Green Tea

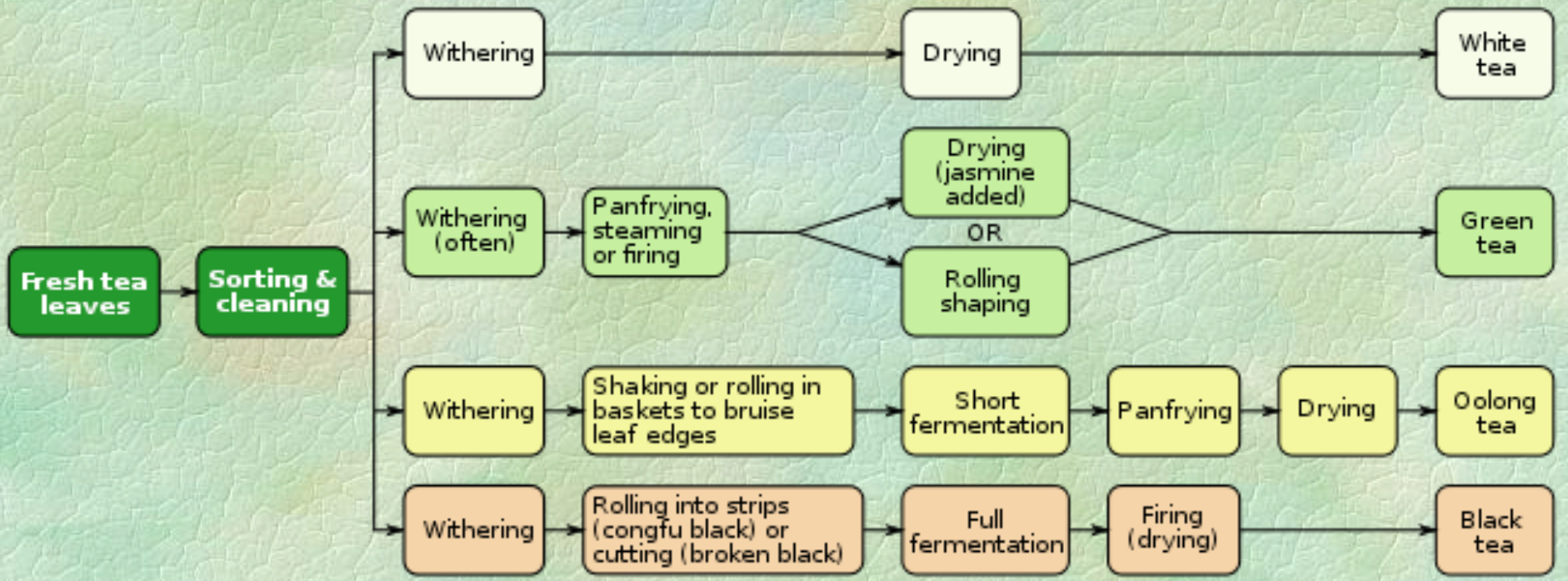
Botany- Camillia sinensis leaves

black tea-fully fermented leaves that are roasted;40mg caffeine/cup
green tea-steamed, dried, nonfermented leaves;20mg/cup
oolong tea-partially fermented
white tea-steamed leaf buds;15mg/cup

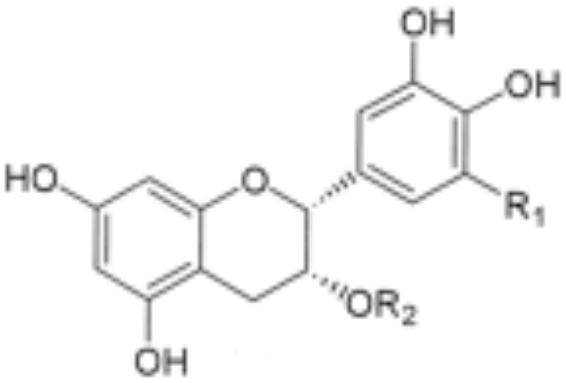
Chemistry- the hot water extract of the leaves contains catechin polyphenols and other antioxidant/free radical scavenging compounds; green and white tea have mainly catechins and flavanols, black tea has theaflavins

Pharmacology- protective activity against experimental cancers in animals and some epidemiological evidence for protective effects for stomach, colon, pancreatic cancers and lower cardiovascular disease risk but these are observational not prospective, controlled trials. There are some new, very promising preliminary studies recently published, however.

Tea (Camellia Sinensis) Processing Chart



FLAVANOLS



	R_1	R_2
EC	H	H
EGC	OH	H
ECG	H	gallate
EGCG	OH	gallate

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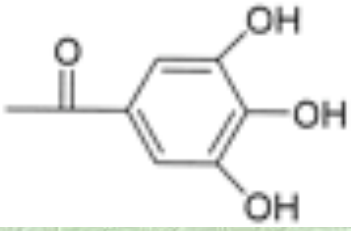
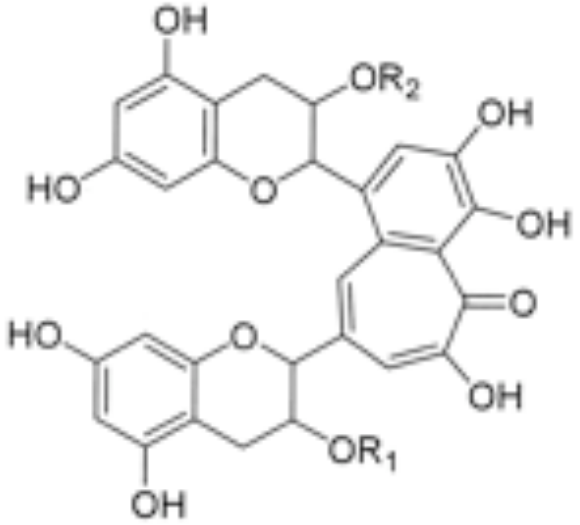


