**Top Selling Botanical Dietary Supplements**

*With Tieraona Low Dog, MD*

**Extent of Use**

- 19% of adult Americans take dietary supplements.
- Most pay out of pocket
- Most use without medical advice.

_CDC Survey 2005_

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**Things to Think About**

- Potential benefit
- Potential adverse events
- Patient’s attitude/belief
- Quality concerns
  - USP seal
  - NSF seal
  - Consumerlabs.com
  - Clinically tested

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**Black Cohosh**

*(Actaea/Cimicifuga racemosa)*

- Approved German health authorities and WHO for relief of menopausal symptoms, PMS, and dysmenorrhea
- 12 comparative or PCT using black cohosh extract for menopause
- Clinical trials suggest that black cohosh extract has a modest effect on menopausal hot flashes, night sweats, anxiety and insomnia.


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**HALT STUDY**

12 month federally funded study of black cohosh failed to find any benefit over placebo.
- 73 women in black cohosh group
- 50% perimenopausal
- 160 mg/d ethanolic extract
- No significant adverse events


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**Other Info on Black Cohosh**

- 52-week study found no endometrial stimulation (360 women; 40 mg/d ethanolic extract).
- 6 month study failed to note any change in breast tissue.
- Four federally funded studies underway.
Clinically Tested Products

- Products studied in majority of clinical trials.
- Dose studied 20-80 mg two times daily.
- NIH studies using product by Pure World Botanicals.

Liver Toxicity?

- Two reviews concluded black cohosh has relatively good safety profile.
- S1 possible cases of hepatotoxicity.
- NIH concluded no conclusive link.
- Australia, Canada and UK require cautionary label on all products.
- USP has revised monograph to include cautionary label.


www.ods.od.nih.gov/

Questions and Answers About Black Cohosh and the Symptoms of Menopause

Office of Dietary Supplements • National Center for Complementary and Alternative Medicine • National Institutes of Health

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- What is black cohosh?
- What are women’s black cohosh preparations?
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- What clinical studies have been done on black cohosh and its effect on menopause?
- How does black cohosh work?
- What is the regulatory status of black cohosh in the United States?
- Where is black cohosh found?
- What side effects and adverse reactions are associated with black cohosh use?
- What is the clinical evidence of efficacy for black cohosh?
- What is the cost of black cohosh supplements?
- How much black cohosh is needed for therapy?
- How can I determine if black cohosh is the right choice for me?
- How can I make an informed decision about using black cohosh?
- How can I ensure the quality and safety of my black cohosh supplement?
- How can I monitor and manage potential side effects or adverse reactions?
- How can I obtain more information about black cohosh and menopause?

Cranberry (Vaccinium macrocarpon)

- Cochrane review found evidence that cranberry reduces number of symptomatic UTIs in women over 12 month period.

Cranberry Database Sys Rev. 2004; (2):CD001321 Evidence Level: A
Recommending Cranberry

- Cranberry juice: 4-6 ounces two times daily.
- Cranberry extract in capsule form:
  - 400-800 mg per day
  - CranActin supported by some clinical research (chewable, capsules, effervescent)

St. John’s Wort (Hypericum perforatum)

- Preponderance of evidence shows beneficial for mild-to-moderate depression.
- Actives unclear
  - 300-600 mg TID SE (hyperforin/hypericin)
- NIH trials underway

NIH Study on SJW

- 340 moderate-severely depressed patients.
- Randomized 900-1500 mg SJW extract, 50-100 mg sertraline or placebo over 8 week period.
- Patients responding to treatment continued for an additional 18 weeks.


NIH Study on SJW

- Full response occurred in:
  - 31.9% of the placebo-treated patients
  - 23.9% of the SJW treated patients (P = .21)
  - 24.8% of sertraline-treated patients (P = .26).
- Neither sertraline nor SJW extract performed as well as placebo in this primary outcome.

Trials on Anti-Depressants

- Review clinical-trial data from nine antidepressants approved by FDA between 1985 and 2000.
- 10,030 patients with depression participated in 52 antidepressant clinical trials evaluating 93 treatment arms.
- Researchers found fewer than half (48%, 45/93) of antidepressant treatment arms showed superiority to placebo.


