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Nutritional supplements, ergogenic aids, and herbals

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Why should dental practitioners know about nutritional supplements, ergogenic aids, and herbal products? Consumers are taking (and usually self-prescribing) dietary supplements at alarming rates and many are not discussing these supplements with their physicians [1]. Consumers are probably even less likely to discuss supplement use with a dental practitioner. Therefore, it is imperative to ask patients about their use of dietary supplements, which encompass vitamins, minerals, herbals, and ergogenic and weight loss aids, in order to provide safe, competent, and comprehensive care. A frank and open-minded discussion with patients will help set goals and desirable outcomes and guide patients to effective and ethical care. Even when practitioners do not embrace or support the same values and ideas as their patients, a complete discussion is warranted so that the patient is advised on appropriate care and averts seeking treatment from sources without scientific background or ethics [2,3].

The availability of supplements is keeping up with consumer demand. The dental practitioner should be aware of various supplements used in wellness and in illness. This article discusses popular dietary supplements, ergogenic aids, and botanicals used in general health and disease, as well as those specifically touted for use in oral health. Side effects and interactions will be noted, along with practice points for interviewing and advising patients in clinical practice.

Dietary supplement regulation

The 1994 Dietary Supplement Health and Education Act defines a dietary supplement as a product that (1) is intended to supplement the diet and

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contains a vitamin, mineral, amino acid, herb, or other botanical; (2) is not represented as a conventional food; and (3) is ingested in the form of a capsule, powder, softgel, or gelcap [4]. As a result of the 1994 Dietary Supplement Health and Education Act, the Food and Drug Administration (FDA) or any other federal agency is not required to oversee the sale of dietary supplements. Unlike FDA-approved medications, dietary supplements are not subject to premarket safety or efficacy trials [5]. Manufacturers of dietary supplements do not need to demonstrate the efficacy of the product or prove its safety before offering the product for sale.

The United States Pharmacopoeia, an independent, nongovernmental organization, set up the Dietary Supplement Verification Program (DSVP) in 2000 to respond to the need to assure consumers that dietary supplements contain the type and amount of ingredients listed on the label [6]. Manufacturers of dietary supplements may voluntarily participate in this program. It subjects products to scientific testing for purity, accuracy of ingredient labeling, and manufacturing practices. When a product passes the United States Pharmacopoeia standards, it may bear the DSVP certification mark.

Another example of an independent, not-for-profit organization offering a voluntary certification program for dietary supplements is NSF International [7]. The certification process includes product testing, good manufacturing practices inspections, and ongoing monitoring in exchange for the NSF mark. The DSVP or NSF marks are desirable to producers and consumers because customers will be able to identify quickly a certified product and confidently make a selection.

Nutritional supplements

Nutritional supplements are defined under the realm of dietary supplements, but are generally limited to micronutrients such as vitamins, minerals, and amino acids. Herbs and botanicals are discussed in a subsequent section. Table 1 lists various supplements, their consumer uses, and concerns to the dental practitioner.

Lysine is one of eight essential amino acids necessary for many metabolic roles in the human body. Supplemental and topical lysine is commonly used in the treatment and prevention of herpes labialis, the most common recurrent infection caused by herpes simplex virus [8]. The main premise of lysine treatment is that it inhibits replication of the herpes simplex virus by limiting the availability of cellular arginine and by competing with the arginine during the herpes simplex virus replication process [9]. Commercially available lysine in the biologically active form (L-lysine) is available as a monohydrochloride salt and is most commonly sold in 500 mg tablets [10]. Monohydrochloride crystalline lysine can be used for topical application of L-lysine to herpes simplex virus infections [11]. Lysine has been shown to

reduce the incidence of ulcers, as well as size, duration, and number of ulcers when they appear, but the studies have used variable dosages ranging from 500 mg/day to 1500 mg/day and show mixed results in the efficacy of the treatments [9–11]. Additional research should be encouraged to determine optimal doses for efficacy while controlling closely for dietary sources of lysine and arginine.

