

Herbal Therapy

What Every Facial Plastic Surgeon Must Know

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Herbal medicine (phytomedicine) uses remedies possessing significant pharmacological activity and, consequently, potential adverse effects and drug interactions. The explosion in sales of herbal therapies has brought many products to the marketplace that do not conform to the standards of safety and efficacy that physicians and patients expect. Unfortunately, few surgeons question patients regarding their use of herbal medicines, and 70% of patients do not reveal their use of herbal medicines to their physicians and pharmacists. All surgeons should question patients about the use of the following common herbal remedies, which may increase the risk of bleeding during surgical procedures: feverfew, garlic, ginger, ginkgo, and Asian ginseng. Physicians should exercise caution in prescribing retinoids or advising skin resurfacing in patients using St John's wort, which poses a risk of photosensitivity reaction. Several herbal medicines, such as aloe vera gel, contain pharmacologically active ingredients that may aid in wound healing. Practitioners who wish to recommend herbal medicines to patients should counsel them that products labeled as supplements have not been evaluated by the US Food and Drug Administration and that no guarantee of product quality can be made.

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The use of herbal medicine is widespread and growing. The actual and perceived relative safety of natural products is a major reason for their popularity with the general public. In 1997, 60 million Americans spent \$3.24 billion on herbs as medical therapy.¹ In 1999, US herbal sales were expected to exceed \$5 billion.² Unfortunately, the explosion in sales of herbs, vitamins, and supplements has brought many products to the marketplace that do not conform to the standards of safety and efficacy that physicians and patients expect. Internet searches for any given herbal medicine routinely yield thousands of links, most of which offer promotional literature and the opportunity to purchase remedies at the click of a mouse button. Pharmacies struggling to profit from small margins on prescription drugs consistently devote prime

display space and marketing dollars to high-profit herbal remedies. Naturally, reports have begun to surface from poison control centers in various states detailing adverse reactions to a broad range of herbal supplements.^{3,4} For example, severe toxic reactions have been reported with the use of chaparral,⁵ germander,⁶ and pennyroyal.⁷ Numerous studies have also demonstrated contamination of herbal medicines with potent synthetic medications.^{8,9} Nonetheless, when considering outcomes for exposures involving dietary supplements (including, but not limited to, herbal preparations) for any reasons (unintentional, intentional, adverse reaction, or other) reported to poison control centers, fewer than 7000 exposures were reported in 1998, compared with more than 1 million exposures reported for all pharmaceuticals.¹⁰ No deaths and only 19 major (0.3%) and 165 moderate (2.4%) effects were attributed to dietary supplement exposures, whereas 868 deaths

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(0.09%), 13 197 major (1.3%), and 58 188 moderate (5.8%) effects were attributed to all pharmaceutical exposures.¹⁰

Unlike other forms of complementary and alternative medicine, herbal medicine may be approached as conventional medicine.¹¹ Many herbal remedies possess significant pharmacological activity and, consequently, potential adverse effects and drug interactions. To paraphrase Simon Y. Mills, PhD, of the University of Exeter, Exeter, England, "Skeptics need only take a few doses of the botanical laxative senna to become convinced of the herb's clinical efficacy" (personal communication, October 1999). Recent articles¹²⁻¹⁵ in peer-reviewed medical journals have acknowledged herbal medicine's unique position in the growing field of complementary and alternative medicine and have provided a context in which clinicians may approach patients using herbal medicines. Nonetheless, many facial plastic surgeons remain unaware of herbal remedies. Indeed, few physicians question patients regarding their use of herbal medicines, and 70% of patients do not reveal their use of herbal medicines to their physicians and pharmacists.¹⁶ It would be difficult to fashion a more dangerous prescription for disaster than that pertaining to the current state of herbal therapy in the United States: physician ignorance of widespread patient use of products with significant pharmacological activity. In this article, we will define herbal medicine and discuss how plants are processed into remedies. We will summarize the history, use, and regulation of botanical medicine in the United States and explore the adverse effects of common herbal remedies. Finally, we will discuss the potential for drug-herb interactions and examine potentially beneficial herbal therapies.

