# Herbal Preparations: A Primer for the Aeromedical Physician

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***Purpose:*** This study was an effort to identify the botanical preparations of potential risk to the aviator and aviation safety, and to ascertain whether aviators are using dietary supplements despite extensive educational efforts discouraging over-the-counter medication use. Herbal preparations may be used by nearly 20% of the adult population. Although the aviator population may be presumed to use them as well, the actual degree of use among aviators is unknown. Use of such substances as health promotion or therapeutic agents may provide health benefits, but may also carry risk. Military and civilian aviators are not currently required to disclose such use, nor are examiners obligated to inquire or counsel aviators about them. This paper examines the trends in post-mortem toxicological samples suggesting botanical preparation use, and develops a rational method for determining suitability for use by the aviator. ***Method:*** The toxicological test results from 3177 mishap pilots performed at the Civil Aeromedical Institute from 1989–1997 were examined for the presence of substances suggesting botanical preparation use. The prevalence of positive test results for ephedrine among mishap pilots was compared with the prevalence of tests positive for chemically and biologically similar non-botanical substances among mishap pilots. A review of existing literature was also performed to identify substances posing possible risk to the aviator health or aviation safety. ***Results:*** Ephedrine was found to be the only substance routinely screened on toxicological specimens that was suitable for association with botanical substance utilization. The percent of specimens positive for ephedrine increased three- to four-fold while the percent of specimens positive for similar non-botanical substances decreased overall. The literature revealed sufficient evidence that a number of open market botanical agents are capable of causing incapacitation by cardiovascular or neuropsychiatric mechanisms, yet are legally permitted for use by aviators. ***Conclusion:*** Aviators are using botanical products with increasing frequency, and many of those substances may pose significant risk of incapacitation, altered sensorium, or adverse health effects. The flight surgeon must be diligent in eliciting a history of use and assisting aviators to minimize personal risk and risks to flight safety. A rational approach to assessing risk is presented.

**Keywords:** alternative medicine, herb, pharmacognosy, botanical, dietary supplement, pilot, aviation.

*Life is short; art is long; opportunity fugitive; experience delusive; judgment difficult. It is the duty of the physician not only to do that which immediately belongs to him, but likewise to secure the co-operation of the sick, of those who are in attendance, and of all the external agents.*

*Hippocrates (24)*

BY THEIR DISTINCTION of being unconventional and rooted in folklore, alternative medical techniques and therapies are often poorly understood, or blithely ignored by conventionally trained physicians. Yet, some therapies may be of use to the mildly injured or ill aviator. These therapies may provide preventive medicine benefits in the maintenance of health, and are also used to maintain or improve performance. Conversely, some therapies may pose significant risks to aviator health and flight safety. Botanical substances are often misperceived as being free from risk or adverse effects as a result of being "natural" substances. They are often not thought of as drugs or medications. The skillful flight surgeon or aeromedical examiner must be aware of these "new" treatment options to properly advise the aviator on the proper use or non-use of unconventional therapies, including those of herbal origin. This article does not attempt to address all alternative therapies but concentrates on oral supplements and treatments of botanical origin.

The large-scale marketing and use of non-regulated, non-standardized, but pharmacologically active food products pose unique challenges to the traditionally trained physician. Although physicians may recognize the names of some botanicals (e.g., *Digitalis purpurea*), many are unfamiliar with the vast array of botanical and non-botanical substances used in today's non-regulated pharmacopoeia. Physicians may not recognize that plants are the source of a wide range of such potent medications as ephedrine, derived from ma huan, pilocarpine from jaborandi, vincristine from the Madagascar periwinkle, reserpine from snakeroot, and more recently taxol from the bark of the Pacific yew. Consequently, the patient's use of non-prescription agents may be overlooked, or not inquired about during patient visits for clinical concerns or aviation examinations. Some of these agents may cause adverse reactions or interactions with prescribed medications, but the patient is unlikely to understand these possibilities

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fully, as there is no method of standardized labeling, and a description of actions and interactions on the product label is rare. Fewer than half of those using alternative medical therapies consult either a physician or a practitioner in alternative medicine (16).

The public is inundated on a daily basis with advertisements for improved health, mentation, vision, and a host of other claims. Nutrition centers and health product outlets have become commonplace in shopping centers, department stores, and through mail-order outlets. Recently, U.S. military bases have included such centers in the base exchanges, and advertising for non-regulated agents has become commonplace among military, veterans, and aviation magazines. Eisenberg et al. (16) have estimated that as much as 42% of the American population currently uses alternative therapies, though the incidence of such use within the aviation community is unknown.

Pilots, with their enhanced national and international mobility, may have greater potential to encounter nonstandard medications and diverse foods. Preparations unavailable in one country may be available next to more familiar products in another. Unfortunately, some popular over-the-counter products have caused or contributed to the sudden incapacitation of their users, either alone or in combination with other pharmaceutical products (1,11,12). Clearly, these products would be unsuitable for use in the aerospace environment. Other products may be sentinels for underlying medical disorders for which physician intervention may be appropriate. None of the products has been studied in the context of high $G_z$, extended duration flight, or high altitude environments. Further, many, and perhaps most, of these products have not been tested in a controlled clinical setting, and side effect profiles are reliant on anecdotal and case reports that may exaggerate or underestimate the actual incidence of adverse effects.

To date the majority of literature concerning herbal preparations has been written in German, Chinese or other non-English language publications. English interpretation is often not available, although the appearance of occasional studies in the mainstream medical literature has fueled interest in alternate medicines. Frequent reports of newly identified side effects, product recalls and changing FDA regulations regarding prescription drugs, in the absence of such literature for herbal preparations may contribute to the perception of reduced toxicity of "natural" substances. This, however, is probably a good example of the effects of reporting bias. Reports of complications of alternate therapies are rarely seen in the lay press.

## METHODS

The literature was reviewed for the aeromedical significance of alternative medicines, concentrating on botanical-derived ("herbal") agents. The Civil Aeromedical Institute maintains a database of in-flight incapacitation episodes and conducts toxicological testing of mishap pilot samples, usually postmortem. This extensive toxicology database was searched for compounds that might suggest the prevalence of herbal preparation use among these mishap pilots. Chemically similar compounds utilizing the same assay technique were then selected as the comparative substances. These were tabulated and trend analysis performed. Then, using summary articles and acknowledging reliance on already translated materials, case reports and anecdotes spanning the past decade, botanical products were categorized according to reported side-effects, mode of action, active constituents, and potential for aeromedically significant effects. The agents were then divided into these categories: 1) those reported to be capable of causing incapacitation or alteration in mentation either alone or due to interaction with other drugs; 2) those known to have other harmful effects; and 3) those of other medical interest to the aviation medicine physician.

## RESULTS

### *Historical Considerations*

Many modern herbal therapies can trace their origins to antiquity, though American herbal preparations in the 1990s have occasionally departed from the carefully prescribed aliquots of the early alchemists to create megadose preparations aimed at faddists. Medicinal use of herbs like garlic and juniper were recorded as far back as c. 1700 BC in ancient Egypt. From nearly 400 BC the Greeks, utilizing the Hippocratic theories of humors and fluids, incorporated Asian and Indian herbs and methods into their practice. Around 70 AD Pedanius Dioscorides codified therapeutic remedies in his classic text *De Materia Medica*. The Romans adopted many of the Greek theories of medical practice and embellished on them. Roman medical practices, though, became lucrative, regimented, and rooted in invasive treatments. Claudius Galenus opposed this trend and codified a less invasive method, reliant on the use of ingested, inhaled or topical potions, in numerous texts that survived to influence European medicine through the Middle Ages.

Following the Dark Ages, European medicine, much of it derived from its Roman ancestry combined with the influences of the Asians and Middle East travelers, became more formalized and regimented. Although the influences of Paracelsus and William Turner helped demystify pharmacotherapy, medicine and the apothecary became increasingly distanced. As the apothecary became more the environ of the alchemist, extensive use of heavy metals and exotic herbs became more common, as did equally exotic claims for their effectiveness (36).

This European tradition of medicine was imported to the Americas with the early settlers. However, it was to become uniquely melded with existing Native American medical practices (the use of saunas) and American herbs (tobacco, boneset). During the Lewis and Clark expedition, there were many exchanges of medical treatments between the Corps of Discovery and the natives. One of the first written accounts of the medicine of native America was reported by Merriweather Lewis in his observations of the team's native American guide Sacagawea's difficult labor. Observing her treatment with a portion of the rattle of a rattlesnake, Lewis

wrote, "This remedy may be worthy of future experiments, but I must confess that I want faith as to its efficacy" (3).

With the immigration of large numbers of Asians and Indians, the influences of Chinese and Ayurvedic medicine were introduced. These blended influences were, to some extent, exported back to Europe where they continue to shape the European practice of herbal medicine. This combination of herbal influences remained the American standard of practice until only about a half century ago with the dawn of the antibiotic age.

