Regulating the Unregulated: Talking to Patients About Use of Dietary Supplements

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Objectives

• List reasons why patients may utilize dietary supplements

• Identify resources available to health care professionals in determining the safety and efficacy of dietary supplements

• Discuss the risks and benefits of taking dietary supplements with patients
Disclosures

- No financial relationships pertinent to this session
- Use of dietary supplements for indications that are not FDA-approved will be discussed
Dietary Supplements & Regulations

• Dietary Supplement Health and Education Act (DSHEA) of 1994
  • Defined dietary supplement as:
    • Vitamin, mineral, herb or botanical, amino acid, dietary substance to supplement the diet
  • Regulations:
    • Labeling cannot assert treatment or prevention ★★
    • Manufacturers responsible for ensuring safety ★★
    • Manufacturers required to register with the FDA
    • Compliance with Good Manufacturing Practices

Available at http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm480069.htm#FDA_role.
Dietary Supplements & Regulations

• Office of Dietary Supplement Programs (ODSP)
  • Constituent of the FDA
  • Enforce regulations outlined in the DSHEA

• FDA’s role with supplements often begins AFTER products enter the marketplace

Which Patients Use Supplements?

- National Health & Nutrition Examination Survey (NHANES), 2003-2006
  - 54% of adults reported dietary supplement use
  - 65%: Age 51-70 years
  - 53%: Female
  - 61%: Education beyond high school
  - 59%: Non-Hispanic white
    - Asian, Pacific islander not reported

Why Supplements are Utilized: Perceived as Natural Mode of Healing

• Represent a plant-based treatment option
  • Perceived as having no/little side effects

• Core part of Traditional Chinese Medicine

• Often used for health promotion, chronic conditions

• Cultural differences in healing practices
Why Supplements are Utilized: Promote a Feeling of Empowerment

• Personal control, ability to do own research
• Easily accessible treatment
• Prescription options may not have worked
Why Supplements are Utilized:
Concern About Side Effects with Prescriptions

Reports in the Media

**FDA Warns Statin Users of Memory Loss and Diabetes Risks**

Popular medications linked to higher risk of kidney failure

Observed Side Effects in Family/Friends
Patient Case

• 56 year old female presents for routine medical exam
• Past medical history significant for deep vein thrombosis and anxiety
• Medications: warfarin
• Discloses use of Kava as needed for anxiety
  • Believes this works effectively
  • Does not produce side effects
  • Prefers to avoid prescription options
  • Feels safer taking a plant-based remedy
### Potential Sources of Information

<table>
<thead>
<tr>
<th>Name</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural Medicines(^2)</td>
<td>naturalmedicines.therapeuticresearch.com</td>
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<tr>
<td>Consumer Labs</td>
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</tr>
<tr>
<td>National Center for Complementary and</td>
<td><a href="https://nccih.nih.gov/health/herbsataglance.htm">https://nccih.nih.gov/health/herbsataglance.htm</a></td>
</tr>
<tr>
<td>Integrative Health</td>
<td></td>
</tr>
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</table>

\(^1\)List is not comprehensive  
\(^2\)Formerly Natural Standard and Natural Medicines Comprehensive Database
Natural Medicines¹

NATURAL MEDICINES

The most authoritative resource available on dietary supplements, natural medicines, and complementary alternative and integrative therapies.

¹Subscription available through Mayo Clinic Library

### Natural Medicines

<table>
<thead>
<tr>
<th><strong>Kava:</strong></th>
<th><strong>Scientific Name</strong></th>
<th><strong>Dosing &amp; Administration</strong></th>
<th><strong>Interactions with Foods</strong></th>
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<td><strong>Background</strong></td>
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<td><strong>Interactions with Herbs &amp; Supplements</strong></td>
<td><strong>Pharmacokinetics</strong></td>
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**Kava** Professional Monograph

Ava Pepper, Ava Root, Awa, Gea, Gi, Intoxicating Long Pepper, Intoxicating Pepper, Kao, Kavain, Kavapipar, Kawa, Kawa Kawa, Kawa Pepper, Kawapfeffer, Kew, Lawena, Long Pepper, Malohu, Maluk, Maori Ka...

**Kava Kava** Commercial Product
Manufactured by Gala Herbs

**Kava Kava** Commercial Product
Manufactured by Quest

**Kava Kava** Commercial Product
Manufactured by Pharmanex

**Kava Kava** Commercial Product
Manufactured by Leiner Health Products

**Kava Kava** Commercial Product
Manufactured by Puritan's Pride

Natural Medicines

Helpful with quick searches

Scientific Name
Piper methysticum.
Family: Piperaceae.

