

COURSE TITLE: Risks and Benefits of Dietary Supplement Use

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COURSE CREDIT HOURS: 2.5 CEUs

COURSE DATE: May 31, 2022

COURSE DESCRIPTION: The purpose of this course is to provide oral health care professionals with current information about the assessment, treatment and management of clients taking selected vitamins, minerals and herbal supplements. Specific course content will focus on current knowledge of the risks and benefits of supplements. Potential applications for supplement use in dentistry will be reviewed.

COURSE OBJECTIVES: Upon completion of this continuing education program, the dental professional will be able to:

1. Discuss how herbal and dietary supplements are regulated in the United States.
2. Discuss potential benefits and harms associated with use of vitamins and minerals.
3. Discuss unique considerations for supplement use in special populations.
4. Identify strategies to reduce risks when managing patients taking supplements.
5. Discuss drug/dietary supplement interactions of significance to dentistry.

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Why are we here today?

- The majority of patients seen in dental practice are using medications (traditional and alternative/complementary) and various health strategies to improve their physical and mental status, and sense of wellness
- These behaviors and substances can dramatically influence overall health but some also can potentially increase risk for adverse reactions

What are Natural Health Products?

- Natural health products (NHPs) are naturally occurring substances that are used to restore or maintain good health.
- They are often made from plants, but can also be made from animals, microorganisms and marine sources.
- They come in a wide variety of forms like tablets, capsules, tinctures, solutions, creams, ointments and drops.
- Natural health products, often called "complementary" or "alternative" medicines, include:
 - Probiotics
 - Herbal remedies
 - Vitamins and minerals
 - Homeopathic medicines
 - Traditional medicines such as traditional Chinese medicines
 - Other products like amino acids and essential fatty acids
 - Many everyday consumer products, like certain toothpastes, antiperspirants, shampoos, facial products and mouthwashes

Natural Health Product Licensing

- All natural health products must have a product license before they can be sold in Canada.
- To get a license, applicants must give detailed information about the product to Health Canada, including medicinal ingredients, source, dose, potency, non-medicinal ingredients and recommended use(s).
- Once Health Canada has assessed a product and decided it is safe, effective and of high quality, it issues a product license along with an eight-digit Natural Product Number (NPN) or Homeopathic Medicine Number (DIN-HM), which must appear on the label.
- This number verifies that the product has been reviewed and approved by Health Canada.
- Search for licensed natural health products using Health Canada's [Licensed Natural Health Products Database](#).

Where do I find credible information about natural health products?

- Natural Medicines. <https://naturalmedicines.therapeuticresearch.com/>
- LexiComp for Dentistry
- National Institutes of Health (NIH) Office of Herbal and Dietary Supplements. <https://ods.od.nih.gov/>
- MedlinePlus. Herbs and Supplements. https://medlineplus.gov/druginfo/herb_All.html
- NIH Center for Complementary and Integrative Health: Herbs At A Glance <https://www.nccih.nih.gov/health/herbsataglance>

- Family Doctor.org. Drug -Nutrient Interactions and Drug-Supplement Interactions. <https://familydoctor.org/drug-nutrient-interactions-and-drug-supplement-interactions-examples-of-dietary-supplement-interactions>
- Herb Research Foundation. <http://www.herbs.org/herbnews/>

What Do We Know About Supplement Use in Specific Populations?

Women of childbearing potential

Prenatal vitamins: Potassium iodide, Calcium, Vitamin D3, **Folic acid** (prevents neural tube defects; take at least 1 month before conception)

- **Vitamin D Deficiency:** sun-blocking pollution, sunscreen; avoiding sun exposure, geographic differences; Many people now require supplements; *avoid need for supplements = go outside* Experts now recommend annual blood test to screen for levels
- **vitamin D test** = 25-OH vitamin D; normal range is 30.0 to 74.0 ng/mL;
- perform test in fall and winter months

Vitamin D Supplements

- **D2 = ergocalciferol:** fungus/yeast-derived product; (ergocalciferol is made from ultraviolet irradiation of ergosterol in yeast); **shorter half-life, decreased potency**
- **D3 = cholecalciferol:** synthesized in humans in skin; form most utilized in clinical trials **more effective at raising and maintaining vitamin D test** (binds better to receptors, longer half-life)
- **vegans may not want to use D3 form** because supplements are derived from animal source cholecalciferol is made from irradiation of 7-dehydrocholesterol from lanolin and the chemical conversion of cholesterol)

What do we know about the effectiveness of HDS?