St. John’s Wort

Dosage and Contra-indications
- Products standardized to 0.3% hypericin and/or 3-5% hyperforin.
- Dose is 900-1800 mg/d.
- SJW fewer side effects compared to prescription antidepressants.
- Rare cases of phototoxicity.
St. John’s Wort

- Clinical trial (n=301)
  - Black cohosh (~80-120 mg/d)
  - SJW (~1200 mg/d)
- Decreased MRS 50% compared to 19.6% placebo at 16 weeks.
  (Goldstein, Obstet Gynecol 2006)
- Hypericum perforatum in
  Relieving Hot Flashes in Women with Non-Metastatic Breast Cancer phase II trial.
  www.cancer.gov/newsatlas/CWPS/BR0301

St. John’s Wort

- St. John’s Wort induces subset of P-450 enzymes, (CYP3A4) that metabolize many pharmaceutical medications.
- SJW also interacts with P-glycoprotein.
- Documented herb-drug interactions include warfarin, digoxin, cyclosporine, indinavir, irinotecan, and oral contraceptives.

Soy (Glycine max)

- 6 RDPPCTs for soy extracts
- Dosage 50-150 mg/d
- Preponderance of evidence suggests soy extracts do not effectively reduce hot flashes
- Caveats noted:
  - inconsistency in products
  - Equal converters?

Soy: Friend or Foe?

- Contradictory and confusing reports.
- Safety likely dependent upon
  - Age and Gender
  - Menopausal status
  - Individual metabolism
- Glycoside form to biologically active aglycones varies: roughly 35% of population can efficiently convert
  - Daidzin ->Daidzein->Equol
NCI Review Panel on Soy and Breast Cancer

“Neither existing animal nor human data allow definitive conclusions to be drawn about the effect of soyfoods or isoflavones on breast cancer risk in high-risk women and on the survival of breast cancer patients.”

Garlic (Allium sativum)

• #1 supplement
• Epidemiology: dietary garlic and onions help reduce the risk of GI cancers.
• Cardiovascular benefit?
• Antimicrobial (diet)
• Anti-inflammatory (diet)

Garlic and Cholesterol

• Three meta-analyses of randomized, placebo-controlled trials found a 5-12% decrease in cholesterol levels in hyperlipidemic patients after at least 30 days treatment with 600-900 mg. of garlic extract.


AHRQ Review

• 37 RCT showed garlic preparations led to short-term reduction of total cholesterol.
• 8 RCT failed to show garlic > placebo at 6 months.
• 27 studies failed to show significant benefit on blood pressure.

http://www.ahrq.gov/clinic/garlicsum.htm

The Problem With “Pooling”

• When comparing products that differ in extraction technique, plant part, delivery system and dose — it makes the question of equivalency valid.
• AHRQ review of garlic: raw garlic, aged garlic extracts, dehydrated garlic and garlic oil macerates pooled together to reach a specific conclusion regarding benefit of garlic to CV health.
Garlic Supplements

- Clinical trials
  - 2.4 to 7.2 g/d (aged garlic, ethanolic extract).
  - 300 mg TID (dried garlic, standardized to 1.3% alliin, 0.6% allicin).
  - 680 mg BID (dried garlic, 0.3% alliin).
  - Dried garlic powder (no characterization).

“Echinacea”

- Cochrane review of 16 RCT
- 3396 participants
- Evidence suggests that some preparations are superior to placebo for acute infection.

Melchart D, Cochrane Database Syst Rev 2005

Echinacea angustifolia

- E. angustifolia extracts
  - Supercritical CO2
  - 60% ethanol
  - 20% ethanol
  - 437 rand to prophylaxis (7 days before challenge) or placebo.
- Challenged with rhinovirus 39, then sequenstered 5 days.

Turner NEJM 2005; 353:341-348

E. purpurea extract

  - 150 subjects, natural colds
  - Treat at onset of 2 symptoms, continue for 7 days.
  - Commercial E. purpurea extract (Echinilin)
  - Statistically significant decrease in symptom scores versus placebo.
  - Authors describe species, plant part, strength, chemistry.

