Love Potions, Witches Brews and the Medicine Bag
- An Update on Herbal Medicine

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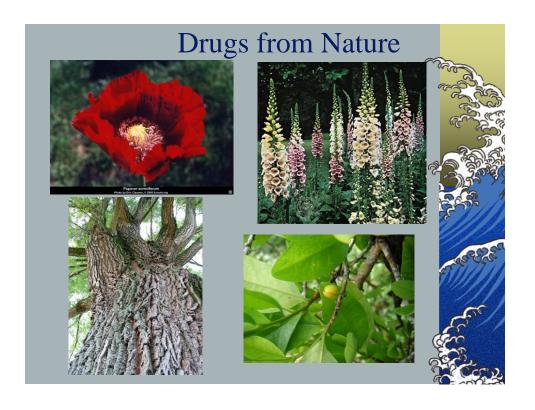
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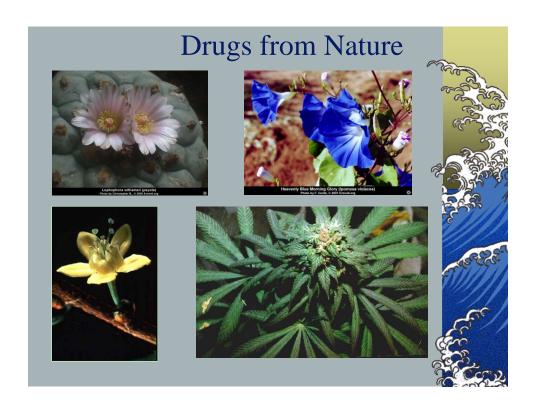


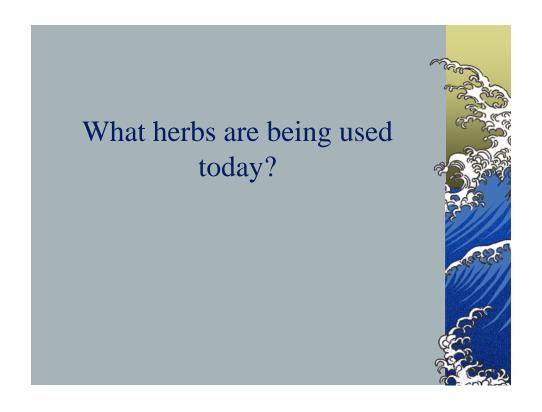
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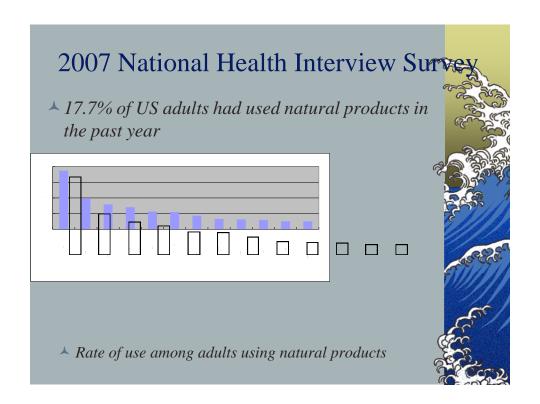
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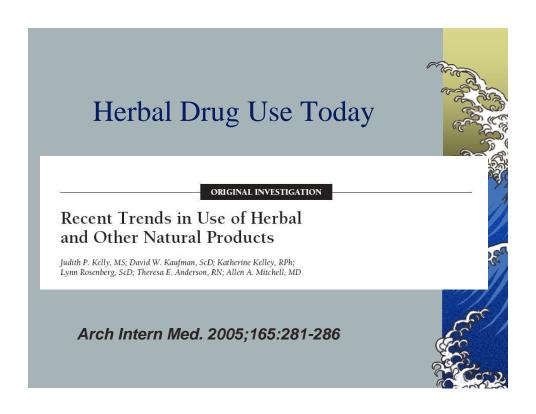