THEAFLAVINS

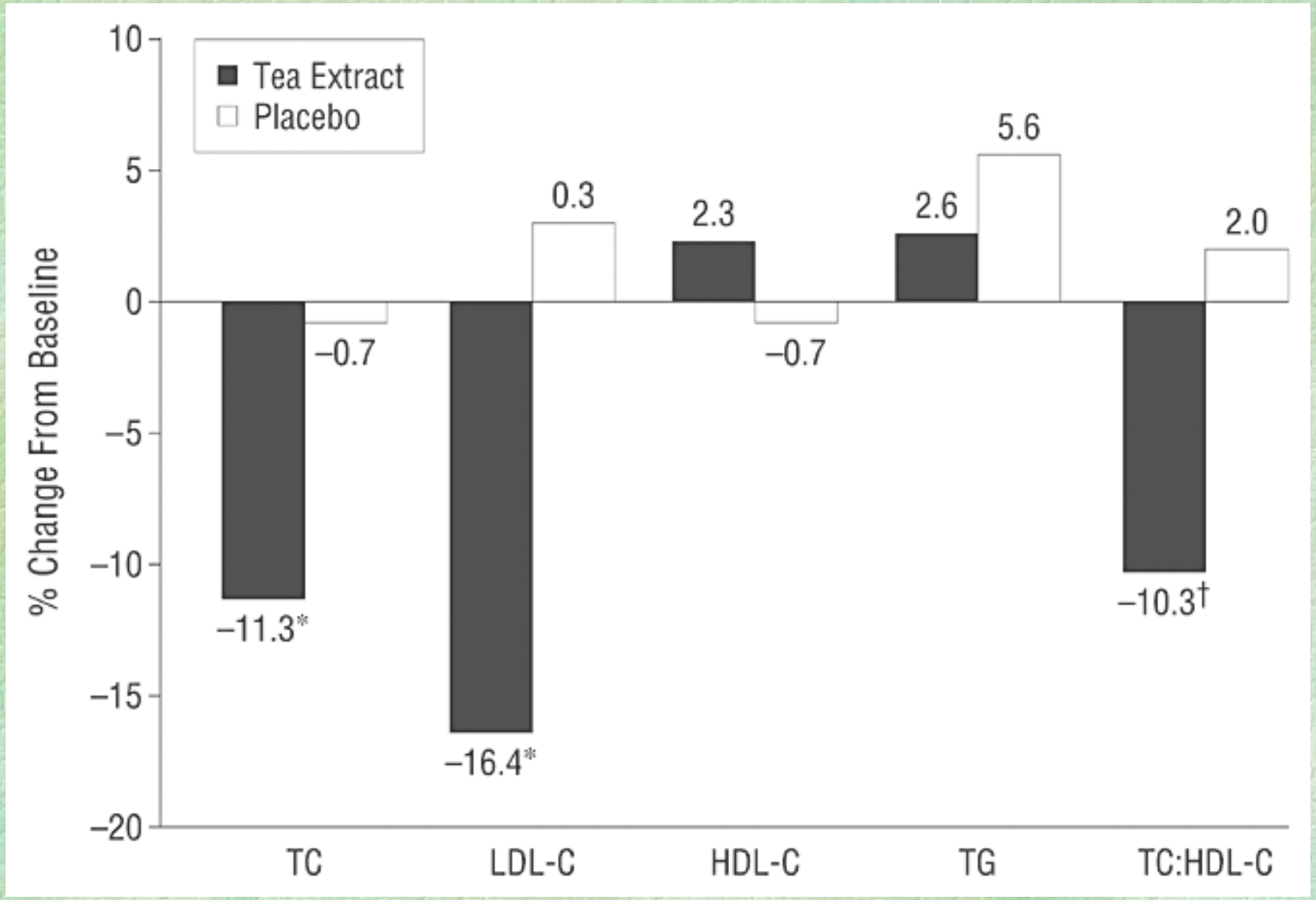


	R_1	R_2
theaflavin	H	H
theaflavin-3-monogallate	gallate	H
theaflavin-3'-monogallate	H	gallate
theaflavin-3,3'-digallate	gallate	gallate

EGCG=epigallocatechin-3-gallate

Uses and Evidence

- Topical use: a special extract with catechins is available on Rx for external genital warts (Veregen, Pharma-Derm, Polyphenon E)
- Cancer: some preliminary evidence for prostate cancer (Bettuzzi et al. Cancer Res 2006;66:1234-1240. n=64) and cervical dyplasia (Ahn et al. *Eur J Cancer Prev*. 2003;12:383-90).
- Also high consumption associated with lower risk for bladder, esophogeal and pancreatic cancers.
- Heart Disease: some preliminary evidence for improved cholesterol levels (see slide)



Archiv Intern Med 2003;163:1448-1453 n=240 12 weeks used theaflavin enriched green tea extract in capsule form

Table 2. Prevalence of prostate cancer in placebo arm and GTC arm (12 months biopsy checkpoint)

Study arm	prevalence of cancer (%)
placebo	30
Green tea extract	3.3
P value	<0.01

Bettuzzi et al. Cancer Res 2006;66:1234-1240. n=64 with early signs of dysplasia; used capsules of a catechin enriched tea extract

