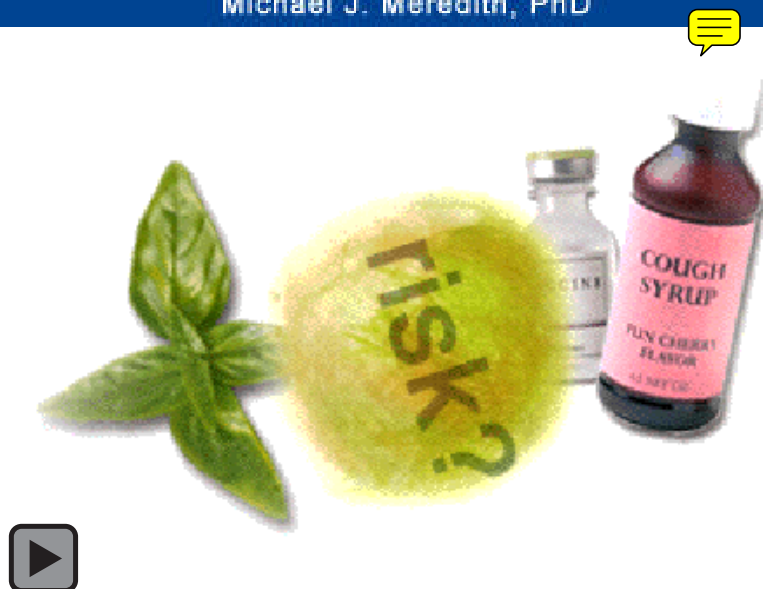


## Herbal Nutraceuticals: A Primer for Dentists and Dental Hygienists

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### Abstract

Herbs have been in use for centuries to prevent and control disease. In recent history demand by the public for herbal supplements has created a multimillion-dollar industry. Herbal extracts are effective because they interact with specific chemical receptors within the body and are in a pharmacodynamic sense, drugs themselves.

A matter for public concern is that herbal supplements are currently independent of regulation by the Federal Drug Administration (FDA). The FDA considers herbal products to be dietary supplements, not drugs. The National Toxicology Program has recently started to examine the composition and standardization of commercial preparations to identify potential health hazards from contaminants or product over use. Many herbal preparations have significant pharmacological effects. The problem that arises for the dental professional is the effect these products have in concert with prescription medications as well as effects on the patient's general response to medication and dental treatment. Drug interactions with the large number of commercially available herbal products can be grouped by the mechanism of most common interactions. These major types of reactions are: (1) alteration of drug metabolizing enzyme activity, (2) interactions with the blood clotting process, and (3) alteration of the inflammatory and immune response.

The widespread use of herbal supplements makes it essential that healthcare providers become informed about this aspect of a patient's personal health practices.

**Keywords:** Nutraceuticals, herbal supplements, monoamine oxidase inhibitor, St. John's wort, mixed function oxidases, kava-kava, goldenseal, ginseng, garlic, evening primrose oil, echinacea, ginger, ginkgo biloba, sanguinarine



## Introduction

Nutriceuticals is a term coined by the popular press as a new way of looking at health maintenance for many people. In ancient times, plants were assigned curative powers based on shape or color; the concept that later became known as the doctrine of signatures in the Hellenistic medical tradition.

Phytotherapy, or phytomedicine, has been a part of both eastern and western medical traditions since the King of Sumaria ordered a summary of current knowledge (about 250 medicinal plants) to be assembled in approximately 2000 BC.

over 2000 plants were thought to have medicinal properties in the ancient world. The Chinese began using ginseng at least 3000 years ago, and Native Americans were using willow bark tea to reduce fever about the time most of the "civilized world" was under Roman rule. Every civilization that has recorded its progress produced a body of knowledge addressing the use of medicinal plants (pharmacognacy). Though displaced to some degree by the rise of "modern medicine," herbalists and herbal preparations have continued to be part of folk and Oriental medical practice. The recent rise in popularity of these materials in American and European societies may reflect a growing discontent with established medical practice, or perhaps an interest in more "natural" modes of healthcare. This is especially true among the elderly.<sup>1</sup> (Table 1)