Herbs were known to be efficacious and from them were derived most medicines prior to the mid-twentieth century. As early as 1803, crystalline morphine was extracted from poppies, aconitine from monkshood, emetine from ipecacuanha, atropine from nightshade, and quinine from Peruvian bark. In 1852 salicin was isolated from willow bark, and in 1899 salicin was improved by the Bayer Corporation as acetylsalicylic acid and formulated for treatment of aches and pains, with less irritation to the stomach than the raw substrate. This was followed by extraction of hundreds of preparations from their natural origins. In this tradition, the first antibiotics were extracted, and the antibiotic era was born. With the rapidly burgeoning pharmacopoeia of the United States, demand for testing and regulating drugs brought about the creation of the Food and Drug Administration (FDA). Public law required standardization of remedies, as well as controlled trials and demonstrated efficacy. Herbal preparations, unpatentable, highly customized in preparation, and poorly standardized, were excluded from the pharmacists' shelves and subsequently fell out of standard medical practice and education (36).

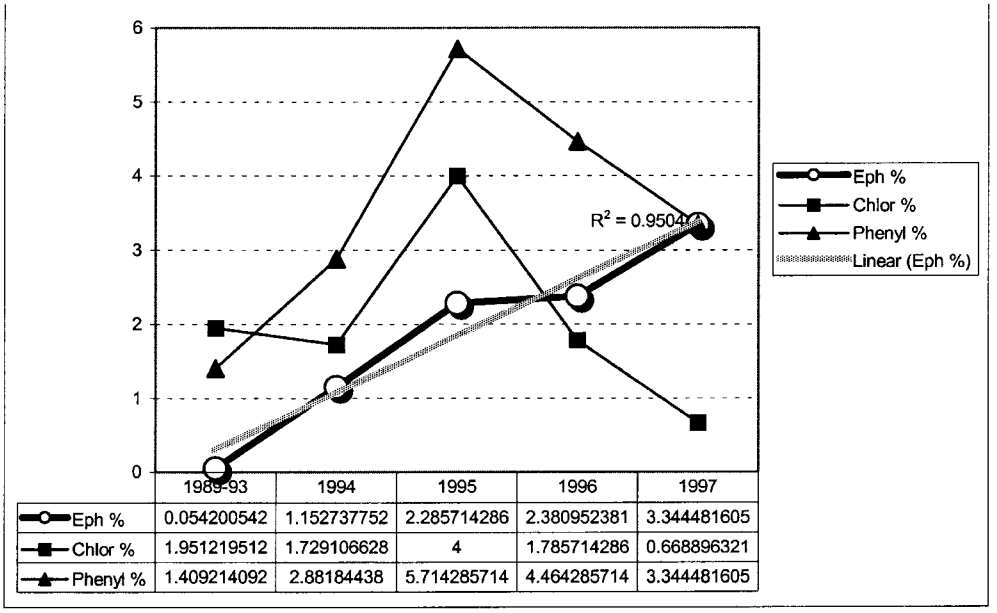
Europe and Asia, however, continued to utilize herbal medications as an adjunct to traditional medical therapy. The United States exported thousands of tons of raw materials to Europe to support this practice. During the late 1980s however, as American disenchantment with mainstream medical practice increased (proportional to skyrocketing medical costs), Congress became less reticent about allowing the marketing of non-regulated pharmaceutical agents. The resultant passage of the Dietary Supplement Health and Education Act of 1994 created a fertile environment for the rapid proliferation of herbal remedies (all called "dietary supplements"). The provisions of the Act permit marketing of the products with suggested dosages but do not require pre-market testing for safety or efficacy, do not require standardization, prohibit direct claims of effect or efficacy, and do not imply FDA approval or sanction (17,18). A pharmacist or knowledgeable equivalent may not be available as these products are frequently sold directly by mail order or over the Internet (40).

*Consumer Demographics and Utilization*

The utilization of unconventional therapies in the United States has proven difficult to quantify. Estimates of patient utilization of alternative medical therapies have ranged from 42% (16) to 57% (18). The use of herbal preparations increased by 380% between 1990 and 1997, and an estimated 1 in 5 individuals taking prescription medication concomitantly use herbal substances. Unfortunately, only about half of those patients taking an herbal preparation and who saw a physician revealed their use of the preparation (16). Elder et al. (18) found no significant demographic predictors to suggest which patients were more likely to discuss their use of herbal preparations with their physician. Eliason et al. (19) described the typical consumer of herbal supplements to be of above average education, insured, and to have a regular physician. However, they too found that the physician was seldom consulted regarding the use of herbal preparations. In their 1995 survey, they reported that the most commonly consumed health foods were herbal preparations, of which Gingko biloba, garlic and ginseng were most commonly purchased. These findings are consistent with the German market experience, which in 1991 saw the consumption of 4.2 million prescriptions of Gingko biloba (13).

*Consumption within the Aviation Community*

The prevalence of herbal preparation use among aviators is unknown. Although regulations and requirements vary by class of aviator in both the military and civilian sectors, the current approach has been to prohibit the use of most Over-The-Counter (OTC) medications while on flight status. Even if an OTC medication is not itself disqualifying, the symptoms or illnesses for which it is being taken may, themselves, be reasons for aviation crewmembers to be temporarily grounded or restricted to non-flying duties. Dietary supplements, since they do not come under the regulatory purview of the FDA as drugs, have not been addressed in military or FAA regulations. Aviators are not required to disclose their use of supplements; nor has it been standard practice for examiners and flight surgeons to inquire specifically about their use. It is likely, however, that aviators, like the rest of the population, use dietary supplements. They may also use diet supplements in lieu of, or in addition to medications while performing flying duties. Aircrew members may use alternative medicines to control distracting symptoms or to enhance their performance. Under current regulations contact with the flight surgeon or civilian aeromedical examiner (AME) is not required and does not constitute use of prohibited medication. Thus, although no regulations are violated, the airman should keep in mind that symptoms for which the non-regulated substances are being used might be temporary disqualifiers for flying duties or for the exercising of civilian airmen certificate privileges. Current regulations require civilian airmen to stop flying, at least temporarily, if their medical circumstances change since their last medical certificate exam and to seek the advice of an AME for other than mild, temporary illnesses. Furthermore, civilian pilots are to report health care provider visits for the past 3 yr at the time of the next medical certificate application. This still leaves in a gray area many potential applications of alternate therapies for such things as prevention of illness, weight loss, feeling better, or improving sexual function, where neither the condition




| | 1989-93 | 1994 | 1995 | 1996 | 1997 |
|---|---|---|---|---|---|
| Eph % | 0.054200542 | 1.152737752 | 2.285714286 | 2.380952381 | 3.344481605 |
| Chlor % | 1.951219512 | 1.729106628 | 4 | 1.785714286 | 0.668896321 |
| Phenyl % | 1.409214092 | 2.88184438 | 5.714285714 | 4.464285714 | 3.344481605 |

**Fig. 1.** Percentage of mishap pilots with detectable tissue or serum levels of selected non-prescription substances.

nor the substance use is reportable for the purposes of medical certification.

Although not indicative of overall consumption of herbal preparations, reviews by the Civil Aeromedical Institute (CAMI) of toxicological results from the pilots of mishap aircraft suggest that use of herbal preparations among pilots may be increasing. Of the more than 150 substances routinely screened for using tissue and fluid samples, only one, ephedrine, is primarily found as a result of dietary preparation use. Therefore, 3177 toxicology cases spanning the period 1989 through 1997 (9) were reviewed for the presence of ephedrine, chlorpheniramine, phenylpropanolamine and many over-the-counter medications. This method was chosen because ephedrine, a common ingredient in dietary supplements is infrequently used medicinally in the U.S. Its stereoisomer, pseudoephedrine, may also occur naturally in the Ephedra species plants, making it unsuitable as a discriminator between pharmaceutical and herbal use. Chlorpheniramine, on the other hand, is a widely used over-the-counter preparation, but does not occur naturally; and Phenylpropanolamine [(±) Norephedrine] is an isomer of ephedrine but is not a major product of Ephedra species plants. Each of these is routinely screened and quantitatively confirmed by utilizing advanced gas chromatographic mass spectrographic techniques in each autopsy specimen from civil aviation mishaps in the United States. The detection of ephedrine in measurable levels may suggest the use of an ephedrine-containing dietary supplement within hours of performing aviation duties. The presence of chlorpheniramine, phenylpropanolamine, and all over-the-counter substances was characterized as percentage of all mishap pilots vs. year of occurrence to reflect overall trends in utilization of over-the-counter drugs operating an aircraft. Detection techniques for these substances were not altered during the study period (9).

