed oil, licorice root
Prolongation of the effects of anaesthetic agents	• Valerian, kava kava, St John's wort • Confusion/sedation: chamomile, ginseng, passion flower, skullcap

Table 2. Summary of some commonly used herbs and their adverse effects

Common name	Biological name	Western use	Chinese use	Adverse effects
Ginger	*Zingiber officinale*	• Food component • Respiratory ailments • Congestion • Sore throats • Body aches • Motion sickness • PONV*	• Food component • 'Evils': expel 'cold', 'wind', and 'damp'	• Possible mutagenesis • Bleeding complications with warfarin • Antiplatelet (decrease aggregation) • Risk of hyperglycaemia
Garlic	*Allium sativum*	• Food component • Natural antibiotic • Promotor of leukocytosis • Blood pressure and lipid-lowering effects	• Food component • Diuretic • Expectorant • Antitussive • Antimicrobial • Diarrhoea • 'Evils': break 'cold'; remove 'damp' • Re-establish blood flow and 'Qi' • Strengthen stomach and spleen	• Antiplatelet • Antithrombolytic • Potentiation of warfarin • Risk of interaction with cardiovascular medications, MAOI†, hypoglycaemics
Ginkgo	*Ginkgo biloba*	• Dementia • Alzheimer's disease • Asthma • Angina • Eye ailments	• Cough and sputum	• Neurotoxicity • Decrease efficacy of anticonvulsants • Decrease seizure threshold • Interaction with MAOI • Antiplatelet (inhibit PAF‡)
American ginseng, Oriental ginseng, Korean red ginseng	*Panax quinquefolius, Panax ginseng*	• Increase energy level • Adaptogenic • Antioxidant • Enhance athletic performance	• 'Heat-raising' • 'Benefits heart, liver, spleen, lung, kidney' • Fatigue and physical stress	• Neuroprotective • Hypoglycaemic effect (diabetics) • Insomnia • Headache • Hypertension • Interaction with cardiovascular medications, digitalis, and MAOI • Vomiting • Antiplatelet (decrease adhesiveness and inhibit PAF) • Decrease warfarin effect
Ephedra	*Ephedra sinica, Ma huang*	• Energy building • Weight reduction	• Asthma • Upper respiratory tract infections	• Autonomic side-effects: tachycardia, hypertension, arrhythmias • Strokes • Seizures • Interactions with MAOI
Dong quai	*Angelica sinensis*	–	• Oestrogen effects • Health promoting	• Contains coumarin derivatives • Prolongs PT/INR§, aPTT‖ • Gynaecomastia
St John's wort	*Hypericum perforatum*	• Depression • Anxiety • Sleep disorders	–	• Serotoninism • Drug interactions with cyclosporine, digitalis, MAOI, warfarin, oral contraceptives, theophylline • Sedative effect

* PONV postoperative nausea and vomiting
† MAOI monoamine oxidase inhibitors
‡ PAF platelet-activating factor
§ PT/INR prothrombin time/international normalised ratio
‖ aPTT activated partial thromboplastin time

Coagulation disorders

Herbs affect coagulation by interfering with platelet functions or potentiating the effects of the anticoagulant warfarin.[9] There have been case reports on the potential bleeding risks of some commonly used herbs (Table 1). Serious bleeding problems have been related to ginkgo. For example, a 61-year-old man developed subarachnoid haemorrhage after taking 120 mg of ginkgo extracts daily for 6 months. His bleeding time normalised after discontinuing the herb.[10] Elsewhere, left frontal subdural haematoma was diagnosed in a 72-year-old woman taking 150 mg of ginkgo daily for 6 months.[11] Ginkgo has also been reported to be associated with intracerebral haemorrhage and bleeding after laparoscopic cholecystectomy. It is perhaps surprising, then, that abnormal bleeding has not been reported in formal randomised clinical trials involving hundreds of patients taking ginkgo extracts to improve cognitive function in dementia or Alzheimer's disease.[12] In one such study, a dose of 120 mg/day for 1 year was used. However, the risk of bleeding from ginkgo cannot truly be assessed. Of all the active constituents, ginkgolide B was found to inhibit platelet-activating factor (PAF),[13] which is important for triggering platelet aggregation and

increasing microvascular permeability. It is still uncertain whether ginkgolide B extracted from ginkgo leaves and root would explain the bleeding episodes reported in the medical literature.