**Table 1. The Top Ten Herbal Remedies**

Common Name	Desired Effect	Known Pharmacological Effect	Drugs Potentially Affected
Ginko	Memory and circulation improvement	Antioxidant, platelet aggregation inhibitor	Anti-coagulants
Ginseng	Improved immune function, stress reduction	Platelet aggregation inhibitor, immune stimulator	Anti-coagulants
Garlic	Cholesterol reduction, cardiovascular health	Platelet aggregation inhibitor	Anti-coagulants
Echinacea	Improved immune function	NK cell increase, IgG/IgM production increase	Cyclosporine, ketoconazole, methyltrexate
Goldenseal	Improved immune function	IgG/IgM production increase	Erythromycin antibiotics
St. John's Wort	Anti-anxiety/anti-depressant	Induce P-450, inhibit MFO, inhibit serotonin uptake	Paroxetine, Sertraline, Nefazadone, Digoxin, Theophylline, Indinavir, Cyclosporin, Oral contraceptives
Saw Palmeto	Prostate health, urinary anticeptic	Diuretic, antiandrogenic	Estrogen replacement, oral contraceptives
Grape seed extract	Antioxidant		
Evening Primrose	Antioxidant, omega fatty acids	Anti-inflammatory	
Cranberry	Urinary tract health		

## Introduction

Herbal remedies are big business, with the top ten selling botanicals accounting for \$600 million to \$2 billion in the United States in 1998.<sup>2</sup> In



1994 Europeans spent \$6 billion, while the Japanese spent \$2.1 billion dollars on herbal preparations.<sup>3</sup> A matter for public concern is that herbal supplements are currently independent of regulation by the Federal Drug Administration (FDA). The FDA considers herbal products to be dietary supplements, not drugs. This means herbal products do not need to meet the "safe and efficacious" standards applied to materials classified as "drugs." However, the National Toxicology Program has recently started to examine the composition and standardization of commercial preparations to identify potential health hazards from contaminants or product over use.<sup>4</sup>

The term nutraceutical refers to doses of vitamins, minerals, nutrients, and micronutrients in excess of the body's needs (2 to 10 times the recommended daily allowance).<sup>5</sup> Consumption of these plant extracts for the purpose of improving or preventing some health related conditions places them in the nutraceutical category, despite the fact the mechanism of action is more often pharmacological in nature than nutritional. Identification of medicinal herbs as natural may be at the center of the increasing concern about these preparations. These plant-derived preparations are often inadvertently omitted from medical histories; there seems to be a lack of understanding of the potent pharmacological actions of many of these extracts. Patients sometimes assume that because these "drugs" were recently green and growing they aren't in the same category as the pills and capsules they more commonly associate with the term "drug."<sup>6</sup>



With the possible exception of meprobamate, the first drug designed from structure/activity relationships, the first examples of most classes of drugs are natural products. Examples of these include: opiates, the salicylates, scopolamine, and the cardiac glycosides like digoxin. Approximately one quarter of all prescription drugs have some component derived from plants. This includes about 100 of the most commonly prescribed drugs.<sup>7</sup>

Herbal extracts are effective because they interact with specific chemical receptors within the body and are in a pharmacodynamic sense, drugs themselves. Current estimates suggest that 18% of Americans take prescription medications in conjunction with herbal remedies.<sup>8</sup> This translates into 15 million people in the United States alone. The potential for interaction between prescription medications and herbal extracts is significant.<sup>9, 10</sup>

This paper will review the pharmacology of the most common herbal nutraceuticals and address the specific mode of interaction with different classes of prescription drugs. No attempt will be made to cover all herbal remedies or all prescription drugs of interest to dental professionals. Only some of the most commonly used herbs and herbal preparations in oral conditions such as inflammation, blood clotting, and alteration of drug metabolism will be covered in this paper.