The results of this investigation are summarized in **Fig. 1**. Prior to 1993, ephedrine was rarely detected, whereas the other over-the-counter sympathomimetic substances were consistently detected, albeit infrequently (between 2 and 6%). However, since that time, ephedrine has been detected with increasing frequency (1% per year) rising linearly to about nearly 4% of mishap pilots ($r^2$ = 0.95), and is now found as frequently as the common over-the-counter preparation phenylpropanolamine and much more commonly than chlorpheniramine. This presumably reflects an increased prevalence of its use among pilots, whereas there has not been a similar increase in use of other over-the-counter agents. Although there is no routinely used serological method to detect the use of other dietary supplements, these data suggest that an increasing number of pilots may be taking dietary supplements and flying. This seems to be occurring despite considerable adverse press about the dangers of ephedrine and the prohibition of its non-prescribed sale in some states.

### *Which Supplements?*

The aviator and aeromedical physician must assess the potential risks inherent in the use of dietary supplements. However, traditional methods of epidemiological evaluation and risk stratification have neither been defined nor applied to the dietary supplements for a number of reasons. Probably the most significant deterrent to study has been the almost infinite number of combinations and preparations. Botanical derived elixirs and preparations have traditionally been individually crafted, and associations of adverse reactions with a particular component of a compound have been difficult to identify. Moreover, the exact ingredients of each compound, even modern commercially produced compounds, differ from batch to batch, may vary in potency, and may lack labeling to assist the consumer or physician in identifying causative ingredients. Furthermore, modern dietary supplements, in addition to

TABLE I. HERBAL SUBSTANCES WITH POTENTIAL HALLUCINOGENIC ACTIONS.

| Hallucinogens |
|---|
| **Reported Cases or Documented Effect** |
| *Psilocybe semilanceata* ("Magic mushrooms") |
| *Exchscholzia californiica* (California poppy) |
| *Piper methysticum* (Kava-kava) |
| *Mandragora officinarum* (Mandrake) |
| *Myristica fragrans* (Nutmeg) |
| *Cantharanthus roseum* (Periwinkle) |
| *Datura stramonium* (Thorn apple) |
| *Corynanthe yohimbe* (Yohimbe bark) |
| **When Smoked** |
| *Humulus lupulus* (Hops) |
| *Cinnamomum camphora* (Cinnamon) |
| *Hydrangea paniculata* (Hydrangea) |
| *Lobelia inflata* (Lobelia) |

botanical products, include a wide variety of amino acids and glandular extracts that have almost no literature associated with them. Efforts are underway in the U.S. and Europe to classify and identify organic herbal type preparations and to study the pharmacoepidemiology of these preparations (13). However, as herbal preparations are typically not patentable, there is little incentive for manufacturers to spend the millions of dollars required to conduct clinical trials, and the trials that have been conducted have frequently been of questionable value. Consequently, the true incidence of adverse effects is not known. These factors, then, make it impossible to quantify risks of a given ingredient. This is particularly vexing for the aeromedical physician, who must make a determination of acceptability for use in the aviation environment. Of the over 800 preparations commonly marketed in the U.S. as dietary supplements or ingredients in such supplements, one group of researchers found fewer than 50 had clinically significant adverse effects reported in MEDLINE listed literature (18). Moreover, even "normal" actions of a botanical substance may have significance in the aeromedical arena. Therefore, decisions regarding the acceptability for use in the aviation environment, for now, must be made based on case reports and probable mechanisms of action.

### *Preparations Capable of Causing Incapacitation or Altered Mentation*

A number of herbal preparations, not all available as dietary supplements, are known to have neurological effects sufficient to cause altered mentation or incapacitation. Others are capable of causing sudden cardiovascular collapse or aggravating existing cardiovascular disease in a manner causing sudden incapacitation. Clearly, these agents are of significant concern to the aviation medical examiner.

*Hallucinogens (**Table I**):* Many naturally occurring herbs and plants have the potential to cause varying degrees of euphoria or hallucinations. The majority of these are not utilized in common herbal preparations, but small amounts may be present in preparations designed to enhance energy. More commonly, however, they are utilized as a "legal" alternative to more expensive street drugs. Probably the most notorious natural hallucinogen is *Psilocybe semilanceata* or "magic mushrooms." Many other herbs are also capable of causing hallucinations when used in high doses or if smoked. The smoking of these herbs may be for medicinal purposes, such as the use of jimson weed (*Datura stramonium*) in the treatment of asthma. The smoke of *Datura* contains potent anticholinergic agents that may relieve symptoms of bronchospasm, but hallucinations may also occur with such use. Other herbs capable of causing hallucinations include *Exchscholzia californiica* (California poppy), *Piper methysticum* (kava-kava), *Mandragora officinarum* (mandrake), *Myristica fragrans* (nutmeg—may cause seizures in extremely high doses), *Cantharanthus roseum* (periwinkle), *Corynanthe yohimbe* (yohimbe bark), and when smoked *Humulus lupulus* (hops), *Cinnamomum camphora* (cinnamon), *Hydrangea paniculata* (hydrangea) and *Lobelia inflata* (lobelia) (12,20,36).

*Sedatives (**Table II**):* Throughout history, a major use of herbs has been as "relaxing nervines," sedatives, or tranquilizers. A number of herbal preparations may be recognized as the progenitors of medicinal sedatives, although others have weak or unpredictable sedative actions. With all, however, the interaction between the sedative herbal preparation and other sedating over-the-counter or prescription medications must be considered. One such sedative herb is *Valeriana officinalis* (valerian). The use of this preparation as a sedative dates at least back to early Greek physicians (36), and it is still a commonly utilized ingredient in antidepressant, stimulant, energy enhancing, and vitamin preparations. The isolated compounds from the herb include isovalerianic acid, borneol, valepotriates, alkaloids, and iridoids. The herb is recognized as effective in the treatment of anxiety and insomnia, according to the German E-commission, and the FDA considers it an anti-insomniac. Interaction with antihistamines and alcohol seems likely, although no such labeling is required on the

TABLE II. PREPARATIONS REPUTED TO HAVE SEDATIVE EFFECTS.

| Sedatives |
|---|
| **Reported Cases or Documented Effect** |
| *Valeriana officinalis* (Valerian) |
| *Rauwolfia serpentina* (Indian snakeroot) |
| *Atropa belladonna* (Deadly nightshade)* |
| **Reputed to Have Sedative Effects** |
| *Chelidonium majus* (Celandine) |
| *Humulus lupulus* (Hops) |
| *Conum maculatum* (Hemlock) |
| *Lycopodium serratum* (Jin Bu Huan) |
| *Papaver somniferum* (Opium poppy) |
| *Passiflora incarnata* (Passion flower) |
| *Scutellaria laterfoloia* (Skullcap) |
| *Lactuca virosa* (Wild lettuce) |
| *Aconitum napellus* (Wolfsbane) |
| *Hyoscyamus niger* (Henbane)* |
| *Datura stramonium* (Jimson weed)* |
| *Scopolia carniolica* (Scopolia)* |
| **Other Herbs Warranting Concern if Used in High Doses** |
| *Salvia officinalis* (Sage) |
| Tryptophan free amino acid preparations |

* Anticholinergic actions.

product (2,12,21,43). Other sedative herbs that may be potentiated by interaction with antihistamines or alcohol include: *Chelidonium majus* (celandine) (12), *Humulus lupulus* (hops) (43), *Conum maculatum* (hemlock) (12), *Lycopodium serratum* (jin bu huan), (25,41), *Papaver somniferum* (opium poppy) (12), *Passiflora incarnata* (passion flower) (12,43), *Rauwolfia serpentina* (indian snakeroot), which can also cause profound depression (2,12), *Scutellaria laterfoloia* (skullcap) (43), *Lactuca virosa* (wild lettuce) (12), and *Aconitum napellus* (wolfsbane) (12). Other sedative drugs derive their action from anticholinergic properties. Most well-known among these is *Atropa belladonna* (deadly nightshade) from which medicinally used belladonna alkaloids derive their names. Other anticholinergic sedatives include *Hyoscyamus niger* (henbane) (12), *Datura stramonium* (jimson weed) (12), *Scopolia carniolica* (scopolia) (12). Of further concern in this family is the occasional adulteration of herbal preparations with pharmaceutical agents. One preparation of "Chinese black balls" utilized for a number of ailments was found to contain significant levels of diazepam as an adulterant (22).

*Other preparations of neuropsychiatric significance: Salvia officinalis* (sage) is a common herb found wild and cultivated in warmer climates of Europe, the Middle East, and the U.S. Although most commonly used as a harmless spice when cooked in foods, this common herb has been utilized as an astringent, antihydriotic, antispasmodic, peripheral dilator, and a cure for epilepsy, insomnia, sea sickness, and even venereal diseases. The tannins it contains are recognized as possessing antiseptic and local anti-inflammatory properties by the German E-commission (21). However, even small doses of the extract taken internally have been reported to cause mental and physical deterioration, and larger doses can cause seizures and loss of consciousness (36,43).