Calcium is essential to maintain bone integrity. Loss of bone density in osteoporosis is systemic, including alveolar bone [12]. Bone resorption and loss are common denominators of both periodontal disease and osteoporosis. Although evidence of a causal relationship between the two remains to be demonstrated in prospective research, analysis of the Third National Health and Nutrition Survey data demonstrated a relationship between low dietary calcium intake and increased risk of periodontal disease [13]. In a study of postmenopausal women, Krall et al [14] demonstrated an association between calcium and vitamin D supplementation and reduced risk of tooth loss; those who experienced tooth loss were significantly more likely to experience systemic bone loss. Research in this area has produced mixed results secondary to small sample sizes, varying definitions of periodontal disease and osteoporosis, and lack of prospective data [12]. Nutritional status, including adequacy of dietary intake of calcium and vitamin D may play a significant role in this relationship.

Calcium intake should come from foods in a varied diet. It is recommended that most adults consume 1000 mg of calcium per day and that adolescents, teenagers, and older adults should consume more than this amount [15]. If it is not possible to achieve the recommended intake of calcium, then supplements may be valuable. Calcium supplements are available in a variety of forms. Depending on the compound combined with elemental calcium, popular supplements are available as calcium carbonate, calcium citrate, and "natural" forms such as oyster shell calcium, bone meal, or dolomite. The amount of elemental calcium per tablet will determine how many tablets are needed to achieve the supplemental dose of calcium desired. Calcium carbonate is best absorbed with food, whereas calcium citrate is absorbed independent of food. For optimal absorption of calcium, it is recommended that a maximum of 500 mg is taken at one time. "Natural" sources of calcium from bone meal, oyster shell, or dolomite should be avoided due to the risk of heavy-metal contamination [16].

Vitamin C is essential to humans for many biologic processes including collagen formation [17]. In the case of ascorbic acid deficiency, gingivae have a decreased ability to resist inflammation and bleeding, and gingivitis occurs [17]. As a result, there is speculation that increasing vitamin C intake will prevent or improve gingivitis and periodontitis. There is only limited evidence that periodontal disease is associated with low vitamin C intake and it appears to be most significant in tobacco users [18]. In a literature review dedicated to vitamin C and oral health, Fontana [19] discussed the oral manifestations of vitamin C deficiency. In periodontal disease, however,

Table 1
Select supplements—uses and concerns for the dental practitioner

Supplement	General use	Oral use	Concerns
Caffeine	Stimulant, ergogenic aid	—	Restlessness, diuresis
Calcium	Bone density	Integrity of maxilla and mandible	Inadequate calcium may be implicated in tooth loss and periodontal disease
Capsaicin	Pain relief	Pain relief for toothache, trigeminal neuralgia	Active compound in chili peppers; irritant to skin and eyes
Coenzyme Q10	Cardiovascular health	Periodontal disease treatment	Research has not demonstrated efficacy in treating periodontal disease
Echinacea	Upper respiratory infections	Antimicrobial for oral health	Research has not demonstrated efficacy
Ephedra	Stimulant, ergogenic aid	—	Tachycardia, hypertension, arrhythmias; possible additive effect with epinephrine
Garlic	Cardiovascular disease	Treatment and prevention of oral candidiasis	Additive effects with blood thinning agents and antagonistic effects with some HIV medication
Ginseng	General tonic, stimulant, improve stress resistance	—	Interferes with platelet aggregation and possibly with other stimulants; may decrease blood glucose levels in type 2 diabetes mellitus
Green tea	Cancer prevention	Oral and esophageal cancer prevention, reduce risk of dental caries	Additional research needed
Guarana	Weight loss, reduce fatigue	—	Avoid use with caffeine, ephedra, or other central nervous system stimulants
Kava	Antianxiety	—	Additive effect with sedatives; implicated in liver failure
Lysine	An essential amino acid in human metabolism	Aphthous ulcers and herpes labialis	Additional research is needed to determine effective dose

