Herbal medicines

Current research on effectiveness, pharmacology, and safety

Guido Masé RH(AHG)
Vermont Center for Integrative Herbalism
www.vtherbcenter.org

Introductory notes

Herbal medicine is an old discipline

Its practice is nature-driven

Traditionally, uses whole plants

High-potency extracts are recent

Effects are generally mild

Habitual use often most effective

Introductory notes

Pharmacology is often complex:

- Multiple countervailing mechanisms
- Synergy

Traditionally understood as a whole "system":

- Plants as personalities
- Ecology-like analogies to describe effects

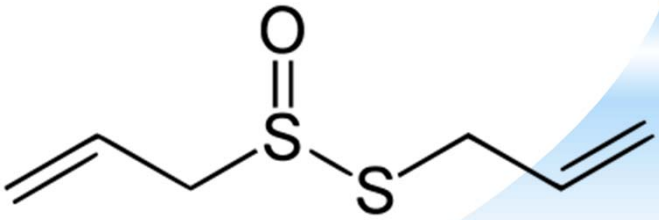
*Garlic

Allium sativum

How used: whole food, proprietary extracts (AGE, Kyolic e.g.)

Why used: Cardiovascular disease. Plasma lipid and cholesterol management, hypertension, potentially stomach and colorectal cancer

Pharmacology: Largely pungent sulfur-containing compounds, such as allicin



*Garlic

Plasma lipid and cholesterol management:

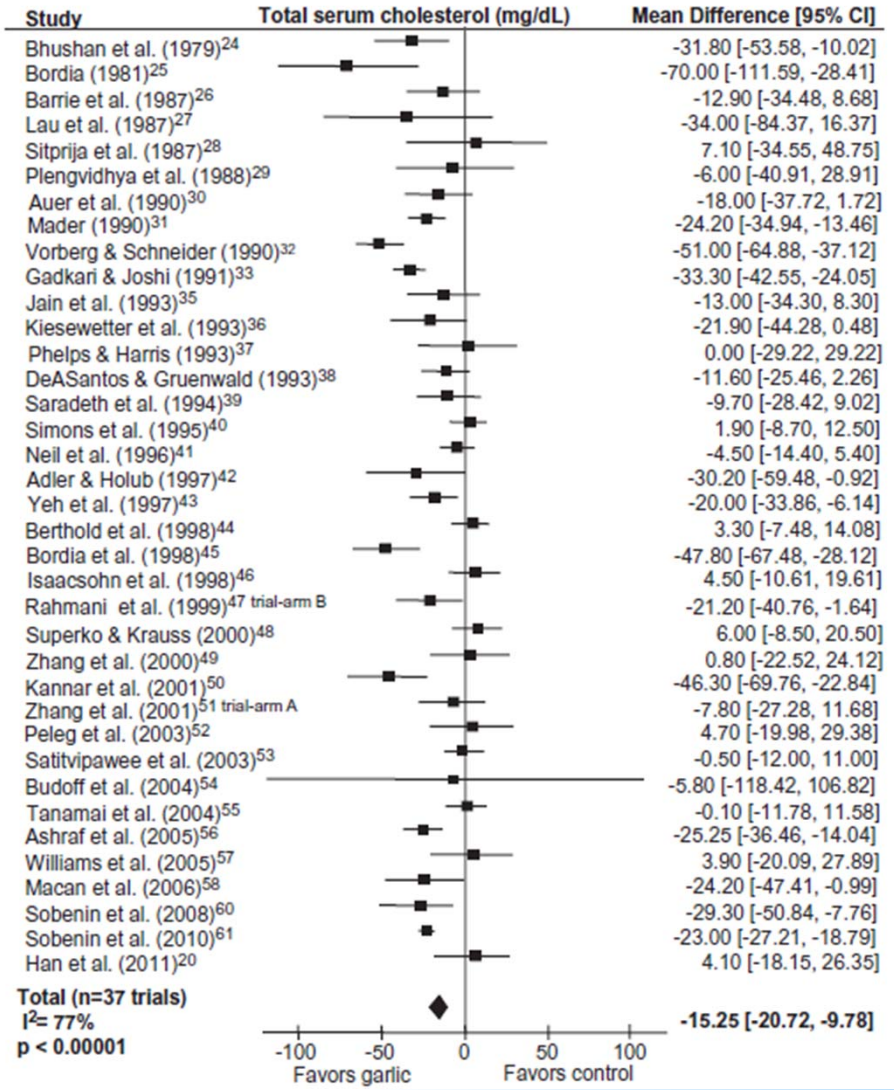
Reid, Toben, Fakler 2013

Building on:

Garlic for treating hypercholesterolemia. A **meta-analysis** of randomized clinical trials.
Stevinson C, Pittler MH, Ernst E.
Ann Intern Med. 2000 Sep 19;133(6):420-9.

The impact of **garlic** on lipid parameters: a systematic review and **meta-analysis**.
Reinhart KM, Talati R, White CM, Coleman CI.
Nutr Res Rev. 2009 Jun;22(1):39-48.

A **meta-analysis** of randomized, double-blind, placebo-controlled trials for the effects of **garlic** on serum lipid profiles.
Zeng T, Guo FF, Zhang CL, Song FY, Zhao XL, Xie KQ.
J Sci Food Agric. 2012 Jul;92(9):1892-902



*Garlic

Risk of cancer:

Fleischauer, Poole, Arab 2000

High heterogeneity of trials
Confounding factors present

VERY high consumption levels in studies showing greatest effects (2 bulbs/d)

Meta-analysis of relative risk (RR) estimates (95% CIs) by cancer site[1]

Model and references	Fixed-effects estimate	Random-effects estimate	P
All cancers, *n* = 22 RRs (4–17, 19, 21–24)	0.65 (0.58, 0.72)	0.63 (0.50, 0.80)	<0.0001
All cancers, excluding the studies by Dorant et al (10, 16, 23, 24),[2] *n* = 18 RRs (4–9, 11–15, 17, 19, 21, 22)	0.57 (0.51, 0.64)	0.54 (0.43, 0.67)	<0.0001
Colorectal cancers, *n* = 8 RRs (5, 11–16)	0.72 (0.61, 0.85)	0.66 (0.48, 0.91)	0.003
Colorectal cancers, excluding the study by Dorant et al (16),[2] *n* = 7 RRs (5, 11–15)	0.67 (0.56, 0.80)	0.60 (0.44, 0.83)	0.02
Colorectal cancers, excluding the studies by Dorant et al (16)[2] and Iscovich et al (11),[3] *n* = 6 RRs (5, 12–15)	0.71 (0.59, 0.86)	0.69 (0.55, 0.89)	0.17
Stomach cancers, *n* = 5 RRs (6–10)	0.57 (0.47, 0.70)	0.61 (0.37, 1.03)	<0.0001
Stomach cancers, excluding the study by Dorantet al (10),[2] *n* = 4 RRs (6–9)	0.54 (0.44, 0.66)	0.53 (0.31, 0.92)	0.0002

[1] Mean (±SD) consumption for the highest category of raw garlic, cooked garlic, or both (RC) was 18.3 ± 14.2 g/wk for all studies combined. Four studies did not report cutoffs for RC garlic consumption.

[2] The studies by Dorant et al examined garlic supplements exclusively and cancer incidence.

[3] Iscovich et al's study combined garlic, onions, and peppers into a single exposure category.

*Garlic

Safety concerns:

Altered coagulability?

Macan et al. 2006, n=30. 5ml aged garlic extract, 12 weeks, while on warfarin revealed no events of hemorrhage.

Scharbert et al. 2007, n=18 healthy volunteers. No effects on platelet function after 1 dose of 4.2g, or after 5 days at same dosage. This is a low dose for colorectal cancer, minimal dose for plasma cholesterol.