May need to search using this term

Safety

**POSSIBLY UNSAFE** ...when used orally. There is concern that kava preparations can induce hepatotoxicity and liver failure in patients taking relatively normal doses, short-term. Kava extracts have been safely used in clinical trials under medical supervision for up to 6 months (2092, 2093, 2094, 2095, 4032, 7325, 15046, 15130, 18314, 18316, 18318, 18320, 29663, 29671). However, there are at least 100 reported cases of liver toxicity following kava use. The use of kava for as little as one to three months has resulted in the need for liver transplants, and even death (390, 7024, 7068, 7086, 7096, 17086, 57232, 57239, 57251, 57252, 57254, 57274, 57297, 57337). However, some experts question the clinical validity of several of these cases (11369, 11371). Kava has been banned from the market in Switzerland, Germany, and Canada, and several other countries are considering similar action. Some patients may be more at risk than others. Patients who are “poor metabolizers” might be at greatest risk, but this has not been verified (7068). Until more is known, tell patients to avoid kava. Recommend routine liver function tests for patients who continue to use kava.

**PREGNANCY:** **POSSIBLY UNSAFE** ...when used orally. There is some concern that pyrone constituents in kava can cause loss of uterine tone (19); avoid using.

**LACTATION:** **POSSIBLY UNSAFE** ...when used orally. There is concern that the toxic pyrone constituents of kava can pass into breast milk (19); avoid using.

Effectiveness

**POSSIBLY EFFECTIVE**

**Anxiety.** The majority of evidence shows that specific kava extracts standardized to 70% kavalactones are superior to placebo (2094, 2095, 7325, 11372, 18315, 18316, 18317, 18320, 29663), and possibly comparable to buspirone 10 mg or low-dose benzodiazepines such as oxazepam 30 mg or (2092, 18314), for relieving symptoms of non-psychotic anxiety. Most of these studies have used a specific standardized extract (WS 1490, Dr. Willmar Schwabe Pharmaceuticals) in daily doses of 150-300 mg. Another specific kava extract (LI 150, Lichtwer Pharma) 400 mg daily has also been used (18314).

However, some contradictory evidence suggests that kava does not significantly decrease anxiety compared to placebo when used for 4 weeks (15046, 18313). Other evidence suggests that it is less effective than oxazepam 30 mg in patients who are anxious when administered as a single, acute dose (18319). Also analysis of three preliminary studies suggests that kava extract standardized to 70% kavalactones providing 140-280 mg kavalactones daily is no more effective than placebo for generalized anxiety disorder (GAD) when used for 4-8 weeks (15130). One reason for the discrepancies may be the duration of treatment. Treatment for at least 5 weeks appears to be necessary for significant improvement in some studies (2094, 7325, 18314, 29663). Other possible reasons for the discrepancies include the severity of anxiety disorder at baseline or the age and gender of the patient. Some evidence shows that kava is more effective in patients with more severe GAD at baseline, while other evidence suggests that it is more effective in female or younger patients (18315, 29663).
Natural Medicines

Kava

Scientific Name
Piper methysticum.

Very detailed, helpful when more thorough review desired

# Natural Medicines

## Kava

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Natural Medicines

Kava Kava by Gaia Herbs

Natural Medicines Brand Evidence-based Rating (NMBER)

Assigned based on safety, efficacy, product quality

Report an Adverse Reaction to Kava Kava

Ingredients:

Kava Kava standardized for 5% kavalactones. Standardized Full Spectrum 136 mg of extract per capsule. Guaranteed Potency 68 mg of extract per capsule.

Brand name products often contain multiple ingredients. To read detailed information about each ingredient, click on the link for the individual ingredient shown above.

May be helpful to utilize with ambiguous names (L-Carnitine vs. levocarnitine)

The most authoritative resource available on dietary supplements, natural medicines, and complementary alternative and integrative therapies.
Natural Medicines

Interactions found!

Click on any interaction below for more information.

**Warfarin <<interacts with>> KAVA**

Interaction Rating = **Moderate** Be cautious with this combination.
ConsumerLab.com

- Dietary supplement reviews
- Independent product testing
- Not available through Mayo Clinic Library
  - Personal subscription $40 per year

Product Review: Echinacea Supplements

Initial Posting: 2/28/16

Sections: Jump to a section by:

- What It Is
- What It Does
- Quality Concerns and Warnings
- What CL Found

Top Picks:
- Test Results by Product

- What to Consider When Buying and Using
- Concerns and Cautions
- Full list of Ingredients by Product
- How Products Were Evaluated

Reviews directed towards advanced consumer or health provider

In this scenario, encourage patient to find alternative product.
### RESULTS OF CONSUMERLAB.COM TESTING OF ECHINACEA SUPPLEMENTS

Click on [Price Check](https://www.consumerlab.com/index.asp) beneath a product name to find a vendor that sells it.

To find retailers that sell some of the listed products [click here](https://www.consumerlab.com/index.asp).