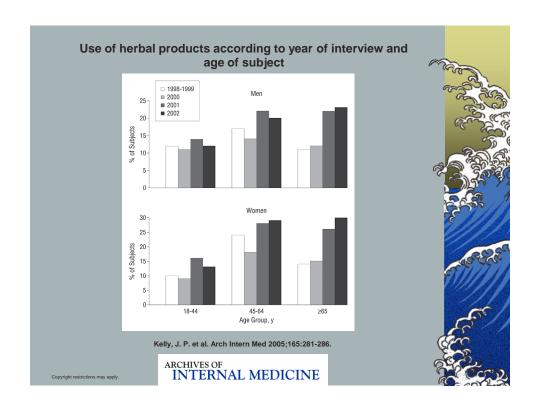


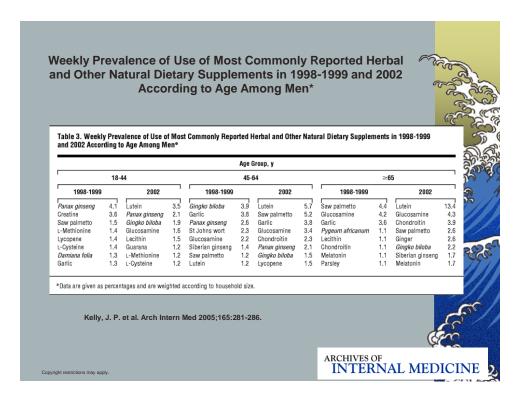


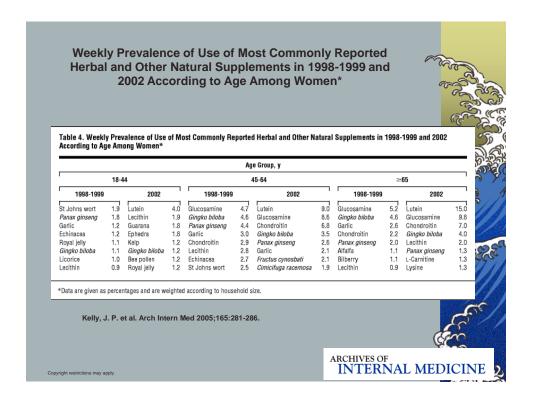












Reasons for Use of Products Containing Herbal and Other Natural Supplements Among Subjects Interviewed in 2002 Table 5. Reasons for Use of Products Containing Herbal and Other Natural Supplements Among Subjects Interviewed in 2002

Men (n = 736)	No. (%)	Women (n = 998)	No. (%)
Vitamin	38 (20.5)	Vitamin	67 (21.0)
Supplement diet	22 (11.9)	Supplement diet	37 (11.6)
Energy	13 (7.0)	Health	23 (7.2)
Prevention, not otherwise specified	12 (6.4)	Physician recommended	15 (4.7)
Physician recommended	11 (5.9)	Energy	13 (4.1)
Health	11 (5.9)	Menopausal symptoms	13 (4.1)
Heart	9 (4.9)	Immune booster	12 (3.8)
Cholesterol	9 (4.9)	Prevention, not otherwise specified	10 (3.1)
Prostate	7 (3.8)	"It is good for you"	9 (2.8)
Mineral supplement	6 (3.2)	Memory improvement	9 (2.8)
Prevent colds	4 (2.2)	Weight loss	8 (2.5)
Do not know	4 (2.2)	Recommended by friend or family	8 (2.5)
Organ health	4 (2.2)	Aging	8 (2.5)
Bodybuilding	4 (2.2)	Mineral supplement	7 (2.2)
Hypertension	4 (2.2)	Digestive	6 (1.9)
Nutrition	3 (1.6)	Organ health	6 (1.9)
Aging	3 (1.6)	Hormone therapy	6 (1.9)
Weight loss	3 (1.6)	Eyes	6 (1.9)
Mental alertness	3 (1.6)	Detoxify	5 (1.6)
Family history	3 (1.6)	Insomnia	5 (1.6)
Antioxidant	3 (1.6)	News report, magazine, or television	4 (1.2)
"It is good for you"	3 (1.6)	Heart	4 (1.2)
Sickness	3 (1.6)	Osteoporosis prophylaxis	4 (1.2)
"I need it"	3 (1.6)	Mood alteration	4 (1.2)
All others	47 (25.4)	Sinus	4 (1.2)
		Antioxidant	4 (1.2)
		Cholesterol	4 (1.2)
		All others	89 (27.9)



Kelly, J. P. et al. Arch Intern Med 2005;165:281-286.