Garlic is generally consumed as a food, a herb, and as herbal tablets. It has been associated with postoperative bleeding after transurethral resection of the prostate in case reports.[14] Spontaneous spinal epidural haematoma developed in an elderly man after taking 2 g of garlic daily for an unknown period. He eventually made a good recovery after he stopped taking the herb.[15] In vitro studies have shown that the garlic constituents allicin[16] and ajoene[17] are antiplatelet agents, which cause decreased thromboxane formation and altered arachidonic acid metabolism. In vivo studies, however, have produced conflicting results. For example, an antiplatelet effect was not demonstrated in a randomised placebo-controlled trial of healthy men fed with unaged garlic extract. By contrast, aged garlic extract had a more consistent antiplatelet action.[18] Ginger is another common food and herb. It decreases platelet aggregation through inhibition of thromboxane synthetase,[19] although adverse bleeding has not been reported. The antiplatelet effect of ginger might be dose- and preparation-dependent.

Herbs may interact with coadministered warfarin to produce bleeding diathesis. Danshen (丹參) (*Salvia miltiorrhiza*) is normally taken for its hypotensive, positive inotropic, antiplatelet, and coronary arterial vasodilatory effects.[20-22] It is prescribed in China for atherosclerosis-related diseases. There were reports of increased international normalised ratio (INR) values, ranging from 5.5 to 8.4,[23,24] in patients taking warfarin and danshen together. The INR returned to its previous level after discontinuing the danshen. Apart from inhibition of platelet aggregation, danshen possesses antithrombin III–like activity and promotes fibrinolysis.[25] Pharmacokinetic studies have shown that danshen increases the maximum concentration of warfarin and decreases its clearance, resulting in an overall increase in anticoagulatory effect.[25]

Other herbs contain coumarins, which are natural vitamin K antagonists. Dong quai (當歸), for example, contains six coumarin derivatives. A 46-year-old woman taking warfarin 5 mg/day consumed dong quai for her menopausal symptoms. Her INR increased to 4.9 before returning to the normal range 1 month after discontinuing the herb.[26] Similar to danshen, both pharmacokinetic and/or pharmacodynamic interactions between dong quai and warfarin may be present.

In summary, special precautions should be exercised in patients taking anticoagulants together with herbs that exhibit antiplatelet or coumarin-like effects. Although randomised trials with ginkgo, garlic, and ginger have not revealed abnormal bleeding complications, anaesthesiologists should be aware of this possible risk. Danshen and dong quai are contraindicated in patients taking warfarin.

Cardiovascular side-effects

Cardiovascular instability can be hazardous to patients during the perioperative period. *Panax ginseng*, the well-known tonic and stimulant, was reported to cause tachycardia or hypertension, particularly in patients taking other stimulants or those with known cardiovascular diseases.[27]

St John's wort is sold over-the-counter (OTC) to treat depression and promote wound healing. It inhibits the reuptake of serotonin and noradrenaline.[28] It also inhibits monoamine oxidase (MAO),[29,30] which accounts for the antidepression effect. Such mechanisms create the potential for important drug interactions with central nervous system (CNS) medications, sympathomimetic agents, and pethidine. Precautionary measures similar to those for patients taking conventional MAO inhibitors (MAOI) should also be applied in patients taking St John's wort.