## Herbal Remedies: Overlapping Pharmacology

Many herbal preparations have significant pharmacological effects. The problem that arises for the dental professional is the effect these products have in concert with prescription medications as well as effects on the patient's general response to medication and dental treatment. Drug interactions with the large number of commercially available herbal products can be grouped by the mechanism of most common interactions. These fall into three major types of reactions:

- Alteration of drug metabolizing enzyme activity
- Interactions with the blood clotting process
- Alteration of the inflammatory and immune response

### **Pharmacology Flashback-**

#### **Monoamine Oxidase (MAO):**

An enzyme that catalyzes the conversion of primary and secondary amines to alkenes and aldehydes. Most commonly associated with the metabolism of epinephrine, norepinephrine, serotonin, dopamine, and other neuroactive amines. Inhibitors of monoamine oxidase (originally hydrazine and hydrazine derivatives) were first introduced in the 50's to treat depression but caused hypotension, leading to their first pharmacological use, the treatment of hypertension. MAO inhibitors were not found to be safe in the hypertensive patient or patients with cardiovascular disease and are now contraindicated by these conditions. Newer MAO inhibitors are currently used to treat depression and as an adjunct to levodopa therapy for Parkinson's disease. These inhibitors are being reexamined for the ability to specifically inhibit the A and B isozymes of MAO, looking for more selective MAO inhibitors, free of the hypotensive/hypertensive side effects.

### **Alteration of Drug Metabolizing Enzyme Activity**

#### **St John's Wort**

St John's wort (*Hypericum perforatum*) is among the most commonly used and well studied herbal remedies.<sup>11</sup> St. John's wort has been in folk wisdom since the time of the ancient Greeks as an agent to promote a feeling of well being, combat insomnia, and depression. However, there is disagreement about the efficacy of St. John's wort in the treatment of depression.<sup>1,12,13</sup>

The active ingredients in St. John's wort are a family of polycyclic compounds, the hypericins, which have a wide variety of physiological properties. Among the most dramatic of these properties is increased photosensitivity.<sup>14</sup> Hypericin and pseudohypericin in or on the skin are photoactivated to produce free radicals that initiate an immediate hypersensitivity-like reaction producing erythema and weal. Although this may seem like more of a problem for the gardener than the pharmacist, photoactivation of hypericin is at the heart of the compound's antiviral and anticancer effects and is currently receiving significant research.<sup>15-19</sup>

St. John's wort is also known to increase sensitivity to ionizing radiation.<sup>20</sup> It's not known if this represents a risk factor for dental radiography, but hypericin may be a risk factor in higher dose ionizing radiation exposure such as cancer radiotherapy. The mechanism by which St. John's wort exerts a beneficial effect on depression is not fully understood. The hypericins are known to be of the chemically active species. When tested, receptor binding was not very strong to likely receptors including adenosine and steroid recep-

tors. The exceptions are the gamma amino benzoic acid (GABA) A and B receptors.<sup>11</sup> GABA is the major inhibitory neurotransmitter in the mammalian central nervous system. Antagonism of the GABA receptors could interfere with the binding of other drugs such as the benzodiazepines and barbiturates as well as produce a direct inhibitory effect on neurotransmissions.

Hypericin and pseudohypericin inhibit MAO activity, but they are not potent MAO antagonists.<sup>21,22</sup> The pharmacological effect of St. John's wort is thought to be initiated by a combination of mild inhibition of MAO, catechol-O-methyl transferase (suppressing dopamine turnover), and inhibition of serotonin reuptake.<sup>22,23</sup> Through these concerted mechanisms, St. John's wort may affect mood by increasing norepinephrine activity and slowing serotonin clearance.

The most significant potential for prescription drug interactions with St. John's wort, acting as an inhibitor of MAO, is with the serotonin-uptake inhibitors. Inconsistencies in the preparation of St. John's wort have led to variable responses and unpredictable effects on mood elevation. Paroxetine<sup>24</sup>, trazodone, sertraline,<sup>25</sup> and nefazadone have all been linked to St. John's wort-induced serotonin syndrome (sweating, hyperreflexia, and shivering) and tremors in mild cases; seizure and coma in severe cases.<sup>26,27</sup> An additional effect of St. John's wort and hypericin caused by MAO inhibition is the alteration of histamine levels. MAO is responsible for production of the major clearance metabolite of histamine. Moreover, MAO inhibitors also block histamine N-methyltransferase, further decreasing histamine turnover.<sup>28</sup> Decreasing the clearance rate of histamine could affect the enhancing histamine-

dependent processes producing physiological responses ranging from the well known allergic



rhinitis to increased HCl secretion by the parietal cells of the stomach, as noted for the MAO inhibitors selegiline.<sup>29</sup>