DEFINING HERBAL MEDICINE (PHYTOTHERAPY)

Herbal medicines are medicinal products that contain plant materials as their pharmacologically active components.¹⁷ For most herbal medicines, the specific ingredients that determine the pharmacological activity of the product are poorly characterized. Most herbal preparations are marketed as dry or fluid extracts, which are made from dried plant parts by maceration or percolation. Schulz et al¹⁷ compare the preparation of herbal medicines with the preparation of wines. Although, generally speaking, a cabernet will be a cabernet, cultivated medicinal plants will yield different vintages, as do cultivated grapes. Naturally, just as processing of the same grapes can yield dramatically different potencies and tastes, so can the processing of medicinal plant extracts yield medicines of varying strength and purity. All extracts are not the same, and commercially available extracts vary greatly in their quality. For example, California investigators in 1998 found that nearly one third of 260 imported Asian herbal remedies were either spiked with drugs not listed on the label or contained harmful materials.³ The California Department of Health Services, Food and Drug Branch, investigated these Asian patent medicines collected from California retail herbal stores and found that 83 of 260 products contained undeclared pharmaceuticals or potentially hazardous levels of lead, arsenic, or mercury.⁴ When prescribing herbal medi-

cines, practitioners are advised to select manufacturers (typically European) who use methods such as high-performance liquid chromatography to generate a characteristic fingerprint spectrum, which they use to maintain consistency across batches.¹⁷ Practitioners should select manufacturers from countries, including those in Europe, Japan, and Australia, where herbal medicines must, by law, be made according to the code of pharmaceutical Good Manufacturing Practice.¹⁸ This fail-safe system of quality assurance and quality control includes high-performance liquid chromatography and other state-of-the-art methods to ensure consistent quality.¹⁷

HISTORY OF HERBAL MEDICINES

The use of plants as medicines predates written human history. A 60 000-year-old Neanderthal burial site in northern Iraq has yielded large amounts of pollen from 8 plant species, 7 of which are used now as herbal remedies.¹⁹ Ancient Chinese,²⁰ Egyptian,²¹ and Assyrian²² texts detail the use of herbal therapies. Hippocrates (c 460-c 375 BC) advised the use of herbal medicines to help balance the humors by removing from the body that which was excessive and augmenting that which was deficient.²³ Finally, herbal medicine found systemized expression in the first European herbal, *De Materia Medica*, which was written by the Greek physician Pednios Dioscorides in the first century AD and which remains an authoritative herbal reference to this day.¹⁷

Herbs, the first human healing system, remain the mainstay of indigenous healing practices. The World Health Organization estimated in 1985 that 75% of the world's population, or 4 billion people, rely on herbs for their medical needs.²⁴ In Germany, where herbs are regulated as drugs, they have been used as adjuncts alongside conventional Western medical therapies for many years and are commonly prescribed. The German Commission E was created in 1988 to evaluate critically the safety and efficacy of herbal medicines. This commission considers traditional herbal uses, assesses the scientific basis for granting an authorized herbal claim, and specifies allowable dosages and limitations on use. The German Commission E has published more than 400 monographs²⁵ and approved more than 200 herbs for use. Six of the top 100 prescribed medications in Germany are herbal preparations, and the top 12 herbals account for 2.25% of all sales of prescribed German medicines.

In contrast with Germany, no enlightened system of laws and regulations governing the sale and use of herbal medicines exists in the United States. The original Food and Drugs Act of 1906 abolished adulterated or misbranded drugs but did not address drug safety or efficacy. As a result, in 1938, the federal Food, Drug and Cosmetic Act required that all drugs sold in the United States be proven safe. The 1962 Kefauver-Harris amendments to this act required that all drugs marketed in the United States be proven safe and effective. During the next several decades, many over-the-counter prescription drugs, including many herbal medicines, failed to receive US Food and Drug Administration (FDA) approval for therapeutic purposes. The landmark Dietary Supplement Health and Education Act of 1994, however, classified herbs as "dietary