FIGURE 2 Changes from baseline to wk 2, 4, 6, 8, 10, and 12 in body weight of overweight or obese adults who consumed a control or catechin-containing beverage

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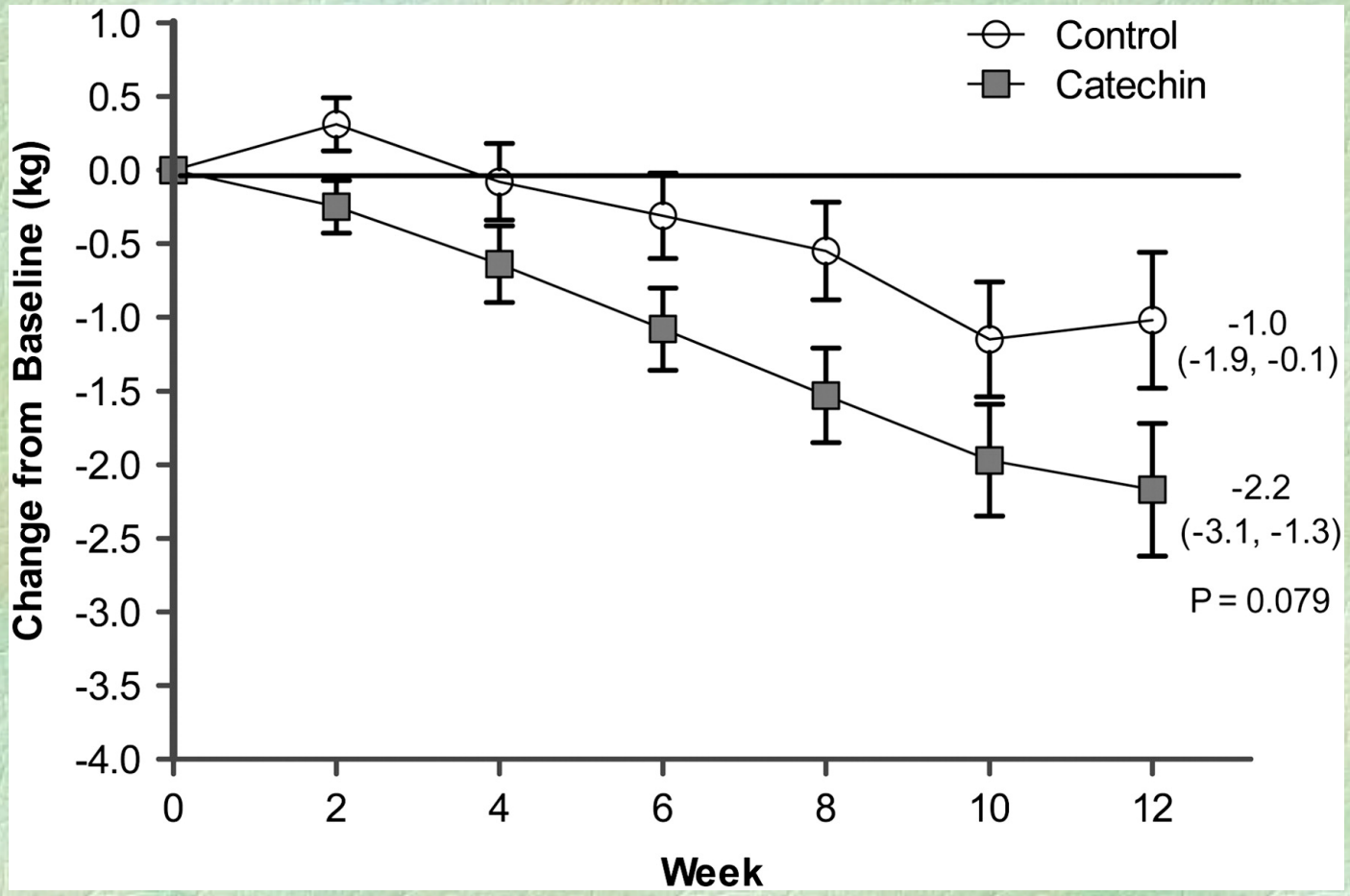

Maki, K. C. et al. J. Nutr. 2009;139:264-270

FIGURE 3 Percent changes from baseline (least squares mean {+/-} SEM and 95% CI) to wk 12 in total fat mass, and total abdominal, abdominal subcutaneous, and intra-abdominal fat areas by treatment group (n = 57 and 52 for fat mass and 55 and 51 for abdominal fat areas in the catechin and control groups, respectively)