Saint-John's-wort	Mild depression	—	Interaction with medications including digoxin, cyclosporin, indinivir; may also cause xerostomia
Tea tree oil	Bacterial and fungal infections of the skin	Bacterial and fungal infections of mucosa, including candidiasis	Oil should not be ingested
Valerian	Antianxiety		Additive effect with sedatives
Vitamin C	Collagen formation and other biologic processes	Integrity of gingivae and improved healing	Research has not demonstrated benefit of vitamin C supplementation for periodontal disease or oral mucosa healing
Yohimbe	Impotence, exhaustion, diabetic neuropathy	—	May cause hypertension

the local irritation is the causative agent, and a suboptimal level of vitamin C may be an aggravating factor but not the cause. There are no published clinical trials with vitamin C for periodontal disease or oral surgery that demonstrate any benefit of supplementation to treat oral disease or enhance healing. Furthermore, objective and controlled studies are needed before vitamin C is routinely prescribed as therapy for oral health. One related research trial is a study on naturopathic medicine to prevent and treat periodontal disease sponsored by the National Center for Complementary and Alternative Medicine. The naturopathic regimen proposes several nutrients, including vitamin C, to improve host resistance to bacteria, as well as an herb combination to combat the bacterial stress [20].

Coenzyme Q10, also known as CoQ10 or ubiquinone, is an endogenous provitamin essential to the synthesis of adenosine triphosphate and possesses antioxidant properties acting in concert with vitamin E [21]. Four recent articles on CoQ10 review the literature on its use, particularly in cardiovascular disease [21–24]. These reviews report that the populations most likely to benefit from supplementation are those with low levels of endogenous CoQ10 [23,24]. It has also been suggested that coenzyme Q10 is effective in the treatment of periodontal disease in people who are deficient in CoQ10; however, recent controlled trials have not been published [25]. Possible interactions with cholesterol and blood pressure–reducing agents should be considered because CoQ10 may cause an additive effect [23]; antagonistic effects may be seen with warfarin [26]. In addition, CoQ10 should not be used with doxorubicin chemotherapy because of possible toxicity [21,23].

Multivitamin and/or mineral supplements may be taken to improve general and oral health. It is the position of the American Dietetic Association that supplemental vitamins and minerals may be beneficial when a well-balanced diet cannot be maintained [27]. No scientific evidence has been found in published research of a select combination of vitamins and minerals in supplement form to enhance oral health. Patients should be encouraged to consume a variety of foods according to the Food Guide Pyramid and to supplement when adequate intake cannot be achieved.

Ergogenic aids

Ergogenic is a term applied to substances or devices that generate or enhance energy production [28]. With the recent increase in use of dietary supplements, there is evidence that the many athletes and body builders are taking various ergogenic aids such as anabolic steroids, creatine, ephedra, and caffeine, which may have reversible and serious nonreversible side effects [28]. Although no supplements of any kind can replace hours of training and conditioning, athletes of all levels—from recreational to professional—may be willing to try an ergogenic aid to gain the competitive

edge. In a recent survey of 674 adolescent athletes, 16% admitted use of creatine and, of those, 26% reported side effects such as muscle cramps, headache, and increased thirst [29]. Similar incidence of use of creatine by college athletes and anabolic steroids by adult athletes has been noted [30].

Caffeine is well known as a central nervous system stimulant. It is considered an ergogenic aid because it may be taken in high doses to enhance endurance. The typical dose of caffeine for an ergogenic effect is 250 mg to 500 mg, the equivalent of three cups of coffee. Side effects include restlessness, insomnia, and diuresis.

