The Use and Misuse of Herbs and Dietary Supplements

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<table>
<thead>
<tr>
<th>Learning Objectives</th>
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<tr>
<td>• Identify the current trends regarding use of herbs and dietary supplements in the US</td>
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<td>• Describe regulations of the herbs and dietary supplement industry</td>
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<td>• Evaluate current literature and information about commonly used herbs and dietary supplements including:</td>
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<tr>
<td>- Common uses or conditions treated</td>
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<tr>
<td>- Latest evidence regarding safety and efficacy</td>
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<td>- Major adverse effects</td>
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<td>- Major drug-herb interactions</td>
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**Background**

- Three-fourths of the world relies on natural medicines
- **JAMA study**
  - 1990 - 34% used > 1 alternative therapy
  - 1997 - 42% used > 1 alternative therapy
- Current use approximately 40-62%[^2][^3]
- $34 billion spent out of pocket annually on CAM[^3]
  - Products, classes, visits to providers
- $15 billion spent on herbs and dietary supplements[^3]

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**Trends in Consumer Use of Herbs and Dietary Supplements**

- **2010 NIH and AARP** surveyed Americans over the age of 50 years old[^1]
  - 37% used herbs and dietary supplements
  - 67% never discuss CAM use with a health care provider
- **2011 Harvard Opinion Research Program**[^2]
  - Conducted telephone survey of 1579 respondents
  - Approximately 4 out of 10 Americans reported using supplements in past 2 years

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[^2]: Barnes PM et al. CDC Advance Data from Vital and Health Statistics No 343; May 2004
**Trends in Consumer Use of Herbs and Dietary Supplements**

- 2011 Harvard Opinion Research Program
  - 36% had not told physician about use of supplements
  - 5% had been told by physician or nurse to stop supplement
  - 25% reported that they would stop using supplement if public health authorities found it was ineffective

2012 National Health Interview Survey

- Supplement to the Census Survey
- Asked about use of 18 non-conventional health care practices

**Results:**
- Found that use of non-vitamin/non-mineral dietary supplements was highest used CAM modality
- Use of these dietary supplements highest in Pacific, Mountain, and West North Central Regions


**2012 National Health Interview Survey**

- Fish oil
- Glucosamine or chondroitin
- Probiotics or prebiotics
- Melatonin
- Coenzyme Q10
- Echinacea
- Cranberry
- Garlic
- Ginseng
- Ginkgo
- Green tea
- MSM
- Milk thistle
- Saw palmetto
- Valerian

NY Times Article on Liver Damage from Dietary Supplements

_Spike in Harm to Liver Is Tied to Dietary Aids_


Liver Injury Related to Dietary Supplements

- Drug-Induced Liver Injury Network (DILIN) established in 2003 to track cases of liver injury
  - In 10 year period, 130 of 839 cases related to dietary supplements
    - First 2 years, dietary supplement injuries = 7%
    - 10 years later, dietary supplement injuries = 20% (p=0.0007)
  - Dietary supplements had significantly more severe cases vs. medications (p=0.002)
  - Quality product selection is an important safety aspect


Dietary Supplement Use in Chronic Kidney Disease

- The National Kidney Foundation webpage for herbal supplement use and kidney disease:
  - https://www.kidney.org/atoz/content/herbalsupp
  - Recommendation to avoid all dietary supplements for patients with kidney disease
  - Lists specific ones to avoid contain potassium or phosphorus and can contribute to hyperphosphatemia
  - Consider those that can affect renal function or worsen other disease states
  - Refer to a nephrologist if patient wants to use

New York Attorney General and Supplements

- February 2015 New York Attorney General accused 4 retailers of selling fraudulent and dangerous supplements
  - GNC
  - Target
  - Walgreens
  - Walmart
  - Testing showed 4 out of 5 products didn’t have labeled ingredients but instead had fillers

New York Attorney General and Supplements

- Walgreens
  - Ginseng contained powdered garlic and rice
- Walmart
  - Ginkgo biloba contained powdered radish, houseplants and wheat (labeled as wheat and gluten free)
- Target
  - 3 out of 6 products didn’t have ginkgo, SJW or valerian but instead powdered rice, beans, peas and wild carrots
- GNC
  - Unlisted ingredients including class of plants that includes peanuts and soybeans