supplements,” and made the FDA responsible for proving in federal court that a product was unsafe before it could be removed from the market. The Dietary Supplement Health and Education Act also allowed manufacturers to make claims of supplement activity on the body’s structure or function, provided these claims were truthful and not misleading; were not claims for a cure, treatment, or prevention of disease; and were based on scientific evidence in company files. Thus, herbal remedies with structural or functional claims carry a disclaimer: “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”^{26(p3)} The *United States Pharmacopeia (USP) and National Formulary (USP24-NF19)* work closely with the FDA and have published authoritative standards for 8 botanical supplements: feverfew (*Tanacetum parthenium*), garlic (*Allium sativum*), ginkgo (*Ginkgo biloba*), Asian ginseng (*Panax ginseng*), chamomile (*Matricaria chamomilla*), saw palmetto, St John’s wort (*Hypericum perforatum*), and powdered valerian. The USP is also developing monographs for other herbal preparations. Physicians may advise patients to purchase products carrying NF or USP on their labels. Federal law requires that products with NF or USP on the label comply with USP24-NF19 published standards. Unfortunately, the use of herbal medicines in the United States has depended largely on popular literature and has been driven by media and Web-based outfitters responding to increasing levels of consumption. Because there is no direct FDA regulation of herbs as drugs, there is no control over product standardization, in terms of either potency or contamination. Each surgeon must take a focused, systematic look at commonly used herbal products, their adverse reactions, and common drug interactions.

ADVERSE REACTIONS

Bleeding

Facial plastic surgeons commonly question patients with regard to aspirin use, yet few explore the use of herbals among their patients contemplating surgery. All surgeons should ask patients about the use of the following common herbal remedies, which may increase the risk of bleeding during surgical procedures: feverfew, garlic, ginger (*Zingiber officinale*), ginkgo, and Asian ginseng. A partial listing of other herbal medicines that may increase bleeding time is provided in **Table 1**.

Feverfew, despite its name, has no fever-reducing powers and is most commonly used for migraines. Feverfew has been shown to inhibit platelet activity²⁷ and must be avoided in patients using warfarin sodium or other anticoagulants. Patients should be advised to discontinue feverfew use before surgery. Unfortunately, abrupt cessation of feverfew therapy may result in a withdrawal syndrome characterized by nervousness, tension headaches, insomnia, stiffness, joint pain, and tiredness.²⁸

Garlic has been widely touted as a cure for colds, coughs, flu, chronic bronchitis, whooping cough, ringworm, asthma, intestinal worms, fever, and digestive, gallbladder, and liver disorders. Recent research has explored its use as a treatment for mild hypertension²⁹ and

Table 1. Some Medicinal Plants Potentially Associated With an Increased Risk of Bleeding

Coumarin-containing plants	
	Horse chestnut bark (<i>Aesculus hippocastanum</i>)
	Sweet clover plant (<i>Melilotus officinalis</i> , <i>Melilotus alba</i>)
	Sweet vernal grass leaves (<i>Anthoxanthum odoratum</i>)
	Sweet-scented bedstraw plant (<i>Galium triflorum</i>)
	Tonka bean seeds (<i>Dipteryx odorata</i> , <i>Dipteryx oppositifolia</i>)
	Vanilla leaf leaves (<i>Trilisa odoratissima</i>)
	Woodruff plant (<i>Asperula odorata</i>)
Plants inhibiting platelet function	
	Bromelain (<i>Ananas comosus</i>)
	Cayenne fruit (<i>Capsicum frutescens</i>)
	Chinese skullcap root (<i>Scutellaria baicalensis</i>)
	Dan shen root (<i>Salvia miltiorrhiza</i>)
	Feverfew (<i>Tanacetum parthenium</i>)
	Garlic (<i>Allium sativum</i>)
	Ginger rhizome (<i>Zingiber officinale</i>)
	Ginkgo (<i>Ginkgo biloba</i>)
	Asian ginseng (<i>Panax ginseng</i>)
	Onion (<i>Allium cepa</i>)
	Papain from leaves and unripe fruit (<i>Carica papaya</i>)
	Reishi fruit bodies (<i>Ganoderma lucidum</i>)
	Turmeric root (<i>Curcuma longa</i> , <i>Curcuma aromatica</i>)
Salicylate-containing plants	
	Black cohosh rhizome (<i>Cimicifuga racemosa</i>)
	Meadowsweet flower (<i>Filipendula ulmaria</i> , <i>Spiraea ulmaria</i>)
	Poplar bark or buds (<i>Populus</i> species)
	Sweet birch bark (<i>Betula lenta</i> , <i>Betula pendula</i>)
	Willow bark (<i>Salix</i> species)
	Wintergreen leaves (<i>Gaultheria procumbens</i>)

hyperlipidemia.³⁰ Heavy consumption may lead to elevated clotting times³¹ and spontaneous hemorrhage.³² Numerous studies³³⁻³⁶ have documented garlic’s inhibitory effect on platelet aggregation in humans, which occurs within 5 days of oral administration.

