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ABSTRACT

The use of herbal medicines has increased dramatically over the past few years. The United States alone noted a 380% increase in the consumption of these products. Although the common practice of taking over-the-counter herbal soups, herbal teas and other such prepacked preparations was not associated with adverse events at large, still, some herbs are known to cause problems, especially when large doses are taken. The American Society of Anaesthesiologist (ASA) has taken a conservative stance and recommended that it is prudent to stop these products at least 2–3 weeks prior to anaesthesia and surgery. This advice may be difficult to implement as most preoperative evaluations occur only a few days prior to surgery. Some of the Ayurvedic preparations have shown to improve the patient outcome when taken during the perioperative period. Hence, the conservative stance by ASA may not always benefit the patient. More scientific studies are needed to have more targeted recommendations. This article puts forward the facts that need to be addressed by researchers in the future.

Key words: Amla, curcumin, garlic, giloe, ginger, ginseng, guggul, therapeutic claims, tulsi

INTRODUCTION

"A potent poison becomes the best drug on proper administration. On the contrary, even the best drug becomes a potent poison if used badly".

Charakacharya in Charak Samhita

The history of modern medicine and herbal medicine is inextricably intertwined. The word "drug" is derived from an ancient word for "root" and, thus, by definition, herbs are drugs. According to the World Health Organization (WHO), 121 prescription medicines are produced directly from plant extracts. Seventy per cent of the patients do not reveal their use of herbal medicines to treating physicians considering "Natural means safe".^[1,2]

A PUBMED and MEDLINE search was conducted using keywords: Garlic, Ginger, Ginseng, *Curcumin*, Tulsi, Amla, Guggul, Giloe, Therapeutic claims. Apart from indexed journals, peer – reviewed non indexed journals were also analysed. Polyherbal preparations were not considered.

AMERICAN SOCIETY OF ANAESTHESIOLOGIST GUIDELINES

In the United States, Ayurveda is considered complementary and alternative medicine (CAM). Because herbs are considered as dietary supplements, they do not meet the same standards and regulations as that of the pharmaceutical industry. The July 2001 issue of JAMA discusses extensively the use of herbal medicines in the perioperative settings.^[1] The American Society of Anaesthesiologist (ASA) has acknowledged the adverse reaction potential of herbal medicines and recommended patients to "stop taking all herbal medications two weeks before surgery".^[1] The ASA has also published a bulletin, "What you should know about herbal and dietary supplement use and anaesthesia" for patient awareness.^[3] However, these recommendations are difficult to implement as most preoperative checks are carried out only a few days prior to the surgery.

In a first of its kind study, Anna Lee and coworkers allowed patients to take herbal products in the

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perioperative period, and the complications arising from this were studied. The researchers concluded that the common practice of taking over-the-counter herbal tea or soups is not detrimental; however, taking traditional Chinese herbal medicines (TCHM) by prescription before surgery is likely to cause problems as they contain potent herbs at higher doses.^[4]

AN OVERVIEW OF THE COMMONLY USED AYURVEDIC MEDICINES

There are a very few randomized double-blind controlled studies available to validate the claim and to study the potential hazards of herbal medicines. The adverse effects can be because of the overdose, contamination or mistaken medicinal plant. There can be an adverse herb–drug or herb–herb interactions.^[2]

Ginger (Adraka, Sunthi, Zingiber officinale, Zo)

In Ayurveda, ginger is commonly prescribed for nausea, vomiting, motion sickness, sore throat, respiratory congestion, hypoglycaemia and vertigo. The Gingerols, in particular 6-gingerol, which give its characteristic taste along with Galanolactone are identified as the active ingredients of the ginger.^[5] The symptoms of seasickness were far lesser in those volunteers who received 1 g of ginger 4 hrs prior to the travel.^[5] One gram of ginger per day in four divided doses offered great symptomatic relief in hyperemesis gravidanum patients.^[6] In patients suffering from leukaemia, ginger reduces the chemotherapy-induced vomiting significantly. Bone and colleagues compared 1 g ginger with 10 mg metoclopramide and a placebo in patients undergoing gynaecological laparoscopic surgeries. During the first 24 hrs, the incidence of nausea was least with ginger as compared with metoclopramide, although it was not statistically significant.^[7] There are many mechanisms that are postulated for the antiemetic action of ginger. 6-gingerols enhances gastrointestinal transport; also, galanolactones are competitive antagonists at ileal 5HT₃ receptors.^[5] Because the herb is commonly used as a food component, one can assume it to be safe. There are reports suggesting that ginger can be mutagenic.^[1] Ginger has been found to cause hyperglycaemia. It is also found to be a thromboxane synthatase inhibitor; thus, it can prolong the bleeding time.^[1] Studies available in which the safety profile of ginger "is tested in patients on anticoagulants, non steroidal anti inflamaratory drugs (NSAID) and colleagues have advised caution for regional anaesthesia in patients who are consuming ginger regularly.^[1]