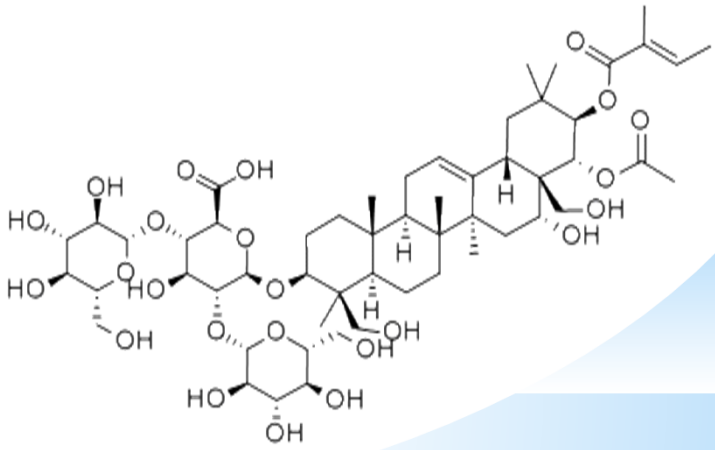
*Horse Chestnut

Aesculus hippocastanum

How used: liquid extracts, encapsulated powdered seed

Why used: Chronic venous insufficiency. Varicosities, incl. hemorrhoids though usually on legs. Includes topical use.

Pharmacology: Anti-inflammatory triterpene saponin, aescin



*Horse Chestnut

Cochrane Collaborative, Pittler and Ernst, 2012:
Six trials (n=543) show reduction in pain, edema, leg circumference and edema. Similar to compression stockings.

Safety concerns: generally low and infrequent adverse events (Greeske 1996; Leskow 1996) reporting pruritus, nausea, gastrointestinal complaints, headache and dizziness in 43 of 6183 patients (0.7%)

In pregnancy: Steiner 1990: n=**52 pregnant women with venous insufficiency**. 300 mg extract (equivalent to 50 mg aescin) or a placebo twice daily for 2 weeks. The extract was superior to the placebo in reducing oedema and symptoms such as leg pain, fatigue and itching. Patients treated with the extract also showed a greater resistance to oedema induction

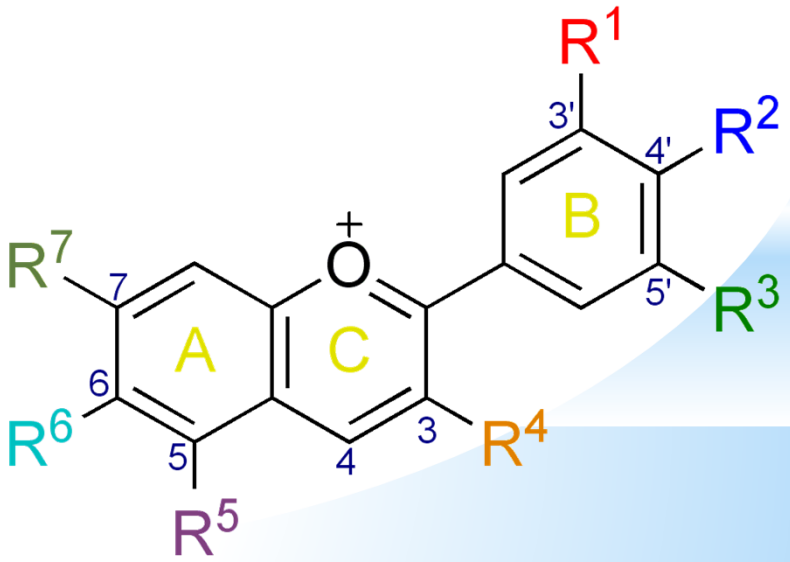
*Hawthorn

Crataegus species (monogyna, oxyacantha, et.al.)

How used: liquid / solid extracts, encapsulated powdered fruit, leaf/flower

Why used: Symptoms of congestive heart failure, esp. angina and dyspnea. Hypertension and hypotension.

Pharmacology: Complex cocktail of bioflavonoids, esp. anthocyanidins



*Hawthorn

Pittler, Guo and Ernst 2008
Cochrane Collaborative

Comparison 1. Hawthorn extract versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maximum work load	5	380	Mean Difference (IV, Random, 95% CI)	5.35 [0.71, 10.00]
2 Exercise tolerance (Watt min)	2	98	Mean Difference (IV, Random, 95% CI)	122.76 [32.74, 212.78]
3 Pressure-heart rate product	5	329	Mean Difference (IV, Random, 95% CI)	-19.22 [-30.46, -7.98]
4 Symptom scores according to v Zerssen	3	239	Mean Difference (IV, Random, 95% CI)	-5.47 [-8.68, -2.26]
5 6-min walk test	1	111	Mean Difference (IV, Random, 95% CI)	-8.0 [-34.49, 18.49]
6 LVEF%	1	40	Mean Difference (IV, Random, 95% CI)	1.7 [0.88, 2.52]

*Hawthorn

Safety concerns: blood coagulability

Dalli et al. 2011

Table 1
Platelet aggregation with ADP, collagen, and arachidonic acid.

	Baseline	*C. laevigata*	Baseline	Aspirin
ADP (Imax) (mm)	107.6 ± 23.6	108.3 ± 29.2	103.6 ± 26.3	64.6 ± 15.7*#
ADP (Imax 5 min) (mm)	100.8 ± 36.9	100.3 ± 44.9	89.0 ± 49.5	20.0 ± 23.1*#
Collagen (Imax) (mm)	127.5 ± 12.5	126.2 ± 9.5	113.5 ± 25.8	39.6 ± 27.6*#
Collagen (Imax 5 min) (mm)	127.5 ± 12.5	126.7 ± 9.6	112.9 ± 28.2	32.1 ± 28.5*#
Arachidonic acid (Imax) (mm)	128.8 ± 11.4	124.8 ± 12.7	120.1 ± 7.6	6.5 ± 7.1*#

Only aspirin inhibited platelet aggregation. * Baseline vs aspirin: $p<0.0001$. # *C. laevigata* vs aspirin post-treatment: $p<0.0001$. Values are mean ± SD.

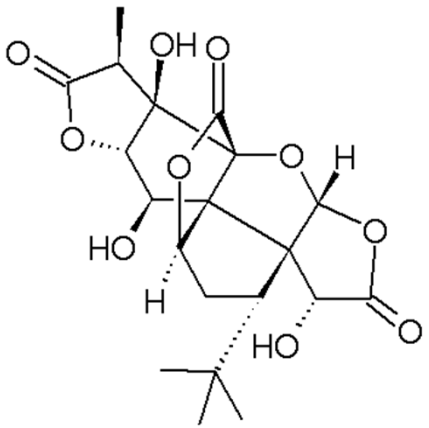
*Ginkgo

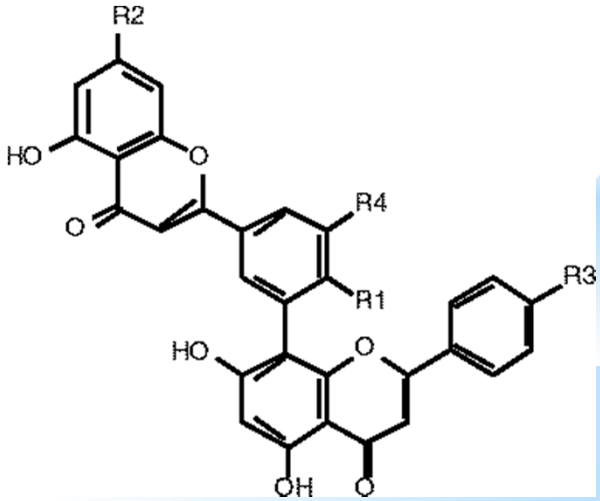
Ginkgo biloba

How used: leaf extract capsules, 24% flavo-glycosides 8% lactones stndz.