*Tryptophan free amino acid preparations:* Although not an herbal substance, the amino acid tryptophan is commonly associated with herbal substances. Ingestion of high doses of amino acids, as commonly sold in health food stores is a common practice. However, after the cessation of manufacture of L-tryptophan following multiple cases of eosinophilia-myalgia syndrome, several high dose amino acid supplements have been marketed without tryptophan. Researchers found that the use of these preparations in doses of 50 g or more causes rapid depletion of internal stores of tryptophan and precipitated profound depression in individuals previously treated successfully for depression (5,35,42).

### *Herbal Preparations Capable of Causing Incapacitation Due to Cardiovascular Effects*

Many herbal preparations have significant cardiovascular effects that may be of concern to the aerospace medicine physician (**Table III**). These herbs often contain substances that are identical or similar to medications utilized in the treatment of cardiac ailments, and interactions with those medications are possible in patients who are using similar prescription drugs.

*Cardiac glycosides:* Among the oldest refined medications in the pharmacopoeia is digitalis, named for and

TABLE III. HERBAL PREPARATIONS CAPABLE OF CAUSING INCAPACITATION DUE TO CARDIOVASCULAR EFFECTS.

| | Reported Cases or Known Effect |
|---|---|
| **Cardiac Glycosides** | |
| *Digitalis purpura* (Purple foxglove) | |
| *Urginea maritima* (Squill) | |
| *Cystisus scoparius* (Broom) | |
| *Convallaria majalis* (Lily of the valley) | |
| *Adonis vernalis* (Pheasant's eye) | |
| *Strophanthus kombe* (Strophanthus) | |
| *Scilla maritima* (White squill) | |
| *Digitalis lanata* (Yellow foxglove) | |
| **Vasoactive substances** | |
| *Ephedra spp* | |
| *Rauwolfia serpentina* (Indian snakeroot) | |

derived from *Digitalis purpura*, the purple foxglove. Although most aeromedical physicians will recognize use of the digitalis plant medicinally as a potential problem in the aerospace arena, some may not recognize the vast assortment of other glycoside containing plants. These plants elaborate cardioactive glycosides that potentiate the effects of digitalis if used concomitantly, and some contain glycosides in sufficient doses to cause cardiac dysrhythmias if utilized in concentrated forms. *Urginea maritima* (squill) is one such herb. Utilized for the treatment of arthritis and as a cardiac "tonic," this herb elaborates cardiac glycosides that are detectable by digoxin assays, and they are cardioactive. The herb, in addition to causing fatal cardiac dysrhythmias, has been reported to cause stomach, kidney, and CNS damage (2). The effects of this dietary supplement may be potentiated by hypokalemia, just as digitalis action would be. Other herbs known to elaborate cardiac glycosides include: *Eleutherococcus senticosus* (Siberian ginseng) (31), *Cystisus scoparius* (broom) (12), *Convallaria majalis* (lily of the valley) (2,12), *Adonis vernalis* (pheasant's eye) (2,12), *Strophanthus kombe* (strophanthus) (12), *Scilla maritima* (white squill) (12), and *Digitalis lanata* (yellow foxglove) (12). *Kyushin*, which contains the dried venom of Chinese toads, includes substances that cross-react with digitalis antibodies, giving the false impression of elevated digitalis levels (12)

*Vasoactive substances:* Among the most widely publicized adverse effects of dietary supplement have been those of ephedrine, derived naturally from *Ephedra* species plants and synthesized artificially as a stimulant additive. This substance has been widely utilized for centuries as a strength enhancer, antiasthmatic agent, and circulatory stimulant. In addition to these uses, however, it has recently been added in high doses to mood enhancing preparations, diet preparations, and "power" supplements aimed at improving strength and endurance. In fact, ephedrine, closely related to epinephrine and other sympathetic amines is a reasonably potent vasoconstrictor, inotrope and chronotrope. It has bronchodilating effects that make it useful in asthma, but it has not enjoyed widespread pharmaceutical use due to its unacceptable side effects. Since the popularity of dietary supplements has exploded, the marketing of ephedrine, often in very high doses, has markedly increased. The supplements are often prepared with a mix of ephedra with caffeine or kola nut, which is very

high in caffeine to enhance the stimulant effect. State health departments and the Centers for Disease Control have received reports of hundreds of adverse events including erythroderma (10), marked hypertension, cardiac dysrhythmias and palpitations, nervousness, overt psychosis, stroke, seizures, and cardiac arrests (2,4,6,14,27,33,34,43). As a result of these reported adverse effects among both food supplement users and illicit users of the substance as an amphetamine analog, some states have banned the over-the-counter sale and distribution of ephedrine containing substances. They remain, however, widely available by mail order.

*Rauwolfia serpentina* (Indian snakeroot) on the other hand, elaborates a potent hypotensive agent. One of the earliest extracted hypotensive agents was derived from the snakeroot, but side effects such as profound depression and gynecomastia limited its utility. Hypertensive persons who are taking prescription antihypertensives must be aware of the potential interaction between their medications and nutritional supplements containing Rauwolfia alkaloids (2,12).

### *Other Herbal Preparations of Interest to the Aerospace Physician*

*Gingko biloba:* Gingko biloba extract, derived from leaves of the prehistoric tree of the same name, has recently enjoyed tremendous popularity for the treatment of circulatory disorders and improved mentation. The German E-commission reports, several clinical trials, and a multivariate analysis have found gingko to be a probable free-radical scavenger, platelet inhibitor, and mild cerebral and peripheral vasodilator that was associated with temporarily improved social and cognitive function of some demented patients (2,29,32,43), although one case report suggests that bilateral subdural hematomas may have been precipitated or aggravated by use of the supplement (37). The vasodilatory effects have made Gingko a possible non-pharmacological alternative for mild claudication (43). The effects of gingko biloba extract on $G_z$ tolerance, or complications as a result of $G_z$ exposure while taking the substance are unknown. Although gingko seems to improve cerebral blood flow, its purported peripheral vasodilatation and unknown effects on splanchnic vessels could theoretically affect $G_z$ tolerance.

*St. John's wort: Hypericum perforatum* (St. John's wort) has become one of the most prescribed pharmaceuticals in Europe, and is rapidly gaining popularity in the U.S. The substance, long used as an antidepressant, anti-inflammatory, antidiarrheal, astringent, and gout treatment (43), has been studied in European and English language literature. Utilizing multiple regression analysis, Linde et al. (30) concluded that St. John's wort was "more effective than placebo for the treatment of mild to moderately severe depressive disorders." Other uses for the herb include external application to mild burns and abrasions (30,36,39,43). Side effects of the supplement have been minimal, with the most commonly reported being photosensitization, following very high doses. The major concern for the aviation medical specialist is the *reason* for its use. As a "natural" alternative to antidepressant medications such as Prozac, *Hypericum* offers an attractive substitute and one, which under current military and civilian aviation regulations need not be reported. A risk, however, is that patients may be tempted to use this preparation en lieu of previously prescribed antidepressant medications. The physician should, therefore, recognize the use of *Hypericum* as a signal to inquire more deeply into the patient's psychomedical history.

TABLE IV. INGREDIENTS OF GENERAL MEDICAL CONCERN.

| Ingredients of General Medical Concern |
|---|
| **Hepatotoxins** |
| *Senecio spp* (Thread leafed groundsel and Life root) |
| *Larria tridentata* (Chaparral) |
| *Symphytum officinale* (Comfrey) |
| *Teucrium spp.* (Germander) |

*The mandrake mistake: Mandragora officinalis* (European mandrake) is a parasympathomimetic hallucinogen. It shares its name, however, with *Podophyllum peltatum* (also called (American) mandrake or mayapple) which is the source of podophyllin used topically for the treatment of condylomata acuminata. Unwary supplement users have mistakenly ingested large quantities of *Podophyllum* mistaking it for *Mandragora officinalis* (26). Furthermore, *Podophyllum* has been identified as an unlabeled adulterant in other herbal preparations (7). *Podophyllum,* when ingested, is a highly potent irritant cathartic capable of causing sudden severe nausea and diarrhea resulting in profound electrolyte disturbances and occasionally encephalopathy (7,2). The unwitting use of such a preparation would be poorly advised in the aviation environment, yet preparations containing the herb may contain no warning as to its potential adverse effects.

### *Ingredients of General Medical Concern (**Table IV**)*

*Hepatotoxins–the toxic pyrrolizidines:* Although not sudden incapacitants, herbs capable of causing fulminant and often fatal hepatic damage should clearly not be used by anyone. Regrettably, several of these herbs continue to be listed ingredients or adulterants in a large number of dietary supplements. These toxins cause a veno-occlusive phenomenon within the liver that ultimately leads to cirrhosis and potential liver failure. Serious cases have been reported following the use of preparations containing *Senecio spp.* (thread leafed groundsel and life root) (26,43), *Larria tridentata* (chaparral) (2,23,38), *Symphytum officinale* (comfrey) (2,26,43), *Lycopodium spp.* (found in jin bu huan) (25), and *Teucrium spp.* (germander) (12,26,28), among others. Several instances of hepatic damage have been associated with other herbs, such as *Scullitaria,* which does not contain pyrrolizidine alkaloids, but have been refuted after careful examination of the preparations revealed the presence of these alkaloids suggesting adulteration with other herbs such as *Teucrium spp.* (43).

