ABSTRACT

Products made from plants that are used to maintain or improve health have a long history of use and claimed health benefits. Most patients fail to report their usage during history taking. However, many herbal supplements have potent pharmacologic activity by themselves and, along with various additives incorporated in various preparations can contribute to adverse effects and drug interactions. The use of herbal supplements by patients in the perioperative period is common and consistent with the substantial increase in the use of alternative medical therapies. We reviewed the literature to examine the constituents, safety, pharmacokinetics, and pharmacodynamics of those herbal supplements that are commonly used. Different supplements possess antiplatelet activity, adversely interact with other drugs, have gastrointestinal manifestations, produce organ toxicities, and produce additive effects when used with sedatives. With the increasing use of herbal supplements by patients, there is now a definite need to screen patients preoperatively for use of these supplements to prevent potential adverse events that may arise from herbal medications taken alone or combined with conventional therapies during the perioperative period. The American Society of Anesthesiologists (ASA) suggests that all herbal medications should be discontinued 2 to 3 weeks before an elective surgical procedure.

Keyword: health, supplements, ASA.

INTRODUCTION

The use of herbal remedies has been around for centuries and their use in both western and eastern societies are increasing. Patient surveys have reported that 12% of Americans, 12% of Australians, and 4.8% of patients in the UK use herbal remedies. The World Health Organization (WHO) estimates that up to 80% of the world's population still depend on...
herbal medicines. Although there has been concern in the medical community about the potential complications arising as a result of patient use of herbal medicines, the exact degree of concern remains unclear as very few of the huge number of remedies have been formally researched. The assumption by patients and healthcare professionals that these products are 'natural' and therefore safe is clearly dangerous. Many patients do not disclose their use and hence the anaesthetist may remain oblivious to potential side-effects and drug interactions. As pharmacokinetic and pharmacodynamic data are lacking, the American Society of Anaesthesiologists recommends that patients discontinue the use of herbal medications 2–3 weeks before surgery. However, patients are often unaware of this recommendation and, furthermore, may present for emergency surgery. There are no formal recommendations or guidelines governing their use for the perioperative period in the UK. Hence, all anaesthetists need to familiarize themselves with the potential perioperative complications that may occur. The aim of this article was to discuss the more commonly used herbal medicines, their side-effects and their effects on the conduct of anaesthesia.

These include echinacea, ephedra, garlic, ginger, gingko biloba, ginseng, herbal diuretics, kava, St John's Wort, and valerian.

**Potential Perioperative Anesthetic/Systemic Side effects**

Areas of concern to the anaesthesiologist in the perioperative milieu may be of concern where herbal medications are involved:

1. Untoward cardiovascular effects,  
2. Enhanced potential for bleeding,  
3. Potential for prolongation or interference with anaesthetic agents,  
4. Possible renal involvement or hepatotoxicity,  
5. Potential for glucose disturbances,  
6. Abnormal thyroid function,  
7. Risk of decreased effectiveness of HIV protease inhibitors.

**St. John's Wort (Hypericum perforatum)**

St John's Wort is used in the treatment of mild to moderate depression. Most preparations are standardized to hypericin content (a naphthodianthrone), but recent data indicate that there are other active ingredients as well, including hyperforin.
Over the past two decades, St. John's Wort has been studied in mild to moderate depression. Most of the clinical trials have shown that it is more effective than placebo and as effective as tricyclic agents for the treatment of mild to moderate depression.

**Garlic (Allium Sativum)**

Garlic is one of the most popular herbal remedies and is available in fresh, dried, and powdered forms. Garlic is used for the treatment of hyperlipidemia and atherosclerosis. Allicin, the ingredient believed responsible for garlic's therapeutic benefit and odor, is highly unstable. Both heat and acid destroy the enzyme allinase, which is necessary to produce allicin, and for that reason garlic is best ingested raw. Garlic is also available over-the-counter in multiple formulations.

Garlic appears to have small effects on cholesterol and very minimal effect of blood pressure and none on glucose levels. The mechanisms of action believed responsible for the lipid-lowering effect include inhibition of HMG-CoA reductase and 14 alpha-demethylase.

Garlic is well tolerated and apparently safe for chronic use. In addition to the well-known breath and body odor, common side effects include gastrointestinal upset, nausea, and flatulence.

**Anaesthetic Implication**

The clinical anaesthesiologist should be aware that garlic may augment the effects of warfarin, heparin, NSAIDs, and aspirin and may result in an abnormal bleeding time, which can lead to an increased risk of intraoperative or postoperative bleeding.

**Gingko biloba**

The dried leaf of the Gingko tree has been used medicinally for thousands of years to improve blood flow in a variety of conditions, including memory impairment, dementia, peripheral vascular disease, and tinnitus. Multiple pharmacologically active compounds have been isolated from gingko, including flavonoid glycosides and terpine lactones (gingkolides). The flavonoids have antioxidant and free radical scavenging ability. The terpine lactones (especially gingkolide B) have platelet activating factor antagonist activity.