Ma huang (麻黃) is another Chinese herb, which is used in the treatment of respiratory illnesses. However, many adverse effects have been reported, including stroke, memory loss, behavioural changes, and panic attacks.[31] By virture of its ephedrine content, ma huang has been reported to enhance the sympathomimetic effects of guanethedine. It can also cause disturbances of cardiac rhythm in conjunction with cardiac glycosides or halothane. Hypertension has been reported with concomitant ma huang and oxytocin therapy.[32]

Water and electrolyte disturbances

Antihypertensives, such as diuretics, commonly cause electrolyte disturbances. Goldenseal (桔梗) (*Hydrastis canadensis*) is used as a natural antibiotic and as an aquaretic: when it is taken, only water is excreted from the kidneys. Thus, concurrent administration of goldenseal with a diuretic will decrease the antihypertensive effect of the latter, particularly because sodium is retained in the body.[31]

Licorice root (甘草) (*Glycyrrhiza glabra*), which is used for chest ailments, as well as heart and gastrointestinal problems, has been reported to cause hypertension, hypokalaemia, sodium retention, and oedema. These effects should return to baseline 3 weeks after stopping the herb. The postulated mechanism of action of licorice root is disruption of corticosteroid metabolism, resulting in prolongation of cortisol's half-life and aldosterone-like effects.[32]

Endocrine effects

There are case reports of ginseng causing postmenopausal bleeding and mastalgia.[33,34] The mechanism of action by which this occurs also relates to augmentation of corticosteroid effects.[31] American ginseng may also affect blood sugar control. In non-diabetics, the herb can attenuate postprandial hyperglycaemia if taken 40 minutes before the 25 g glucose challenge. In type 2 diabetics, postprandial

hyperglycaemia is attenuated, regardless of whether the herb is taken before or at the time of the glucose challenge.[35] Other herbs, such as bitter melon, fenugreek, gurmur, goat's rue, and bilberry, are reported to have hypoglycaemic effects.

Saw palmetto (銀棕櫚) (*Serenoa repens*) is believed to be useful for benign prostatic hypertrophy. It acts by inhibiting dihydrotestosterone binding at androgen receptors and decreasing 5α-reductase activity on testosterone.[31] Echinacea (松果菊/紫椎花) (*Echinacea purpurea)*, another natural antibiotic, has immunostimulating properties. It may interact with cyclosporine and steroids, decreasing their active effects.[31]

Dong quai is widely believed to possess oestrogen-like activities. However, Liu et al[36] were able to show only weak binding of dong quai extracts to oestrogen receptors. Gynaecomastia was reported in a man who ingested dong quai pills, although it was alleged in this case that the pills he took may have contained a higher phytoestrogen content than the original herbal product.[37]

Potential for hepatotoxicity

It is vitally important to be aware of the possibility of liver damage by herbal medicines. Valerian (纈草) (*Valeriana officinalis*), skullcap, and chaparral-containing herbal tea have all been reported to be associated with acute hepatitis.[38] One Chinese herbal preparation, jin bu huan, which is a sedative and analgesic, has caused seven cases of acute hepatitis.[39]

Herbs may also enhance the hepatotoxic effects of other pharmaceutical drugs. Chronic use of echinacea, for example, can potentiate the liver toxicity of agents, such as steroids, amiodarone, methotrexate, ketoconazole, and halothane. The concurrent use of echinacea with these drugs is thus not recommended.[31]

Prolongation of the effects of anaesthetic agents

Various herbs can prolong or potentiate the effects of anaesthetics. Valerian is most commonly employed as a sedative herb. A randomised double-blind study revealed a significant decrease in sleep latency with a nightly dose of 450 mg of valerian compared with placebo.[40] This herb has the potential to prolong thiopentone- and pentonbarbitone-induced sleep,[41] and is thus not recommended for use with barbiturates.

Kava kava (卡瓦胡椒) (*Piper methysticum*) is a herbal anxiolytic used for insomnia and nervousness. Long-term use of kava kava is not advisable because of the possibility of developing tolerance to the herb, called kawaism. This is characterised by dry, flaking, discoloured skin, and reddened eyes. Concomitant use of kava kava with benzodiazepines could result in potentiation of the latter's effects. There was a case report describing a 54-year-old man on regular alprazolam, cimetadine, and terazosin therapy who went into a coma for several hours after consuming kava kava concurrently for 3 days.[42] This kava kava–benzodiazepine interaction was thought to be related to the weak agonist effect of α-pyrone, the active component of the herb, on the γ-aminobutyric acid (GABA)/benzodiazepine receptor.