Why used: Cognitive symptoms associated with vascular dementia, peripheral vascular disease

Pharmacology: Unique lactones (ginkgolides) and flavonoid glycosides





*Ginkgo

Weinmann et al. 2010

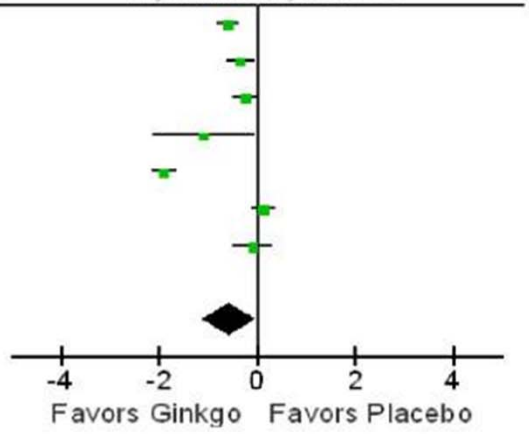
"Effects of Ginkgo biloba in dementia: systematic review and meta-analysis."

Generally effects are more conclusive in vascular dementia than Alzheimer's dementia, for which Ginkgo does poorly. Napryeyenko 2007 – outlier. Most effects are modest.

	Ginkgo			Placebo				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Ihl 2008	-1.4	2.8	202	0.3	2.8	202	15.2%	-0.61 [-0.81, -0.41]	
Kanowski 1996	-2.1	3.15	106	-1	3.05	99	14.9%	-0.35 [-0.63, -0.08]	
LeBars 1997	-0.3	5.35	134	1	5.32	134	15.0%	-0.24 [-0.48, -0.00]	
Maurer 1997	-2.9	2.5	9	0.8	3.8	9	10.3%	-1.10 [-2.10, -0.09]	
Napryeyenko 2007	-3.2	2.3	198	1.3	2.4	197	15.0%	-1.91 [-2.15, -1.67]	
Schneider 2005	1.6	5.8	169	0.9	5.6	174	15.1%	0.12 [-0.09, 0.33]	
vanDongen 2000	0.8	4.1	79	1.2	3.8	40	14.4%	-0.10 [-0.48, 0.28]	
Total (95% CI)			**897**			**855**	**100.0%**	**-0.58 [-1.14, -0.01]**	

Heterogeneity: Tau² = 0.53; Chi² = 178.92, df = 6 (P < 0.00001); I² = 97%

Test for overall effect: Z = 2.01 (P = 0.04)



Safety concerns: blood coagulability

Kellerman and Kloft 2011

- **Pooled 18 trials, n=1985. 13% healthy volunteers**
- **Blood viscosity decrease favors Ginkgo (better tissue perfusion)**
- **No alteration in ADP-induced platelet aggregation, fibrinogen, PT**

- *Standardized GBE does not carry a higher risk of bleeding, even at higher (240mg+ QD) doses*

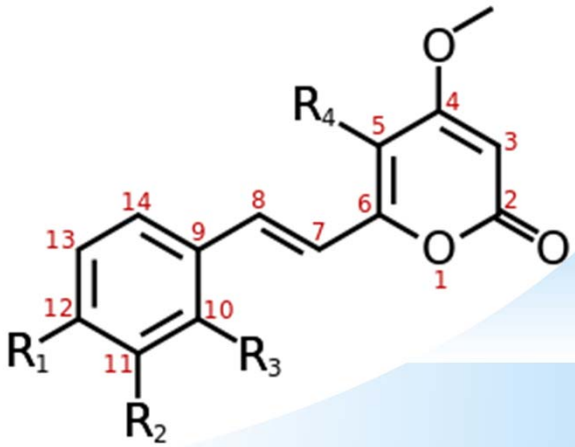
*Kava-Kava

Piper methysticum

How used: liquid extracts, extract capsules, traditional preparations of root

Why used: Anxiety

Pharmacology: Lactones (kavalactones – relatively unique pungent bitters)

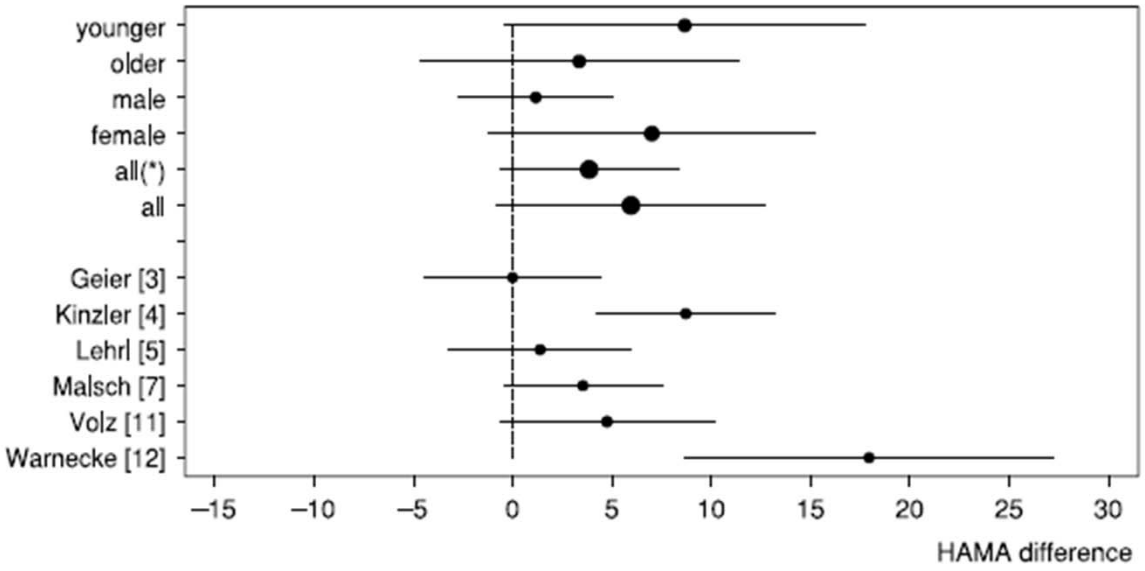


*Kava-Kava

Ernst and Pittler,
Cochrane Collaborative 2003

Effective for anxiety,
Safe 1-24wks

Witte, Loew,
Gauss 2005
5.94pt improvement
on HAMA
Greater effect in:
women,
younger patients



*Kava-Kava

Safety concerns: liver damage, driving, interactions with pharmaceuticals

Stevenson, Huntley and Ernst 2002 Safety review

Kava extracts do not impair cognitive performance and vigilance;
Do not potentiate the effects of central nervous system depressants.
Possible interaction with benzodiazepines has been reported.

Teschke, Genthner, Wolff 2009, Journal of Ethnopharmacology

- Hepatotoxicity isn't related to solvent (acqueous or ethanolic)
- May be related to poor quality / incorrect raw material