In general, gingko is well tolerated in healthy adults at recommended doses for up to 6 months. Allergic skin reactions, gastrointestinal disturbances and headache occur in fewer than 2% of patients. There are theoretical concerns about a risk of increased bleeding because antiplatelet activating factor activity has been demonstrated in vitro. Several cases of
increased bleeding have been reported (two patients were also taking aspirin or warfarin). Although no bleeding complications have been reported in any clinical trials and causality has not been clearly established. Therefore, caution should be exercised when combining gingko with anticoagulants.

**Anaesthetic Implications**

Concomitant use of gingko biloba with aspirin, NSAIDs, warfarin and heparin is not recommended because gingko may increase the potential for bleeding in these patients. In addition, it has been recommended that gingko should be avoided in patients taking tricyclic antidepressant agents, because it might potentiate the seizure threshold-lowering action of these drugs.

**Echinacea**

Echinacea ranks among the top-selling herbs in the United States. In 1920s, Echinacea tincture was a popular anti-infective agent until the discovery of antibiotics. Several active ingredients have been identified, including polysaccharides, glycoproteins, alkaloids, and flavonoids. In vitro and animal studies suggest that these ingredients cause stimulation of the immune system (natural killer cells, macrophages, and cytokine activity) and that they possess anti-inflammatory, free radical-scavenging and antiviral activity. There is not sufficient evidence to support the use of Echinacea to prevent upper respiratory tract infection. In general, Echinacea is well tolerated, with few reported adverse events. Rare allergic reactions have been reported (especially in patient with ragweed allergies).

**Anaesthetic Implications**

The immunostimulatory effects of Echinacea may antagonize the immunosuppressive actions of corticosteroids and cyclosporine. Because the herb can cause inhibition of the hepatic microsomal enzymes, its concomitant use with drugs such as phenytoin, rifampin, and phenobarbitone, which are metabolized by the hepatic microsomal enzymes, should be avoided, because echinacea can precipitate toxicity of these drugs.

**Kava kava(Piper methysticum)**

Kava is prepared from the dried rhizome of the piper methysticum plant. Traditionally, it was used to prepare a ceremonial drink in the South Pacific Islands. Its present day uses include the treatment of anxiety, stress, and insomnia. The active ingredients (kavapyrones) have central muscle–relaxing properties and anticonvulsant activity. The precise anxiolytic
mechanism of action is not fully understood but many involve enhanced binding of gamma-aminobutyric acid in the central nervous system.

**Anaesthetic Implications**
Antinociceptive effects produced by kava kava may be similar to local anaesthetic responses and appear to be mediated through a non-opiate-dependent pathway. Ethanol can increase the hypnotic effects of kava kava. It should be avoided in patients with endogenous depression and can potentiate the effect of barbiturates and benzodiazepines and cause excessive sedation.

**Ginseng (Panax Ginseng)**
Ginseng root has been used for medical purposes in Asia for over 2000 years. There are three major forms of ginseng in use today. Panax Ginseng known as Asian Ginseng, is commonly used in the United States. Panax quinquefolius, known as American ginseng, is cultivated in the United States and exported to China. Possible drug interactions have been reported between P. ginseng and warfarin, calcium channel blockers, digoxin, and alcohol.

**Anaesthetic Implications**
Ginseng should be avoided with patients on anticoagulant medications such as warfarin, heparin, NSAIDs, and aspirin. Because ginseng can cause hypertension, the clinical anaesthesiologist should be focused on clinical consequences of long-term use of this agent. As a result of its potential to exert hypoglycaemic effects, ginseng should be used cautiously in diabetic patients on insulin or oral hypoglycaemic medications. It would therefore follow that the anaesthesiologist would need to have appropriate evaluation of blood glucose levels peri-operatively for applicable patients.

**Saw Palmetto**
Traditionally, the fruit of the dwarf palm tree (Serenoa repens) was used by Native Americans for urinary complaints. Saw palmetto is now widely used to treat benign prostatic hyperplasia. The mechanism of action is unclear; but there is evidence for inhibition of 5 alpha-reductase activity and dihydrotestosterone binding at the androgen receptor. Two small European studies suggest that the herb is slightly less effective than prazosin and alfuzosin an alpha-adrenergic antagonist.
Adverse reactions to saw palmetto are rare, with occasional reports of mild gastrointestinal symptoms and headaches.

**Anaesthetic Implication**
Although no detailed studies have been done with regard to the anaesthetic interactions, caution should be used if the patient is using benzodiazepines (e.g. alprazolam) or medications such as dextromethorphan because saw palmetto can alter pharmacokinetics of these medications. Elaborate clinical trials on anaesthetic-herb interactions are warranted.