- Studies have found that some dietary supplements may have: some benefit, such as melatonin for jet lag
 - little or no benefit, such as ginkgo for dementia
- Supplements bought from stores or online may differ in important ways from products tested in studies
- Most research shows that taking multivitamins doesn't result in living longer, slowing cognitive decline, or lowering the chance of getting cancer, heart disease, or diabetes

What do we know about the safety of HDS?

- Taking a multivitamin is unlikely to pose any health risks
- DS may cause drug interactions and use poses risk with some medical conditions and/or if about to undergo surgery
- Many dietary supplements have not been tested in pregnant women, nursing mothers, or children Some products marketed as dietary supplements—promoted mainly for weight loss, sexual enhancement, and bodybuilding—may contain prescription drugs not allowed in dietary supplements or other ingredients not listed on the label
 - Some of these ingredients may be unsafe

HDS and Emergency Room Visits

- Dietary supplements result in an estimated 23,000 emergency room visits every year in the United States
- Many of the patients are young adults having heart problems from weight-loss or energy products and older adults having swallowing problems from taking large vitamin pills

Recalled Supplements Remain on Market

- sports enhancement supplements
- weight loss supplements
- sexual enhancement supplements

Liver Injury with HDS

- Although it's still rare, more cases are being reported of acute (sudden) liver damage in people taking dietary supplements in the United States and elsewhere.
- Liver injury: can be severe; can require an emergency liver transplant; is sometimes fatal **Use of unregulated herbal or dietary supplements associated with liver injury** Prospective study using 8 sites within the Drug-Induced Liver Injury network
 - 839 people with drug-induced liver injury caused by HDS or conventional medications (excluding acetaminophen cases)
- During 10 year study period, proportion of cases linked to HDS use increased from 7% to 20% Products commonly used for bodybuilding or weight loss in middle-aged women
- HDS products associated with death or need for transplant included: energy boosters
 - herbal "Viagra"
Chinese herbal mixtures
ayurvedic compounds
 - colon and "cleanse" products
- Liver injury cases are more likely to require transplantation than with hepatotoxicity associated with conventional medications

Safety Considerations

Are there risks?

- False labeling
- Risks: interact with medications, complicate medical problems, risks if undergoing surgery
- *Most dietary supplements have not been tested in pregnant women, nursing mothers, or children*

ANTIOXIDANT SUPPLEMENT USE AND CANCER

- It is estimated that > 50% of patients with chronic diseases or cancers use HDS
- 64% to 81% of cancer survivors take vitamin and mineral supplements
14% to 32% of patients begin using supplements

Tsai HH, Lin HW, Simon Pickard A, Tsai HY, Mahady GB. *Evaluation of documented drug interactions and contraindications associated with herbs and dietary supplements: a systematic literature review. Int J Clin Pract. 2012;66(11):1056-1078.*

Identified 1,491 pairs of HDS-drug interactions: 213 HDS , 509 medications

- **Greatest number of documented interactions with medications:**
 - St. Johns wort, magnesium, calcium, iron, ginkgo
- Of a total of 509 drugs, most were used for: CNS disorders (100)
 - cardiovascular system disorders (90) systemic anti-infectives (75)
- **Greatest number of reported interactions with HDS: warfarin;** most HDS interactions(100+): **insulin, aspirin, digoxin, ticlopidine**
- HDS products containing **herbs** were more likely to have documented interactions with medications and contraindications than vitamins, minerals and other types of dietary supplements.
- Patients using medications that have a **narrow therapeutic range** (i.e. warfarin, digoxin) =
- **greater risk for adverse outcomes because of HDS–drug interactions**
- Important for patients on anticoagulants (i.e. warfarin) who concomitantly took HDS products that had antiplatelet or anticoagulant effects

Be Aware! *Coumadin* has the **most drug and herbal dietary supplement interactions of all prescription drugs**

Interaction Risks

- Herbal interactions with prescription medications or other chemicals can:
 - interfere with how the drug may be broken down in the body
 - enhance side effects of prescription medications
 - block the intended therapeutic effect of a drug

Drug-Herb Actions and Interactions of Significance to Dentistry Herbs and Bleeding

- Many herbs act as anti-platelet or anticoagulant medications
- Effects may be additive if taking one or more of these herbs and/or if taking aspirin, ibuprofen, warfarin, etc.
- Patients are **unaware** of these effects
- Many herbal products contain multiple herbs: patients may not always know what is contained within their supplements
- There is limited evidence to support the bleeding effects of herbal medications
 - Anecdotal evidence
 - Case studies
 - Animal studies; laboratory studies