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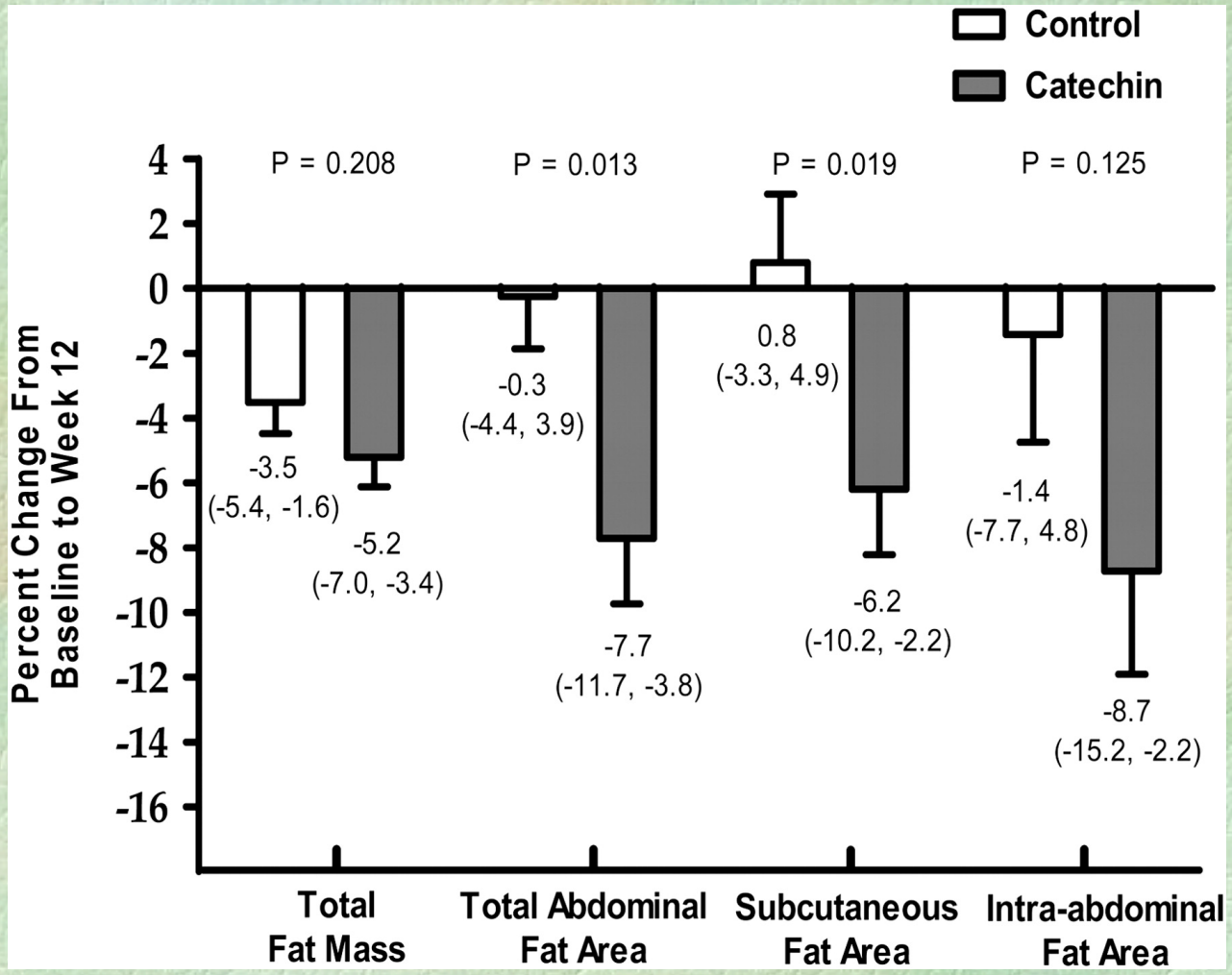


Maki, K. C. et al. J. Nutr. 2009;139:264-270

June 30, 2005, FDA denied health claim for Green Tea

1. "Two studies do not show that drinking green tea reduces the risk of breast cancer in women, but one weaker, more limited study suggests that drinking green tea may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of breast cancer."

2. "One weak and limited study does not show that drinking green tea reduces the risk of prostate cancer, but another weak and limited study suggests that drinking green tea may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of prostate cancer."

Green Tea

Summary

- **Efficacy: Increased consumption *may* be somewhat protective against certain cancers and heart disease.**
- **Safety: good; caffeine content is significant; several reports of hepatotoxicity associated with green tea extracts. Causal?**
- **Drug interactions: antihypertensives? (caffeine); does contain vitamin K so large amounts might counteract warfarin.**
- **Product selection: Most are not standardized to catechins or polyphenols**
- **Dose: tea? Maybe 3 cups/d; extracts? Maybe 200mg TID containing 80% catechins and 50% EGCG**
- **Questions remaining:**
- ***How much benefit and how much tea consumption? Black tea? Do capsules act the same as the tea? What to standardize on?***

GWE: safe enough and maybe some benefit but ??

Evening Primrose Oil

Botany

Oenothera biennis., a wildflower/weed on the East USA coast

The seed is pressed to yield an oil

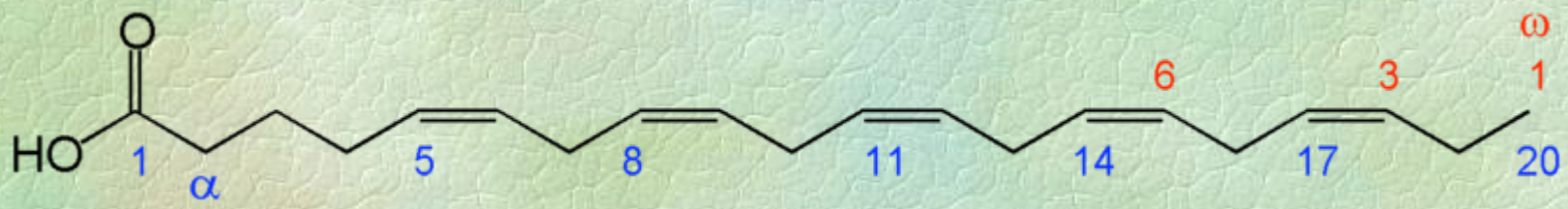
History

Many native American uses for the plant

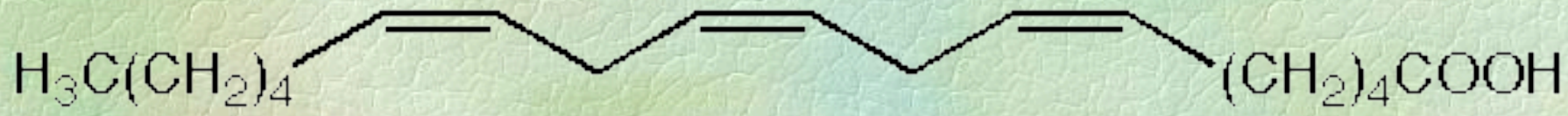
Recent years have focused on the uses of the seed oil