Caffeine is often mixed with ephedra (*Ephedra sinica*), an herbal supplement also known as ma huang having a molecular structure similar to amphetamine and norephedrine [31]. The two products are often combined in weight-loss supplements to provide energy, decrease appetite, and increase metabolic rate. Ephedrine and pseudoephedrine are the active constituents in ephedra that are noted to have several drug interactions. These interactions may also be significant in the ''natural'' or herbal form [26]. Although there are no published reports of interactions at this time, the dental practitioner should be aware of theoretic interactions of ephedra with epinephrine because it has similar effects as ephedrine [32]. Side effects of ephedra alone may include tachycardia, hypertension, arrhythmias and, in some cases, death. A review of reported adverse effects attributed to ephedra is detailed by Haller and Benowitz [33] who concluded that the use of supplements containing ephedra by some susceptible populations pose a serious health risk that includes fatal myocardial infarction and lethal cardiac arrhythmias. Patients seeking dental care with local anesthesia should avoid taking any ephedra-containing products for at least 12 hours prior to the appointment to reduce the risk of interactions.

Anabolic steroids are derivatives of testosterone used to increase muscle size and strength. The steroids have anabolic action on muscles but the user risks sexual, psychologic, and serious irreversible side effects. Dehydroepiandrosterone (DHEA) is a precursor in the gonadal steroid pathway and is used similarly as anabolic steroids without supportive research for efficacy. Also like anabolic steroids, DHEA can have undesirable side effects ranging from the development of masculine features in women to hepatic toxicity at high doses [26]. The National Collegiate Athletic Association and the United States Olympic Committee have established general guidelines of banned substances, but each individual sports organization has specific rules. A list of individual organizations can be found at http://www.healthycompetition.org/. In addition to a ban by sporting organizations, it is illegal in the United States to obtain anabolic steroids without a prescription [28].

Creatine is used for performance enhancement by increasing the amount of phosphocreatine for faster generation of adenosine triphosphate. It may be used to decrease rest time between bouts of physical exertion and to gain energy. Creatine helps delay muscle fatigue and soreness by buffering lactic acid production. Weight gain is a known side effect. Long-term side effects

are unknown due to the fact that the duration of research on creatine has been 3 months or less [28].

Several other herbs are used for their ergogenic effect, such as ginseng, green tea, guarana and yohimbe; these are discussed in the section on herbal supplements.

Herbal supplements

For centuries, herbal preparations have been used as medications. Herbs may be in the form of a tea, tincture, pill, cream, or lozenge but are all derived from botanical components such as leaves, roots, bark, or flowers of plants. Traditional Chinese medicine uses several herbs in combination (usually given in tea form) for a synergistic effect. In the United States, many consumers of herbs do not consult with health providers or qualified healers but are lured by product marketing and the convenience of over-the-counter access. With greater availability of supplements in pill form, there is an increased risk of misidentification, contamination with impurities, and enhanced doses beyond the traditional intended level [34]. This article focuses on several herbs with potential issues related to dental practice.

Capsaicin is an active component of the *Capsicum* herb (eg, cayenne and chili peppers). It is recognized as a pain reliever by the action of the capsaicin constituent that causes the release of substance P in nerves. With repeated applications, as substance P is depleted, the sensation of pain diminishes. In oral health, capsaicin has been reportedly used for toothaches, trigeminal neuralgia, and as an ingredient in a gargle for laryngitis [26]. Published clinical trials of capsaicin and oral health are lacking; however, the National Institute of Dental and Craniofacial Research is sponsoring a study to test the efficacy of capsaicin after third-molar extraction [20]. Proven results of effectiveness will be beneficial for reducing postoperative pain and decreasing the use of analgesic medications. If patients do choose to use capsaicin, then it should be applied with a cotton swab, and care should be taken because it may irritate eyes and skin.

Echinacea (*Echinacea angustifolia* or *Echinacea purpurea*) is recognized for its antimicrobial properties and is commonly used in treating general upper respiratory infections [26]. In the realm of oral health, some proponents of herbal medicine advocate Echinacea in mouth rinses and toothpaste [3]. Although there may be some theoretic basis to the action of Echinacea as an antiseptic in oral hygiene products, there is no published research (to this author's knowledge) separating the action of tooth brushing and mouth rinsing from that of the added herb.