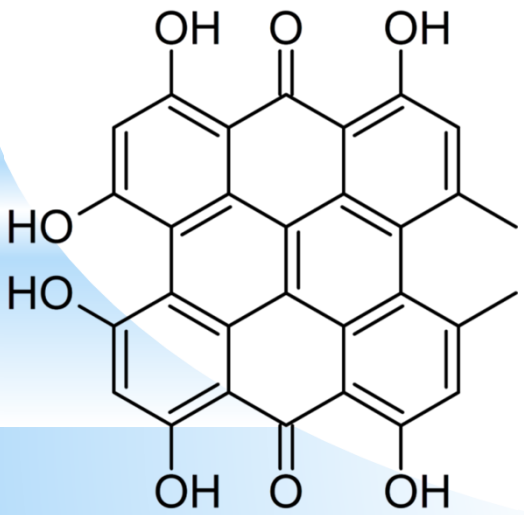
*St. Johnswort

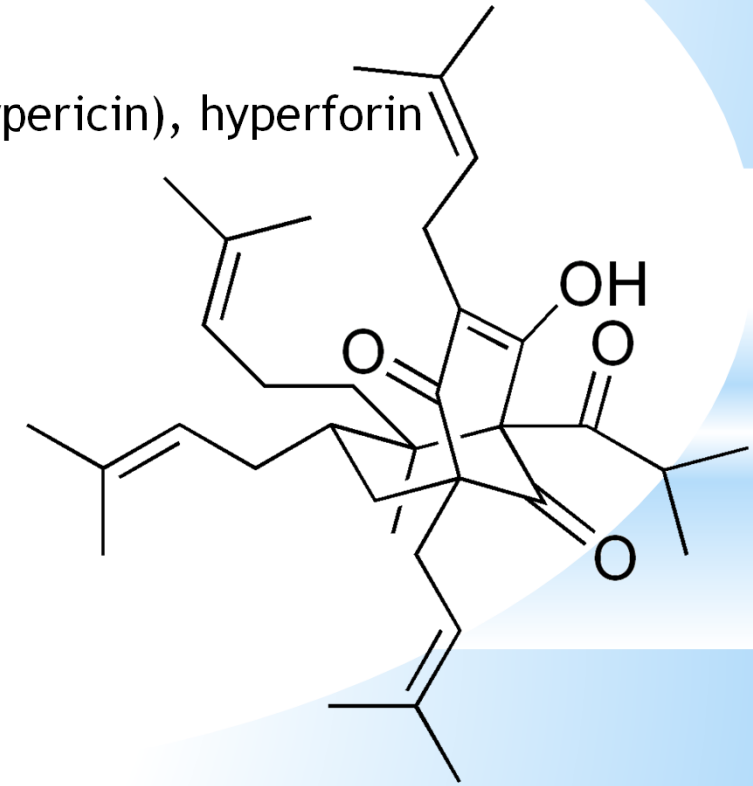
Hypericum perforatum

How used: liquid extracts, extract capsules

Why used: Depression

Pharmacology: Complex. Resin w/ quinones (hypericin), hyperforin



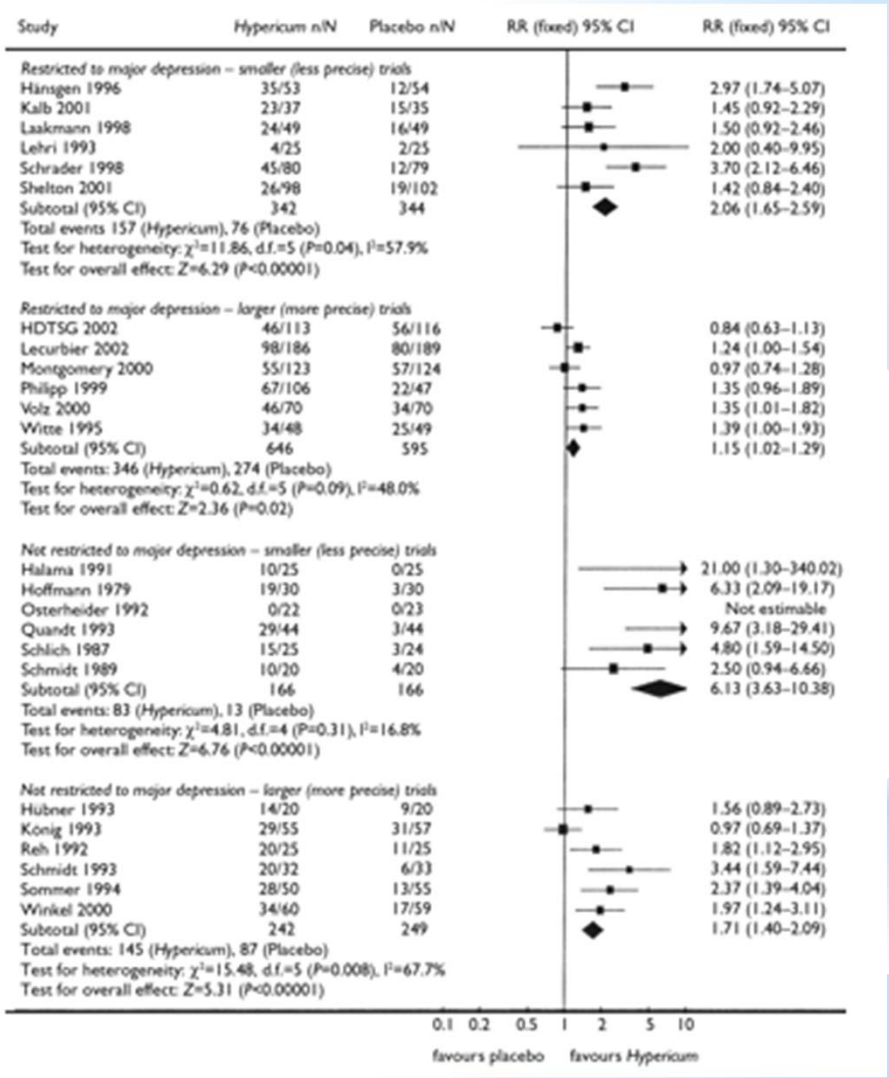


*St. Johnswort

Linde et al. 2005 Meta-review
Cochrane Collaborative
Depression (broad range)

Compared small vs large trials
Compared major vs non-major

Similar to standard antidepressants



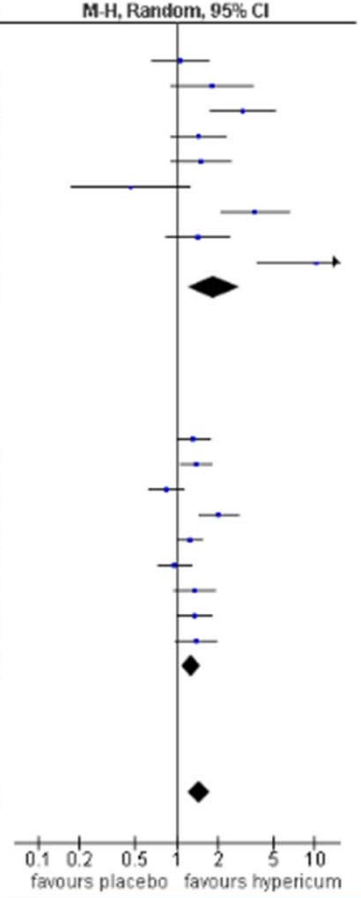
*St. Johnswort

Linde et al. 2008
Meta-review update
Cochrane Collaborative
Depression (major only)

Similar to standard
antidepressants
but with
fewer side-effects

Figure 1. Forest plot of comparison: 1 Hypericum mono-preparations vs. placebo A. Dichotomous measures, outcome: 1.1 Responder - grouped by precision - primary analysis.