Chemistry

- Seed contains about 14% oil of which half is gamma linolenic acid (GLA); this is a omega –6 essential fatty acid;
- note: omega –3 fatty acids are present in fish oils and flaxseed oils and have different uses (e.g. lower cholesterol and risk of cancer
- GLA is a precursor to prostaglandin E1 which modulates (reduce) inflammation
- Other rich sources of GLA are borage seed oil (20%GLA) and black currant oil (15% GLA)



EPA (eicosapentaenoic acid) omega – 3 fatty acid



γ-Linolenic Acid

6,9,12 octadecatrienoic acid

Linoleic is 9,12 octa decadienoic acid-plentiful in diet

Omega – 6 fatty acid

Pharmacology of GLA

- GLA is precursor to several prostaglandins and leukotrienes that influence pain and inflammation
- The idea is to "flood the system" with precursor to enhance synthesis.
- Linoleic acid is an essential amino acid widespread in our diet
- GLA is formed from linoleic acid and is not found in common foods

Uses of GLA and Evening Primrose Oil

- Cyclic mastalgia
- PMS
- Diabetic neuropathy
- Eczema
- Arthritis, fatigue, digestive, asthma, weight loss, and many others

Evidence

- The evidence is surprisingly weak for most uses
- Several placebo controlled trials in the 1980s showing improvement in breast pain associated with menses; a recent study showed no effect (Am J Obstet Gynecol. 2002 Nov;187(5):1389-94).
- No strong evidence to show improvement of other symptoms of PMS or post menopausal symptoms
- Eczema use has been not effective in recent studies
- Use in diabetic neuropathy and rheumatoid arthritis looks promising based on a small number of older controlled studies
- More evidence is needed to support use of EPO in Raynauds syndrome, ADD, osteoporosis,as an adjunct treatment for breast cancer,for obesity,and hyperlipidemias

Safety: No special concerns at present

Dose: 2-6g of EPO/d or even higher

Evening Primrose Oil

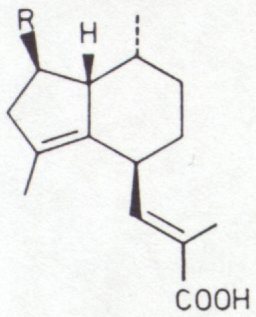
- **Summary**
  - **Efficacy: uneven evidence for most uses; best for diabetic neuropathy, cyclic breast pain, and possibly rheumatoid arthritis. May have application in helping treat breast cancer.**
  - **Safety: good**
  - **Drug interactions: none noted so far but increased blood clotting time has been noted. Caution with warfarin.**
  - **Product selection: Efamol is the best studied; has 1g/ capsule**
  - **Dose: 2-6g/d**
  - **Questions remaining include**
    - ***Does EPO really work for its many suggested uses?***

Valerian

- **Botany**
  - Valeriana officinalis, garden heliotrope
  - roots and rhizomes used
    - powder
    - tincture
- **History**
  - roots long used as tranquilizer and sedative

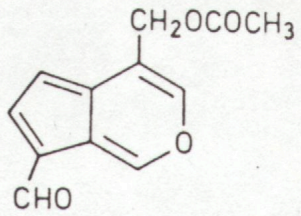
Valerian

- **Chemistry**
  - 0.1%-0.3% volatile oil in roots
  - contains sesquiterpenes e.g. valerenic acid
  - contains valepotriates
  - contains baldrinal and other decomposition products
- **Pharmacology**
  - volatile oil is sedative in animals
  - valepotriates have tranquilizer activity
  - water extract is sedative and has neither!
  - ? Active components
  - in vitro-
    - aqueous extracts causes release of GABA (similar to benzodiazepines)
    - inhibit GABA breakdown
  - mechanism unknown, active components unknown!

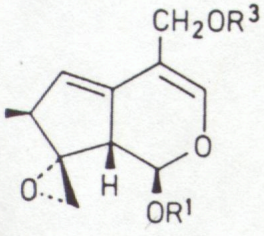


Valerenic acid R = H

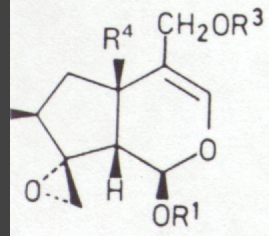
Acetylvalerenic acid: R = $OCOCH_3$



Baldrinal



	R^1	R^2	R^3
Valtrate	Isovaleryl	Isovaleryl	Acetyl
Isovaltrate	Isovaleryl	Acetyl	Isovaleryl
Acevaltrate	Isovaleryl	β-Acetoxyvaleryl	Acetyl



	R^1	R^2	R^3	R^4
Didrovaltrate	Isovaleryl	Acetyl	Isovaleryl	–H
IVHD-Valtrate	Isovaleryl	Acetyl	2-(Isovaleryloxy)-isovaleryl	–OH