Garlic (*Allium sativum*) is a popular supplement in the prevention of heart disease by way of decreasing blood pressure and improving lipid profiles [26]. Garlic is considered safe when ingested regularly as part of foods. Short-term improvements in cholesterol have been noted but not proven superior to placebo beyond 6 months [35]. It has also been suggested that an

aqueous solution of garlic extract as an oral rinse may reduce the occurrence of chronic candidiasis by reducing the adhesion of *Candida* to epithelial cells [36]. Oral supplements of garlic in high doses can have several side effects. Consumers have complained of offensive halitosis and body odor when using garlic, and manufacturers have responded with "odorless" supplements that may be more acceptable. Practitioners should be aware of garlic's interactions with other supplements and medications when garlic is used in doses greater than that of food seasoning. For example, when garlic is combined with fish oils or other "blood thinning" supplements such as ginger, ginkgo biloba, or ginseng, the antithrombotic effects may be exaggerated. With regard to medications, close monitoring is recommended when patients insist on using garlic supplements in a regimen with anticoagulant/antiplatelet drugs such as warfarin or aspirin [26,37]. Garlic supplements should be avoided in some HIV/AIDS treatments because they have been shown to decrease levels of saquinavir [38].

Ginseng is available as American ginseng, Panax ginseng, or Siberian ginseng. Although these ginseng preparations are used in different ways, the major uses of the ginseng family are as a tonic or stimulant and for improving stress resistance. Panax ginseng has also been recommended for use in people with type 2 diabetes mellitus to lower blood glucose levels. Ginseng may interact with other stimulating substances such as caffeine or guarana, interfere with platelet aggregation, and have an additive effect with hypoglycemic agents [26].

Green tea (*Camellia sinensis*) is used generally in cancer prevention because of its polyphenol compounds [39]. Epidemiologic evidence supports the fact that green tea may reduce the risk of cancers (eg, esophageal, oral) [40] by way of the mechanism of polyphenol-induced apoptosis [39,40]. In oral health, green and black tea have been reported to prevent dental caries due to the bactericidal effect on *Streptococcus mutans* and the inhibition of salivary amylase [41]. Additional research is warranted because only small clinical trials have been reported; however, constituents in tea may prove beneficial to reduce the incidence and severity of caries [42,43].

Guarana (*Paullinia cupana*) is used for weight loss, enhanced athletic performance, and reduction in fatigue. It is a natural source of caffeine, so concomitant use with caffeine or ephedra should be avoided due to the risk of overstimulation to the central nervous system [26].

Yohimbe (*Pausinystalia yohimbe*) is used by consumers for impotence, exhaustion, and diabetic neuropathy. The active constituent, yohimbine, can cause hypertension [44]. Consumers may not be aware of increased blood pressure from yohimbe. This supplement is considered unsafe by the FDA [26].

Tea tree oil, also known as *Melaleuca alternifolia*, is a natural remedy for bacterial and fungal infections of the skin and mucosa, including candidiasis [26]. Jandourek et al [45] found that a solution of tea tree oil was effective against oral candidiasis in AIDS patients when used as an oral rinse.

Valerian and Kava are used as antianxiety agents or sedatives for relaxation. They can have additive side effects when combined with similar agents. In addition, Kava has recently been implicated in liver failure [46].

Saint-John's-wort (*Hypericum perforatum*) is used systemically for mild depression and associated symptoms such as fatigue, loss of appetite, and anxiety. Topically, Saint-John's-wort may be used for relieving inflammation and promoting healing [26]. Adverse effects when Saint-John's-wort is taken systemically may be dry mouth, dizziness, photosensitivity to sunlight, and interactions with medications. Drugs that are metabolized through the P450 cytochrome system interact with Saint-John's-wort. For example, concomitant use of Saint-John's-wort diminishes the efficacy of drugs such as cyclosporine, digoxin, indinivir, and warfarin [47].