Common herbs: ginkgo, garlic, ginseng, ginger

- *Antagonize platelet activating factor*
- **All herbal medicines should be discontinued for 14 days prior to surgery (including oral surgery)**
- Mnemonic: A “Few G’s” will help you remember:
- When the “g” is followed by a vowel (e.g. **g**inkgo), the herb is associated with a bleeding effect
- When the “g” is followed by a consonant (e.g. **g**reen tea), there is not a concern for bleeding
- A Few G’s include: fever**f**ew, **g**inkgo biloba, **g**inger, **g**arlic, **g**inseng

Echinacea

- **Use:** common cold, cough and bronchitis
- **Hepatotoxic**, especially when used with other hepatotoxic meds:
 - Limit use to 10 days
- **May decrease effectiveness of corticosteroids**

Feverfew

- Anti-inflammatory (rheumatoid arthritis) Preventive for migraine headache
- Muscle soreness
- Effect: Inhibits platelet aggregation Active: sesquiterpene lactone, parthenolide
- **May cause irritation of oral mucosa and tongue**
- Increases risk for photosensitivity
- **Use:** migraine prophylaxis; fever reduction; anti-inflammatory (RA, muscle soreness) Abrupt discontinuation: rebound headaches, joint pain and stiffness, anxiety
- **Inhibits platelet activity**
- **Up to 15% of users may develop aphthous ulcers May cause irritation of oral mucosa/tongue Contraindicated in pregnancy**
- Increases risk for photosensitivity
- May increase the risk of bleeding, especially in people with blood-clotting disorders or using blood thinners to help prevent clots, for example:
- Aspirin warfarin heparin and low molecular weight heparins (enoxaparin, dalteparin) clopidogrel (Plavix) dabigatran (Pradaxa) rivaroxaban (Xarelto)
- 41 drug interactions

Garlic: Anti-lipidemic, Antimicrobial, Anti-asthmatic, Anti-inflammatory

Components implicated with bleeding

- **Ajoene**
- **Allicin** – strong odor and flavor; platelet effect is *irreversible*
- **Sulfur containing compounds**
- Effect: **antiplatelet** = inhibits production and/or release of chemical mediators: Platelet activating factor
- Adenosine (decreases platelet function)
May affect blood glucose levels
- 187 drug interactions

Ginger:

- best with dried formulation; anti-inflammatory effects; relieve motion sickness and morning sickness; relieve upset stomach
- **antiplatelet** = reduces platelet thromboxane, inhibits platelet aggregation; 55 drug interactions

Ginkgo biloba

- Prevent decreased cerebral function
- Peripheral vascular insufficiency associated with Alzheimer's disease or age-related dementia
Improve memory and cognition
- Components implicated in bleeding:
 - **Terpenoids**
 - Potent antagonists of platelet activating factor
 - Long-lasting and rapid onset with oral dosing
- Effect: **antiplatelet** = increases prothrombin time and decreases platelet activity
Many case reports of severe bleeding
- **Risk for severe spontaneous bleeding with concurrent use of aspirin and warfarin**
- 269 drug interactions: avoid taking with blood thinners and anticonvulsants

Ginseng

- Anti-cancer
- Slows aging
- Prevent heart attack
- Improve digestion
- Reduce hypertension
- Strengthen immunity
CNS stimulant
- Components implicated in bleeding: **Ginsenosides**
- Effect: **antiplatelet** = inhibit PAF, platelet aggregation, thrombin and thromboplastin
Interacts with 102 drugs
- Antagonizes the effect of warfarin (decreasing effectiveness)
- **Potentiates bleeding with aspirin, NSAIDs, warfarin, heparin**

Kava

- **Use:** anxiety, stress relief; acts like a minor tranquilizer; skeletal muscle relaxant
Potentiates CNS effects of other CNS depressants: alcohol, BDZs, barbituates, sedatives, general anesthesia = **caution with sedation dentistry**
- **FDA monitoring for hepatotoxicity** (In Europe, over 20 cases of cirrhosis, hepatitis and liver failure; 1 liver transplant needed)
- **Contraindicated in pregnancy, lactation and Parkinson's disease** (may cause dopamine antagonism)
- Interacts with 253 drugs

Licorice

- **Use:** gastric disorders; antitussive; aphthous ulcers; herpes simplex
- **May cause hypertension:** monitor vital signs
- **May alter platelet aggregation**