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GENERAL CONSIDERATIONS

- ▲ Herbs are drugs
 - ▲ *Side effects*
 - ▲ Drug-drug interactions
 - **▲** *Un-regulated*
 - ▲ Variability in preparations
 - ▲ Testing of brands
 - ▲ http://www.consumerlab.com/





DSHEA Act of 1994

▲ Definition of dietary supplement:

A product intended to supplement the diet that contains a vitamin, mineral, an herb or other botanical, an amino acid, ...a dietary substance for use by man to supplement the diet by increasing the total dietary intake; (or a concentrate, metabolite, constituent, extract or combination of any ingredient described above)



DSHEA Act of 1994

- ▲ Supplements are not 'food additives'
- ▲ Statements of nutritional support allowed
 - ↑ This statement has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease."
- ▲ The burden of proof that a product is unsafe or adulterated lies with the FDA
 - ▲ Examples tryptophan, ephedra (Ma Huang)

Supplement Labeling

- ▲ What must it tell you?
- ▲ What can it tell you?
- ▲ What it doesn't tell you?



What *must* it tell you?

- ▲ Statement of identity
- ▲ Net contents
- ▲ *Manufacturer name and address*
- ▲ Supplement Facts panel
 - ▲ Serving size
 - ▲ *Ingredient listing (name/part/herb or extract)*
 - ▲ Amount per serving (herbs or "Propietary blend")



What can it tell you?

- ▲ Structure-function claim (w/ FDA disclaimer)
- ▲ Expiration date
- ▲ Relevant precautions
- "Standardized" or "Full spectrum"
 - ▲ Neither of these terms has a definition in the U.S.



What it doesn't tell you?

- ▲ Preparation of the herb
 - ▲ Agricultural history of extract
 - ▲ Preparation of extract
- ▲ Standardization (in U.S.)
 - ▲ Contact manufacturer FMI
- ▲ Indications
- ▲ Dose



Why standardize?

- ▲ Assure consistent quality
- ▲ Avoid adulteration or substitution
- △ "Define" the extract for clinical trials and/or patent protection



2007 – FDA ruling

- New June 2007 FDA ruling: to require "current good manufacturing practices" (cGMPs) for dietary supplements.
 - ▲ This rule to take effect in June 2008 for large companies.
 - ▲ Smaller companies 2010 to comply.
- ▲ *GMP* ensures
 - ▲ Production in a quality manner without contaminants and with accurate labeling, so product contains what the label states!



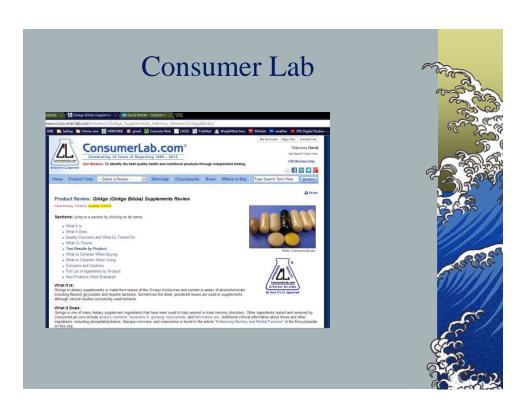
2007 – FDA ruling

- ▲ To try to get accurately labeled herbals advise patients to look for the following symbols on labels
 - ▲ GMP (Good Manufacturing Practices)
 - *▲NSF* (*National Safety Foundations*)
 - *▲ USP (United States Pharmacopeia)*
 - Note: This does not mandate proof of clinical efficacy or mandatory reporting of side-effects.



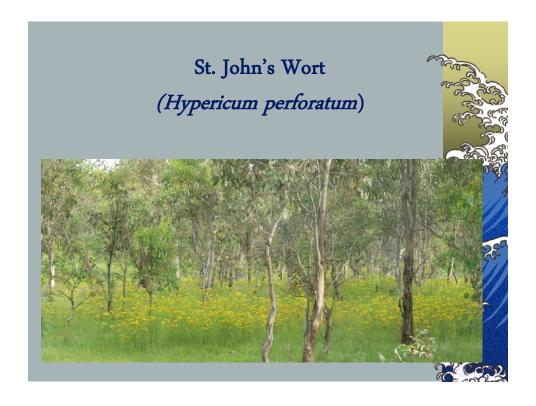










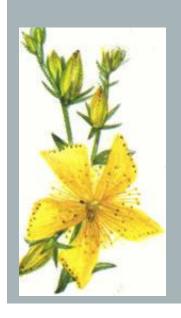




St. John's Wort

Allooms on St. John the Baptist's birthday and is said to bleed red on the day in August he was beheaded