There is a strong possibility that St. John's wort acts to counter the effect of antihistamines increasing the histamine levels competing for receptor binding site occupancy. MAO

inhibitors vary in the degree of anticholinergic effect observed (xerostomia, decreased gastric motility, etc.). Tranylcypromine is known to have pronounced anticholinergic properties, while selegiline and phenylzine are not noted for these effects. Variability is probably due to the number of biological amines antagonized by the drug. It is not known whether hypericin's antagonism is limited to serotonin or extends to dopamine and norepinephrine.

### Kava-Kava

St. John's wort is not the only herbal preparation to alter MAO activity. Kava-Kava (*Piper methysticum*) is a popular herb from the South Pacific with significant MAO inhibitory activity.<sup>23-31</sup> The kavapyrones have been shown to have great potential for reducing anxiety and stress without the side effects associated with the tricyclic antidepressants.<sup>32</sup> Levels of serotonin are significantly increased which accounts for the sleep inducing properties.<sup>33</sup> It has been shown to be a safe and effective tranquilizer and antidepressant<sup>34</sup> perhaps resulting from the ability to inhibit norepinephrine and epinephrine uptake at neuronal surfaces.<sup>35</sup> The potential drug interactions resulting from kava-kava would be similar to those observed with St. John's wort; decreased serotonin uptake and decreased dopamine oxidation. However, an important addition for the dental practitioner should be made. As with cocaine, the inhibition of epinephrine uptake by kava-kava could have

profound cardiac consequences for patients receiving local anesthetics containing epinephrine.

### Compounds in Foods

There are many other possible interactions of MFO inhibitors outside besides those associated with prescription drugs. Foods containing tyramine (aged cheese; yeast extract; soy sauce; fava bean or broad beans; smoked meats; pickled meats; poultry and fish (lox, smoked salmon); pickled fish; bananas and avocados just to name a few) should be avoided as well as foods and beverages containing caffeine and theobromine (such as tea and coffee). Caffeine can produce a severe hypertensive crises or dangerous cardiac arrhythmias in patients taking an MAO inhibitor.

### Monoamine Oxidase (MAO) Inhibitors and Dental Treatment

In dental practice, perhaps the most significant possibility for acute drug interaction between MAO inhibitors, such as St. John's wort, is with epinephrine. Drugs that block MAOs lead to the accumulation of serotonin and norepinephrine within the central nervous system. Epinephrine can increase the effect of norepinephrine resulting in unexpected transient hypertension. This risk is most severe in the elderly patient or the patient with a history of heart disease. The potential for unexpected elevation and blood pressure when using epinephrine in local anesthesia suggests the cautious use of this vasoconstrictor in patients taking MAO inhibitors, including St. John's wort.

### Mixed Function Oxidase (MFO) Alteration

#### St. John's Wort

St. John's wort leads the list of herbs that have been suggested to alter Cytochrome P-450 MFO activity, however, there is disagreement about the direction of the effect, induction,<sup>36</sup> or inhibition.<sup>37</sup> The balance of data suggests that St. John's wort leads to an increase in Cytochrome P-450 MFO induction, producing selective



increases in biotransformation and faster clearance of drugs metabolized by the increased P-450 species.

### **Pharmacology Flashback:**

The cytochrome P-450 mixed function oxidases (MFO's) are a large family of heme containing microsomal enzymes that begin the process of biotransformation by adding polar substituents such as hydroxyl groups or by dealkylating, i.e., demethylation. These modifications of drugs and other compounds lead to less reactive, more water-soluble molecules. In most cases, Cytochrome P-450 dependent metabolism is the first step in drug clearance. However, some drugs are activated by P-450 dependent metabolism. The cytochrome P-450 MFOs are coded for by many separate genes, arranged into gene families. Each enzyme is regulated independently in response to changing metabolic needs. The presence of a substrate for a particular P-450 MFO can cause induction, an increase in its synthesis, increasing the rate of clearance for that molecule. An inhibitor of P-450 activity can lead to the accumulation of drugs that metabolize via that cytochrome P-450 isozyme. Substrate specificities are very broad and substrates for one cytochrome P-450 are often inhibitors or inducers of another. This is the basis of acquired drug cross-tolerance.