- ***Contraindicated in pregnancy, lactation, liver or renal impairment***

Melatonin

- Natural hormone that helps to regulate the sleep-wake cycle: Insomnia, Jet lag, Shift work sleep disorders
- Because melatonin causes drowsiness, avoid use with:
 - Alcohol Benzodiazepines, sedatives, hypnotics
 - Sedating antihistamines Opioid analgesics
 - Muscle relaxants
 - Other herbs that cause drowsiness: Kava, St. John's Wort
- As with many herbal products, blood clotting may be affected with use of melatonin with anticoagulants

St. John's Wort

- Weed-like plant
- Most widely studied herb with demonstrated efficacy Reduce mild to moderate depression
- Mechanism of St. John's wort
- The exact mechanism = unclear
- Mechanism is believed to involve inhibition of serotonin reuptake The major active antidepressive constituents in St John's wort:
 - *hyperforin* and *hypericin* flavonoids and *tannins*

Efficacy of St. John's wort

- An early meta-analysis indicated that extracts of *Hypericum* may be ***more efficacious than placebo for the treatment of mild to moderately severe depressive disorders.***
- This study, which covered the results from 23 smaller, earlier studies, is perhaps the most oft-cited by manufacturers and other supporters of St John's wort.
- This study was later updated to include further studies, for a total of 27, to form a **Cochrane Review:** The updated review found that *Hypericum* preparations were ***significantly superior to placebo and similarly effective as standard antidepressants***

St. John's Wort

- Components implicated in bleeding: **hypericin**
- Effect: ***induces some cytochrome P450 liver enzymes***
- **Reduces anticoagulant effect of warfarin (increases clotting) and lowers the INR**
- Decreases effects of many medications:
- **Many drug interactions:** Interacts with 527 drugs
 - Decreases effectiveness of drugs for HIV
 - Induces liver enzymes
 - Prolongs effects of general anesthetics Increases photosensitivity of tetracyclines
 - Reduces effect of glucocorticoids Decreased efficacy of anticoagulants

Valerian

- **Use:** mild sedative; mild anxiolytic; anxiety, depression, insomnia Causes drowsiness and sedation
- **Potentiates the effects of CNS depressants, including barbiturates**
- Interacts with 235 drugs

Vitamin E

- **Use:** fat soluble vitamin
- **Antioxidant**
 - Prevents oxidation of vitamins A and C
 - Protects polyunsaturated fatty acids in membranes from free radical damage Protects RBCs against hemolysis
- **May alter the effect of vitamin K on clotting factors**
 - Interacts with warfarin: increases hypoprothrombinemia = delays clotting and increases risk for spontaneous hemorrhage

Other Notable Interactions

Potential of Stimulants

Ephedra, yohimbe, guarana, ginseng

Potential of CNS effects of sedatives

Valerian, kava, St. John's wort

Effects on platelets

Risk for serotonin syndrome

antidepressants and St. John's wort

Potential of glucose lowering effects

Hypoglycemics, bilberry, bitter melon, dandelion, garlic

Immune system alteration

Echinacea, astragalus

Dental Considerations

- Synergistic drug effects with aspirin, NSAIDs: seek alternative analgesics Monitor patients on warfarin for herbal use and counsel appropriately
- Cross-reference all herbal and prescription medications prior to prescribing to ensure compatibility
 - Use a database that contains common herbal supplements (e.g. LexiComp for Dentistry)
- **Some HDS alter response to general anesthesia Also consider increased bleeding risk Discontinue all herbs 14 days prior to surgery**

Polyherbacy for Chronic Pain Avocado-soybean unsaponifiables

- 4 studies have shown that 300 to 600 mg of avocado sterol compounds per day are associated with reduced knee/hip pain and swelling after 3 to 6 months of use
- Reduces use of NSAIDs in some users

Omega-3 fatty acids

- fatty acids, especially 2 to 4 g of marine-based docosahexaenoic acid and eicosapentaenoic acid
- **may be helpful for arthritis**

Tumeric

- low quality evidence
- curcumin 1 to 2 g per day **may be beneficial for joint pain** **best taken with fatty meal**
- absorption may be improved if taken with black pepper

Cat's claw (*Uncaria tomentosa*)

- may be helpful for joint pain
- pentacyclic and tetracyclic alkaloids in cat's claw are associated with immunostimulant properties:
- increased phagocytosis
- anticancer
- antioxidant
- anti-inflammatory

Glucosamine: Inconclusive; large meta-analyses conclude only small improvements versus placebo or no improvement at all may work for specific subsets of individuals