St. John's Wort - Then



- ▲ Used to protect against wounds in battle
- ▲ Used to ward off evil spirits
- ▲ Used to reveal witches and to make them speak the truth

St. John's Wort - Then

- ▲ *Medicinally*
 - ▲ Antiseptic (used in the crusades??)
 - ▲ Anti-viral
 - ▲ Nerve tonic
 - ▲ Anti-depressant
- ▲ St Johns Wort is good in tertian and quartan agues (Malaria) and is also used to destroy worms.
- "A tincture of its flowers in spirit of wine is commended against Melancholy and Madness".

Blackwell's Curious Herbal, 1735



St. John's Wort - Today

- ▲ One of most widely used \$48,000,000 in U.S. in 1997
- ▲ Standardized to hypericin
- ▲ Many studies use an extract of SJW hypericum extract
- Hypericum may work as re-uptake inhibitor for serotonin and norepinephrine



- ▲ Systematic review showed 8 trials with almost 1000 patients
- ▲ Against placebo or TCA
- ▲ Significantly better than placebo (4 trials)
- ▲ Equivalent to low dose TCA (4 trials)
- ▲ Gaster and Holroyd, Arch. Intern. Med., 2000



- ▲ Imipramine (75 mg bid) vs STJ (hypericum extract ZE117 bid)
- ▲ 324 patients, mild to moderate depression
- ▲ Randomized, DB, 6 weeks
- Comparable decrease in depression scores for imipramine and SJW
- ▲ Adverse side effects 39% for SJW and 63% for imipramine
- ▲ Woelk et al., BMJ, 2000



- → Hypericum (900 mg LI 160) vs sertraline (75 mg/d)
- ▲ 30 patients, mild to moderate depression
- ▲ DB, randomized
- ▲ 47% of patients improved on SJW and 40% improved on sertraline
- ▲ Small group, small effect size
- ▲ Brenner et al., Clin. Ther., 2000



- ▲ SJW vs. placebo
- ▲ 300 pts, major depression, 8 weeks
- ▲ No differences in depression scores
- ▲ Greater number of patients reaching remission 14.3% vs 4.9%
- ▲ Shelton et al., JAMA, 2001



- ▲ Adverse side effects
 - **▲** *Dry mouth*
 - ▲ GI disturbances
 - **▲** *Photosensitivity*
 - **▲** Sedation



- *▲Drug-drug interactions*
 - ▲ Serotonin syndrome
 - ▲ When combined with other anti-depressants
 - ▲ Restlessness, muscle twitches, myoclonus, sweating, hypertension, may lead to coma



- *▲Drug-drug interactions*
- ▲ Induces CYP450-3A4
 - ▲ Major liver enzyme
 - ▲ Decreases serum concentration of other drugs
 - **▲** Cyclosporin
 - **▲** Oral contraceptives
 - ► HIV anti-viral drugs
 - **▲** Digoxin



- ▲ Proposed trials
 - ▲ Anxiety and social phobia
 - ▲ Minor depression
 - ▲ *Obsessive-compulsive disorder*



St. John's Wort

- ▲ Useful in mild to moderate depression
- ▲ Ineffective in major depression
- ▲ Well tolerated with few adverse side effects
- ▲ Significant drug-drug interactions



Kava kava

- ▲ Piper Wichmanii
- ▲ Piper Methysticum





"I drink kava each Friday evening, after a week's worth of teaching high schoolers. Ordinarily on Fridays, the events of the week loop repeatedly yet pointlessly through my mind. Kava's relaxing properties allow me to drop this loop, and concentrate on whatever I like. Nicest of all is the way kava affects my dreams. On kava nights, my dreams involve long, epic voyages through blue-green seas, populated by strange, friendly water animals. Like last night - my travel and conversation partner was a manatee with violet eyes. These are more like the dreams I remember having as a child, and a total departure from my usual stressinduced dreams of grading papers, running out of chalk" - J. Prince (Seattle, WA)