Regulations

- 1951: 2 classes of drugs were established (prescription and non-prescription (OTC))
- 1962: Kefauver-Harris Amendment
- 1994: Dietary Supplement Health and Education Act (DSHEA)
- 2006: Dietary Supplement and Nonprescription Drug Consumer Protection Act
- June 22, 2007: New Dietary Supplement Current Good Manufacturing Practices (cGMPs) Final Rule Issued by FDA

DSHEA

- Signed into law on October 25, 1994
- Herbal supplements, vitamins and minerals considered dietary supplements not drugs
- Dietary ingredients in supplements no longer subject to pre-marketing safety evaluations
- Labeling criteria
  - Body structure and function claims
  - Cannot make therapeutic claims
  - Must state not approved by FDA
  - Must have manufacturer’s name and address
  - Not required to have lot numbers, expiration dates or contraindications

Dietary Supplement and Nonprescription Drug Consumer Act

- Passed by Congress on 12/26/06; effective 12/26/07
- Known as the Adverse Event Reports Bill (S. 3546)
- Amends the Federal Food Drug and Cosmetic Act and requires manufacturers to report serious adverse events for OTC drugs and dietary supplements
- Requires manufacturers to submit report of adverse event within 15 business days of receipt
- Requires labels to have address or phone number so that patients can report serious adverse events
Herbs and Dietary Supplements

Fish Oils

- Can consume in diet through cold water fish that are high in omega-3 fatty acids or through other natural products like avocado or almonds (alpha-linolenic acid)
- Uses include treatment of high triglycerides, reduction in risk of death from heart disease, cognitive function
- Look for EPA and DHA as active ingredients
- FDA approved products: Lovaza, Vascepa, and Epanova

Fish Oils

- Summary of clinical studies:
  - Appears to reduce triglycerides by 20-50%
  - May decrease risk of coronary heart disease death by 25% in healthy patients
  - May decrease overall cardiac mortality and MI risk in secondary prevention 16-20%
  - No apparent benefits in patients with atrial fibrillation
  - Controversial study related to prostate cancer

Fish Oils

- Side effects include fish aftertaste, burping/belching, flatulence
- Important Drug Interactions
  - Contraceptives may decrease the triglyceride lowering effect of fish oils
  - May increase risk of bleeding with antiplatelets and anticoagulants with high dose fish oils
  - Orlistat decreases absorption of fish oils
**Probiotics**

- Available as bacteria:
  - *Lactobacillus* species (L. acidophilus, L. rhamnosus, L. bulgaricus, L. reuteri, L. casei)
  - *Bifidobacterium* species (B. infantis, B. breve, B. longum, B. lactis)
- Available as yeast: *Saccharomyces boulardii*
- Benefits of probiotics are strain specific

**Probiotics**

- Summary of clinical studies:
  - Acute infectious diarrhea
    - S. boulardii (Florastor®), Lactobacillus GG (Culturelle®), L. reuteri and some mixtures are most beneficial
    - May reduce risk of antibiotic associated diarrhea by ~50%
  - IBS
    - L. casei (L. acidophilus and S. boulardii (Florastor®))
    - B. infantis (Align®), B. animalis (Activia®) and a combination product (VSL#3) may reduce symptoms of IBS

**Probiotics**

- Side effects include mild abdominal discomfort, flutulence
- Important Drug Interactions:
  - Separate antibiotics by 2 hours with bacteria-based probiotics
  - Avoid yeast-based probiotics with antifungals
- Use caution with immunocompromised patients

**Melatonin**

- FDA approved products for use in blind children to reset circadian rhythm for sleep
- Often used for treating jet lag
- New studies showing benefits with young children and difficulty sleeping
**Melatonin**

- Summary of clinical studies:
  - Orphan drug status for circadian rhythm sleep disorders in blind patients
  - May be beneficial for sleep wake cycle disturbances
  - May be beneficial for jet lag
    - 0.3-5mg at bedtime
  - Possibly effective for insomnia, nicotine withdrawal and preoperative anxiety and sedation
  - May be helpful with benzodiazepine withdrawal
  - Limited studies with cluster headaches
    - 10mg daily

**Melatonin**

- Side effects include daytime drowsiness
- Important Drug Interactions:
  - Anticoagulants/antiplatelets
  - Hypoglycemic agents
  - Calcium channel blockers
  - Fluvoxamine