St. John's wort contains at least 10 families of compounds that are known to induce P-450 activity.<sup>38</sup> Among these are the xanthenes, flavinoids, bioflavonoids; all demonstrated inducers of the P-450 isozyme CYP3A. Recently, St. John's wort was found to be the cause of an acute heart transplant rejection. Use of St. John's wort by the recipient caused an increase in the P-450 isozyme that oxidizes cyclosporin, producing a drop in cyclosporin level and rejection of the transplanted heart.<sup>39</sup>

A similar situation was found for another CYP3A substrate, indinavir, an HIV protease inhibitor. St. John's wort was found to induce P-450 MFOs leading to a reduction by 50% in the plasma levels of indinavir.<sup>40</sup> Since members of the cytochrome P-450 CYP3A MFO family are involved in the metabolism of other HIV protease inhibitors and non-nucleotide reverse transcriptase inhibitors, St. John's wort should be avoided during these antiviral treatments. The anti-herpetic, Acyclovir, often prescribed by dentists, would not fall under this warning. Other substrates of this MFO include diazepam, caffeine, theophylline, digoxin, and, very significantly, most oral contraceptives.<sup>41</sup>

Inhibition of this cytochrome P-450 isozyme has additional significance in dentistry because the erythromycin antibiotics (including clarithromycin; no data is available on azithromycin) are substrates for CYP3A.<sup>42,43</sup> The erythromycins (including clarithromycin and azithromycin) are generally thought of as inhibitors of drug metabolism. To be more specific, the 3A3 isozyme of cytochrome P-450 MFO is responsible for the

metabolism of carbamazepine, codeine, and a number of other drugs of dental importance. However, in this case, erythromycin can be thought of as being cleared more rapidly due to MFO induction. Increased P-450 activity could alter the clearance time for these important antibiotics

The full extent of the ability of St John's wort to induce the MFOs is not known. It is very probable that other specific isozymes of the cytochrome P-450 MFO are induced or inhibited by this botanical. The potential for interaction with prescription drugs is, therefore, very significant and worse yet, unknown.

The opposite is true of Goldenseal, a herb which is a potent inhibitor of CYP3A.<sup>44</sup> Therefore, goldenseal, which is used to treat a wide variety of skin related problems as well as constipation, menstrual pain, and digestive disorders could potentially cause an increase in the serum levels of the erythromycins and other substrates of these cytochrome P-450 MFOs.

### **Interactions with the Blood Clotting Process**

It's common knowledge among hay producers that red clover hay improperly dried produces several compounds that inhibit blood clotting. The best known of these is the coumadin group, including dicumarol. Numerous congeners of dicumerol have been made, and fortunes have been made along with them. One of them, Warfarin (Wisconsin Alumni Research Foundation-arin), is perhaps the world's most common rodenticide.

Many plant products can act to inhibit coagulation. Almost all act as Vitamin K analogs, blocking the fibrin-clotting cascade. These include three of the most popular herbal supplements: ginkgo biloba, garlic, and ginseng. Ginger has also been found to have an effect on blood clotting. Ginkgo, garlic, ginger, and ginseng have all been found to slow clotting. The mechanisms by which they work differ significantly.