Garlic (Allium sativum L, As)

During both World Wars I and II, soldiers were given garlic to prevent gangrene. Garlic clove when crushed activates the enzyme allinase, which converts allin to allicin, an active form of garlic, liberating sulphur, which gives garlic its characteristic smell.^[1] In Ayurveda, garlic is used as a natural antibiotic. It is prescribed as antitussive, expectorant, diuretic, lipid and blood pressure lowering drug. Twelve per cent reduction in serum cholesterol and serum triglycerides is achieved by 600-900 mg of garlic everyday for 1 month.^[8] Garlic causes a fall in the systolic blood pressure more than the diastolic blood pressure, and is found to be useful in the treatment of mild hypertension.^[9] Garlic, by strengthening the immune system, helps the body fight diseases such as cancer. People who have garlic in their diet are less likely to develop certain types of cancers, namely colon, stomach, breast, larynx and prostrate.^[10] Dietary garlic can also reduce the side-effects of chemotherapy, such as anorexia and fatigue.^[11] Aged garlic extract has been shown to delay the reperfusion or ischaemia-induced neuronal injury.^[12] Garlic is considered safe by US FDA as it has very low toxicity. The side-effects of garlic include stomach upsets, bad breath, bad odour and, rarely, skin rashes. Garlic has blood-thinning properties. Spontaneous spinal epidural haematoma has been reported in an old man taking 2 g of garlic for an unknown period.^[1] Garlic has also been associated with postoperative bleeding following trans urethral resection of prostrate (TURP.)^[1] Allicin and ajoene, the main constituents of garlic, are antiplatelet agents. In vitro studies have shown that both can decrease thromboxane formation and alter arachidonic acid metabolism. They can also block cyclooxygenase pathways and prevent formation of inflammatory prostaglandins.^[1] Garlic can enhance the effects of NSAIDs, aspirin, warfarin, heparin and other antiplatelet agents. It is advised to discontinue garlic at least 7 days prior to surgery due to its antiplatelet effects.^[1] However, dietary use is safe.^[13]

Indian Ginseng (*Withania somnifera, Ws*, Ashwagandha, Winter Cherry, Ajagandha, Kanaje, Ayamodakam, Samm Al Ferakh, Amukkrang Kilangu)

Ashwagandha, in Sanskrit "horse's smell", refers to the odour of its root that resembles horse's sweat. In Latin, somnifera means sleep inducing. Ashwagandha is used in Ayurveda in a similar way to that of ginseng in TCHM. It is one of the most expensive and most widely used herb in the world. Ginsenoside, an active compound in ginseng, is sympathomimetic.^[1] The drug is abused by the athletes to increase their energy levels. Ginsenosides can also interact with mono amine oxidase inhibitors (MAOI) and can cause manic episodes in patients with MAOI^[1] Ayurveda recommends this herb as an aphrodasiac, antiaging and energy-enhancing tonic. Adverse effects of ginseng may include irritability, insomnia, hypoglycaemia, hypertension, skin rashes and nervousness.^[1,2] Ginseng can cause tachycardia and hypertension, particularly in those patients who are on other stimulants or have a cardiovascular disease. The herb is shown to attenuate postprandial hyperglycaemia in both type 2 diabetics as well as in normal healthy individuals.^[14] Ginseng interacts with oral anticoagulants, antiplatelet agents, corticosteroids and hypoglycaemic agents.^[1] Herb may predispose the patient to perioperative bleeding.^[1] It may be a concern for neuroaxial blockade. Ginseng should be avoided for at least 7 days before surgery. Patients who are on NSAIDs, aspirin, warfarin, other antiplatelets and on oral hypoglycaemic agents need special attention.^[1]