Given the availability and the popularity of herbs and supplements in the United States, dental practitioners may better serve patients by understanding some of the direct and indirect effects of these supplements. Herbs and supplements may be used to treat an oral condition or may be encountered in the dental office as a treatment for a chronic disease. If the supplement is used for an oral condition, then the dental practitioner should be asking why. Is it a substitute for a failed conventional treatment or simply enhancing the treatment's efficacy without adverse side effects? If the supplement is used for a general chronic condition, then the dental provider should be aware of side effects and consider interactions with any planned treatment or medications.

Research issues

Conventional medicine philosophy dictates that rigorous scrutiny needs to be conducted with the scientific model of double-blind placebo-control clinical trials [48]. Rigorous research studies are not available for herbs and supplements. Most of the documented research has been conducted outside the United States or has been faulted for being of short duration or sponsored by herb/supplement manufacturers. Because natural products cannot be patented, researchers may be inclined to isolate active compounds. This may actually help clarify the side effects and the way in which the substance works [49]. As a practitioner, it is important to describe the mechanism of action, efficacy, and known safety or side effects [28,50].

Supplement interactions

Although many consumers believe it is safe to take herbs and supplements because they are "natural," dietary supplements are subject to the same mechanisms of interactions as pharmaceutical drugs. Pharmacokinetic interactions are related to absorption, displacement, and metabolism, whereas pharmacodynamic mechanisms refer to additive, opposing, or

transport changes. These pharmacokinetic or pharmacodynamic interactions may occur with food, medications, or other supplements. For example, kava and valerian may have additive effects when combined with alcohol or prescribed sedatives; anticoagulants such as garlic can have additive effects with warfarin; and Saint-John's-wort has been implicated in pharmacokinetic interactions with several drugs using similar metabolic pathways [51]. Current information on drug interactions and advisories can be obtained from the National Center for Complementary and Alternative Medicine Web site at http://nccam.nih.gov/health/.

Practice points for dental practitioners

An open dialogue with all patients is essential. Practitioners should discuss the subject of supplements as part of routine care. Pertinent questions to ask are "what, why, when, where, and how" (Table 2). Practitioners should learn about common supplements most likely to be used by the population they serve. Familiarity with herbs and supplements may ease any tension in the discussion. In addition and, perhaps most important, to increase the likelihood of honest responses, patients should understand why their practitioner is inquiring about dietary supplements within dental care.

In evaluating the potential for a supplement, practitioners should consider the following five factors: method of action, available research, adverse effects, legality of use, and professional ethics [52]. When patients make an informed decision to take supplements, practitioners should advise them to buy from well-known, reputable companies to reduce the risk of supplement contamination and adulteration [53]. Consumers should be educated to look for quality-control standards such as the DSVP or NSF certification. Consumer and practitioner collaboration will be critical to safe and rational use of supplements [49].

Additional information is available from online resources such as the National Center for Complementary and Alternative Medicine (http://nccam.nih.gov/), the Office of Dietary Supplements (http://dietary-supplements.info.nih.gov/), the American Botanical Council (www.herbmed.org), and the Herb Research Foundation (www.herb.org). Electronic sources are usually resources with the most current information. Text references such as the

Table 2
Questions to ask regarding supplement use

What	What are you taking? What dosage do you take?
Why	Why are you taking it (for a symptom, disease, or disease prevention)?
When	When did you start taking it? When in the day do you take it?
Where	Where did you obtain your information? Where do you buy the product?
How	How is it working?

Natural Medicines Comprehensive Database, the *Physician Desk Reference for Herbal Medicine*, and the *Physician Desk Reference for Dietary Supplements* would make valuable additions to any practitioner's reference library.

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