### Garlic

Besides improving the flavor of food, garlic is taken in large doses to reduce serum cholesterol and blood pressure. This is one of the more thoroughly studied medicinal plants and is reviewed with regard to cardiovascular health elsewhere.<sup>45</sup> In perhaps the best controlled experiments, garlic was found to reduce serum cholesterol by 0.65 mmol/l, or about 25 mg/dl (from a study group mean of 268 mg/dl).<sup>46</sup> Recent studies have shown little or no effect on any aspect of cholesterol metabolism.<sup>47</sup> Studies of garlic's effect on blood pressure show a slight reduction in about half the subjects, although the effect was not consistently on the systolic or diastolic pressure.<sup>48</sup> Studies of garlic pharmacology are notoriously hard to do properly because it is impossible to blind the subjects due to the smell. Since the effects of garlic are associated with the low molecular weight sulfide components of the herb (allylic sulfides), placebos altered to mimic the odor possess some unintended pharmacological effect by inadvertently supplying active pharmacological materials. Garlic oil is known to inhibit platelet aggregation.<sup>49,50</sup> While there is no evidence garlic can effect clotting time in a healthy patient, several reports of garlic potentiation of warfarin and other anticoagulants can be found.

### Ginger

Ginger has been found to be useful in the treatment of motion sickness and vertigo.<sup>51,52</sup> Single doses of ground ginger root performed better than standard prescription drugs in preventing nausea and vomiting in several trials. However, ginger is a potent inhibitor of thromboxane synthetase,<sup>53,54</sup> thereby, inhibiting blood clotting. Again, potentiation of anticoagulants is a risk. As with garlic,

effects in a healthy patient are unknown but it seems very likely that ginger could induce excessive bleeding during dental procedures if consumed in high levels. It's interesting to note that consumption of food items (for example, the Chinese hot and sour soup or the pickled ginger served with sushi) could easily provide the one gm dose of ginger root found to be pharmacologically active in clinical trials.

### Ginkgo biloba

Ginkgo biloba is the most popular herb in Europe and has recently been approved in Germany to treat dementia.<sup>56</sup> Ginkgo extracts contain a large number of flavinoid and terpenoid compounds that are thought to provide the extract's antioxidant capacity. Among these, ginkgolide B, a glycosylated flavinoid, is known to be a potent inhibitor of platelet aggregation.<sup>57</sup> Cases of spontaneous hematomas have been reported as well as hyphemia.<sup>58</sup> Use of ginkgo extract must be closely monitored in patients on anticoagulant therapy, or those who suffer bleeding disorders of any sort regardless of whether the disorder is nutritionally-induced or from such conditions as extended NSAID use.

### Ginseng

Ginseng has been recommended for everything from mood enhancement to hypertension and may well have an effect on all of them. Ginseng extracts contain a very wide variety of known pharmacologically active compounds. However, standardization and outright fraud has been a problem. Analysis of saponin and panoxide showed that only about 25% of early commercial "ginseng" extracts contained any ginseng at all.<sup>59</sup> Consumer Reports found striking differences in the ginsenoside contents of 10 brands tested.<sup>60</sup> Additional confusion arises due to different sources of what is called ginseng: Siberian ginseng, American ginseng, Oriental ginseng, different species within the genus *Panax*. Along with ginger and garlic, ginseng (in a standardized product) has been found to be useful in reducing blood glucose in type II diabetics.<sup>61</sup> The mechanism of action is unknown, making ginseng/drug interactions less clear. Ginseng has a central nervous system stimulant activity and may be working through an unidentified steroid receptor. Other ginseng effects are better understood. Many of the polycyclic aromatic components of ginseng, found in all ginseng varieties tested, are



known to antagonize platelet function. This accounts for the numerous reports of bleeding related events ranging from destabilization of dicumarol therapy<sup>62-64</sup> to vaginal bleeding.<sup>65</sup> Recent reports showing a limited interaction with ginseng and warfarin notwithstanding, it is probably prudent to consider

ginseng use detrimental to patients with bleeding problems or look to ginseng as a possible source of unexpected clotting delays.<sup>66</sup>

