



2019 Community Oncology Conference

Ensuring quality, affordable & accessible cancer care

Safety of Herbals, Dietary Supplements and Aromatherapy in Cancer Patients

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Objectives

- Review the history of herbal and dietary supplements
- Discuss safety concerns with herbal and dietary supplement use in oncology
- Review possible supplement benefit in oncology
- Discuss aromatherapy use and safety



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Overview of Herbal and Dietary Supplement Use

Popularity and Public Perception

- 2000: \$4.2 billion in herbal supplement sales
- 2010: More than 15 million people in the U.S. consume herbal remedies or high-dose vitamins
- 2015: \$21 billion in vitamin and herbal sales
- 2017: \$8 billion in herbal supplement sales
- Increased sales 8.5% from 2016
- Fastest growth is in direct sales
- Regarded as food products, so not subject to the same scrutiny and regulation as medications

Dietary Supplement Background

- Herbal medications have been around for a very long time
- Reports of Ma-Huang being used during the Ming Dynasty (1368-1644)

Dietary Supplement Background

- Treatment based on “traditional” or “folk” medicine
- African, Asian, Latin countries use traditional medicine for their healthcare needs
- 80% of the African population use traditional medicine as their primary care

Natural Prescription Drug Examples

- Cancer Treatment Medications

- Vincristine/
Vinblastine:
 - Periwinkle Flower
- Taxol/Taxotere:
 - Yew Tree

Other Medications

- Penicillin - Mold
- Aspirin – Willow Bark
- Digoxin – Foxglove Plant
- Warfarin – Sweet Clover
- Atropine – Deadly Nightshade

Herbal Supplements

- Became the same as “dietary supplements” after the Nutrition and Labeling Act of 1990
- Before 1990 dietary supplements were only essential nutrients such as vitamins, minerals , and proteins
- After 1990 dietary supplements included herbals



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The Dietary Supplement Health and Education Act of 1994

Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), the dietary supplement manufacturer is responsible for ensuring that a dietary supplement is safe before it is marketed

Dietary Supplement and Health Education Act of 1994

- Structure/function claims permitted
 - Truthful and not misleading
 - OK: “improves memory”
 - Not OK: – “prevents Alzheimer’s”
- Disclaimers
 - Statement has not been evaluated by the FDA
 - Not intended to "diagnose, treat, cure or prevent any disease"

Food and Drug Administration (FDA)

FDA regulates dietary supplements under a different set of regulations than those covering "conventional" foods and drug products (Prescription and Over-the-Counter)

FDA

- FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market
- FDA Issues Dietary Supplements Final Rule :
“Manufacturers are required to evaluate the identity, purity, strength, and composition of their dietary supplements.”



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FDA Final Rule (cont.)

“If dietary supplements contain contaminants or do not contain the dietary ingredient they are represented to contain, FDA would consider those products to be adulterated or misbranded”.

So...

Herbal and dietary supplements are regulated like foods NOT drugs....

Herbal Supplements and Safety

- “Natural” doesn’t mean it is safe
 - Kava kava
 - Comfrey
- Herbals can act like drugs
- Herbals interact with, each other Rx and OTC medications

Herbal Supplements and Safety

- Herbals do not have to meet the same standards as drugs and over-the-counter medications for proof of safety, effectiveness
- Active ingredients in these products are many times not known
- There is no legal definition of standardized, certified, or verified for herbals



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Herbal Supplements and Safety

- Some herbals have been found contaminated with metals, unlabeled prescription drugs, microorganisms, or other substances
- The Federal Government has taken legal action against a number of company sites because they have been shown to contain incorrect statements and to be deceptive to consumers



What is “Natural”?

- Anything I say it is....
- Used extensively in marketing of herbal supplements
- Think about it: Can't the “natural” argument be made about anything?
- Keep in mind natural has to do more with marketing than anything else



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Oncology Therapy Cautions

Panax Ginseng

- Use: Breast cancer (IE), CA related fatigue (IE)
- Inh. **CYP3A4: imatinib → hepatotoxicity**, etoposide, paclitaxel, vinblastine, vincristine, vindesine
- Inh. Platelet aggregation, decrease BG, estrogenic, increase Q-T prolongation

Insufficient evidence = (IE)

Bilgi N, Bell K, Ananthakrishnan AN, Atallah E. Imatinib and Panax ginseng: a potential interaction resulting in liver toxicity. Ann Pharmacother 2010;44(5):926-8.