Ginger has been used for millennia in China as a digestive aid and to remedy stomach upset, gassy indigestion, bloating, and cramping. Recent studies³⁷⁻³⁹ have confirmed its use as an anti-nauseant in motion sickness. Ginger is a potent inhibitor of thromboxane synthetase and can theoretically prolong bleeding times with long-term use.⁴⁰

Use of ginkgo was recognized by the 1994 German Commission E for treatment of cognitive disorders, including dementia, intermittent claudication, and tinnitus or vertigo of vascular or involuntal origin.²⁵ Recent publicity about its use as a treatment for Alzheimer disease⁴¹ has boosted sales of standardized *G biloba* extract to unprecedented levels. Reports of spontaneous hyphema⁴² and of spontaneous bilateral subdural hematomas⁴³ underscore ginkgo’s potent inhibitory effect on platelet activating factor and, consequently, on platelet aggregation.⁴⁴

Asian ginseng has become popular as a key to vitality and longevity, the herb to take in cases of physical or mental fatigue or lowered resistance to infection.²⁶ The herb exhibits antiplatelet effects,⁴⁵ and its concomitant use with warfarin, heparin, aspirin, and nonsteroidal anti-inflammatory drugs should be avoided.¹³ This effect has not been shown with Siberian ginseng (*Eleutherococcus senticosus*), which has also been promoted for its adaptogenic properties.

Numerous plants contain salicylate and should be used with caution, although some authors have con-

Table 2. Some Medicinal Plants With Potential Photosensitizing Effect

Carrot family
Angelica root and fruit (<i>Angelica</i> species)
Celery (<i>Apium graveolens</i>)
Dill (<i>Anethum graveolens</i>)
Fennel (<i>Foeniculum vulgare</i>)
Khella fruit (<i>Ammi visnaga</i>)
Lomatium root (<i>Lomatium dissectum</i>)
Lovage root (<i>Levisticum officinale</i>)
Cow Parsnip (<i>Heraclium lanatum</i>)
Parsley (<i>Petroselinum sativum</i>)
Queen Anne's lace (<i>Daucus carota</i>)
Other plant families
Agrimony (<i>Agrimonia eupatoria</i>)
Bergamot peel (<i>Citrus bergamia</i>)
Bitter orange peel (<i>Citrus aurantium</i>)
Buttercup plant (<i>Ranunculus</i> species)
Fig (<i>Ficus carica</i>)
Goosefoot (<i>Chenopodium</i> species)
Lemon peel (<i>Citrus limonia</i>)
Psoralea seeds (<i>Cullen corylifolia</i> , <i>Psoralea corylifolia</i>)
Rue leaves (<i>Ruta graveolens</i>)
St John's wort (<i>Hypericum perforatum</i>)
Yarrow plant (<i>Achillea millefolium</i>)

tended that natural sources of salicylates seem to lack aspirin's effect of inhibiting platelet aggregation.⁴⁶ These plants include black cohosh rhizome (*Cimicifuga racemosa*), meadowsweet flower (*Filipendula ulmaria* and *Spiraea ulmaria*), poplar bark or buds (*Populus* species), sweet birch bark (*Betula lenta* and *Betula pendula*), willow bark (*Salix* species), and wintergreen leaves (*Gaultheria procumbens*).⁴⁶ Other plants contain coumarin, and their use should be strictly avoided perioperatively (Table 1). Herbal medicines such as chaparral⁵ and germander⁶ have also been associated with toxic effects in the liver, which can lead to an altered clotting function. Finally, herbal medicines not known to cause bleeding may be adulterated with synthetic agents known to increase the risk of bleeding during surgical procedures.