Study or Subgroup	Hypericum Events	Hypericum Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Less precise trials						
Bjerkenstedt 2005	22	54	21	55	5.3%	1.07 [0.67, 1.70]
Fava 2005	17	45	9	43	3.7%	1.80 [0.90, 3.60]
Hänsgen 1996	35	53	12	55	4.8%	3.03 [1.77, 5.17]
Kalb 2001	23	37	15	35	5.4%	1.45 [0.92, 2.29]
Laakmann 1998	24	49	16	49	5.1%	1.50 [0.92, 2.46]
Moreno 2005	4	20	11	26	2.4%	0.47 [0.18, 1.27]
Schrader 1998	45	80	12	79	4.6%	3.70 [2.12, 6.46]
Shelton 2001	26	98	19	102	4.9%	1.42 [0.84, 2.40]
Uebelhack 2004	41	70	4	70	2.4%	10.25 [3.88, 27.09]
Subtotal (95% CI)		**506**		**514**	**38.8%**	**1.87 [1.22, 2.87]**
Total events	237		119			
Heterogeneity: $Tau^2 = 0.32$; $Chi^2 = 38.33$, df = 8 ($P < 0.00001$); $I^2 = 79\%$						
Test for overall effect: $Z = 2.88$ ($P = 0.004$)						
1.1.2 More precise trials						
Bracher 2001	64	109	48	109	7.0%	1.33 [1.02, 1.74]
Gastpar 2006	71	131	51	130	7.0%	1.38 [1.06, 1.80]
HDTSG 2002	46	113	56	116	6.8%	0.84 [0.63, 1.13]
Kasper 2006	159	243	26	81	6.5%	2.04 [1.47, 2.83]
Lecrubier 2002	98	186	80	189	7.4%	1.24 [1.00, 1.54]
Montgomery 2000	55	123	57	124	6.9%	0.97 [0.74, 1.28]
Philipp 1999	67	106	22	47	6.4%	1.35 [0.98, 1.89]
Volz 2000	46	70	34	70	6.8%	1.35 [1.01, 1.82]
Witte 1995	34	48	25	49	6.5%	1.39 [1.00, 1.93]
Subtotal (95% CI)		**1129**		**915**	**61.2%**	**1.28 [1.10, 1.49]**
Total events	640		399			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 20.33$, df = 8 ($P = 0.009$); $I^2 = 61\%$						
Test for overall effect: $Z = 3.17$ ($P = 0.002$)						
Total (95% CI)		**1635**		**1429**	**100.0%**	**1.48 [1.23, 1.77]**
Total events	877		518			
Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 68.87$, df = 17 ($P < 0.00001$); $I^2 = 75\%$						
Test for overall effect: $Z = 4.21$ ($P < 0.0001$)						



*St. Johnswort

Safety concerns: hepatic CYP450 induction Russo et al. 2013 review

Prescribed drug	Clinical results of the interaction with HP	Possible mechanism	References
Antihistamine			
Fexofenadine	Increased the maximum plasma concentration and decreased the oral c learance		Wang *et al.*, 2002; Di *et al.*, 2008
Bronchodilator			
Theophylline	Decreased plasma concentration	Induction of hepatic cytochromes	Chen *et al.*, 2012
Cardiovascular			
Warfarin	A loss of the anticoagulant effect; significant reduction in the pharmacological effect of racemic warfarin	Particle formation in aqueous solution with HP; induction of CYP3A4	Gröning *et al.*, 2003; Jiang *et al.*, 2004
Phenprocoumon	Decreased plasma levels	Induction of CYP3A4	Chen *et al.*, 2011
Nifedipine	Induced metabolism with increased plasma concentrations of dehydronifedipine	Induction of CYP3A4 and CYP2C19	Wang *et al.*, 2007
Verapamil	Reduced bioavailability	Induction of first-pass CYP3A4 metabolism	Tannergren *et al.*, 2004
Digoxin	Decreased intestinal absorption; reduction of plasma AUC and C_{max}	Induction of the P-gp	Gottesman *et al.*, 1996; Johne *et al.*, 1999
Hypolipidemic			
Atorvastatin	Increased LDL Increased total cholesterol	Increases CYP3A4 and P-gp activity	Holtzman *et al.*, 2006; Markowitz *et al.*, 2003
Simvastatin	Increased LDL	Decreased plasma concentrations	Sugimoto *et al.*, 2001
Gastrointestinal			
Omeprazole, esomeprazole,	Decrease plasma concentration of proton pump inhibitors	Induction of CYP2C19	Wang *et al.*, 2004

*St. Johnswort

Safety concerns: hepatic CYP450 induction. Russo et al. 2013 review

Loperamide	Brief episode of delirium	Theoretically induces a monoamine oxidase inhibitor–drug reaction	Khawaja *et al.*, 1999
Oral contraceptives			
Etinilestradiol and desogestrel	Reduction of plasmatic concentration, bleeding, and pregnancies	Induction of CYP3A4	Zhou *et al.*, 2004; Hall *et al.*, 2003; Borrelli and Izzo, 2009; Dresser *et al.* 2003; Izzo, 2004
Etinilestradiol and noretindrone	Increased clearance of noretindrone and decreased half-time of etinilestradiol Increased metabolism of noretindrone and etinilestradiol		
Non-steroidal antiinflammatory drugs			
Ibuprofen	Reduction of plasmatic concentration	Increase expression of glycoprotein G	Bell *et al.*, 2007b; Zhou *et al.*, 2004; Izzo, 2004; Dresser *et al.*, 2003
Corticosteroids			
Dexamethasone, prednisone, and budesonide	Reduction of plasmatic concentration	Induction of CYP3A4	Izzo, 2004; Bell *et al.*, 2007a
Opioids			
Methadone and pethidine	Reduction of plasmatic concentration and	Induction of CYP2D2	Dostalek *et al.*, 2005
Dextromethorphan	abstinence syndrome		
Oxycodone	Reduction of plasmatic concentration Reduction of plasmatic concentration	Induction of CYP3A4	Nieminen *et al.*, 2010
Antimicrobial			
Voriconazole	Decreased AUC	Induction of CYP3A4, CYP2C19, and CYP2C9	Borrelli and Izzo, 2009
Erythromycin	Increased metabolism of erythromycin (decreased AUC)	Induction of CYP3A4 (40%)	Borrelli and Izzo, 2009

*St. Johnswort

Safety concerns: hepatic CYP450 induction. Russo et al. 2013 review

Antineoplastic			
Imatinib	Decreased plasma concentration	Induction CYP3A4 and	
Irinotecan	Altered hepatic metabolism	P-gp	Caraci *et al.*, 2011
Docetaxel	Decreased clinical efficacy		Izzo and Ernst, 2009
Immunosuppressants			
Cyclosporine	Decreased plasma concentration	Induction enzymes	He *et al.*, 2012; Hu *et al.*, 2005
Tacrolimus	Organ rejection	cytochrome and P-gp	Mai *et al.*, 2003
Hypoglycaemic agents			
Gliclazide	Decreased plasma concentration	Induction enzymes	Izzo and Ernst, 2009
Tolbutamide		cytochrome and P-gp	Di *et al.*, 2008

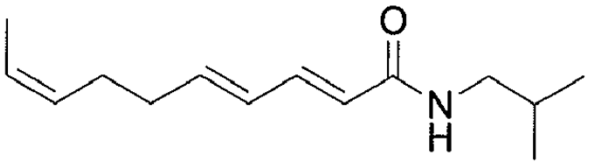
*Echinacea

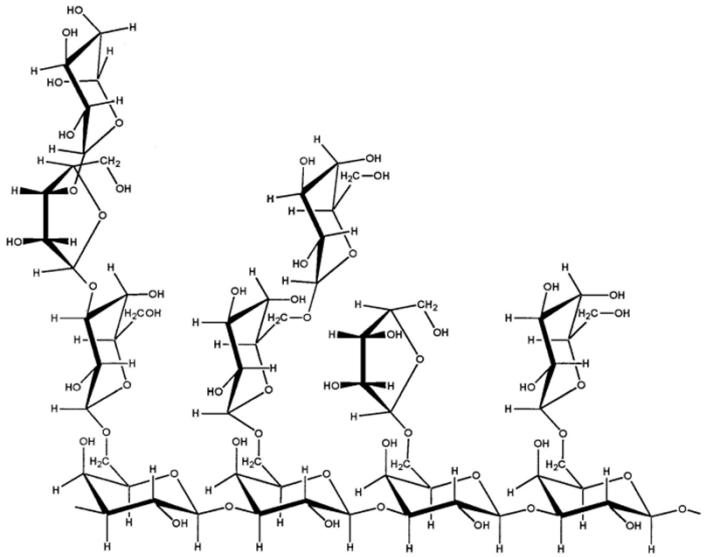
Echinacea species (purpurea, angustifolia, pallida)