Turmeric (Curcumin Ionga, CI, Haldi, Sarvoshadhi)

In Sanskrit, turmeric is called as sarvoshadhi, meaning medicine for all diseases. Turmeric, which was used initially as a dye and food component, is nature's most powerful healer. Curcumin is the main constituent, which gives turmeric its vellow colour. Turmeric is used historically as an antiseptic, antibacterial, anti-inflammatory, pain killer, hepatoprotector, cosmetic cream and as a weight-reducing herb. In vitro and animal studies suggest the *curcumin* may have antitumour, antiarthritic, antioxidant and antiinflammatory activities.^[15] Turmeric is a natural cox2 inhibitor.^[16] In vivo, curcumin has been found to inhibit the formation of beta amyloid oligomers and fibrils in the brains of Alzheimer's disease patients.^[17] Curcumin acts as a free radical scavenger and is also a potent inhibitor of cytochrome P450 and hence can decrease the metabolism of drugs like alfentanyl, midazolam, lignocaine, calcium channel blockers, warfarin and theophylline. In TCHM, curcumins are used to treat depression and stress. This is supported by the fact that *curcumins* reversed impaired hippocampal neurogenesis,^[17] which is responsible for stress, depression and anxiety. The various studies have described cell proliferation and cell survival pathways to prove the anticancer effect of curcumin. It is used widely in the treatment of colonic, breast and prostrate cancer. It is also useful in leukaemia, multiple myeloma and pancreatic cancer.^[18] A combination of ginger and *curcumin* has been shown to increase collagen production and is found useful in "at risk" skin in reducing the formation of nonhealing wounds.^[19] *Curcumins* have been found to reverse paracetamolinduced liver damage, and are useful in toxic liver injuries.^[20] *Curcumin* has been found to be safe even at high doses of 2–10 g. Very rarely, *curcumin* may cause iron deficiency in susceptible individuals.^[21] *Currently*, there are no recommendations regarding the use of *curcumins* in the perioperative period.

Tulsi (Oc*imum sanctum Linn, Os*, Holy Basil, Maduruthala)

Charakacharya in Charaksamhita described Tulsi as elixir of life for its diverse healing properties, and is also believed to promote longevity. In Ayurveda, Tulsi is recommended for respiratory diseases such as bronchitis, common colds, bronchial asthma, heart diseases, malaria, diarrhoea, skin diseases, arthritis, chronic fever and insect bite. It is also used as an anticancer, antidiabetic, antifungal, hepatoprotective, antiemetic, analgesic, adaptogenic and antispasmodic. Tulsi can be taken in many forms, such as herbal tea, dried powder or fresh leaf. Eugenol has been identified as the active constituent of Tulsi, which is responsible for its therapeutic effects.^[22] In one study, 27 type 2 diabetics on oral hypoglycaemic drugs when supplemented with Tulsi powder showed a considerable reduction in blood glucose, glycated protein, total amino acids, total cholesterol, low density lipoproteins (LDL), very low density lipoproteins (VLDL) and serum triglycerides, but the high density lipoproteins (HDL) was normal.^[22] However, in another study, the HDL was found to increase.^[23] The extract of Os improved memory deficits and learning associated with Alzheimer's disease.^[24] The effect was due to the antioxidant activity of Os. Tulsi has been found to protect against noise-induced stress.^[25] It is also found to protect the heart from chronic restraint stress in animal experiments. Os is also useful in preventing drug-induced extrapyramidal side-effects.^[26] Os has been shown to possess significant antioxidant and wound-healing activities, which may be useful in the management of abnormal healing such as keloids.^[27] There are no known side-effects of Tulsi. Currently, there are no recommendations for the use of Tulsi in the perioperative period.