Echinacea Use

- Good safety profile - can cause allergic reaction in some individuals, especially if atopic.
- Herbalist experience - use tincture (1:5 strength) 3-5 ml every 3-4 hours for first 24-48 hours of feeling cold/flu.
**Ginseng (Panax ginseng)**

- Tonic, adaptogen
- German Commission E and WHO + monographs
- SE: 100-600 mg/d (4% ginsenosides)
- Research mixed:
  - Mood
  - Concentration
  - Fatigue
  - Well-being

**Ginseng**

- Two primary species
  - Panax ginseng (Asian, Chinese, Korean)
    - White - crude, unprocessed
    - Red - steamed
  - Panax quinquefolius (American)
  - Siberian ginseng is Eleutheroc - not a true ginseng.
- Tonic, adaptogen
- Recognized by German Commission E and WHO for mental & physical fatigue.
- SE: 100-600 mg/d (4% ginsenosides)

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**Ginkgo (Ginkgo biloba)**

- Neuroprotective, Antioxidant
- GEM Study: 3000 healthy adults (75 and older) followed average 6 years
- 240 mg/d ginkgo extract did not delay or prevent dementia more than placebo
- DeKosky, et al. JAMA 2008

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**Ginkgo and Research**

- Systematic reviews suggest:
  - Ginkgo superior to placebo for intermittent claudication.*
  - Promising evidence may improve symptoms of early dementia.**
  - Limited evidence of benefit for tinnitus.***
  - Limited evidence for acute ischemic stroke.****

* Atherosclerosis. 2005 Jul;181(3):3-7
** Cochrane Database Syst Rev. 2002(4):CD003120
*** Cochrane Database Syst Rev. 2004(4):CD001682

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**Ginkgo and Bleeding**

- 15 published case reports describe temporal association between ginkgo and a bleeding event, including 8 episodes of intracranial bleeding.
- 13/15 case reports identified other risk factors for bleeding.
- 6 reports clearly described that ginkgo was stopped and bleeding did not recur.

**Study**

- RDBPCT 32 healthy male volunteers studied three dosages of Egb 761 (120, 240, and 480 mg/day).
- No significant modification of bleeding time, platelet function, or coagulation factors at any dosage compared with placebo.


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**Milk Thistle**

* (Silybum marianum)

- Systematic review of 13 RCT (n=915) milk thistle extracts for alcoholic and/or hepatitis B or C.
- No significant benefit reported with milk thistle extract.
- Large NCCAM research initiative underway.


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**Saw palmetto**

* (Serenoa repens)

- Meta-analyses show reduced symptoms in enlarged prostate.
- Moved to USP from NF.
- German Commission E and WHO have positive monographs.
- 320 mg/day SE

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**Changes in Primary and Secondary Outcome Measures**

![Table of changes in outcome measures](image)

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**Bilberry/Blueberry**

* (Vaccinium myrtillus)

- Basic science...
  - Rich in anthocyanins
  - Potent antioxidants
  - Positive benefits on vascular system

German Comm E approves dried fruit for acute nonspecific diarrhoea.

Common uses:
- Prevent retinopathy
- Vascular disorders
- Acute nonspecific diarrhoea

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**Chaste Tree Berry**

* (Vitex agnus castus)

- German Commission E approves for menstrual cycle irregularities, PMS, and mastodynia.
- Dose is typically 500 mg dried fruit taken once each morning.
Chaste Tree

- Chaste tree preparations act, in part, by reducing prolactin via binding D2 receptors, increasing progesterone in the luteal phase, and binding opiate receptors.
- Safety profile good: theoretically could interact with dopaminergic medicines and OCP.

Devil’s Claw
(Harpagophyllum procumbens)

- S. African plant
- Harpagoside marker
- Fever, aches, arthritis

Issues...
- Bitter
- Stomach upset
- Caution with certain patients
- Use with acute inflammatory conditions.