How used: liquid extracts, encapsulated root and/or leaf

Why used: Prevention and treatment of the common cold

Pharmacology: Complex. Alkyl amides, hmw polysaccharides





*Echinacea

Shah et al.
Lancet
Meta-review 2007

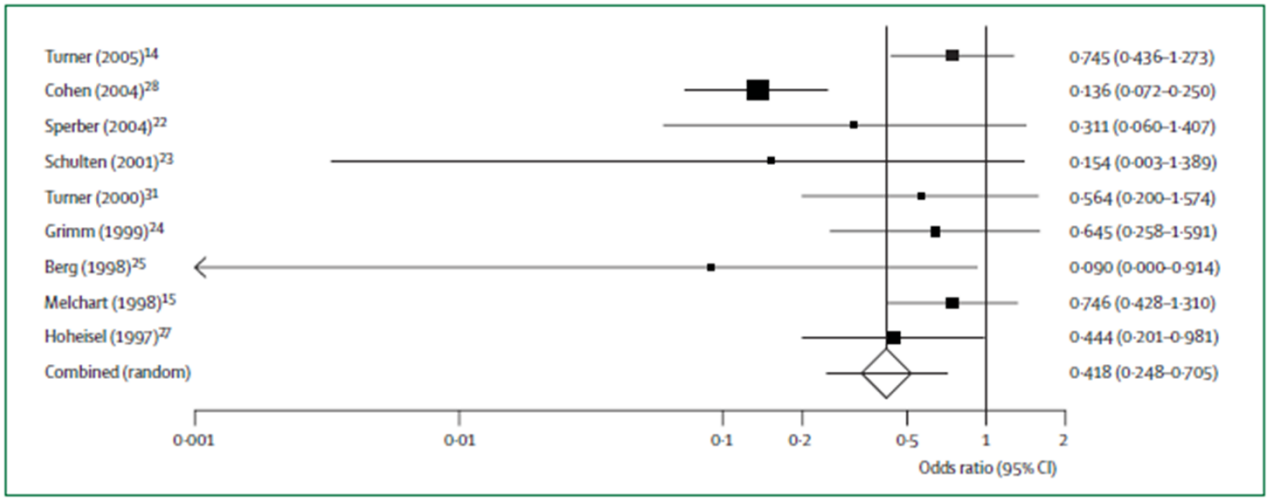


Figure 3: **The effect of echinacea on incidence of common cold**
The squares represent individual studies and the size of the square represents the weight given to each study in the meta-analysis. Error bars represent 95% CIs. The diamond represents the combined result. The solid vertical line extending upwards from 1·0 is the null value.

But…
Barrett et al 2010
N=719, 4 groups
Showed no effect

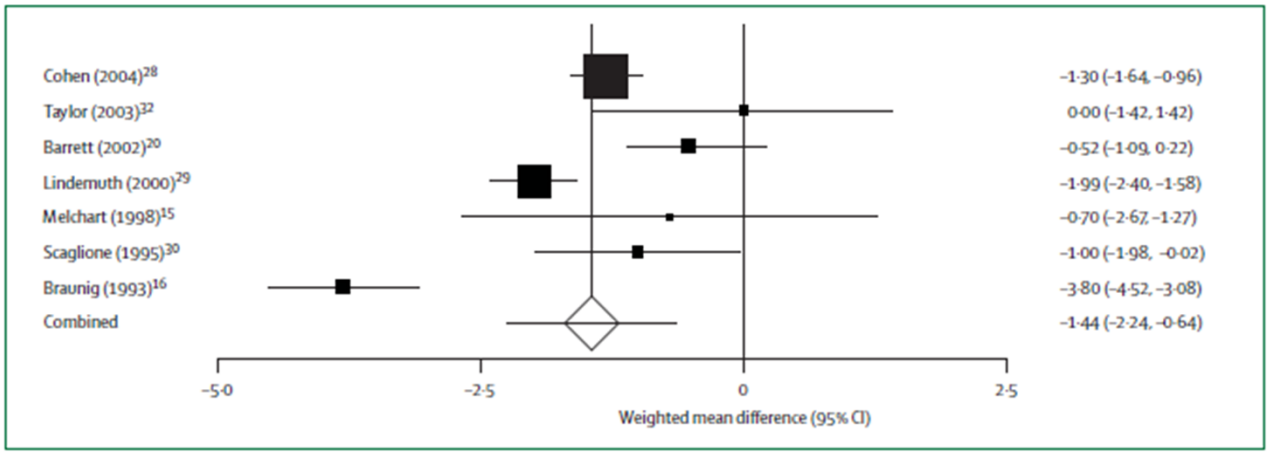


Figure 4: **The effect of echinacea on duration of common cold**
The squares represent individual studies and the size of the square represents the weight given to each study in the meta-analysis. Error bars represent 95% CIs. The diamond represents the combined result. The solid vertical line extending upwards from 0 is the null value.

*Echinacea

Safety concerns:

antiretroviral interaction? Moltó J et al 2011 found no effect w/etravirine

Contraindicated in autoimmune disease? Theoretical from T-cell activation potential *in vitro*.
Neri et al 2011 found no effect on idiopathic autoimmune uveitis

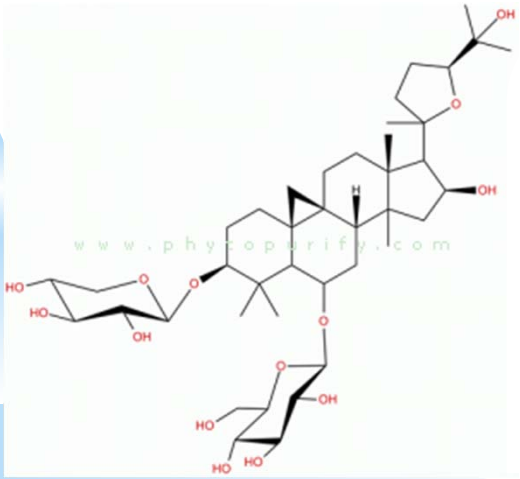
*Astragalus

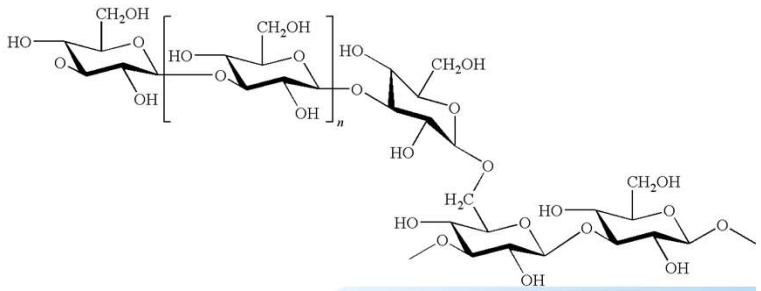
Astragalus membranaceus. aka huang-qi

How used: liquid extracts, encapsulated or sliced dry root

Why used: Renoprotective in nephrosis, chemotherapy adjunct

Pharmacology: Steroidal saponins (astragaloside), hmw polysaccharides





*Astragalus

Preventing infection w/nephrotic syndrome in children:
Wu et al., Cochrane Collaborative 2012
(RR 0.62, 95% CI 0.47 to 0.83)

Alongside platinum-based chemotherapy for NSC lung cancer
McCulloch et al 2006 Pooled 34 trials for 2,815 patients
Increased tumor response, survival.
Very safe, free of side effects