Kava Kava

- *▲Natural valium??*
- ▲ Mild stimulant
- *▲ Anti-Anxiety*
- ▲ Anti-Fatigue
- ▲ Active constituents kavapyrones (4) and other kava alkaloids
- ▲ May increase GABA receptor
- ▲ May inhibit reuptake of norepinephrine
- ▲ May increase dopamine



Kava kava

- ▲ Clinical trials
- ▲ As effective as oxazepam (38 pts with anxiety)
- ▲ More effective than placebo (58 patients with anxiety)
- ▲ More effective than placebo for 8 weeks (101 patients with anxiety)
- ▲ Anxiety Level of evidence A



Side Effects and Interactions

- ▲ Liver toxicity (case reports)
 - ▲ Withdrawn in Europe and Canada
- ▲ Potentiate benzodiazepines and other sedatives
- ▲ May increase activity of anti-coagulants
- ▲ May worsen symptoms of Parkinson's disease
- ▲ May inhibit P450 metabolism
- **▲** Dependence





Cannabis Indica

▲ Given in full dose to man, this drug causes exhilaration and periods of constant laughter arising from the slightest cause, the person seeming convulsed with merriment; in other cases the sensations are disagreeable, and even death may seem imminent to the deranged mind. – Practical Therapeutics, Hare, 1895.



Marijuana

- Common name for a tall annual herb (Cannabis sativa) of the family Cannabinaceae
- ▲ Native to Asia but now widespread because of its formerly large-scale cultivation for the bast fiber (also called hemp) and for the drug it yields



Marijuana - Then

▲ When a patient suffers from sleeplessness which is due in part to pain and in part to nervousness, the following prescription may be given:

CANNABIS INDICA.

113

B.—Chloralis
Sodii bromidi
Ext. belladonnæ fl. f3j (4.0).
Ext. cannabis indicæ fl. f3j (4.0).
Syr. acaciæ f3y (192.0).—M.
S.—Tablespoonful (16.0), in water, at a dose at night, to be repeated once.

In headaches at the menopause cannabis indica is useful, and if the are associated with constipation and anæmia, iron and aloes be given simultaneously. Where headaches are due to retinal a very useful prescription, according to de Schweinitz, is

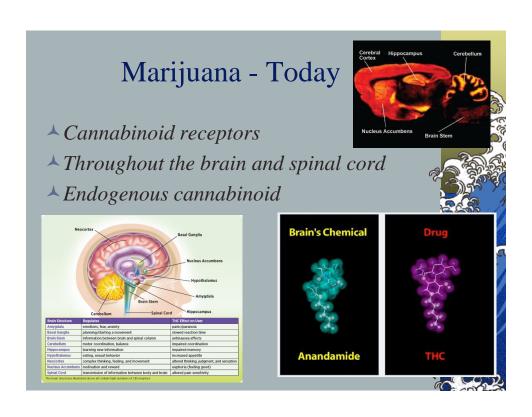
Marijuana - Then

- *▲ Other uses (1895)*
 - ▲ Chronic inflammation
 - ▲ Gastralgia
 - **▲** Metorrhagia
 - ▲ Nervous and spasmotic dysmenorrhea
 - **▲** Gonorrhea
 - ▲ Sexual stimulant



Marijuana - Then

▲ The employment of this most valuable remedy is handicapped by its frequent lack of power — a fault which is largely dependent upon its preparation. The drug as prepared by Parke, Davis and Co. has proved efficacious in the author's hands for a number of years. The physician should always employ some preparation known by him to be active by personal trial before condemning the drug as a failure in a given case. — <u>Practical Therapeutics</u>, Hare, 1895.