Vorbach et al. Psychopharmakotherapie 3:109-115,1996

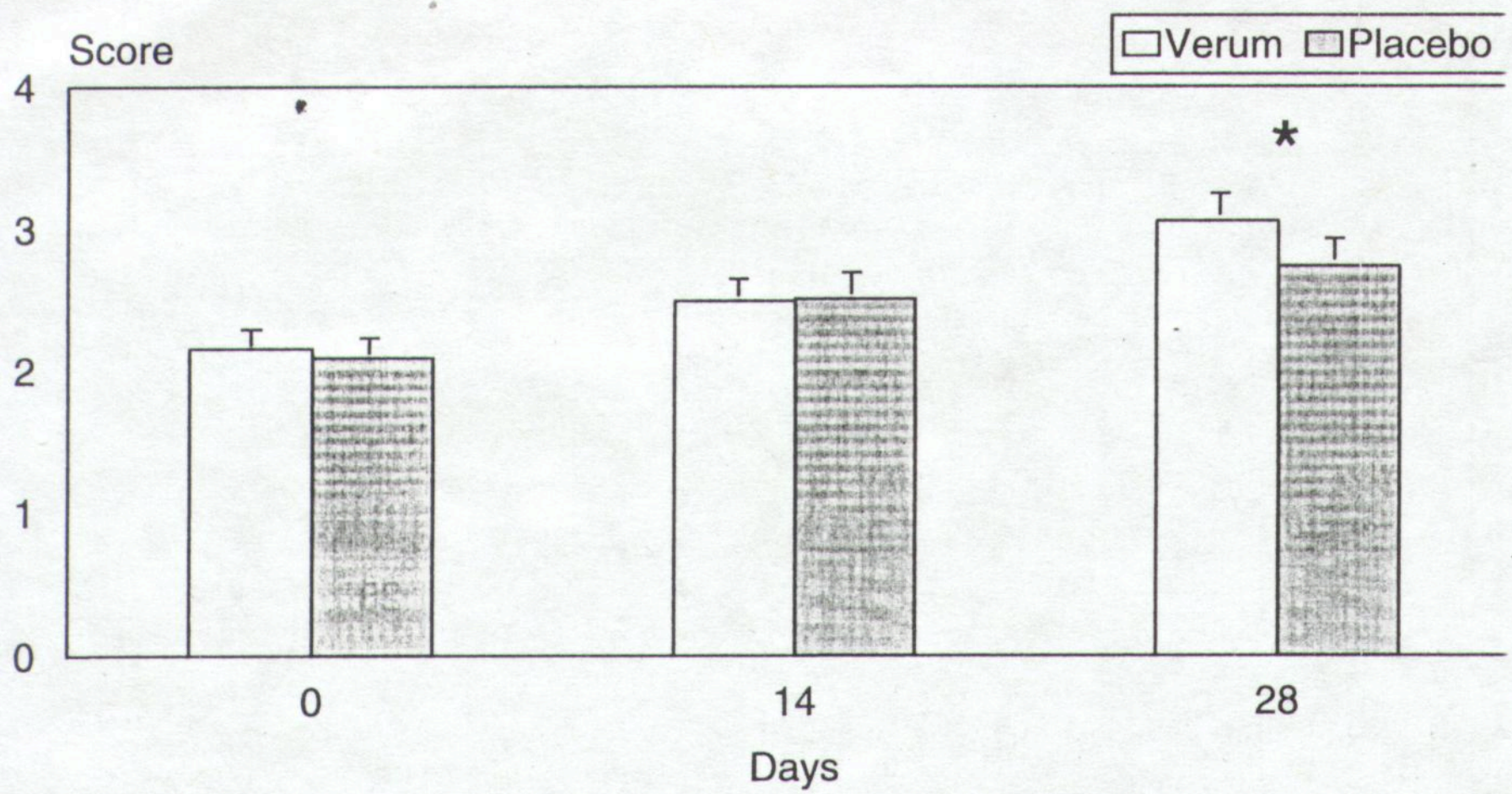


Fig. 2.16. Effect of 4 week's treatment with an ethanol valerian extract (600 mg/day) compared wit a placebo. The results were assessed by the Görtelmeyer sleep questionnaire (SF-B) and statisticall evaluated. A significant difference between valerian and placebo is seen only after a 4-week cours of treatment (Vorbach et al., 1996).