- Injection included
- Combination formulas included

McCulloch et al 2006

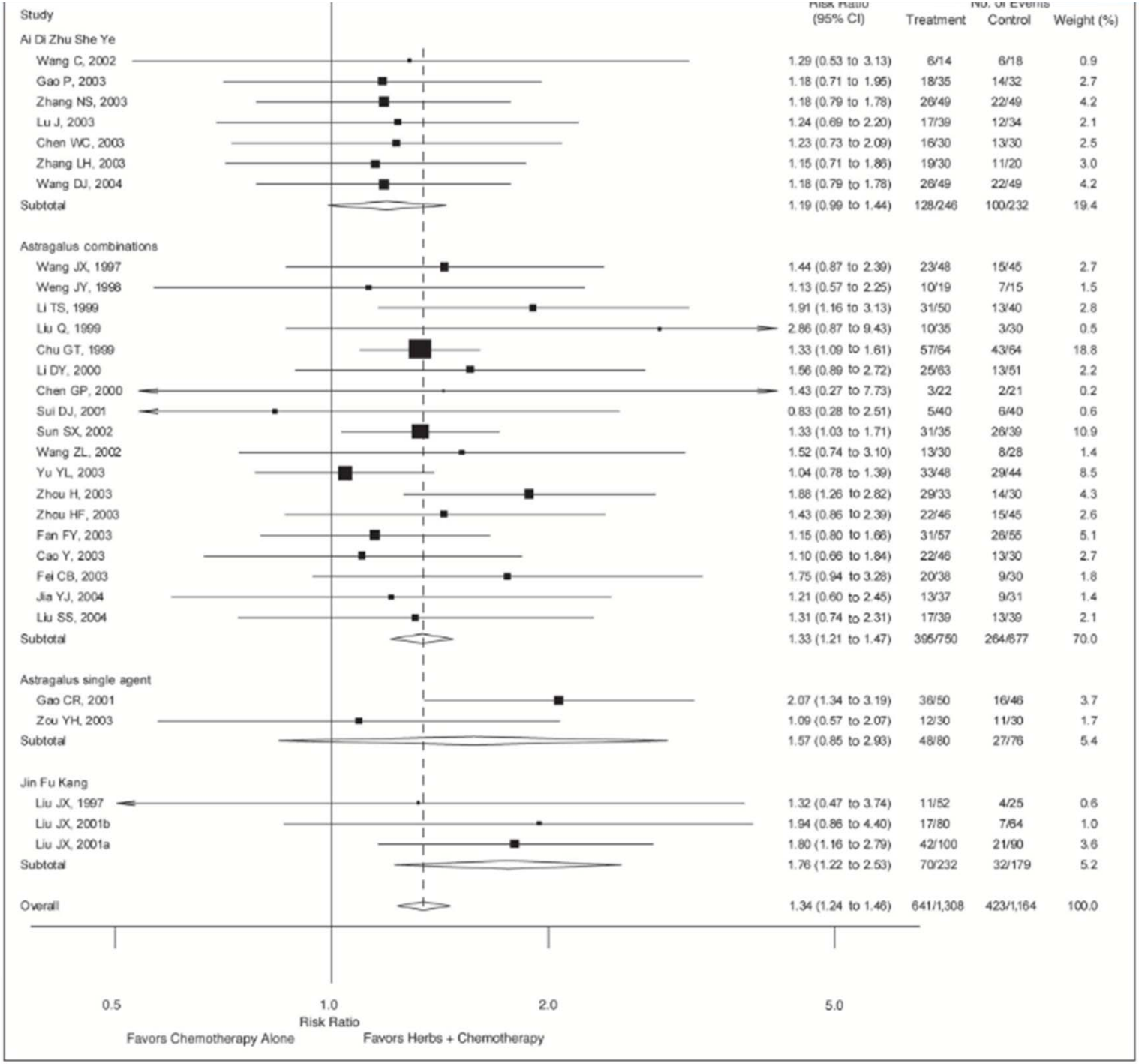


Fig 4 Tumor response with *Astragalus*-based herbs and platinum-based chemotherapy versus platinum-based chemotherapy alone

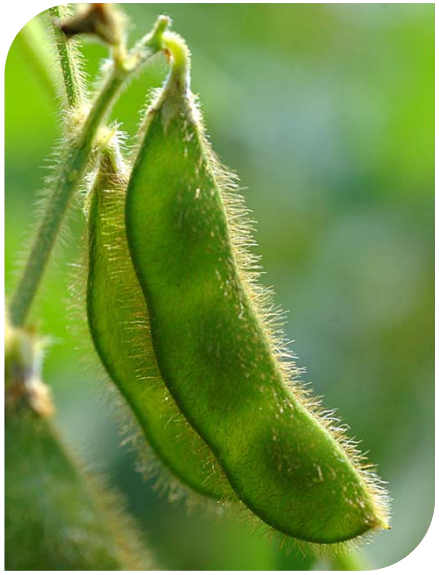
*Soy

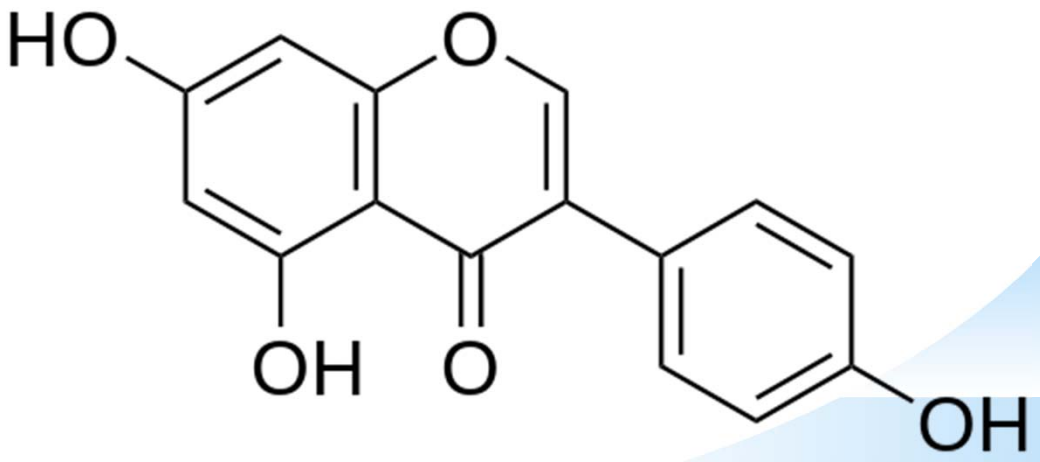
Glycine max

How used: food, protein isolate, isoflavone isolate capsules

Why used: Plasma lipid and cholesterol management, menopausal symptoms

Pharmacology: Isoflavones (genistein, daidzein)