In treating depression, St John's wort can produce sedation and confusion. However, the suggestion that St John's wort may prolong anaesthesia has not been confirmed in controlled clinical studies.[43] The postulated mechanism of action of St John's wort is inhibition of synaptic reuptake of serotonin, noradrenaline, and dopamine.[44] Down-regulation of cortical β-adrenoreceptors and up-regulation of postsynaptic serotonin 5-HT_{1A} and 5-HT_2 receptors may also play a part.[45]

Commonly used herbal medicines in Hong Kong

In TCM, herbalists previously prescribed herbs in fresh, dried, or processed forms. A combination of herbs is decocted in a pot of water over heat for several hours to make the tea. Different diseases in different persons required different combination of herbs. Nowadays, some herbal combinations are made into powder, concentrates, or tablets. These products can be prescribed by a herbalist or bought OTC for the treatment of specific ailments. Herbs can also be used externally in the form of various creams, gels, oils, aromatics, or baths. Some are preserved in alcohol or vinegar. Herbs may be found in dietary supplements or health foods claiming to promote wellness. Traditional Chinese medicine emphasises a holistic approach to care, recognising that diet is important in promoting health, as well as treating or preventing diseases. Indeed, some herbs have become part of the normal Chinese diet in soups or spices. Clearly, it is essential to be aware of some of the common herbs and their anaesthetic implications, which will be discussed.

Ginger (Zingiber officinale)

The rhizome of ginger is used as a herbal medicine and food component. Western herbalists believe it is useful for healing respiratory ailments. It helps to relieve nasal congestion, sore throats, and decrease headaches and body aches. Its effectiveness is enhanced by the addition of other herbs. It also helps to decrease motion sickness, particularly during pregnancy. Ginger is used in TCM to expel the 'cold', 'wind', and 'damp' 'evils', and it can stop the reverse flow of 'Qi'.

Ginger has been studied as an antiemetic after gynaecological and day-surgery operations. Early studies showed a positive effect. For example, in a randomised placebo-controlled study of 60 women undergoing major gynaecological operations, ginger root was similar to metoclopramide, and both the herb and drug were better than placebo in reducing the incidence of postoperative nausea and vomiting (PONV).[46] However, recent studies involving larger

numbers of patients and different doses of ginger were unable to show a benefit over placebo. One such study showed that both 2 g of ginger root and droperidol 1.25 mg were ineffective in reducing PONV after out-patient gynaecological laparoscopy.[47] A systematic review that pooled the absolute risk reductions in the incidence of PONV in randomised clinical trials found no significant difference between ginger and placebo.[48] In pregnant women, 1 g of ginger can reduce hyperemesis gravidarum,[49] but this must be balanced against possible mutagenic effects. The postulated antiemetic mechanisms of ginger include actions at the gut and brain. The 6-gingerols in ginger can enhance gastrointestinal transport and galanolactone, another active constituent, can act as a competitive antagonist at serotonin 5-HT_3 receptors. The central action of 6-gingerols is effective in seasickness and chemotherapy.

The antiplatelet effect of ginger demands extra caution, as this herb is present in many food products. If the concomitant use of ginger in patients taking anticoagulants cannot be avoided, the clotting profile should be monitored very closely. This notwithstanding, further studies are needed to determine whether this will affect the choice of regional anaesthetic technique(s) in patients who regularly consume this herb.

Garlic (Allium sativum)

The use of garlic as a herb in China was described in Ming Yi Bei Lu (Miscellaneous Records of Famous Physicians) written at about AD 510. Garlic is prescribed as a diuretic, expectorant, antimicrobial, and antidiarrhoeal agent. It is useful in breaking the 'cold' and removing the 'damp' 'evils'. Blood flow and 'Qi' can be re-established and the 'stomach' and 'spleen' strengthened.