Skin Reactions

Numerous herbal medicines may profoundly affect the skin and thereby adversely interact with the facial plastic surgeon's efforts to improve skin quality through resurfacing techniques. Kava (*Piper methysticum*) preparations are an herbal alternative to synthetic anxiolytics and tranquilizers and are frequently found in "herb drinks."⁴⁷ A characteristic "kava dermatopathy" may develop if the herb is used continuously for several months.⁴⁸ Symptoms include reddened eyes, scaly skin eruptions, and a yellowish discoloration of the skin, hair, and nails, attributed to 2 yellow pigments in the plant.⁴⁹ Fortunately, these effects appear to be reversible on discontinued use of the herb. St John's wort is licensed in Germany for the treatment of mild depressive states, anxiety, nervous unrest, and sleep disorders.²³ Sales of the herbal preparation have boomed because of the public's perception that it is a safe alternative to prescription antidepressants. St John's wort poses a risk of photosensitivity reaction attributed to its hypericin component.⁵⁰ Concomitant use with other pho-

tosensitizing agents, such as tetracycline hydrochloride, fluoroquinolones, and sulfonamides, should be avoided. Retinoids, such as tretinoin, and similar dermal irritants should be administered with caution in conjunction with St John's wort because of the possibility of augmented phototoxic effects. Certain medicinal plants of the carrot family (*Apiaceae* species) contain furocoumarins and can also cause a photodermatitis in humans from sensitization of the skin to UV light. Use of any herbal medicines containing furocoumarins (**Table 2**) should be avoided while undergoing cosmetic UV light exposure or in conjunction with other photosensitizing agents or dermal irritants.⁴⁶

Estrogen Effects

Many facial plastic surgeons advise patients who are postmenopausal to consult their primary care physicians regarding the risks and benefits of estrogen replacement therapy. More than 500 plant species contain phytoestrogens, naturally occurring substances functionally similar to estradiol.⁵¹ Phytoestrogens may potentiate or antagonize estrogen effects. Accordingly, these compounds may contribute to changes in skin pigmentation following resurfacing procedures. Moreover, use of some phytoestrogens in conjunction with estrogen replacement therapies may result in symptoms such as nausea, bloating, hypotension, breast fullness or tenderness, migraines, and edema. Among the more commonly used phytoestrogen-containing herbs are dong quai (*Angelica sinensis*), red clover (*Trifolium pratense*), alfalfa (*Medicago sativa* var *italica*), licorice (*Glycyrrhiza glabra*), and black cohosh.^{52,53}

POTENTIALLY BENEFICIAL WOUND HEALING HERBAL MEDICATIONS

Botanical remedies have long been used as topical preparations to enhance wound healing. These topical preparations may be administered in vehicles with high water content, such as moist compresses, hydrogels, and tinctures, or may be applied in formulations with high fat content, such as lipophilic creams and ointments. The German Commission E has approved 25 herbs for dermatologic indications, including chamomile, witch hazel leaves and bark (*Hamamelis virginiana*), podophyllin (*Podophyllum peltatum*), calendula flowers (*Calendula officinalis*), bitter-sweet (*Solanum dulcamara*), purple coneflower (*Echinacea purpurea*), St John's wort oil, arnica flowers (*Arnica montana*), and comfrey leaves and root (*Symphytum officinale*).¹⁷ Facial plastic surgeons must be aware of arnica and comfrey, both of which have a long tradition in European folk medicine for the treatment of posttraumatic and postoperative discomfort, ecchymosis, and edema. In vitro studies have demonstrated anti-inflammatory⁵⁴ and antimicrobial⁵⁵ effects attributable to arnica's helenalin component. Although topical application may cause irritant or allergic dermatitis, arnica may safely be recommended for use on unbroken skin to lessen posttraumatic ecchymosis, inflammation, and edema. Undiluted arnica, however, is toxic if taken internally, and the claim that homeopathic arnica is efficacious beyond a placebo effect is not supported by rigorous clinical trials.⁵⁶ Physicians should

caution against use of comfrey because of the herb's constituent pyrrolizidine alkaloids,⁵⁷ which have shown hepatotoxic,⁵⁸ carcinogenic,⁵⁹ and mutagenic⁵⁹ properties in rats. Although topical formulations have been approved by the German Commission E for short-term use on unbroken skin, comfrey preparations in the United States are not standardized and may contain high levels of pyrrolizidine alkaloids and contaminants such as nightshade (*Atropa belladonna*) and foxglove (*Digitalis purpurea*).²