## DISCUSSION

### *The Physician's Responsibility*

The physician may discover an ethical quandary when dealing with the patient who is using herbal

preparations in conjunction with or en lieu of conventional therapy. Conventional wisdom certainly suggests that the physician should inquire about the use of unconventional therapies, and should consider their risks and potential benefits when formulating a treatment plan for the patient. However, as most non-traditional medications have neither been shown to be effective or nor safe, the physician must consider whether advising or permitting the use of the medications constitutes endorsement of unproved therapies. Should a major adverse event occur due to the herbal preparation used with the physician's approval, would the physician be liable or partially liable for the event? Conversely, not inquiring carefully about the use of herbal preparations could lead to unexpected interaction between herbal preparations and prescribed medications. Were the physician to not inquire about drug allergies or other medications currently being used prior to prescribing a pharmaceutical, he or she would likely not meet accepted standards of care. The same logic could be similarly applied to the patient who is using herbal dietary supplements. These ethical issues are further complicated by inconsistently applied labeling standards for the products and reported inconsistencies in formulation even within the same preparation.

In the final analysis, however, the patient's best interest must prevail and the physician should engage in a partnership with patients who account for their use of unconventional therapies. Only by engaging in such a dialogue can the physician prevent untoward outcomes that result from side-effects of the supplement or interaction of the supplement and prescribed medications. However, the physician must be careful not to simply proscribe all therapies not specifically issued by him or herself. As half of patients already fail to reveal their use of alternative therapies to their physician for fear of ridicule or simple belief that the traditional physician lacks the expertise to reliably advise them about it (19), a general proscription of all unconventional therapies would likely result in undisclosed use of the therapies, potentially to the patients' harm.

*The Aerospace Medicine Physician and the Aviator*

The military flight surgeon has a unique responsibility that transcends traditional medical therapeutics. He or she also has the responsibility to treat and prevent illness and incapacitation, to assess the risk of either when determining suitability for flying duties, and to maintain the effectiveness of aviation crewmembers to carry out their mission in stressful and hostile circumstances. The civilian AME has the responsibility to properly represent the Federal Air Surgeon in the application of the regulatory standards and guidelines for the medical certification assessment of pilots. For both groups of physicians, their responsibilities extend beyond the simple assessment of a single affected system, illness, or injury and encompass the whole person and his or her environment. In this manner, then, the aerospace medicine physician has an obligation to inquire about and understand the effects of all pharmacologically active substances the patient may be taking.

Unfortunately, due to lack of clinical information, quantified methods of aeromedical risk assessment cannot currently be used to determine if an herbal preparation is safe to consume during aviation duties, which leaves the aeromedical physician in a quandary once the patient has revealed the use of such preparations. In the absence of such quantifiable risk data, the physician must utilize some other artful algorithm to guide his decision-making processes. These questions should be considered:

1. Is the use of the preparation due to signs or symptoms that suggest an underlying medical problem separate from the preparation in question?
2. Is any component known to have potential impairing, incapacitating or neuropsychiatric effects (including sudden unpredictable side effects)?
3. Does the preparation seem likely to contain unlabeled or incorrectly labeled ingredients?
4. Is the preparation being used in a dose range far outside that of current experience or in an extremely concentrated form?
5. Is any component of the preparation known to cause physical harm (even infrequently, unless the quantified incidence of adverse effects is known)?
6. Is the preparation an alcohol based tincture, tonic or elixir?

If the answers to all of these questions are negative, the aeromedical physician is unlikely to be able to justify an absolute prohibition of their use as legal dietary supplements. However, if the answer to any of the above questions is affirmative, a potential risk exists that should be managed by correcting or properly treating the underlying illness, urging the patient to discontinue use of the preparation and prohibiting aviation duties while harmful or incapacitating substances are used, and by prohibiting the use of alcohol based elixirs while performing aviation duties. Adverse aeromedical experiences with dietary supplements should be disseminated promptly.

*Limitations of this Review*

The reader must be reminded that the true incidence of adverse effects, either as a predicted action or an undesirable side-effect, is not known, and until costly clinical trials are conducted, are likely to remain so. Moreover, the entire body of literature researched and tabulated does not cover all of the thousands of substances potentially utilized in the non-regulated pharmacopeia. This study did not try to answer whether particular mishaps were caused by the use of these substances or the illnesses they may have been treating. Accident analysis is a complex multifactorial process, often with multiple active and latent root causes. In a future study, the NTSB accident coding will be used to look at approved and unapproved medication-related mishaps and mishaps with illnesses or impairment root causes. In the meantime, however, investigators should remain alert to substances listed in our table (**Table V**) that can cause pilot incapacitation. The use of postmortem toxicological testing, as a method to infer patterns of utilization among the rest of the flying population, is problematic and may only be considered circumstantial

TABLE V. SELECTED COMMINLY USED BOTANICAL SUBSTANCES.

| Common Name(s) | *Scientific Name* | Aeromedical Considerations | General Medical Considerations | Other Names | Common uses | Some Evidence of Effectiveness for |
|---|---|---|---|---|---|---|
| **Agrimony** | ***Agrimonia eupatonia*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Astringent, sore throat, cystitis, stomach upset, gall bladder disorders, incontinence, analgesic, antiviral, anti-inflammatory | Internal: mild acute diarrhea; inflammation of the mouth and throat. Externally: Astringent, may be used for mild inflammation of skin 45 |
| **Akee** | ***Blighia sapida*** | | Reported to have mild hypoglycemic effects | | Anti-diabetic | |
| **Aloe** | ***Aloe*** | | | Barbados aloe, Curacao aloe | Emollient, laxative, burn treatment | Internally: Effective laxative |
| **Ammi** | ***Ammi majus*** | | Contains psoralens, may cause photosensitivity | | | |
| **Angelica** | ***Angelica archangelica*** | | | | Emmenagogue, abortifacient, carminative, stomachic, expectorant, relieves menstrual cramps and insomnia, diuretic. Topical anti-inflammatory | Possible spasmolytic, may relieve mild dyspepsia |
| **Anise** | ***Pimpinella anisum*** | | **Allergic reactions** have been reported | Aniseed | Antispasmodic, aromatic, expectorant, tonic carminative, aphrodisiac, emmenagogue, galactagogue | Expectorant actions, may be used for respiratory catarrh, weakly spasmolytic |
| **Aristolochia** | ***Aristolochia spp*** | | **Interstitial Nephropathy** following ingestion has been | | Frequently cited adulterant or substitute | |
| **Arnica** | ***Arnica montana*** | | | Leopard's Bane | anti-inflammatory (topical), immunostimulant | |
| **Balm** | ***Melissa officinalis*** | | | Balm mint, bee balm, cure-all, dropsy plant | Antispasmodic, calmative, carminative diaphoretic, hypotensive, stomachic, emmenagogue, insomnia, depression, relief of menstrual cramps, asthma, migraine, relief of toothache and treatment of cold sores | May have mild sedative effects useful for nervous disorders of sleep |
| **Bayberry bark** | ***Myrica Pennsylvania and M. Cerifera*** | | | | Astringent, circulatory stimulant, diaphoretic, colds, hemorrhoids, diarrhea | Some mineralocorticoid activity |
| **Bearberry** | ***Arctostaphylos uva-ursi*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Diuretic, astringent, anti-microbial, demulcent | |
| **Black cohosh** | ***Cimicifuga racemosa*** | | | Black snakeroot, rattle weed, rattle root | Dysmenorrhea, antispasmodic, astringent, diuretic, expectorant, promotes labor, sedative, rheumatism, pms, menopausal symptoms | May reduce LH secretion, possibly effective for premenstrual discomfort, dysmenorrhea and climacteric symptoms |
| **Boneset** | ***Eupatorium perfoliatum*** | | May cause nausea if taken orally. Contains toxic alkaloids | Feverwort | Diaphoretic, cathartic, emetic, febrifuge, breaking up mucous | May increase sweating |
| **Borage** | ***Borago officinalis*** | | Slight constipating effect, Contains pyrrolizidine alkaloids | | Diuretic, astringent, febrifuge, tonic, galactagogue, antipyretic, diaphoretic, expectorant, laxative, anti-inflammatory, adrenal restorative | Weak astringent, mild expectorant |
| **Boron** | ***Boron*** | | | | Increase testosterone levels and muscle mass | No benefit demonstrated |
| **Broccoli** | ***Brassia spp*** | | Concentrated Vit. K may antagonize anticoagulants | | | |
| **Broom** | ***Cysticus scoparius, Sarothemanus scoparius*** | • Elaborates cardiac glycoside. may precipitate dysrhythmia alone or in combination with other glycosides | Has diuretic effects, may potentiate effects of concomitantly used diuretics | Scotch broom, Irish broom, Broomtops, Besom | Cardiotonic (used for CHF), diuretic, hypertensive, astringent. | |
| **Bryony** | ***Bryonia dioica*** | | | | | |
| **Buchu** | ***Barosma betulina*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | Bucco | Diuretic, Urinary antiseptic | |
| **California poppy** | ***Exchscholtzia californica*** | • Hallucinogen | | | Sedative/hypnotic nervine | |
| **Capsicum or Cayenne pepper** | ***Capsicum spp*** | | | Chile peppers | Stimulant, carminative, tonic, antiseptic, rubefacient, sialogogue, reduces cold symptoms, stomachic, useful in the treatment of Delirium Tremens | Topical analgesic |
| **Cascara** | ***Rhamnus purshiana*** | | | Sacred bark, Chittem bark | Laxative, bitter tonic, gallstones, liver ailments | FDA approved as a laxative |
| **Catnip** | ***Nepaeta cataria*** | | | | Bronchitis, antidiarrheal agent, antiflatulent, digestive aid, astringent, antispasmodic, sedative, diaphoretic, mind altering effects if smoked | |
| **Celandine** | ***Chelidonium majus*** | • Potential Sedative Effects. may potentiate other sedative agents | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Astringent, cholagogue | |
| **Chamomile (German and Hungarian)** | ***Matricaria recutia, chamaemelum nobile*** | | persons allergic to ragweed, asters or chrysanthemums should use this herb with caution | | Carminative, anti-inflammatory, anti-spasmodic, anti-infective, diaphoretic, analgesic, local healing, anxiolytic / mild sedative | Anti-inflammatory and antispasmodic effects |