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Milk Thistle

- Use: Cisplatin-induced nephrotoxicity, capecitabine induced hand-foot syndrome (IE)
- P-gp, glucuronidation inhibition
 - Incr. absorp. etoposide, paclitaxel, vinblastine, vincristine, vindesine. Alter tamoxifen metabolism ? (CYP2D6)

Shahbazi F, Sadighi S, Dashti-Khavidaki S, et al. Effect of Silymarin Administration on Cisplatin Nephrotoxicity: Report from A Pilot, Randomized, Double-Blinded, Placebo-Controlled Clinical Trial. *Phytther Res.* 2015;29(7):1046-53.

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Red Clover

- Use: Breast (IE), endometrial cancer (IE)
- Inh. CYP1A2, CYP2C19, CYP2C9, CYP3A4
- Incr. Methotrexate (MTX) levels
- Incr. bleeding
- Estrogenic → decr. efficacy of tamoxifen

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Valerian

- Use: Sleep (possibly effective)
- CYP3A4 (dose dep), UGT 1A1 inh.
- Decreased estrogen, irinotecan metabolism
- Sedation
- Some patients are already UGT1A1 poor to intermediate metabolizers

Houghton PJ. The scientific basis for the reputed activity of Valerian. *J Pharm Pharmacol* 1999;51:505-12.

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Turmeric (Curcumin)

- Use: Colorectal cancer (IE)
- Chemotherapy effects controversial/paradoxical
- **Cyclophosphamide**
 - Reduced efficacy possible
- **Camptothecin:**
 - One *in vitro* study suggests that curcumin inhibits camptothecin-induced apoptosis of breast cancer cells by up to 71%
- **Doxorubicin:**
 - Inhibited apoptosis of breast cancer cells by doxorubicin.

Shah BH, Nawaz Z, Pertani SA. Inhibitory effect of curcumin, a food spice from turmeric, on platelet-activating factor- and arachidonic acid-mediated platelet aggregation through inhibition of thromboxane formation and Ca²⁺ signaling. *Biochem Pharmacol* 1999;58:1167-72..

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Turmeric

- **Mechlorethamine:**

- Possibly inhibits mechlorethamine-induced apoptosis of breast cancer cells by up to 70%

- **Paclitaxel:**

- Enhanced bioavailability of paclitaxel
- May induce bleeding if low platelet count. Stop 2 weeks before surgery

Shah BH, Nawaz Z, Pertani SA. Inhibitory effect of curcumin, a food spice from turmeric, on platelet-activating factor- and arachidonic acid-mediated platelet aggregation through inhibition of thromboxane formation and Ca²⁺ signaling. *Biochem Pharmacol* 1999;58:1167-72..

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Cannabis

- Use: Neuropathic pain (Possibly effective), cachexia (IE), CINV (IE)
- P-gp substrates inhibited: etoposide, paclitaxel, vinblastine, vincristine, vindesine
- THC inh. P-gp, CYP3A4. Induce CYP2E1: APAP, chlorzoxazone, ETOH, theophylline, inhaled anesthetics-halothane, etc.
- Inh. Platelet aggregation, CNS depression

Pellinen, P., Honkakoski, P., Stenback, F., Niemitz, M., Alhava, E., Pelkonen, O., Lang, M. A., and Pasanen, M.

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Oncology Therapy Promise

Lactobacillus

- Possibly effective: Chemo-induced diarrhea
- Colorectal cancer patients receiving chemotherapy with 5-fluorouracil took a Lactobacillus rhamnosus, Lactobacillus GG
- Significantly reduced severe diarrhea, less abdominal discomfort, reduced hospital care, and fewer chemotherapy dose reductions due to gastrointestinal side effects

Barley, Rice Bran, Oats

- Epidemiologic evidence suggests that consuming a diet that includes dietary cereal fiber, including oats and oat bran, might reduce the incidence of stomach cancer

