

Safe Use of Dietary Supplements

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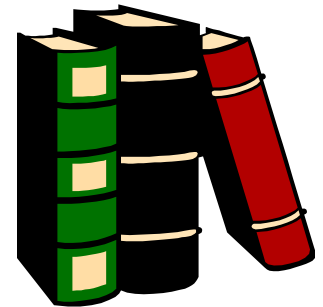
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Objectives

- Discuss facts and fiction regarding supplements
- Appropriate sources of information
- Considerations when searching the internet



Basic Definitions

- Dietary supplements
 - “... a product taken by mouth that contains a dietary ingredient intended to supplement the diet...”¹
- Dietary ingredients may include:
 - Vitamins
 - Minerals
 - Herbs or botanicals
 - Amino acids
 - Other substances



¹<http://cfsan.fda.gov/~dms/ds-oview.html>



Epidemiology of Use



- National Center for Health Statistics
 - Data from NHANES (2003 to 2006)
 - 72 million; 44% - males 53% - females
 - Multivitamin/multimineral supplements most used – 33%
 - Botanicals – 14%
 - Amino acids – 4%
- Council for Responsible Nutrition, Natural Marketing Institute, Nutrition Business Journal have other statistics
 - CRN: 66% of US adults use supplements
 - NMI: 47%
 - NBJ: \$26.1 billion/year industry (\$93 billion by 2015 in global market)



Reasons for Use

- Baby boomers
- Interested not only in longevity but “wellness”
- Certain products used
 - Supplements
 - Multivitamins, multiminerals
 - Probiotics
 - Turmeric
- Disease modulation
 - Omega 3 fatty acids (\$5 billion/year)
 - Fish oil, krill, algae
 - Flax, chia



Why Be Cautious? Facts and Fiction

- Facts – Supplements contain active chemical constituents
 - Fiction: Supplements are “natural”
- Fact – Supplements may have disease interactions
 - Fiction: Supplements may be taken in any disease
- Fact – Supplements may cause adverse effects
 - Fiction: Unlike drugs, supplements do not cause side effects
- Fact – Supplements may interact with drugs or other supplements
 - Fiction: Supplements do not have drug interactions



Why Be Cautious? Facts and Fiction

- Facts – Study design for supplement trials often “flawed” and with low numbers; Surrogate markers often used
 - Fiction: Supplements are well studied
- Facts – Supplements are considered foods; few dose-ranging studies; impurities/undeclared ingredients
 - Fiction: Supplements are FDA-approved
- Facts – Takes time to remove DS from market
 - Fiction: FDA must remove DS from market immediately; report to *MedWatch (www.fda.gov/medwatch)



Supplements

- Does natural mean safe?
- Natural products contain pharmacologically active ingredients and thus one may see not only a pharmacologic effect but possibly side effects and drug interactions¹

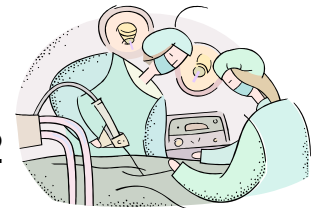
1 <http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM420449.pdf>





Reasons for Caution

- Product variability
- Adverse Effects^{1,2}
- Drug interactions^{3,4}
- Surgery precautions^{5,6}



1 Drug Safety 1997;17:342-56 2 N Engl J Med 2000;342:1686-92

3 JAMA 1998;280:1569-75 4 Lancet 2000;355:134-38

5 www.asahq.org/PublicEducation/herbal.html

6 AORN J 1999;69:173-5,177-8,180-3



Other Reasons for Caution

- Recalls¹
- Illegally sold treatments²
 - “Lowers your blood sugar naturally”
 - “Replaces your diabetes medicine”
- Confusing labeling (mislabeling) and information^{3,4}

¹ JAMA Internal Medicine 2013;April 15:1-3. doi: 10.1001/jamainternmed.2013.379

² <http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM361807.pdf>

³ N Engl J Med 1998;339:827-30.