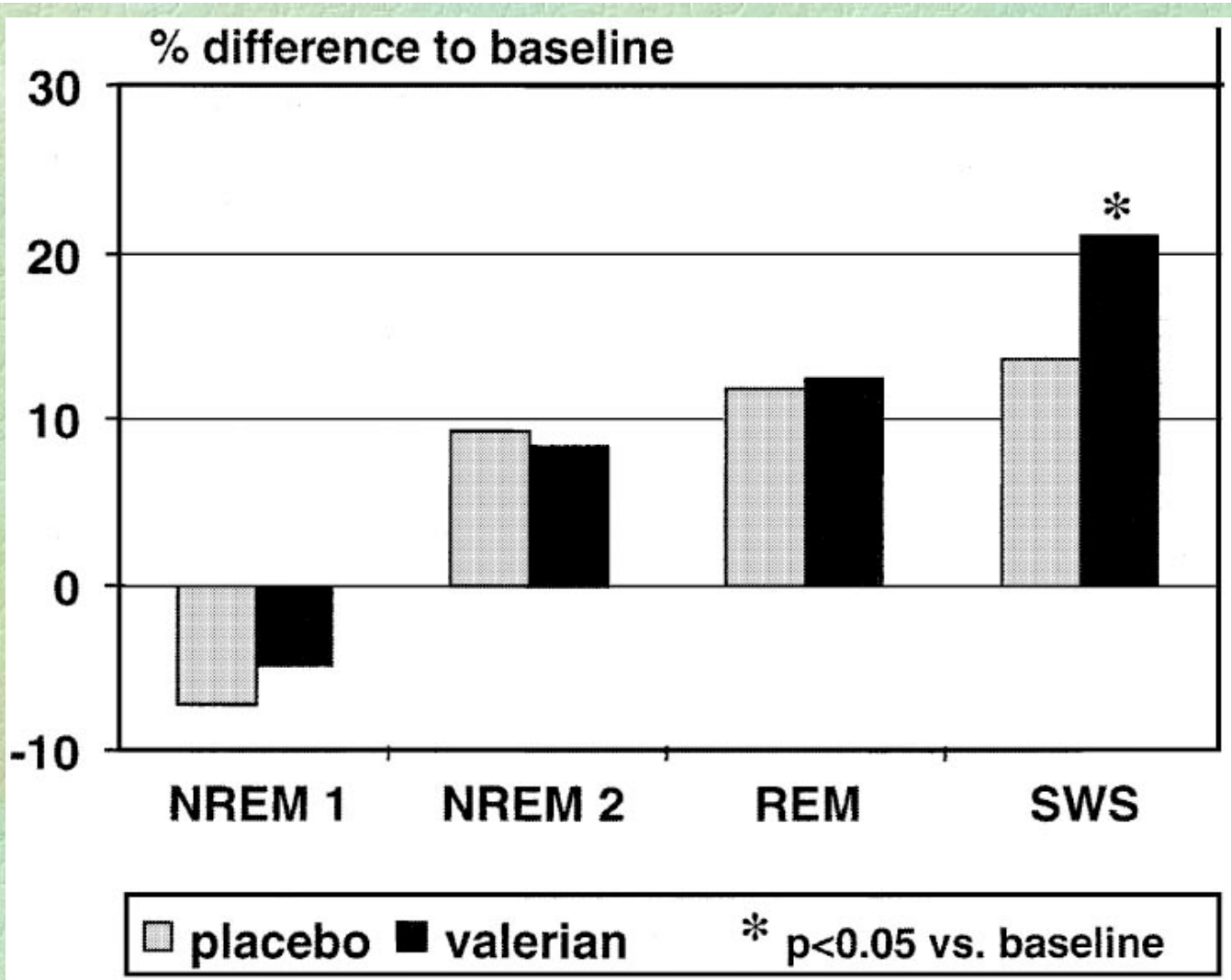


Fig. 2 Differences in sleep stages: NREM 1, NREM 2, REM, and slow-wave sleep (SWS) between baseline and long-term treatment under placebo and valerian.

Donath et al. Pharmacopsychiatry 2000;33:47-53. N=16; valerian for 14d; crossover study