Numerous botanical remedies formulated as essential oils have been shown to have antimicrobial and anesthetic effects, including tea tree oil (*Melaleuca alternifolia*), peppermint oil (*Mentha piperita*), and various conifer-derived oils. Tea tree oil's primary antimicrobial ingredient has been identified as terpinen-4-ol,⁶⁰ which has demonstrated in vitro efficacy against numerous bacteria and fungi, including methicillin sodium-resistant *Staphylococcus aureus*.⁶¹ In a 1990 clinical study involving 124 individuals with mild to moderate acne, 5% tea tree oil in a water-based gel significantly reduced the mean number of acne lesions by the end of 3 months, with fewer reported adverse effects than those associated with 5% benzoyl peroxide lotion use.⁶² Peppermint oil has also demonstrated antibacterial,⁶³ antiviral, and antifungal⁶⁴ effects in several in vitro studies. Numerous analgesic creams include peppermint oil or its distillate menthol because of the oil's long-lasting cooling effect on the skin.⁶⁵ Surgeons should approach the use of essential oils with caution, however, because they may irritate sensitive skin and cause contact dermatitis.⁶⁶

Aloe vera (*Aloe vera*) gel is commonly incorporated in many cosmetic products for its wound-healing properties. Aloe vera gel, or mucilage, is a thin, clear, jellylike substance obtained from the parenchymal tissue making up the inner part of the *A vera* plant leaf. It must not be confused with aloe juice (also known as latex), which is a cathartic, bitter yellow juice extracted from specialized cells of the plant's inner leaf.² Fresh aloe vera gel promotes the attachment and growth of normal human cells in vitro and enhances the healing of wounded monolayers of cells.⁶⁷ Aloe vera contains several pharmacologically active ingredients, including a carboxypeptidase that inactivates bradykinin in vitro, salicylates, and substances that inhibit the local vasoconstrictive effect of thromboxane in vivo.⁶⁸ Controversy exists as to whether these wound-healing effects can be seen with commercially prepared products, many of which contain minimal amounts of *A vera*. Quality aloe vera gel products typically contain more than 95% pure *A vera* and have proven effective in preserving skin circulation following frostbite injury⁶⁹ and in accelerating wound healing in patients who have undergone full-face dermabrasion.⁷⁰ Aloe vera gel improves the anti-inflammatory effect of hydrocortisone acetate when used as a vehicle for topical application on mice.⁷¹ In an excisional wound model in rats, aloe vera gel accelerated wound contraction and neutralized the toxic effects of topical antimicrobials to fibroblasts and keratinocytes. Consequently, aloe vera increased collagen activity and enhanced the breaking strength of scars resulting from excisional wounds.⁷² Aloe vera gel may aid in superficial wound healing (dermabrasion and minor surface wounds), although at least one study⁷³ has indicated it may delay recovery in complex wound heal-

ing by secondary intention. The evidence for a potential beneficial wound-healing effect from aloe vera gel is sufficient to warrant the design and implementation of well-controlled clinical trials. Several reputable suppliers produce a stabilized aloe vera gel for use and are working toward isolating and eventually providing verified active ingredients in dosable quantities.⁷⁴

CONCLUSIONS

Facial plastic and reconstructive surgeons work with patients seeking to maintain their appearance of health and vitality. Eisenberg et al note that 58% of alternative therapies in 1997 were used, at least in part, to "prevent future illness from occurring or to maintain health and vitality."⁷⁵(p1574) Clearly, all patients should be asked about the use of herbal medicines and should have their responses documented in the medical record.⁷⁶ Surgeons must be aware of adverse reactions stemming from herbal medicine use, especially with regard to perioperative bleeding. They must caution patients that lack of standardization, quality control, and regulation may result in variability in herbal content, efficacy, and frank contamination. Well-controlled clinical trials may yield valuable new herbal medicines or validate ancient remedies, but each surgeon should discuss proven treatment options with patients before consideration of herbal therapies.

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