Marijuana - Today

- ▲ Nausea and vomiting (FDA approved as THC extract Marinol)
- ▲ Glaucoma
- *▲ Wasting syndromes*
- ▲ Pain level of evidence B
- ▲ Symptoms of MS level of evidence B



Marijuana - Today

- ▲ Side effects and Toxicity
 - **▲** Psychoactive
 - **▲** Hypotension
 - **▲** Dependence



Chondroitin Sulfate in Osteoarthritis

Chondroitin Sulfate in Osteoarthritis

- ▲ Bourgeois P, et al.
 - ▲ 127pts, 1,200 mg, effective at 3 months
- ▲ Bucsi L, et al.
 - ▲ 80pts, 800 mg, effective over 6 months
- ▲ Conrozier T.
 - ▲ 104 pts, 800 mg, effective after 1 year
- ▲ *Morreale P, et al.*
 - ▲ 146 pts, 1,200 mg, effective for 6 months
- ▲ *Uebelhart D, et al.*
 - ▲ 42 pts, 800 mg, effective over 1 year
- ▲ *Verbruggen G, et al.*
 - ▲ 119 pts, 1,200 mg, effective over 3 years



How Chondroitin Sulfate Eases Osteoarthritis

- ▲ Increasing levels of chondroitin sulfate available to articular cartilage.
- ▲ Increasing levels of other important proteoglycans available to the articular cartilage.
- ▲ Decreasing activity of elastase, thus decreasing the degradation of collagen.
- ▲ Decreasing inflammation
- ▲ Level of evidence B



Chondroitin Sulfate's Atherosclerotic Promise

- ▲ Decreasing plasma levels of cholesterol and other lipids.
- ▲ Decreasing atherosclerotic plaque formation.
- ▲ Decreasing inflammation
- ▲ Level of evidence D









Panax Ginseng

- ▲ Asian ginseng (Panax ginseng C.A., Meyer)
 - ▲ Panax, Chinese, or Korean ginseng.
- ▲ American ginseng (Panax quinquefolius L.)
- ▲ Siberian ginseng, also called eleuthero (Eleutherococcus senticosus Rupr ex Maxim),



Panax Ginseng

- ▲ Enhances immune system Level of evidence B
 - ▲ *Antiviral activity*
 - ▲ Decreased colds and flu
 - ▲ Decreased recurrance of herpes simplex with eleuthero
- ▲ Enhances mental activity Level of evidence B
 - ▲ Variable results some positive
- ▲ Enhances general well-being
 - ▲ 200 mg per day for 8 weeks
 - ▲ Energy, mood and vigor



Panax Ginseng

- ▲ Doses
 - ▲ 200 mg daily of extract containing ginsenosides
 - ▲ 300-400 mg of Siberian ginseng (eleuthero)
- ▲ Side effects rare
 - ▲ Estrogen-like effects
 - ▲ Mania with anti-depressants
 - ▲ Reduced efficacy of coumadin
 - ▲ May interfere with tests for digoxin
 - ▲ May reduce insulin requirements





Ginko Biloba



- ▲ Typically extract of leaves of Ginko biloba tree ?
 - ▲ Oldest surviving species of tree
 - ▲ Extinct in Europe but survived in Asia
 - ▲ Some trees cultivated for over 1,000 years
 - ▲ Original Chinese medicine used seeds
- ▲ Huperzine A is extract from leaves of Chinese toothed club moss (Huperzia serrata or synthetically manufactured.

Ginko Biloba

- ▲ Alzheimer's Disease
 - ▲ German Commission E
 - ▲ As effective as any approved medication for Alzheimer's disease
 - ▲ Mildly effective in elderly with memory loss
 - ▲ Weak in younger patients
- ▲ Intermittent claudication



Ginko Biloba

- ▲ Preliminary double-blind trials
 - **►**PMS
 - *▲ altitude sickness*
 - **▲** Glaucoma
 - <u> ▲ macular degeneration</u>
 - **▲** <u>Vertigo</u>
 - <u> ***** sudden hearing loss</u>
- ▲ *Increases blood flow*



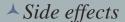
Ginko Biloba



▲ Dosage

▲ 40-80 mg 3 times a day of 50:1 extract standardized to contain 24% ginkgo-flavone glycosides

Ginko Biloba



▲ Relatively safe

- ▲ Not established in young children, pregnant women or in kidney or liver disease
- ▲ Anti-coagulant
 - ▲ Interactions with anti-coagulants
- ▲ Lowers seizure threshold
- ▲ Reduces efficacy of calcium channel blockers
- ► May increase efficacy of anti-psychotic drugs





▲ Mosquito repellant - Level of evidence C



Chinese herbal medicine A different approach

- **▲** 22,000 herbs
- *▲ 3000 years*
- combinations of herbs individually prepared after patient history
- *▲ specialty medicine*



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