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**Coenzyme Q10**

- Used widely in Japan and on some hospital formularies in US
- FDA approval for mitochondrial encephalopathy and Huntington’s Disease
- Used in patients with congestive heart failure
  - May improve exercise tolerance
  - May improve symptoms and/or classification of heart failure severity

**Coenzyme Q10**

- Summary of clinical studies:
  - FDA approved products:
    - UbiQGel® - Orphan Drug Status for Mitochondrial encephalomyopathies
    - Ubiquinol ® – Orphan Drug Status for Huntington’s disease
  - May have additive effects with conventional therapy on QOL and NYHA classification and symptoms of CHF
  - May have additive effects with antihypertensive agents
  - May help with migraine control
  - Unclear if beneficial in diabetes
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<th><strong>Coenzyme Q10</strong></th>
<th><strong>Echinacea</strong></th>
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<td>• Generally a well tolerated medication</td>
<td>• Native to North America; used to be treatment of choice for upper respiratory infections (URI)</td>
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<tr>
<td>• Important Drug Interactions:</td>
<td>• Uses include prevention and treatment of upper respiratory infections and fungal infections and dermatological conditions</td>
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<tr>
<td>– May have additive effects with anti-hypertensive agents</td>
<td>• Comes in many forms – angustifolia, purpurea and pallida</td>
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<td>– HMG Co-A reductase inhibitors may reduce CoQ10 levels</td>
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<td>– May reduce effects of warfarin</td>
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<tr>
<th><strong>Echinacea</strong></th>
<th><strong>Summary of clinical studies</strong></th>
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<tr>
<td>• Uses include prevention and treatment of upper respiratory infections and fungal infections and dermatological conditions</td>
<td>• Majority of studies find no benefits in prevention of URI</td>
</tr>
<tr>
<td>• Comes in many forms – angustifolia, purpurea and pallida</td>
<td>• May be useful for decreasing symptom severity and duration of URI</td>
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<td>• 2012 Jawad et al study in Evidence-Based Complementary and Alternative Medicine</td>
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<td></td>
<td>• 755 patients in a 4 month study looking at E. purpurea for safety, efficacy, and prevention of common cold</td>
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<td>• No difference in adverse effects</td>
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<td></td>
<td>• Echinacea reduced number of cold episodes and cumulated episodes</td>
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<td></td>
<td>• Echinacea showed some antiviral properties</td>
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<td></td>
<td>• May be useful in combination with antifungal drugs – decreased rate of recurrence of infection by 76% with Spectazole</td>
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<th><strong>Echinacea</strong></th>
<th><strong>Side effects include allergic reaction which can range from mild to anaphylactic reaction, unpleasant taste</strong></th>
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<tr>
<td>• Important Drug Interactions:</td>
<td>• May counteract the effect of immunosuppressants</td>
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<td>• Inhibits metabolism through CYP450 3A4 and 1A2</td>
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Kava

- Consumed as social drink in South Pacific
- Uses include anxiety, stress, insomnia
- Withdrawn from market in some European countries and Canada
- Concern due to risk of liver-related adverse effects, not considered safe for use

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Kava

- Summary of clinical studies
  - Thought to be effective for anxiety
    - Appears to be as effective as low dose benzodiazepines
    - May take 1-8 weeks for efficacy
  - May be beneficial with withdrawal of benzodiazepines
  - Increase dose of kava over 1 week while withdrawing dose of benzodiazepine over 2 weeks
  - Not considered safe enough to recommend for any use currently

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Kava

- Side effects include hepatotoxicity, unclear effect on cognitive function and concerns with long term, high dose, chronic use
  - Over 100 cases of liver damage including hepatitis, cirrhosis, fulminant liver failure
  - Theory of genetic component to ADRs with kava: poor metabolizers of CYP450 2D6 develop hepatotoxicity
- Important Drug Interactions:
  - Inhibits CYP 450 2D6, 2C6, 3A4, 1A2, 2C19
  - Use with CNS Depressants may increase risk of drowsiness and motor reflex depression
  - Hepatotoxic drugs may increase risk of liver damage

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Integration into Practice: Role of the Health Care Provider

- Provide unbiased and knowledgeable information
- Be informed of safety and efficacy literature
- Focus on being an educator, partner, and supporter for the patient
- Be a liaison between patient and other health care providers
**Integration into Practice: Role of the Health Care Provider**

- Be a willing participant in integrative medicine
- Promote personalized health care for patients
- Involve the patient in their own health care