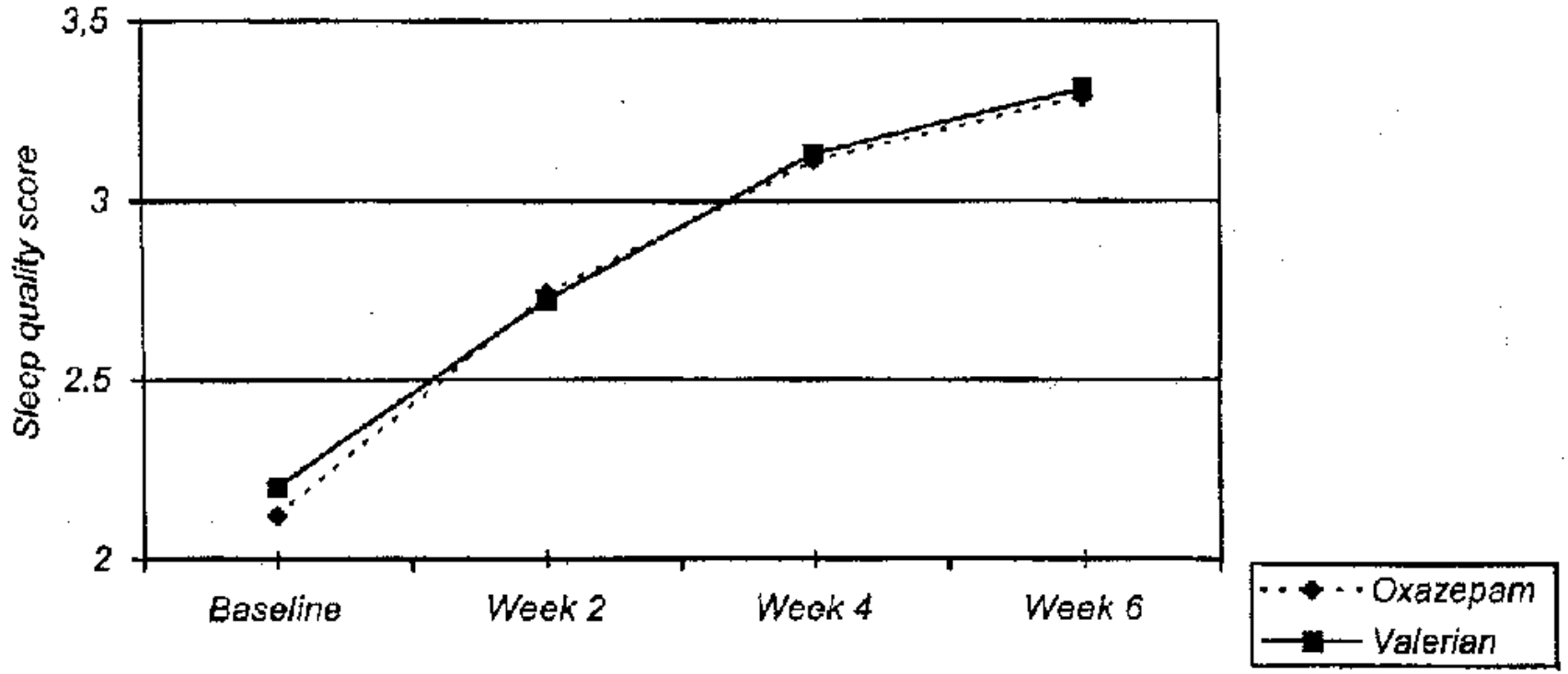
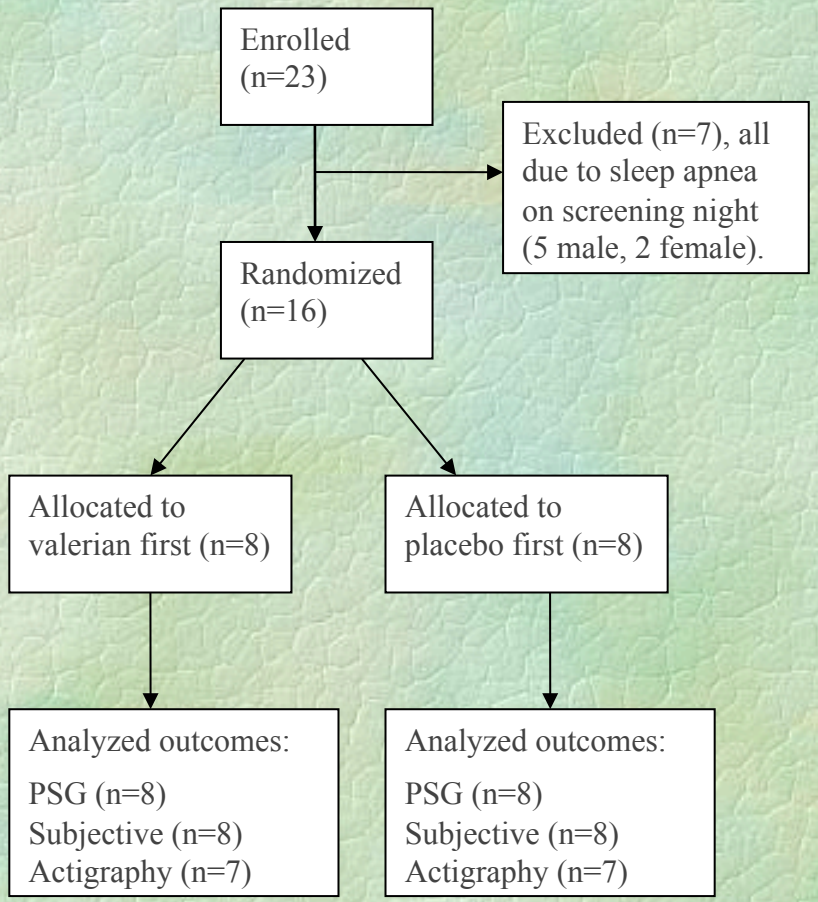


Fig. 2. Mean Sleep quality (SQ) at baseline and after 2, 4 and 6 weeks of treatment (PP analysis).

Ziegler et al. European J Med Res 2002;7:480-486. N=202

A randomized clinical trial of valerian fails to improve subjective and objective sleep quality of older women with sleep disturbance . Taibi et al. Sleep Med. 2009;10(3):319-28.



Results: no difference between placebo and valerian in subjective and objective sleep in this UW study

Valerian

- Precautions
  - drowziness, avoid alcohol
  - restlessness,nausea
  - worry over valepotriate epoxide (liver damage) but commercial products have little
  - not pregnancy, not infants, not nursing
  - limit use to 2 weeks, withdrawal signs have been reported but these reports are suspect
  - acute overdose (20x) gave only mild effects
- Dose
  - 400mg –600mg of an extract at hs
  - 2-3g of powder to make tea
  - 1-3ml of tincture
- Products
  - valerenic acid as marker

Valerian

Summary

- **Efficacy: long historical use; limited number of controlled studies; not all show efficacy. Acute use may be ineffective. Recent studies are negative including one we did.**
- **Safety: good but be careful as with any sedative**
- **Drug interactions: none noted so far**
- **Product selection: many products failed consumerlab.com's testing**
- **Dose: about 600mg of a root extract at HS**
- **Questions remaining include**
  - ***How effective is this for occasional use?***
  - ***How effective is this for chronic insomnia?***
- ***GWE: I don't recommend valerian***

Horny Goat Weed (really!!)

- Botany — Epimedium species, usually E. grandiflorum; leaves or root used
- History — long used in traditional Chinese medicine (TCM) and called Ying Yang Huo
- Chemistry — flavonoids, icariin (a flavonol glycoside), polysaccharides; active components are unknown
- Pharmacology — animal studies show some effects in increasing semen, increasing growth of prostate and testicular tissue, lowering blood pressure and decreasing platelet adhesion. In vitro inhibitory effects on cancer cells
- Use — impotence, aphrodisiac, tonic and a variety of other uses in TCM including for heart disease

Horny Goat Weed

- Evidence: animal studies support some hormonal effects and hypotensive action
- Safety:a report of tachyarrythmia and hypomania with use in a patient with CHD.
- Drug Interactions:caution with anti-platelet adhesion drugs, anticoagulants and antihypertensives
- Products:no recommendations; most contain 500mg crude plant; some are extracts
- Summary:avoid this unproven and poorly studied product