Amla (*Emblica officinalis, Eo*, Amalaki, *Phyllanthus emblica*, Indian gooseberry, Dhatriphala)

Ayurveda believes that amala can maintain balance between all three doshas. It is used in two of the most commonly consumed Ayurvedic preparations, namely chyawanprash and trifala. Amla is the richest natural source of Vitamin C. One hundred grams of amla contains 700 mg of Vitamin C, which is 30-times the amount found in oranges. In addition, it also contains sugar, phosphorus, tannic acids, carbohydrates, protein, iron and calcium. In Ayurveda, amla is used to treat hyperacidity and ulcers. It is also used as a cardiotonic, to build up immunity, improve eye sight, regulate the sugar, free radical scavenger, increase haemoglobin, reduce cholesterol and for asthma. Amla has shown to reduce elevated serum creatine and blood urea nitrogen in aged rats. Thus, it would be a very useful antioxidant for the prevention of agerelated renal disease.^[28] Topical application of amla has been found to accelerate wound healing in in vivo studies.^[29] Amla extract has been found to reverse the atheromatous plaque formation in the blood vessels of rabbits.^[30] It has been shown to decrease serum cholesterol, triglycerides, LDL, VLDL, C-reactive protein and increase HDL, haemoglobin, red blood cells (RBCs) and other cells in human studies. Thus, amla, by reducing dyslipidaemia and inflammation, decreases the risk of coronary artery disease.^[30] In uremic patients, amla decreases the oxidative stress by increasing the plasma antioxidant power.^[31] As such, there are no side-effects of amla; however, it is not advisable to take amla during the night time as it may be bad for the teeth. There are no targeted recommendations for amla by ASA.

Guggul (*Commiphora mukul*, *Cm*, Indian Bdellium gum, guggulipid)

Guggul has been used for the treatment of heart diseases since historic times. It is found in northern India, Rajasthan and Gujrat. G.V. Satyavati in 1966 published the first study of the effects of guggul on rabbits.^[32] After the mid-1990s, there was a considerable interest shown by the western world in guggul as a hypocholesterolaemic drug. In Ayurveda, it is considered as an antioxidant, anti-inflammatory, hypolipidaemic, antiobesity herb.

The Z and E isomers of guggulosterone are biologically active constituents of guggul and are responsible for its therapeutic effects.^[32] Numerous clinical studies have reported its hypolipidaemic effect. In the study by Nityanand *et al.*, when patients were given 500 mg of guggul daily for 12 weeks, total cholesterol and triglycerides were reduced by 24% and 23%, respectively.^[33] When guggul was compared with clofibrate, it showed an identical fall in serum cholesterol and triglycerides. However, clofibrate had no effect on HDL while guggul increased HDL in 60% of the patients.^[33] It has been found that guggul, along with dietary modifications, can further reduce total cholesterol, LDL and triglycerides by 11.7%, 12.5% and 12%, respectively.^[32] After treatment with guggul for 6 months in 200 patients with ischaemic heart disease with abnormal electrocardiogram (ECG), a fall of 39%, 51% and 32% in total cholesterol, triglycerides and total blood lipids was seen, with 26% of the patients having a normal ECG and another 59% showing improvement in ECG.^[32] Guggul has been shown to decrease high-sensitivity C-reactive protein (hs-CRP), an index of inflammation, by 29%.^[33] Guggul at 500 mg three-times a day when given to knee arthritis patients improved their Western Ontario and McMaster Osteoarthritis index total score.^[32] Guggul is regarded as a generally safe drug, with a few side-effects like mild nausea and hiccup. Currently, there are no targeted guidelines on the use of guggul in perioperative settings by ASA.

Giloe (*Tinospora cordifolia, Tc,* Guduchi, Gulvel, Gulancha, Somida, Sindal, Sittamrytu)