⁴ Consumer Reports September 2012 “10 surprising dangers of vitamins and supplements”



Other Reasons for Caution

- Quality issues

Ocean sources may be contaminated¹

Animal origin products may be contaminated²



Animal sources may transmit disease²

Misidentification, mislabeling, adding other substances³

¹ JAMA 2000;284:1425-9

² <http://www.centerforfoodsafety.org/page285.cfm>

³ N Engl J Med 1998;339:827-30.



Problematic Supplements?

- Weight loss products
- Body building products
- Men's health products

- JAMA study: supplements recalled by FDA for containing banned substances (sibutramine, steroids, sildenafil, fluoxetine) back on the shelf 6 mo later
<http://time.com/3554782/dietary-supplement-safety/>



Supplements + Medications?

- Fish oil
 - In combination with antihypertensives = ↓↓ BP
 - OCPs attenuate TG lowering effect of fish oil
 - High doses of fish oil + ginkgo = possible bleeding
 - High doses of fish oil + high dose Vit E = possible bleeding
- Echinacea + prednisone
 - Interferes with drugs that suppress the immune system
- Melatonin
 - May ↓ clotting; so in combination with blood thinners = possible bruising
 - May ↑ BP; offsets possible benefits of antihypertensives
 - ↑ ↑ sedation with other sedating products (valerian, SJW)





Evaluating Internet Information

- How to evaluate information on the internet –
<http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm110567.htm#tips>
- Ask these questions:
 - Who operates the website?
 - What is the purpose of the website? (Educate or sell products?)
 - What is the source of information? (Published studies/testimonials?)
 - Is the information current? (Date posted)
 - How reliable is the internet? (Easy way to spread myths, beware of overly emphatic language (ALL CAPS) or “This is not a hoax” or “Send this to everyone you know”)



Internet Information



- Examples of “suspect” statements:
 - “These are not medicines so taking these herbs in larger amounts or over a long period of time is not harmful”
 - “There are no ingredients available for this product”
 - To “determine dose for a child or pet, divide the weight by 150 and that determines the fraction of the adult dose”





Appropriate Patient References

- FDA websites
 - Tips for the Dietary Supplement User
<http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm110567.htm>
 - Do I need to think about my diet?
 - Should I check with my doctor?
 - Are there any interactions (supplements/meds)
 - What should I do if I am going to have surgery?
 - Who is responsible for safety of the products?



Appropriate Patient References

- FDA websites
 - Tips for Older Dietary Supplement Users –
<http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm110493.htm>
 - Are there any risks because of my age?
 - Should I stop my regular medicines?
 - Should I check with my doctor?
 - Should I take the products in to checkups?



Appropriate Patient References

- FDA websites
 - MedWatch
www.fda.gov/medwatch
 - Problems with products listed
 - Reporting problems





Appropriate Patient References

- Read FDA 101: Dietary supplements
<http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/ucm050824.pdf>



Appropriate References: Providers

- Natural Medicines Comprehensive Database (www.naturaldatabase.com)
 - Maintained by Pharmacist's Letter/Prescriber's Letter
 - Approximately 1100 ingredients reviewed in evidence-based monographs
 - Index containing over 38,000 brand names
 - Section on other alternative therapy modalities – acupuncture, balneotherapy, colonic irrigation, aromatherapy, shiatsu, reiki, etc.
 - USP-verified product names
 - References!!



Appropriate References: Providers

- Natural Standard (www.naturalstandard.com)
 - Multidisciplinary research collaboration that uses evidence-based criteria to evaluate different products and enable decision-support
 - Excellent job of appraising original research on herbs/supplements
 - Monographs reviewed by Western-trained clinicians and CAM practitioners
 - Evidence grade
 - A – Strong positive scientific evidence
 - B – Positive scientific evidence
 - C – Unclear scientific evidence
 - D – Negative scientific evidence
 - F – Strong negative scientific evidence



Appropriate References:

Providers

- The Cochrane Collaboration – <http://www.cochrane.org>
 - International organization providing up to date information about health care information interventions
 - Cochrane Library has regularly updated databases and systematic reviews of different treatments
 - Regularly updated evidence-based information
- National Center for Complementary and Alternative Medicine (NCCAM – free) - <http://nccam.nih.gov>
 - Information for clinicians and the public
 - Access information under “Research, Clinical Trials, Training, and Health Information”
- The Review of Natural Products
 - Comprehensive chemistry, pharmacology, toxicology



Choosing an Appropriate Product

- Choose a reputable manufacturer – appropriate information on a label?
- Information about dietary supplements
<http://ods.od.nih.gov/>



Choosing an Appropriate Product

- Ask yourself:
 - Is this too good to be true?
 - Think twice about chasing the latest headlines
 - Can you contact the manufacturer and what type of information is provided?
- Consider use of testing services
 - USP – <http://www.usp.org>
 - Consumer Lab – <http://www.consumerlab.com>
 - NSF International – <http://www.nsf.org/consumer>
 - Natural Products Association – <http://www.npainfo.org/>





“DB”

- A 48 y/o woman with type 2 DM and PCOS is on metformin and basal/bolus insulin, an ACEI/HCTZ and a calcium channel blocker for HTN, simvastatin for high cholesterol, warfarin post DVT, and sertraline for depression. She has high triglycerides, insulin resistance (\uparrow HOMA-IR), muscle aches, knee pain, \downarrow energy.
- What supplements might be considered?
- Which supplements may interact with medications this person is taking?
- If the person decides to take any products, what should she be told?



Which Agents? Popular Products

- Cinnamon
- Ginseng
- Milk thistle
- St. John's wort
- CoQ10
- Magnesium
- Turmeric
- Others



Cinnamon

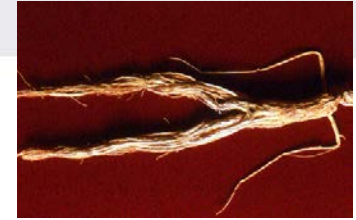


- Active ingredient: Procyanidin type-A polymers (Cinnamaldehyde)
- Decreases fasting glucose and lipids
- May enhance insulin sensitivity
- May also delay gastric emptying; decrease PPG
- Side effects mostly benign
 - Hepatotoxicity?
- Contains coumarins
 - Caution with concomitant anticoagulants
- Most appropriate form: aqueous form?





Ginseng



- Side effects - \uparrow BP, anxiety, insomnia
- Drug interactions – warfarin (\downarrow INR), attenuates effects of BP meds
- Other effects
 - Enhanced effects of polyvalent flu vaccine, \downarrow colds/flu
 - Some benefits on “ED”
- Diabetes – modest benefit for PPG; only studied in type 2 DM
 - \downarrow PPG, plasma insulin, improved insulin sensitivity
- Varying contents (Am J Clin Nutr 2001;73:1101-6)
 - Evaluation found quantities varied from less (12%) to more (137%) than indicated on the bottle
- American ginseng, no added benefit from > 3 g/day
- Take within 2 h of meal to avoid potential hypoglycemia
- Use: 2-week holiday q 2-3 weeks; others say limit use to 3 months (concerns about hormone-like effects)





Milk Thistle

- Background
 - Aster family (daisies, thistles)
 - Silymarin
- Mechanism
 - Inhibits hepatotoxin binding
 - Antioxidant
 - Restores MDA levels (marker of oxidative stress)
 - May benefit pts with insulin resistance secondary to hepatic damage
- Uses
 - Hepatic disorders
 - Hepatoprotectant
 - Diabetes
- Side Effects
 - GI, sweating, estrogenic effects
- Drug Interactions
 - Beneficial interactions with hepatotoxins
 - ↑ Cl of estrogens taken by mouth
 - Inhibits CYP 2C9





St John's Wort

- Hippocrates/Galen: for “demonic possession”
- Active ingredients: hyperforin, hypericin, quercetin
- Inhibits neurotransmitter re-uptake
- Preparations vary widely
- Major/severe depression: inconsistent effects
- Major drug interactions: Potent inducer of metabolism (CyA, HIV meds, warfarin, OCPs)
- Pharmacodynamic interactions: Other antidepressants, SSRIs, sympathomimetics, narcotics