**Ephedra**
The dried young stems of Ephedra sinica have been used for thousands of years in traditional Oriental medicine to treat respiratory disorders, especially bronchospasm and congestion. Ephedra is widely marketed for its stimulant and appetite suppressant effects (alone or in combination with caffeine-like herbs). Ephedra's alkaloids are structurally similar to amphetamines. Sympathomimetic side effects include tremors, severe hypertension, seizures, and arrhythmias. These may lead to myocardial infarction, stroke, and death.

**Anaesthetic Implication**
The use of ephedrine–containing over-the-counter products is highly relevant to the perioperative period. The possibility of hypertension causing myocardial ischaemia or stroke needs to be considered. Ephedra can potentially interact with volatile general anaesthetic agents (e.g., halothane, isoflurane, desflurane) and cardiac glycosides (e.g., digitalis) to cause cardiac dysrhythmias. Patients taking ephedra for prolonged periods of time can deplete peripheral catecholamine stores. Thus, under general anaesthesia, these patients can potentially have profound intraoperative hypotension, which can be controlled with a direct vasoconstrictor (e.g., phenylephrine) instead of ephedrine.

**Ginger (Zingiber officinale)**
Ginger has been used for the treatment of nausea, vomiting, motion sickness, and vertigo. Western herbalists believe it is useful for healing respiratory ailments. It helps to relieve nasal congestion, sore throats, and decrease headaches and body aches. Side effects of ginger include bleeding abnormalities and its use is contraindicated in patients with coagulation dysfunction or those on anticoagulant medications such as NSAIDs, aspirin, heparin, and warfarin.
Anaesthetic Implications
Ginger may increase bleeding risk, therefore, its use should be avoided in patients on anticoagulants like warfarin and heparin or drugs such as NSAIDs and aspirin. Large quantities of ginger may also cause cardiac arrhythmias and central nervous system depression.

Feverfew (Tanacetum parthenium)
The herbal agent feverfew is used to treat headache and fever, prevent migraines and treat menstrual abnormalities. Like most herbal compounds, analysis of feverfew-based products have yielded significant variations in the parthenolide contents, a proposed active ingredient between feverfew products.

Feverfew has demonstrated inhibition of serotonin release from aggregating platelets. Adverse reactions to feverfew include aphthous ulcers, abdominal pain, flatulence, nausea, vomiting, and rebound headache with an abrupt stoppage of the herb.

Anaesthetic Implications
Because feverfew can inhibit platelet activity, it is reasonable to avoid the concomitant use of this herb in patients taking medications such as heparin, warfarin, NSAIDs, aspirin, and vitamin E. For patients with perioperative bleeding abnormalities, the use of feverfew should be considered in the differential diagnosis. Furthermore, tannin-containing herbs like feverfew can interact with iron preparations, thereby reducing the bioavailability of such preparations.

Table: Common Herbal Medications and Anaesthetic Considerations

<table>
<thead>
<tr>
<th>Herbal Medication</th>
<th>Anaesthetic Considerations</th>
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<tbody>
<tr>
<td>Echinacea</td>
<td>May potentiate barbiturate toxicity, possible renal involvement or hepatotoxicity</td>
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<tr>
<td>Ephedra</td>
<td>May interact with volatile anaesthetics, i.e., halothane and cause fatal cardiac dysrhythmias. Profound intraoperative hypertension controlled with phenylephrine and not pseudoephedrine.</td>
</tr>
<tr>
<td>Garlic</td>
<td>Increased risk of intraoperative bleeding, risk of decreased effectiveness of HIV protease inhibitors, abnormal thyroid function.</td>
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<tr>
<td>Medication</td>
<td>Effects</td>
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<td>------------------</td>
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<tr>
<td>Gingko biloba</td>
<td>Increased intraoperative and postoperative bleeding tendencies, may decrease effectiveness of intravenous barbiturates, may cause glucose disturbances, cause untoward cardiovascular effects.</td>
</tr>
<tr>
<td></td>
<td>Increased risk of intraoperative haemodynamic instability, causes untoward cardiovascular effects, enhances bleeding potential, potential for prolongation or interference with anaesthetic agents.</td>
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<tr>
<td>Kava kava</td>
<td>May potentiate the effect of barbiturates/benzo-diazepines, thereby resulting in excessive sedation</td>
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<tr>
<td>St. John’s Wort</td>
<td>Pseudoephedrine, MAOIs should be avoided, potential for prolongation or interference with anaesthetic agents, risks of decreased effectiveness of HIV protease inhibitors</td>
</tr>
<tr>
<td>Ginger</td>
<td>Increased risk of intraoperative haemodynamic instability</td>
</tr>
<tr>
<td>Feverfew</td>
<td>Increased risk of intraoperative bleeding, discontinue 2 to 3 weeks before surgery</td>
</tr>
<tr>
<td>Saw palmetto</td>
<td>Untoward cardiovascular effects and enhanced bleeding potentials.</td>
</tr>
</tbody>
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REFERENCES