### Echinacea

The best known and most widely used plant altering inflammation and immune response is the American Coneflower, *Echinacea* sp. These plants are part of the Native American pharmacopoeia in all areas of North America where *Echinacea* is indigenous. Wustenberg<sup>67</sup> describes these preparations as "immunobalancing" and "phytoimmunomodulators," and Sun et al<sup>68</sup> suggests a prophylactic role by nonspecific immune stimulation. Some effect on the immune system has been demonstrated. Rehman et al<sup>69</sup> found an increase in IgG and IgM production after treatment. An increase in natural killer cells (NK cells) and antibody dependent immunity was observed by See and coworkers.<sup>70</sup> Some recent success in treating colds has been noted,<sup>71</sup> but based on clinical studies, only a 10% risk reduction for upper respiratory infection could be attributed to *Echinacea*.<sup>72</sup> Others conclude it may be of some limited benefit.<sup>73</sup> Hepatotoxicity has been observed with *Echinacea* and treatment should be limited to 8 weeks or less continuous exposure<sup>74</sup> and not used with other drugs producing liver effects such as methylnitroimidazole, ketoconazole,<sup>63</sup> and phenytoin.<sup>75</sup> Since *Echinacea* may function as an immunostimulant, use with immunosuppressants like corticosteroids and cyclosporine is contraindicated. However, this does not preclude the use of prednisone for control of acute inflammation, i.e., after dental extraction, in patients taking *Echinacea*. An additional problem with *Echinacea* preparation has been standardization. The pharmacologically active

glycosides are not highly soluble in alcohol so methods of extraction are crucial to the efficacy of the preparation.<sup>76</sup> Water versus alcohol extraction yields a product with widely varying ingredients.

Use of *Echinacea* to relieve colds may be of limited value, but these plants may have a useful role in regulating the inflammatory response. Alkarnides isolated from *Echinacea* roots have been shown to inhibit both cyclooxygenase and 5-lipoxygenase.<sup>77,78</sup> By inhibiting the production of the prostaglandin-2 and leukotriene-4 series of inflammatory mediators, *Echinacea* may serve as an effective inhibitor of the inflammatory response.

### Sanguinarine

Another plant product proposed to alter the inflammatory response is sanguinarine, derived from the bloodroot, *Sanguinaria canadensis*. Although a modest inhibitor of 5-lipoxygenase,<sup>79</sup> no inhibition of cyclooxygenase by sanguinarine was found, thereby, only suppressing one side of the proinflammatory lipid synthesis. Moreover, topical sanguinarine is unlikely to have sufficient time to exert an effect by this mechanism. Sanguinarine has been marketed in the past as a plant derived inhibitor of oral inflammatory response (gingivitis) as an ingredient of a common mouthwash.



### Goldenseal

Goldenseal (*Hydrastis canadensis*) has also been found to be an immune modulator. Used as a tonic for fever and cough by native Americans of the East, goldenseal has a similar effect on IgG and IgM production in rats.<sup>69</sup> Goldenseal's use may be limited by its ability to inhibit cytochrome P-450 as noted above.<sup>44</sup>

### Evening Primrose Oil

An interesting and little known modulator of inflammation is evening primrose oil. An excellent source of the polyunsaturated fatty acid gamma-linolenic acid (18:3n-6, known as GLA), evening primrose oil has been tested as a possible means of controlling inflammatory conditions such as arthritis.<sup>80</sup>

and more significantly for dentistry, Sjögren syndrome. GLA levels are depressed in patients with Sjögren syndrome.<sup>81</sup> GLA is elongated to form DGLA (20:3n-6), the precursor of prostaglandin

E1, an anti-inflammatory prostaglandin as well as an inhibitor of the 5-lipoxygenase and the production of the proinflammatory prostaglandin, leukotriene B<sub>4</sub>. The net result is a movement of the immune system away from inflammation.<sup>82</sup>



Early studies showed evening primrose oil, combined with B-complex vitamin supplementation, had a positive effect on Sjögren syndrome after 8 weeks of treatment as measured by tear production.<sup>81,83</sup> However, larger studies have not been done to investigate these findings further. No further information is available on the efficacy of evening primrose oil in treating Sjögren's syndrome. This is unfortunate since there are very few or some would say no effective treatments for Sjögren syndrome. Nutritional modulation of inflammatory response could be a useful strategy against Sjögren syndrome and other inflammatory related conditions.

### **What Should Patients be Told About Herbs**

Any discussion the health professional has with a patient about herbal supplements should be conducted with caution. Patients are likely to feel an herbal supplement is of value to their health and well being, thus, making it difficult to give guidance without interfering with the patient's ideas of self-determination. The dental aspects of herbal supplementation are not as diverse as those faced by the physician. However, plant extracts affecting inflammation and bleeding are of significant interest to the dental professional.