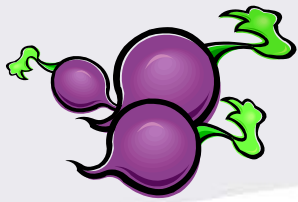




Turmeric

- *Curcuma longa* (curcumin)
 - Diferuloylmethane (polyphenol)
- GRAS status
- Arthritis, other inflammatory disorders
 - COX-2 inhibition
 - Inhibits PGs, leukotrienes, thromboxanes
- Cancer
 - Apoptosis of some cancer cell lines
 - Inhibits angiogenesis
- Diabetes (pre-diabetes)
- ADRs – GI, nephrolithiasis, ↓ BG
- Interactions: Antiplatelets





CoQ10

- Vitamin-like substance; ↑ ATP production; Scavenges OFRs; Membrane stabilizer
- Small studies have resulted in slight ↓ in FBG and A1C (NS)
- HF symptom improvement; may ↓ BP, improve angina, Parkinson's, ↓ statin myopathy
- Long-term safety - 6 years
- Soybean oil formulation ↑ absorption
- Side effects
 - GI, rash, increased LFTs
- Drug interactions
 - Warfarin, statins, BP meds
 - Adriamycin® (less cardiac toxicity but less efficacy?)
- Some evidence for use in several diseases
- DM dose – 100-200 mg/day

Natural Medicines Comprehensive Database 13th ed.
Stockton, Calif., Therapeutic Research Faculty, 2013





Magnesium



- Highly used supplement
- DM pts consume fewer foods containing Mg – green, leafy vegetables, grains/nuts, meats, dairy products
- Many persons don't meet RDA for Mg (320 mg/day for women, 420 mg/day for men)
- Many meds deplete Mg: diuretics, PPIs, beta-2 agonists
- May improve insulin resistance and ↓ fasting glucose in overweight, insulin resistant persons
- 15% risk reduction for T2DM with 100 mg/day of Mg
- May ↓ fasting glucose and ↑ HDL in T2DM
- Less neuropathy in T1DM
- Monitor renal function and potential drug interactions (may impair absorption of some antibiotics, Ca)



Turmeric



- *Curcuma longa* (curcumin)
 - Diferuloylmethane (polyphenol)
- GRAS status
- Arthritis, other inflammatory disorders
 - COX-2 inhibition
 - Inhibits PGs, leukotrienes, thromboxanes
- Cancer
 - Apoptosis of some cancer cell lines
 - Inhibits angiogenesis
- Diabetes
- Taken with fat or black pepper, easily absorbed, ↑ SDCs
- ADRs – GI, nephrolithiasis, ↓ BG
- Interactions: Antiplatelets
- 2000 mg/day in divided doses



“DB”



- A 48 y/o woman with type 2 DM and PCOS is on metformin and basal/bolus insulin, an ACEI/HCTZ and a calcium channel blocker for HTN, simvastatin for high cholesterol, warfarin post DVT, and sertraline for depression. She has high triglycerides, insulin resistance (\uparrow HOMA-IR), muscle aches, knee pain, \downarrow energy.
- What supplements might be considered?
- Which supplements may interact with medications this person is taking?
- If the person decides to take any products, what should she be told?



Supplement Use: Guiding Patients



- Determine why you want to use a supplement
- What are your goals for supplement – be specific
- Consider that products may cause side effects or drug interactions
- Select single-ingredient products
- Discuss use to determine appropriate length of treatment
 - Don't stop or start without discussion since this may affect the other medications being taken
- Don't stop taking your other medications
- Don't share the products
- Consider that you must still eat healthy and exercise





Counseling Patients

- Providers must be respectful of patients beliefs
- Provide evidence-based information
- Discuss target goals, evidence (benefit or not?)
- Assess potential side effects; drug interactions
- Help evaluate whether brand is appropriate
- Emphasize role of conventional medications
- Be informed and supportive



QUESTIONS???