| Common Name(s) | Scientific Name | Aeromedical Considerations | General Medical Considerations | Other Names | Common uses | Some Evidence of Effectiveness for |
|---|---|---|---|---|---|---|
| **Chaparral** | ***Larrea tridentiata*** | | **Hepatotoxin**, contains toxic pyrrilozidine alkaloids | | Bronchitis, colds, rheumatic pains, stomach pain, chickenpox, and snakebite, anti-oxidant | |
| **Chaste tree berry** | ***Vitex agnus-castus*** | | | Vitex | PMS, dysmenorrhea, climacteric symptoms | May alter prolactin secretion |
| **Chromium picolinate** | ***Chromium picolinate*** | | | | Insulin regulator, maximize glycogen use, increase muscle uptake of amino acids | Limited evidence that chromium can slightly lower cholesterol, some evidence of improved glucose tolerance in NIDDM |
| **Cinnamon** | ***Cinnamomum camphora*** | • Hallucinogen (when smoked) | | | Topical anti-inflammatory | |
| **Clamshell** | | | Heavy Metal (Mercury, Lead) toxicity reported | Hai gai fen | Mineral supplement, strength enhancer | |
| **Cluster bean** | ***Cyamopsis tetragonolobus*** | | May reduce absorption of some antibiotics | | | |
| **Comfrey** | ***Symphytum officinale*** | | **Hepatotoxin,** contains toxic alkaloids | Knitbone | Remedy for stomach ulcers, cancer, and astringent salve for sprains and abrasions, demulcent, emollient, expectorant, hemostatic, refrigerant, hoarseness, treatment for intestinal problems, bronchitis, pleurisy, rheumatism | Some topical antiinflammatory action, promotes callus formation |
| **Couchgrass** | ***Agropyrum repens*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | Twitchgrass, Quickgrass, Doggrass | Diuretic, demulcent, urinary anti-microbial | |
| **Damiana** | ***Turnera aphrodisiaca*** | | | | Aphrodisiac, laxative anti-anxiety, urinary antiseptic, antidepressant | |
| **Damsissa** | ***Amni visnaga*** | | | | | Hypoglycemic effects |
| **Dandelion** | ***Taraxacum officinale*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | Tang kuei, dang qui | Digestive aid, laxative, diuretic, liver and gallbladder protectant, prevents iron deficiency anemia, pms, breast tenderness | |
| **Deadly nightshade** | ***Atropa belladonna*** | • Anticholinergic<br>• Sedative | | | Hay Fever, Peptic ulcer disease, Migraine HA | Known anticholinergic and sedative actions |
| **Echinacea** | ***Echinacea purpurea (leaves/flowers) Echinacea angustifolia, E. Pallida, E. Purpurea*** | | High doses reported to cause nausea and dizziness | Purple Coneflower | Ameliorate flu-like conditions, urinary and resp. Tract infections, antiseptic, digestive, eczema, acne, migraine, antipyretic, antiflatulent<br>Immune stimulant: Increase number and activate granulocytes, increase tumor necrosis factor release and decrease hyaluronidase activity | Some evidence of immune stimulant effect |
| **Ephedra** | ***Ephedra spp*** | • Potent vasoconstrictor / Hypertensive agent. Stimulant. has been associated with MI, stroke, seizures and sudden death | Erythroderma reported | Ma Huan, Epitonin | Appetite suppressant, strength enhancer, enhances concentration,<br>Antiasthmatic, nasal decongestant, vasodilator, anti-allergic, hypertensive, circulatory stimulant, weight loss, legal stimulant (especially if bolstered with caffeine), mood enhancing, aphrodisiac | Some evidence of efficacy as an appetite suppressant, effective nasal decongestant |
| **Eucalyptus** | ***Eucalyptus spp*** | | May cause nausea, vomiting and diarrhea when taken orally | | Antiseptic, deodorant, expectorant, stimulant, indigestion, respiratory ailments | Secretomotor, expectorant, weakly spasmolytic |
| **Evening primrose** | ***Oenothera biennis*** | | | | Astringent, demulcent, depression, stimulating effect on liver, spleen and GI tract, skin rashes, pms, weight loss | No evidence of efficacy |
| **False hellebore** | ***Veratrum viride*** | | | | | |
| **Fennel** | ***Foeniculum vulgare*** | | | | Demulcent, stomachic, antispasmodic, aromatic, carminative, diuretic, expectorant, stimulant galactagogue, aromatic, rubefacient | May have utility for dyspepsia, and as respiratory secretolytic, |
| **Fenugreek** | ***Trigonella foenum-graecum*** | | May cause local inflammation if used topically | | Aphrodisiac, antidiabetic (hypoglycemic), expectorant, gout, demulcent, restorative, neuralgias, skin irritations, menstrual cycle stabilizer | No data on efficacy |
| **Feverfew** | ***Tanacetum parthenium*** | | | | Alleviate migraine headaches, anti-inflammatory, relaxes blood vessels, digestive stimulant, expels worms | |
| **Garlic** | ***Allium sativum*** | | | | Antibiotic, antiplatelet, antihyperlipidemic, Antihelminthic, antispasmodic, diuretic, carminative, digestive, expectorant | Average decrease in total cholesterol and TG by 10% and 15%. Probable antiplatelet effect, may reduce blood pressure |
| **Germander** | ***Teucrium spp*** | | **Hepatotoxin,** elaborates toxic alkaloids | | Implicated as an adulterant or substitute | |
| **Ginger** | ***Zingiber officinale*** | | | | Appetizer, carminative, diaphoretic, stimulant, prevention of motion sickness, rubefacient | Some antiemetic effects |
| **Gingko** | ***Ginkgo biloba*** | • Anti-platelet activity<br>• Possible vasodilator. Unknown effects on Gz tolerance | | Ginkgo | Treatment of circulatory disorders, claudication, memory improvement,<br>Enhance cerebral blood flow, tinnitus, vertigo, Alzheimer's, hemorrhoids, antidepressant, antioxidant, peripheral vasodilator | Possible free-radical scavenger and antiplatelet agent.<br>"Egb was safe and appears capable of stabilizing and in a substantial number of cases, improving the cognitive performance and the social functioning of demented patients for 6 months to 1 year." (29) |