If the conversation is initiated by observations made by the dentist or hygienist during treatment, direct inquiries are certainly justified. This is especially true of circumstances leading to unusu-

al bleeding. If the patient inquires about the effects of a particular herb, it is essential the facts about herbal supplements be presented as dispassionately as possible to allow the patient to make an informed decision. However, the dental professional is also obliged to supply professional judgment. Based on the current understanding of the interactions and mechanisms of action of these supplements as well as the patient's medical history, a clear and reasoned recommendation can be made without producing patient resistance or antagonism.

A more difficult question to answer is about the benefits of herbal supplements. Whatever the dental professional says, will either conflict or confirm the patient's preconceived notions. Therefore, factual knowledge is essential. In this scenario the practitioner can intervene to provide the patient with good information about herbal supplements and sufficient knowledge of available resources.

Patients need to understand that the FDA regulates herbal products as food supplements, not drugs. Therefore, they don't have to pass the safe and efficacious standards to which prescription medications are held. The labels are not obliged to point out risks, nor do they guarantee the herb products are marketed in a composition or form that can be absorbed. Also, these products may have other ingredients in addition to those on the label.<sup>7</sup>

### **Guidelines for Patients Using Herbal Supplements**

A set of useful guidelines for patients using or interested in using herbal supplements would include the following:

- Disclose to the health provider all non-prescription medications and vitamins, since herbal supplements are known to interact with prescription drugs.
- Be sure to follow instructions for taking the herbal supplement. It may be inappropriate to take too much, or too little and the patient may be putting themselves at risk for potential side effects



- Pregnant or breast-feeding women should avoid herbal supplements. Remember some herbal preparations are known to be teratogenic.
- Avoid mixtures of herbs to minimize unexpected effects and unlisted contaminants.

•Any unexpected reaction while taking herbal supplements should be reported to the health practitioner. These include abdominal cramping, abnormal bleeding, bruising, changes in pulse or heart rate, dizziness, visual aberrations, hives, rash, or other allergic symptoms.

•Herbal supplements should never interfere with standard medical care.

•Children and elderly patients should not use herbal supplements without appropriate medical consultation.

•For questions about herbs, seek advice from your healthcare provider or ask for a referral to someone with the proper knowledge of the subject. Keep in mind that the clerk in a health food store is there to sell products, not act as a health care information provider

### Information Resources

Patient information on herbal supplements is available from an increasing number of sources. The dental health professional is in an ideal position to be a good source for this valuable information, however this is seldom the case. The news media and advertisements supply a vast amount of information about herbal supplements, most of it is to motivate sales, rather than provide helpful

information. There are many good sources of unbiased information on this subject. The Complete Guide to Herbal Medicine (Fetrow and Avilia 2000) is an excellent reference guide, mixing scientific and cultural information about many plant products in a useful and informative fashion. Information is also available online at many web sites dealing with herbal preparations. However, sales are the goal of most of these sites, not patient information. The American Society of Pharmacology and Experimental Therapeutics, a major scientific pharmacology professional society, maintains a plant medicine informational site (<http://www.faseb.org/aspet/H&MIG7.htm#top>) that can act as an entry into this subject for professional and patient.

The University of Washington maintains a very excellent site, "The Medicinal Herb Garden" (<http://www.nlm.nih.gov/pnr/uwmhg/>). This is perhaps the best informational Internet site on herbal remedies. Adding to the value of this site is the direct link to the National Library of Medicine's Pub-Med search engine. This provides immediate updating of patient information with current scientific papers on all of the plants listed. Other web sites are also available and can be useful sources of information if the patient is well informed about how to evaluate material found online.

### Conclusion

The widespread use of herbal supplements The herbal supplement question is no longer an exception. makes it essential for healthcare providers to become informed on this topic. Up-to-date, scientifically substantiated information tempered with an understanding of the patient's needs is always the best response when a patient asks for a healthcare provider's opinion.

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