<table>
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<tr>
<th></th>
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<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Nature's Sunshine® Echinacea (2 capsules, three times daily)</td>
<td>1,200 mg E. purpurea powder (aerial) 1,200 mg E. purpurea powder (root) 18 mg TPCs</td>
<td>NOT APPROVED</td>
<td>[Cost for Per 10 mg of TPCs] Other Notable Features(^4) Price Paid</td>
</tr>
<tr>
<td>Dist. by Nature's Sunshine Products, Inc. Ingredients</td>
<td></td>
<td></td>
<td>Found 2.2 mcg lead per daily serving (0.92 mcg per gram)</td>
</tr>
</tbody>
</table>

\(^1\) Expected Minimum of Total Phenolic Compounds (TPCs)

\(^2\) Arsenic

\(^3\) Salmonella

\(^4\) Other Notable Features:

- Price Paid: $0.84
- [Kosher](https://www.consumerlab.com/index.asp) $0.22
- $25.15/180 capsules

In this scenario, encourage patient to find alternative product.
Cinnamon

On This Page
- Introduction
- What the Science Says
- Side Effects and Cautions
- For More Information
- Key References
## Summary

<table>
<thead>
<tr>
<th>Name</th>
<th>Cost</th>
<th>Quality of Reviews</th>
<th>Commercial Product Testing</th>
</tr>
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<tbody>
<tr>
<td>Natural Medicines</td>
<td>Free through Mayo Clinic Library</td>
<td>Excellent</td>
<td>No</td>
</tr>
<tr>
<td>Consumer Labs</td>
<td>$40 per year</td>
<td>Very good</td>
<td>Yes</td>
</tr>
<tr>
<td>National Center for Complementary and Integrative Health</td>
<td>Free</td>
<td>Directed toward patients, very summarized</td>
<td>No</td>
</tr>
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</table>
Supplements with Multiple Ingredients

- If bottle is not present, try searching product online to determine ingredients
- Search supplements individually
Communicating with Patients

- Important to avoid displaying an overall dislike of supplement use
  - Perceived negatively by patients
  - Detrimental to provider-patient relationship
  - Preclude patients from disclosing use
  - Force patients toward less reliable resources
    - Retailers, internet
- Most of these patients want to be healthy!
Discussions about Supplement Use

1. Inquire about use
   • Most patients do not volunteer use
   • Concern for disapproval
   • Inquire about reasons for use

2. Discuss the regulatory issues
   • Assumed safe unless proven otherwise

Discussions about Supplement Use

3. Evaluate the supplement
   • Familiarize yourself with available references
   • Review for potential drug interactions
   • Consider keeping printed resources available

4. Discuss available safety and efficacy data
   • Often limited to small studies, but growing
   • Searches can be complicated by different names
     • Utilization of controlled terms may help
       • MeSH (Medical Subject Headings)

Discussions about Supplement Use

5. Compare risks and benefits to conventional therapy
   • Patients may be unaware or have misconceptions of prescription options

6. Allow the patient to make an informed decision

7. Monitor for adverse effects and response
   • Event reporting through FDA MedWatch
     • www.fda.gov/Safety/MedWatch

Discussions about Supplement Use

• C: communicate freely about supplements
• A: acquire knowledge, find an easy reference
• R: report adverse events
• E: evaluate the literature

Will the FDA Remove Products Found to be Harmful?

• FDA has authority to enforce manufacturers to discontinue production and recall existing products
• FDA can advise consumers to avoid use

Available at
Audience Question

Which is most likely a reason why patients may utilize dietary supplements?

1. Prescription options did not help.
2. Prescription options been been negatively displayed in the media.
3. Dietary supplements may be perceived as natural treatment options.
4. All of the above.
A patient presents to clinic for a general medical exam and states she is taking cranberry to prevent urinary tract infections. Which resource would be most appropriate to look up efficacy data?

1. Micromedex
2. Natural Medicines
3. National Center for Complementary and Integrative Health
4. *New England Journal of Medicine*
A patient is admitted to the hospital with cellulitis. During the admission medication history, he tells you that he takes Hydroxycut, a weight loss supplement. What is the most appropriate action?

1. Look up the ingredients of Hydroxycut and discuss the risks and benefits of continued use.
2. Do nothing, this is unrelated to his primary problem.
3. Ask him to discuss use of Hydroxycut with his primary care provider.
4. Tell him your personal opinion of supplements.
Clinical Pearls with Supplement Use

- Avoid use with narrow therapeutic index agents
  - St. John’s Wort is a CYP isoenzyme inducer
    - Case reports of acute transplant rejection
- Some “G” supplements (garlic, ginkgo) have antiplatelet effects
  - Screen for interactions with anticoagulants
- Weight loss supplements often contain stimulants
  - Advise caution in cardiovascular disease

Clinical Pearls with Supplement Use

- Advise caution with proprietary blend products

![Supplement Facts]

- Encourage patients to bring bottles in for visits
Clinical Pearls with Supplement Use

• Look for United States Pharmacopeia (USP) Verified options
  • Contains ingredients in declared amounts
  • No harmful contaminants
  • Has been made under Good Manufacturing Practices
  • List of products available at www.usp.org
Take Home Points

• Patients utilize dietary supplements for multiple reasons, often with intention to enhance their well-being

• Health care professionals are encouraged to find a resource that helps with better understanding dietary supplements

• Discussing the risks and benefits with patients may be challenging, but the key is to have open communication
Questions & Discussion
Most Popular Supplements

1. Vitamin D
2. Fish oil
3. Coenzyme Q10
4. Multivitamins
5. Probiotics
6. B vitamins
7. Magnesium
8. Curcumin/tumeric
9. Vitamin C
10. Calcium
11. Melatonin
12. Protein/nutrition powers and drinks