| Common Name(s) | *Scientific Name* | Aeromedical Considerations | General Medical Considerations | Other Names | Common uses | Some Evidence of Effectiveness for |
|---|---|---|---|---|---|---|
| **Ginseng** | ***Panax ginseng, P. Quinque-folius*** | | May potentiates gynecomastic and galactorrheic effects of calcium channel blockers, digitalis glycosides, ethionamide, griseofulvin, methyldopa, phenothiazines, spironolactone | Ginseng | Adaptogen, demulcent, anti-stress, aphrodisiac, menopausal symptoms<br>Performance enhancer | No clear evidence of efficacy |
| **Ginseng, Siberian** | ***Eleutherococcus senticosus*** | | Contains eleutherosides, chemically related to cardiac glycosides that may cause false laboratory levels | Eleuthero | Aphrodisiac, Anti-inflammatory, metabolic stabilizer | |
| **Goldenseal** | ***Hydrastis canadensis*** | | | Orange Root, Yellow Root | Bitter tonic, digestive aid, genitourinary conditions, menorrhagia, upper respiratory ills, irritate gums, canker sores, ringworm treatment atrophic vaginitis | Astringent, weak antiseptic |
| **Goosegrass** | ***Galium aparine*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | Cleavers | Diuretic, lymphatic cleanser, astringent, anti-inflammatory | |
| **Gotu kola** | ***Centalla asiatica*** | | | | Aphrodisiac, promotes longevity, phlebitis, heal episiotomies, expectorant, leprosy, hypertension, ulcers, rheumatism, hot flashes, improve memory, antidepressant | May have some anti-inflammatory effects |
| **Ground holly** | ***Chimaphilia umbellata*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **Guarana root** | ***Pasta guarana*** | | | | Increase stamina, energy and concentration | Caffeine effects |
| **Gymnema** | ***Gymnema sylvestre*** | | | | Appetite suppressant | Gymnemic acid obtunds taste of bitter and sweet. Possibly effective at curbing sugar urges |
| **Hawthorne** | ***Crataegus monogyna, C. Laevigata, C. Oxycantha*** | • Positive inotropic and chronotropic effects<br>• Possible weak peripheral vasodilator, unknown effects on Gz | | | Antispasmodic, sedative, coronary vasodilator, possible use in atherosclerosis and as an antihypertensive | Slow acting coronary vasodilator at high doses, Positive inotropic and chronotrope, increased myocardial circulation may have utility for NYHA class I and II cardiac insufficiency |
| **Hellebore** | ***Veratrum viride*** | | | | | |
| **Henbane** | ***Hyoscyamus niger*** | • Powerful anticholinergic<br>• Potential Sedative Effects, may potentiate other sedative agents | | | Used in the treatment of nervousness, melancholy or mania | |
| **Holy thistle** | ***Cnicus benedictus*** | | | | Bitter tonic, astringent, diaphoretic, antibacterial, expectorant | May have utility for mild dyspepsia |
| **Hops** | ***Humulus lupulus*** | • Hallucinogen (when smoked)<br>• Potential mild Sedative Effects, may potentiate effects of other sedatives | | | Sedative, mind-altering action, appetite stimulant, antiflatulent, anti-septic, astringent, anti-insomniac | |
| **Horse chestnut** | ***Aesculus hippocastanum*** | | | | Astringent, anti-inflammatory | |
| **Hydrangea** | ***Hydrangea paniculata, Hydrangea arborescens*** | • Hallucinogen (when smoked) | Has diuretic effects, may potentiate effects of concomitantly used diuretics | Seven barks, Wild Hydrangea | Diuretic, treatment for prostatitis and urolithiasis | |
| **Ink cap** | ***Coprinus atramentarius*** | | Disulfiram type reaction with alcohol | | | |
| **Inosine** | | | | | Energy enhancer | No published evidence |
| **Ipecac** | ***Cephaelis ipecacuanha*** | | | | Expectorant (for use with bronchitis, Emetic, Sialogogue | Effective emetic in prescribed formulations |
| **Jimson weed** | ***Datura stramonium*** | • Anticholinergic<br>• Potential Sedative / Hypnotic. Effects, may potentiate other sedative agents | | Thorn Apple | Inhaled anticholinergic, useful for asthma | |
| **Jin bu huan** | ***Lycopodium serratum*** | • Potential Sedative Effects, may potentiate other sedative agents | | Jin Bu huan Anodyne | Sedative analgesic, useful for stage fright | |
| **Juniper** | ***Juniperus communis*** | | Renal toxicity reported with prolonged use | | Diuretic, antiseptic, carminative, stomachic, tonic, urinary anti-microbial, rubefacient, antirheumatic, gastrointestinal infections | |
| **Karela** | ***Mormodica charnatia*** | | Hypoglycemic, use caution in conjunction with other antidiabetic agents | | | |
| **Kava** | ***Piper methisticum*** | • Hallucinogen | | Awa, Waka, Lavena, Yaqara | Diuretic, sedative, narcotic-like hallucinogen effects | |
| **Kelp** | ***Fucus vesiculosus*** | | High potassium iodide content, may affect thyroid function | | | |

| Common Name(s) | *Scientific Name* | Aeromedical Considerations | General Medical Considerations | Other Names | Common uses | Some Evidence of Effectiveness for |
|---|---|---|---|---|---|---|
| **Kola nut** | ***Cola acuminata, C. vera*** | | | | Increase stamina, energy enhancer, diuretic, anti-depressant | Caffeine and theobromine containing. Typical caffeine effects. Actual concentrations vary widely in preparations |
| **Kyushin** | | | Cross reacts with digitalis antibodies giving false elevated readings | Derived of toxin from poison toads | | |
| **Lady's mantle** | ***Alchemilla spp.*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Astringent, anorexia, diuretic, rheumatism, diarrhea, enteritis, menstrual problems, decreases menstrual flow leukorrhea | Astringent |
| **Larch** | ***Larix americana*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **Life root** | ***Senecio aureus*** | | **Hepatotoxin,** elaborates toxic alkaloids | Squaw Weed, Golden Senecio | Emmenagogue, uterine diseases, diaphoretic, diuretic, abortifacient, urinary problems, expectorant | |
| **Lily of the valley** | ***Convallaria majalis*** | • Elaborates cardiac glycoside, may precipitate dysrhythmia alone or in combination with other glycosides | | | Cardiac stimulant | |
| **Liquorice** | ***Glycyrrhiza glabra*** | | Sodium and water retention, may worsen hypertension | | Expectorant, demulcent, rheumatism, prevents cavities, prevents growth of tumors, stabilizes menstrual cycle, anti-inflammatory effects | Expectorant, antitussive, anti-inflammatory and antiallergic properties |
| **Lobelia** | ***Lobelia inflata*** | • Hallucinogen (when smoked) | | Pukeweed, Indian Tobacco | Anti-asthmatic, emetic, nervine, expectorant | |
| **Magic mushroom** | ***Psilocybe semilanceata*** | • Potent hallucinogen | | | No medicinal uses | |
| **Male fern** | ***Dryopteris filix-mas*** | | | | | |
| **Mandrake (European)** | ***Mandragora officinarum*** | • Hallucinogen, anticholinergic | | | Nervine, hypnotic | |
| **Mandrake (American)** | ***Podophyllum peltatum*** | | Severe nausea followed by intense diarrhea if taken orally. | Long dam cho, Mayapple | Cathartic | Topical treatment of condyloma acuminata |
| **Marshmallow root** | ***Althaea officinalis*** | | May inhibit absorption of some drugs | | Diarrhea, cystitis, demulcent, diuretic emollient | May be useful for inflammation of mucous membranes and GI tract<br>May inhibit mucociliary activity |
| **Melatonin** | ***Melatonin*** | • May cause undesired drowsiness | | | Sleep agent | Possibly effective |
| **Menispermum** | ***Menispermum conadense*** | | Contains toxic alkaloids | | Muscle building, testosterone increase | No evidence of benefit |
| **Milk thistle** | ***Silybum marianum*** | | | | Liver protectant, galactagogue, demulcent | Contains silymarin may exert a protective effect on the liver |
| **Mistletoe** | ***Viscum album*** | | CNS, Cardiac and GI toxicity | | Anti-hypertensive (not currently available commercially) | |
| **Myrrh** | ***Commiphora spp.*** | | | | Astringent, fragrance, antiseptic, carminative, stomachic, asthma, antimicrobial, anti-catarrhal, emmenagogue | Mild astringent |
| **Nettle** | ***Urtica diocia*** | | | Stinging Nettle | Cystitis, diuretic, astringent, antiasthmatic, treatment of BPH, menorrhagia | Diuretic, some possible symptomatic benefit in BPH |
| **Nutmeg** | ***Myristica fragrans*** | • Hallucinogen / Seizures reported with very high doses | | | | |
| **Opium poppy** | ***Papaver somniferum*** | • Sedative Effects, may potentiate other sedative agents | | | | |
| **Pansy** | ***Viola tricolor*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Expectorant, ant-inflammatory, diuretic, anti-rheumatic, laxative | |
| **Pareira brava root** | ***Chondodendron tormentosum*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Diuretic | |
| **Parsley** | ***Petroselenium crispum*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Diuretic, expectorant, emmenagogue | |
| **Pasque flower** | ***Anemone pulsatilla*** | | | Wild Flower, Meadow Anemone | Nervine, anti-spasmodic, anti-bacterial | |
| **Passion flower** | ***Passiflora incarnata*** | • Potential Sedative Effects, may potentiate other sedative agents | | | Sedative, hypnotic, decreases muscle tension, headaches | May have both mild stimulant and sedative effects |