Garlic has natural antimicrobial properties that do not disrupt the body's normal flora. It is effective against *Helicobacter pylori* and good for other infections, such as common colds. The herb industry claims that garlic promotes leukocytosis and lowers blood pressure and serum lipids. A meta-analysis of eight randomised controlled trials demonstrated a reduction in systolic and diastolic blood pressure in three and four trials, respectively.[50] The effect on serum cholesterol, however, is controversial. Some studies showed a reduction in serum cholesterol and triglyceride levels with 900 mg of garlic daily for 12 weeks,[51] whereas others did not. A recent meta-analysis of 13 randomised controlled trials showed that although garlic is superior to placebo in reducing total cholesterol levels, the size of the effect is modest and its robustness is debatable.[52] The antiplatelet effect of garlic has important implications for clinicians and the importance has been discussed previously.

Ginkgo (Ginkgo biloba)

Ginkgo has been used as a medicinal plant for centuries in China and Japan. It is also very popular in Europe as a herbal treatment to improve cognitive function in dementia. It contains several flavonoids and terpenoids (eg ginkgolides), which can act as free radical scavengers. Ginkgo was found to be superior to placebo in improving cognitive function in a study of 2020 patients with dementia without significant complications.[12] Other herbal uses include alleviating asthma, angina, and eye ailments. Chinese herbalists also prescribe ginkgo tree seeds and leaves for respiratory symptoms, such as cough and sputum production. Although ginkgo can improve cognitive function, ginkgo leaves may contain a neurotoxin that can lower the seizure threshold.[53] This neurotoxin is thought to antagonise the action of vitamin B_6. Epileptic patients should be advised not to take ginkgo, as it may decrease the efficacy of anticonvulsants. Drugs that can decrease seizure threshold, such as tricyclic antidepressants, should not be taken concomitantly with ginkgo.

Ginseng

Ginseng is described in the Shen Nong Bencao, and is used in TCM as a superior herb for tonification of the 'heart, liver, spleen, lung, and kidney'. It can stimulate the body, increasing the ability to cope with fatigue and physical stress. There are several types of ginseng for medicinal use including American ginseng *(Panax quinquefolius)*, Oriental ginseng *(Panax ginseng)*, and Korean red ginseng. The active constituents vary according to the different species. Ginseng is consumed as a raw herb, a powder, or made into ginseng tea. It is believed to be 'heat raising' for the haematological and circulatory systems.

Ginsenosides are the active constituents found in ginseng. The ginsenoside R_b-1 in American and Oriental ginseng has been shown to exert a neuroprotective effect by blocking the inactive state of sodium channels and preventing abnormal influx of sodium during ischaemic episodes.[54] It also helps to regulate GABAergic transmission in the brainstem.

The hypoglycaemic effect of ginseng in diabetic patients is related to the ginsenoside R_b-2. Korean red ginseng has been shown to improve endothelial dysfunction in hypertensive patients, possibly through increasing synthesis of nitric oxide.[55] The ginsenosides R_g-1 and R_b-1 can also relax pulmonary vessels.[56]

The reported adverse effects of ginseng include insomnia, headache, hypertension, and vomiting.[57] Ginseng can also decrease platelet adhesiveness[58] and antagonise PAF,[59] but adverse bleeding has not been reported. On the contrary, ginseng was reported to have decreased the anticoagulatory effect of warfarin in a 47-year-old man with a mechanical heart valve. The INR decreased from 3.1 to 1.5 after 2 weeks of taking ginseng and returned to 3.3 after discontinuing the herb.[60] The exact mechanism of action is unknown, but may be related to vitamin K antagonism.