Devil’s Claw: RCT

Review: RCT
- Chronic low back pain
- Acute exacerbation
- Devil’s Claw, Placebo, Devil’s Claw+NSAID
- Superior to placebo, equiv. to conventional med

Feverfew
(Tanacetum parthenium)

- Cochrane review 5 RCT (343 patients) - mixed results.
- 3 RCT S- in severity, duration, frequency.
- Parthenolide probably not active – used as marker compound.
- Dose: 125-250 mg/day
- Safety note:
  - Withdrawal HA/GI upset
  
Goldenseal Root
(Hydrastis canadensis)

Contains berberine & related alkaloids
- Antibacterial, antifungal
- No clinical trials though widespread use

N. American plant
Folk tradition

Feverfew
(Tanacetum parthenium)

Migraine Prevention
- Combination product
  - Riboflavin
  - Magnesium
  - Feverfew
- Dose: 125-250 mg/day
- Parthenolide probably not active – used as marker compound.
Goldenseal Root
*(Hydrastis canadensis)*

- Traditional use: gastritis
- Goldenseal extract
- Bactericidal to H. pylori

Outside the GI tract?
- Lung infections
- Renal/Urinary infections

Also Berberine rich...
- Oregon grape root
- Barberry root bark

Safety...
- Interactions with drug-metabolizing enzymes
- Pregnancy

Meta-analysis of 6 RCT...
- Seed extracts very effective
- for chronic venous insufficiency

Use in patients with Lymphedema
Dose: 300 mg BID
- standardized to provide
50-75 mg escin per dose

Good safety profile.

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Horse Chestnut
*(Aesculus hippocastanum)*

Licorice Root
*(Glycyrrhiza glabra; G. uralensis)*

Consider these similar for benefits/risks
- Western: glabra
- Eastern: uralensis

Licorice often found in herbal formulations for cough, colds, sore throat, GERD, gastritis or IBD.

Gastroprotectant effects of licorice root known for centuries.

Compounds in licorice increase local prostaglandin levels that promote mucus secretion and cell proliferation in the stomach

Licorice root likely safe in healthy adults when used at doses not exceeding 3 grams/d for periods up to 3-4 weeks.

Glycyrrhizin (glycyrrhizinic acid) is the compound responsible for symptoms of pseudohypokalemia with excess or prolonged ingestion.

Symptoms include hypertension, edema, hypokalemia.

Be cautious with large doses of crude form, especially with certain patients.

Preparations available without glycyrrhizin are called DGL.
- Commonly used for GERD
- No long term safety concerns

DGL: Dose
- 700-800 mg (760 mg)
- Chewable tablets
- 20 minutes prior to meal
- 2-3x/day 4-6 wks; 1 at largest meal

Usd as spice (curry) and medicinal agent for at least 2000 yrs.

USA: common in Yellow Mustard

Yellow Pigments: Curcumin considered major active component.
Curcumin vs Turmeric

- 1200-2400 mg/d curcumin for IBD
- India: average daily consumption = 60 mg curcumin (2.5 gm/d of Turmeric)

NIH Studies

- Colon cancer prevention
- FAP
- Prostate cancer, Skin cancer
- IBD: Crohn’s, UC
- Rheumatic conditions

Curcumin/FAP Study

Pilot Study: FAP
~ curcumin & quercitin
~ 66% reduction in polyp formation

Turmeric (Curcuma longa)

Good safety profile
- high doses: bleeding risks
- caution: Warfarin interaction

- Bactericidal
- Anti-adhesive
- Antimicrobial

Curcumin & The Bowel

Curcumin stays in GI tract.
Systemic absorption increased by taking with fatty meal.

For Bowel:
- Empty stomach
- Not with fat
- Avoid specialized products

Absorption research:
- 20 mg black pepper/1 kg curcumin
- 2000% increase

Valerian (Valeriana officinalis)

The German Commission E recognizes the use of valerian root for restlessness and sleeping disorders based on nervous conditions.

Research for sleep...
- Mixed results
- Effective: 7-10 days
Combination with Hops

Valerian
- Not habit forming
- Good safety profile
- Theoretical interactions
- Effectiveness studies for insomnia not clear
- Use for anxiety...
  - small doses throughout day
  - combo with lemon balm

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