| Common Name(s) | *Scientific Name* | Aeromedical Considerations | General Medical Considerations | Other Names | Common uses | Some Evidence of Effectiveness for |
|---|---|---|---|---|---|---|
| **St. John's wort** | ***Hypericum perforatum*** | | | Multiple preparations | Antidepressant, antiinflammatory, antidiarrheal, astringent, rheumatism, gout, diuretic, gastritis | "There is evidence that extracts of hypericum are more effective than placebo for the treatment of mild to moderately severe depressive disorders." 27<br>Topical astringent |
| **Stephania** | ***Stephania tetrandra*** | | | | | |
| **Stone root** | ***Collinsonia candensis*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **Strophanthus** | ***Strophanthus kombe*** | • Elaborates cardiac glycoside, may precipitate dysrhythmia alone or in combination with other glycosides | | | | |
| **Thread-leafed groundsel** | ***Senecio longilobus*** | | **Hepatotoxin** | | | |
| **Tryptophan** | ***Tryptophan*** | • Profound depression precipitated when tryptophan *FREE* amino acid preparations used in large doses. | Eosinophilia-myalgia syndrome | | | |
| **Valerian** | ***Valeriano officinalis*** | • Sedative | | | Sedative / hypnotic, Carminative, antidepressant, hypotensive | Insomnia, note that 5-10% may have paradoxical stimulant effects |
| **Water plantain** | ***Alisma plantago*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **White squill** | ***Scilla maritima*** | • Elaborates cardiac glycoside, may precipitate dysrhythmia alone or in combination with other glycosides | | | Cardiac tonic | |
| **Wild carrot** | ***Daucus carota*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Diuretic, anti-lithic, carminative, anti-spasmodic | |
| **Wild lettuce** | ***Lactuca virosa*** | • Potential Sedative Effects, may potentiate other sedative agents | | Lettuce opium | Hypnotic sedative, anti-spasmodic | |
| **Witch hazel** | ***Hamamelis virginiana*** | | | | Astringent, hemostatic, sedative, tonic, vaginitis, hemorrhoids, menorrhagia, analgesic, anti-inflammatory | Effective, FDA approved astringent |
| **Wolfsbane** | ***Aconitum napellus*** | • Potential Sedative Effects, may potentiate other sedative agents | | | Rash and fever of measles, varicella, colds and treatment of insomnia | |
| **Wood sorrel** | ***Oxalis acetosella*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **Wormwood** | ***Artemisia absinthum*** | | Massive rhabdomyolysis and renal failure reported with ingestion of liquor | absinthe | Bitter digestive tonic, uterine stimulant, menstrual regulator, anti-rheumatic | |
| **Yellow foxglove** | ***Digitalis lanata*** | • Elaborates cardiac glycoside, may precipitate dysrhythmia alone or in combination with other glycosides | | | | |
| **Yellow jasmine** | ***Gelsemium sempervirens*** | | | | | |
| **Yohimbe** | ***Corynanthe yohimbi*** | • Hallucinogen (Bark) | | | Increase muscle mass, strength and density | A2 adrenergic blockade. Negligible effects on impotence |
| **Yohimbe** | ***Pausinystalia yohimbe*** | | Hypertension at low doses, Heart failure in those at risk | | Vitalizing agent for men, male impotence | |

| Common Name(s) | Scientific Name | Aeromedical Considerations | General Medical Considerations | Other Names | Common uses | Some Evidence of Effectiveness for |
|---|---|---|---|---|---|---|
| **Pellitory** | ***Anacyclus pyrethrum, Parietaria diffusa*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Diuretic, demulcent | |
| **Pennyroyal** | ***Mentha pulegium or Hedeoma pulegoides*** | | Hepatotoxin | | Abortifacient , carminative, stimulant | |
| **Peppermint** | ***Mentha piperita*** | | | | Stomachic, carminative, antispasmodic, diaphoretic, antiseptic, analgesic | May soothe some GI symptoms |
| **Periwinkle** | ***Catharanthus roseum*** | • Hallucinogen | | | Not currently used in phytomedicine | Source of vincristine, vinblastine |
| **Pheasant's eye** | ***Adonis vernalis*** | • Elaborates cardiac glycoside, may precipitate dysrhythmia alone or in combination with other glycosides | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **Plantain** | ***Plantago major*** | | | Greater plantain | Expectorant, demulcent, anti-inflammatory, astringent | |
| **Psyllium** | ***Plantago psyllium*** | | | | Laxative, decreases cholesterol | Effective laxative |
| **Purple foxglove** | ***Digitalis purpurea*** | • Elaborates cardiac glycoside, may precipitate dysrhythmia alone or in combination with other glycosides | | | | |
| **Ragwort** | ***Senecio spp*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Diuretic | |
| **Rauwolfia** | ***Rauwolfia serpentina*** | • Sedative, Hypotensive agent | May cause depression, sedation Contains estrone, estradiol and estriol, secondary gynecomastia reported. | Indian snakeroot | | |
| **Red raspberry** | ***Rubus idaeas*** | | | | Astringent, uterine stimulant, antiemetic, laxative | |
| **Rupture wort** | ***Herniariea glabra*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **Sage** | ***Salvia officinalis*** | • Seizures and loss of consciousness with very large doses | | Garden Sage | Astringent, antihydriotic, antispasmodic, dries mothers milk, epilepsy insomnia, measles, sea sickness, veneral diseases, rheumatism, peripheral vasodilator | Antiseptic and local anti-inflammatory due to tannins |
| **Sarsaparilla** | ***Smilax spp*** | | Potential carcinogen | | Diuretic, expectorant, flavoring agent, menstrual stabilizer, carminative, diaphoretic, rheumatism, colds, fevers, treatment of psoriasis | Diuretic, laxative, expectorant |
| **Sassafras** | ***Sassafras albidum*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | | |
| **Saw palmetto** | ***Serenoa repens*** | | | Sabal | Diuretic, BPH, urinary antiseptic, aphrodisiac, GI infections, increase breast size, increase sperm production, reverse atrophy of testes and mammary glands | Possibly effective for mild BPH symptoms |
| **Scopolia** | ***Scopolia carniolica*** | • Anticholinergic. Potential Sedative Effects, may potentiate other sedative agents | | | | |
| **Senna** | ***Cassia spp.*** | | | | Cathartic | Effective laxative agent |
| **Shepherd's purse** | ***Capsella bursa-pastoris*** | | Has diuretic effects, may potentiate effects of concomitantly used diuretics | | Diuretic, uterine stimulant, astringent | |
| **Skullcap** | ***Scutellaria laterfolia*** | • Potential Sedative Effects, may potentiate other sedative agents | | | Antispasmodic, diuretic, relaxing nervine used to treat delirium tremens, rabies, menstrual cramps , epilepsy | No evidence of efficacy |
| **Slippery elm** | ***Ulmus rubra, U. fulva*** | | | | Demulcent, emollient, nutrient, astringent | Oral demulcent |
| **Squill** | ***Urginea maritima*** | • Elaborates cardiac glycoside, may precipitate dysrhythmia alone or in combination with other glycosides | | | Arthritis, cardiac remedy | |

evidence to support an increase in utilization patterns. This study does, however, suggest the need for continued research into the aeromedical implications of the use of non-regulated pharmacologically active substances.

## SUMMARY

Alternative medications may offer the advantages of self-medication, reduced cost, easy availability, and in some cases, less toxicity and side effects. Their disadvantages, though, include poor standardization, no clinical trials, unknown or unpredictable side effect profiles, and few, if any, comparisons with existing modalities. Deaths due to herbal preparations have occurred, particularly with the ephedra group. The aeromedical physician must, then, proactively seek information regarding the patient's use of herbal preparations, despite a current lack of official guidance on the subject from regulating authorities. This inquiry carries with it the tacit understanding that the intent is to guide and inform patients regarding the use or non-use of potentially harmful substances, and to minimize the risk of in-flight incapacitation. Unlike some other purified and concentrated pharmaceutical agents, however, there is little evidence to suggest that the vast majority of these agents have an immediate harmful potential. There is, therefore, no justification for a blanket prohibition on the consumption of substances that are, in essence, foods, except for those preparations the use of which results in an affirmative answer to the guideline questions above. This approach certainly requires the physician to deal with each case on an individual basis; however, this approach with existing medications and medical conditions is also what sets the aerospace medicine practitioner apart from the common "cookbook" approaches arising in the broader practice of medicine in this country. More definitive science-based guidance is not likely to be readily available in the absence of large clinical trials that are, likewise, unlikely to be conducted. This summary outlines a rationale to serve the aeromedical physician's endeavor to earn the trust of their aircrew patients so that in the area of alternative treatments, as in other personal and sensitive aspects of their lives they will be willing to discuss their concerns in an open therapeutic relationship.

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