Ma huang (Ephedra sinica)

Ephedra is a widely grown family of herbs. It has been used to relieve asthma and other respiratory ailments in China for more than 4000 years. Ephedra is also used in herbal medicine for headache, fever, cold, and hay fever. The

active alkaloids found in ephedra are mainly ephedrine and pseudoephedrine. Ephedrine is an indirect-acting sympathomimetic agent commonly employed to treat mild hypotension in anaesthesia. Apart from being a bronchodilator and nasal decongestant, it can stimulate the CNS. It can also increase the body's metabolic rate and is thus currently being investigated for use in obesity. Herbal tablets for colds and allergies may contain ephedra, and dieters have used this herb to suppress appetite.

There are concerns about the cardiovascular and CNS side-effects of ephedra. Among the 140 adverse events relating to the use of this herb reported to the FDA, 31% could be directly attributed to ephedra alkaloids. Cardiovascular symptoms, such as hypertension, palpitations, and tachycardia, and CNS symptoms, such as strokes and seizures, accounted for 47% and 18%, respectively, of the adverse events associated with ephedra alkaloids. Permanent disability and even death have been reported.[61] Indiscriminate use of ephedra has to be advised against in view of all of these adverse effects.

Dong quai (Angelica sinensis)

Dong quai is a herb commonly used in the Chinese community to promote health in women and, in combination with other herbs, to treat menopausal or menstrual complaints. Apart from phytoestrogens, it contains coumarin-like substances and vitamins E, A, and B_{12}. The balancing effect on women's health may be related to the acids and various polysaccharides contained in the root of dong quai, which cause relaxation of peripheral blood vessels. Dong quai is contraindicated in patients taking warfarin and can cause gynaecomastia in men.[37]

St John's wort (Hypericum perforatum)

St John's wort is used as a herbal remedy, particularly in Germany, to ease depression, anxiety, and sleep disorders. A meta-analysis of 23 randomised clinical trials involving 1757 patients concluded that 300-1000 mg/day of St John's wort extract was superior to placebo, and similar to conventional tricyclic antidepressants, in the treatment of depression. It also had fewer side-effects than the comparator antidepressants.[62] In a recent trial of 324 patients in Germany, 250 mg of St John's wort twice daily was found to have equivalent antidepressant efficacy to that of imipramine 75 mg twice daily after 6 weeks of treatment, but with fewer side-effects.[63]

St John's wort induces the activity of hepatic cytochrome CYP3A4,[64] and reduced therapeutic efficacy has been reported with drugs, such as cyclosporine, digoxin, warfarin, oral contraceptives, theophylline, digoxin, and indinavir. Discontinuing St John's wort after protracted use may lead to a rebound increase in plasma concentrations of these drugs. As St John's wort inhibits MAO and reuptake of serotonin and noradrenaline, it has the potential to prolong the effects of anaesthetics and cause cardiovascular side-effects. Patients taking St John's wort should avoid tyramine-containing foods so as to prevent the serotonin syndrome. Concomitant use of sympathomimetic amines or MAOI with St John's wort is not advised. The herb should be stopped 2 weeks before surgery to avoid interactions with anaesthetic drugs.

Miscellaneous herbs

There are also other fairly toxic herbs for which problems have been reported. *Aconiti radix*, one of the alleged contents of mafesian, is used as an analgesic for joint pains and headache in TCM. It can bind to the tetrodotoxin binding site of sodium channels, suppressing their inactivation, and cause laboured breathing and ventricular arrhythmias. Thorn apple, another alleged constituent of mafesian, can be used to treat cough, asthma, and arthralgia. It contains atropine, hyoscyamine, and hyoscine, and has been used in China as a herbal anaesthetic.[65] The use of these toxic herbs must be carefully regulated.

Conclusions

Herbal products may affect normal functions of the body and cause adverse drug interactions. Recent studies have uncovered some of these mechanisms, but much remains unknown. Some herbs cause problems when taken in large quantities or for prolonged periods, while others may affect perioperative care even when taken in small quantities in susceptible patients. Before all relevant potential adverse herb-drug interactions have been elucidated, anaesthesiologists should adopt a prudent attitude in the perioperative care of patients. A history of taking herbal medicine must be obtained in all patients. If in doubt, a herbal medicine should be stopped for 2 weeks before proceeding to anaesthesia and surgery.

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