Calcium

- Population studies suggest that high intake of dietary or supplemental calcium is associated with a reduced risk of colorectal cancer
- Clinical trials show that taking calcium supplements 1.2-2 grams daily for up to 4 years can reduce the risk of colorectal adenoma recurrence by up to 29%

Beta-Carotene

- There is some preliminary evidence that a diet rich in beta-carotene may reduce the risk of breast cancer in premenopausal women
- Especially those at high risk due to family history or high alcohol intake
- An analysis of clinical studies suggests that beta-carotene can decrease breast cancer risk by up to 18%

Caffeine (Guarana)

- A review of available population research shows that increased caffeine intake from any source is associated with a 14% reduction in the risk of developing non-melanoma skin cancer. Consumption of caffeinated coffee, but not non-caffeinated coffee, is associated with an 18% reduced risk

Marijuana (Cannabis)

- Use: Neuropathic pain
- A meta-analysis of five small clinical studies shows that inhaling marijuana providing tetrahydrocannabinol in doses of 1.6-96 mg daily for up to 2 weeks reduces the intensity of neuropathic pain caused by HIV, trauma, diabetes, chemotherapy, and other conditions



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Aromatherapy

Aromatherapy

- Aromatherapy is the therapeutic use of essential oils (also known as volatile oils) from plants (flowers, herbs, or trees) for the improvement of physical, emotional, and spiritual well-being
- Used by oncology patients most often for supportive care and general well-being

History of Aromatherapy

- Gattefosse-French chemist coined the term in 1937; “one rinse of essential oil of lavender” stopped infection of wounds with gas gangrene
- Dr. Jean Valnet- French army physician wrote first aromatherapy book by a doctor; book full of case studies and references

History of Aromatherapy

- Marguerite Maury- nurse who classified use of essential oils into various clinical departments; developed topical application and established first aromatherapy clinics in Paris, Great Britain, and Switzerland

Essential Oils

- Volatile liquid substances extracted from aromatic plant material by steam distillation or mechanical expression
- Available for inhalation and topical application- topical treatment should be diluted

Effects of Aromatherapy

- May result from the binding of chemical components in the essential oil to receptors in the olfactory bulb, impacting the limbic system (brain's emotional center)
- Topical application may exert antibacterial, anti-inflammatory, and analgesic effects

Chemistry- A Pharmacist's Dream!

- Basic frame of carbon and hydrogen to which a “functional group” is added
- Functional group determines characteristic chemical properties
- Six classes of functional groups are important to aromatherapist- alcohols, aldehydes, esters, ethers, ketones, phenols

Chemistry- A Pharmacist's Dream!

- Minor components can be important in aromatherapy
- Synergy- whole essential oil has natural synergy of the combined action of individual molecules; complete oils more effective than isolated constituents
- Blending more than one oil also creates synergy

Safety of Aromatherapy

- Aromatherapy has a relatively low toxicity profile when administered by inhalation or diluted topical application

Quality Supplier

- Should produce GC-MS reports- identifies individual components of essential oils
- Unadulterated- traders can add cheaper oils or synthetics to genuine oils
- Organic-herbicides, pesticides, fungicides are toxic and can contaminate oils

Lavender Essential Oil *(Lavandula angustifolia)*

- May be helpful in the treatment of anxiety and depression; may also improve breathing, relaxation, and sleep
- Has weak hormonal activities so long-term oral or topical use should be avoided in patients with hormone-sensitive cancers

Lavender Essential Oil *(Lavandula angustifolia)*

- ONS study showed decrease in trait anxiety and a significant change in sleep quality measures in patients undergoing chemotherapy who used lavender oil aromatherapy

Lemon Essential Oil (*Citrus limon*)

- May be useful in nausea, uplifting to mood, may increase concentration and mental performance
- Caution: topically may be phototoxic



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Popularity is increasing- education is key

“Future Market Insights has recently published its study on the global aromatherapy market, projecting the US\$ 3.8 billion market to soar at a healthy 7.7% CAGR and reach US \$8,058.8 million valuation by end of 2026. Over the next decade, awareness regarding healing benefits of aromatherapy is expected to gain momentum.”

About Herbs/Herbals

- Website, app, and newsletter updated by a pharmacist and botanicals expert
- Useful for providers and patients
- <https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs>
- Also: Natural Medicines Database



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Thank you!

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Questions?