In Sanskrit, Tc is called as guduchi, meaning plant that protects from diseases. In Avurveda, Tc is advocated as cardiotonic, expectorant, aphrodisiac, antiasthmatic, analgesic, antipyretic, anti-inflammatory and antidiabetic.^[34] The phytochemical analysis of Tc shows that it has numerous alkaloids, sterols, lactones and glycosides,^[34] the prominent being clerodane furanoditerpene glycoside, cordioside, syringin, cordifolioside A and B and cordiol.^[34] The antidiabetic effect of *Tc* is attributed to its antihyperglycaemic, renoprotective, antihyperlipidaemic and antioxidant effect. The animal studies in the late 1960s have been shown to increase glucose tolerance and decrease fasting blood sugar.^[34] In alloxan-induced diabetic rats, a 5 g/kg dose of the aqueous extract of Tc was found to be equivalent to 600 μ g/kg glibenclamide, but was not as effective as protamine zinc insulin 6 U/kg.^[34] The effect of Tc is found to be maximum with mild and poor with severe hyperglycaemia.^[34] *Tc* is valuable in reducing albuminuria and polyuria associated with diabetes.^[34] *Tc* is found to be better than glibenclamide, but not as well as protamine zinc insulin, in controlling hyperlipidaemia.^[35] Tc has been found to delay the diabetic cataracts.^[34] An aqueous extract of Tc when given to diabetic foot ulcers patients showed a statistically significant reduction in the number of surgical debridements.^[36] The Tc has been found to be effective against drugs causing insulin resistance, namely dexamethasone and fructose.^[37] In obstructive jaundice patients, when Tc 16 mg/kg/day was added to conventional treatment, it showed a reduction in the mortality rate from 61.54% to 25% in patients with percutaneous transhepatic biliary drainage (PTBD) and from 39% to 6.25% in patients without PTBD, with less patients developing septicaemia,^[38] improved appetite and decreased nausea in the Tc group.^[38] The asymptomatic hepatitis B carriers showed a three-times higher rate of seroconversion (37.5% versus 11.1%) when treated with Tc than when treated with placebo. In cirrhotic patients, Tc therapy showed an improvement in the Child-Pugh scores, shortened the prolonged antipyrine half-life and increased the phagocytic and killing capacity of monocytes.^[34] The antioxidant effects of *Tc* have been studied in animal and in *in vitro* studies. Tc is found to be useful in ischaemic brain damage, ischaemic myocardial damage and radiation toxicity.^[34] Tc has been shown to offer protection against infections induced by Escherichia coli, Staphylococcus aureus, Candida albicans and Klebsiella pneumoniea.^[34] Tc promotes leukocytosis with neutrophilia in a dosedependant manner.^[34] Tc, when given as an adjuvant to chemotherapy to tuberculosis patients, showed an improvement in the clinical symptom score and weight gain, reduced the sputum conversion time and fastened the radiological recovery.^[34] In thermal burns patients, Tc therapy had increased the survival rate, IgG levels and white blood cell count.^[34] When Tc-pretreated rats were exposed to stress, they showed significant decrease in the stress-induced rise in plasma corticosteroid levels.^[34] Tc has antineoplastic activity and it protects from chemotherapy-induced toxicity.^[34] Tc also has anti-inflammatory, analgesic, antipyretic, antiallergic and diuretic properties.[34] Numerous safety studies have shown Tc to be a safe drug.^[34] Currently, there are no targeted guidelines by ASA on the use of *Tc* in perioperative settings.

CONCLUSION

When studying this difficult subject, one must remember that natural does not necessarily mean safe. The conservative stance taken by ASA to stop herbs 2 weeks prior to surgery cannot be justified. As such, anaesthesiologists do not interact with the patient 2 weeks prior to surgery. According to the World Health Organization (WHO) 75% of the world's population uses herbs for basic healthcare needs. Assuming that one out of three patients is on dietary supplements, we still do not encounter many problems while administering anaesthesia. Ayurvedic preparations are generally considered as safe. Herbs like guggul, amla and giloe are cardioprotective. If statins are allowed to be continued during the perioperative period, then why should amla be discontinued 2 weeks prior to surgery, especially when it has proven its worth in modifying all the factors responsible for myocardial ischaemia, namely hypercholesterolaemia, inflammation and immunity? Turmeric and giloe have been effective in improving wound healing, Tulsi is helpful against stress and giloe is useful in obstructive jaundice and cirrhotic patients. Hence, the ASA guidelines need to be modified in view of these clinical studies. It is imperative that more clinical studies be done and more targeted guidelines be formed considering the usefulness of these herbs in improving the patient outcome.

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