*Soy

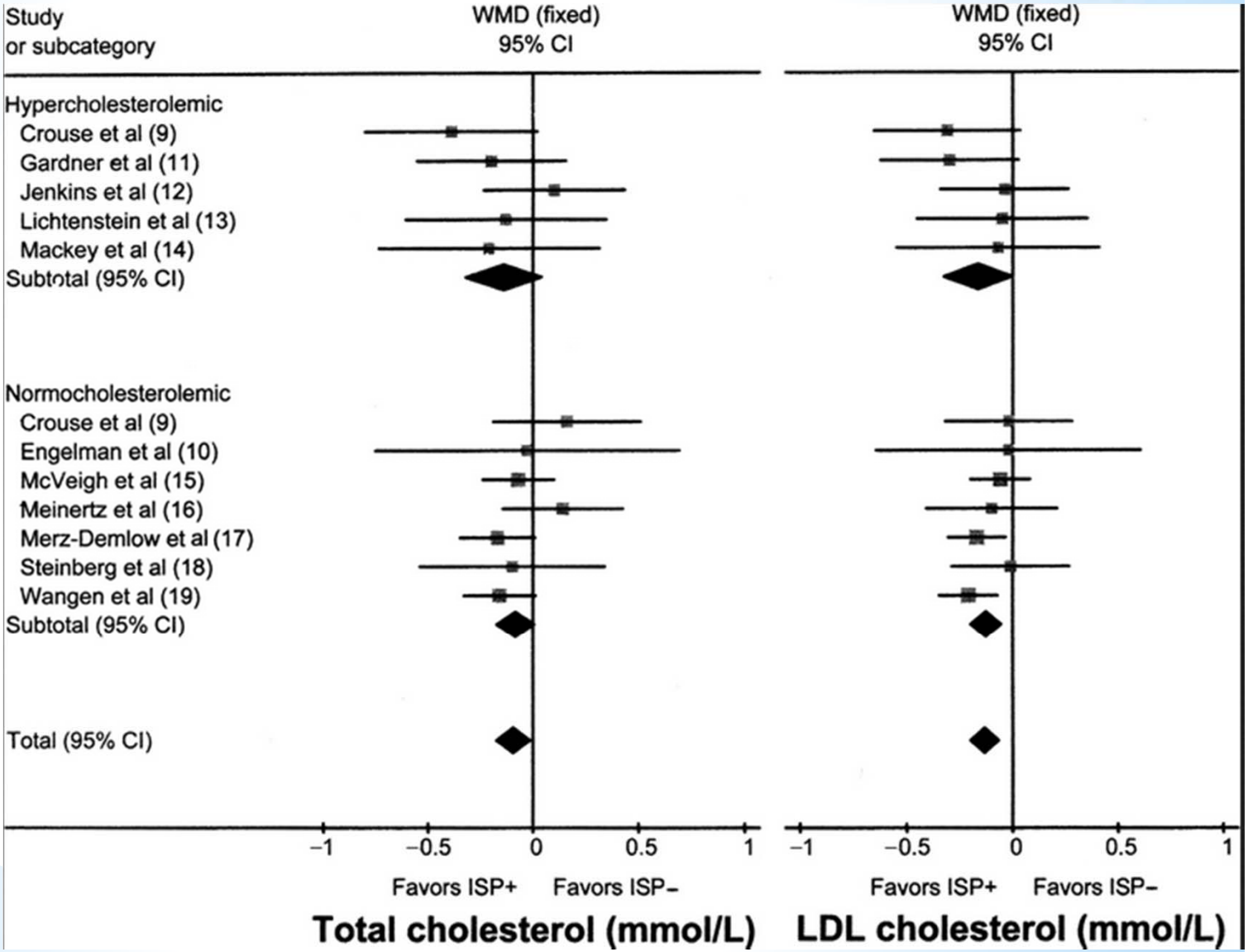
Plasma lipid and cholesterol management:

Anderson and Bush 2011, Meta-analysis.
4-5% reduction in LDL, 3.2% increase in HDL, 10.6% reduction in TG

Builds on
Taku et al. 2007, Meta-analysis.
Similar results on reducing LDL and TC

*Soy

Taku et al. 2007



*Soy

Menopausal symptoms:

Taku, Kyoko, et al. "Extracted or synthesized soybean isoflavones reduce menopausal hot flash frequency and severity: systematic review and meta-analysis of randomized controlled trials." *Menopause* 19.7 (2012): 776-790. Frequency reduced 20%, severity 26%

Bolaños, Rafael, Angélica Del Castillo, and José Francia. "Soy isoflavones versus placebo in the treatment of climacteric vasomotor symptoms: systematic review and meta-analysis." *Menopause* 17.3 (2010): 660. Frequency reduced 39%, high heterogeneity of pooled trials

*Soy

Bone density:

Some reviews, such as
Wei et al. 2012,
show modest effects on bone mineral density.
Others, such as
Ricci 2010
show no effects.

Taku et al 2010
Found modest effects on BMD in the spine of post-menopausal women.

*Soy

Safety considerations: phytoestrogen content in ER-dependent tumors

Dong et al. 2011 reviews prospective studies on incidence / recurrence
.89 HR on average for incidence
.76 HR for incidence in Asian women, not significant in Western women
.84 HR for recurrence on average

Xu et al. 2013, building on previous retrospective work at Vanderbilt,
Reviews retrospective studies on post-diagnosis survival / recurrence

Soy intake is associated with
.85 HR for mortality
.79 HR for recurrence
Best outcomes in ER- and ER+/PR+ tumors, postmenopausal women

*note: may be useful for lung, colorectal tumors as well

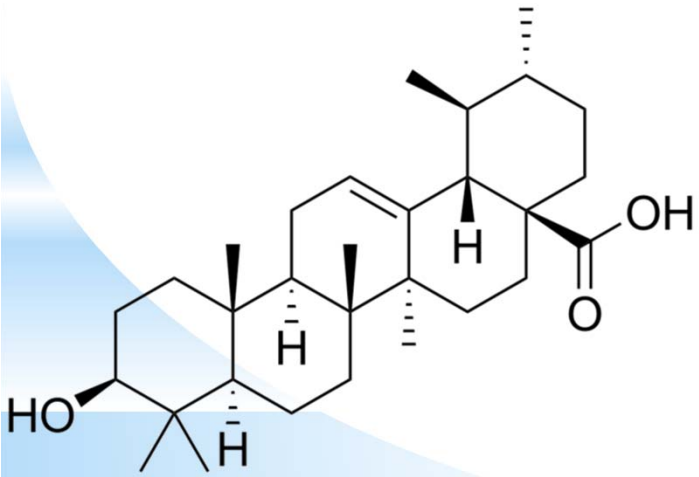
*Devil's Claw

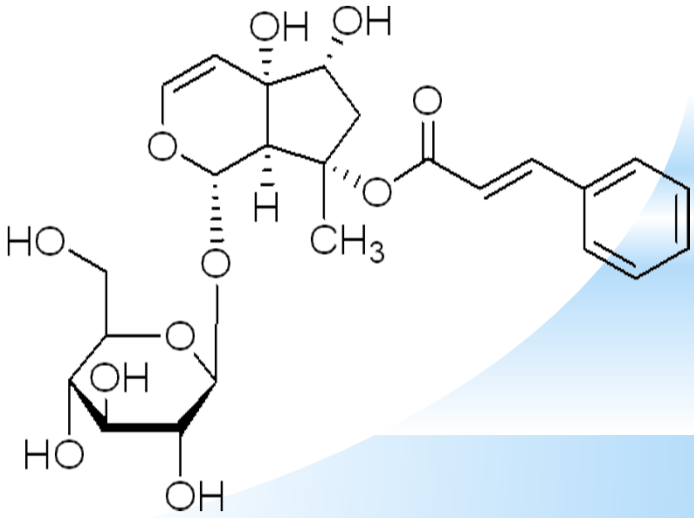
Harpagophytum procumbens

How used: liquid extracts, extract capsules

Why used: Back pain, osteoarthritis, rheumatoid arthritis

Pharmacology: Triterpinoids, iridoid glycosides in resin





*Devil's Claw

Osteoarthritis / back pain:

Gagnier et al 2007 (Cochrane Collaborative): higher quality trials (3) demonstrate benefit in spine / low back pain

Wegener T, Lupke NP. Treatment of patients with arthrosis of hip or knee with an aqueous extract of devil's claw (Harpagophytum procumbens DC.). Phytother Res 2003;17:1165-1172.
*open-label. Pain scores reduced 20-24% after 12 weeks

Chantre P, Cappelaere A, Leblan D, et al. Efficacy and tolerance of Harpagophytum procumbens versus diacerhein in treatment of osteoarthritis. Phytomedicine 2000;7:177-183
Pain reduced similarly between groups, less rescue medication, fewer side eff

*Devil's Claw

Safety considerations:

May affect GI tract: bitter irodoids, resins. Caution in GI ulceration
May affect CYP450 enzymes (inihibitor of isoforms 2C8 3A4)

Unger and Frank, 2004

Herbal medicines

Current research on effectiveness, pharmacology, and safety

Guido Masé RH(AHG)
Vermont Center for Integrative Herbalism
www.vtherbcenter.org