Top 20 Selling Herbals for 2008- Mass Market HerbalGram 2009;82:58-61

Product	M $	% change	rank in 2007
1. cranberry	25	+5.2	2
2. soy	22	-13	1
3. garlic	19	-5.7	3
4. saw palmetto	18	+3.2	5
5. ginkgo	15	-2.6	4
6. echinacea	15	+4.5	6
7. milk thistle	09	+7.9	8
8. St. John's Wort 08	+1.5	10	
9. ginseng	08	-3.7	9
10. black cohosh	08	- 7.1	7
11. green tea	06	+5.3	11
12. evening primrose oil	04	- 7.1	12
13. valerian	03	+11	13
14. horny goat weed	02	+8.7	14

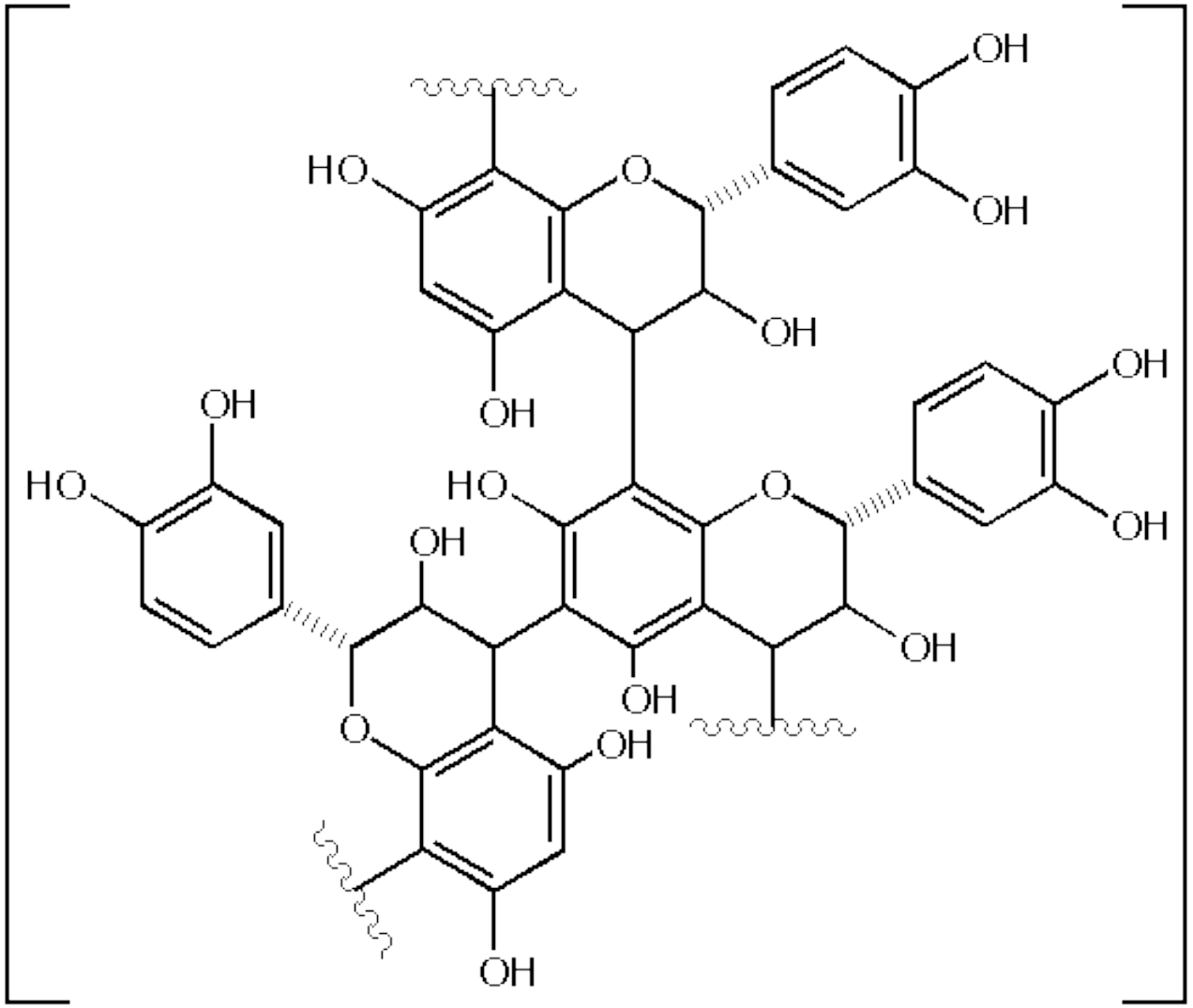
Top 20 Selling Herbals for 2008- Mass Market HerbalGram 2009;82:58-61

Product		M $	% change	rank in 2007
15. grape seed		02	+7	16
16. elderberry		02	+124	none
17. bilberry		02	+1.9	15
18. ginger	01	+42	20	
19. horse chestnut seed		0.8	-19	19
20. yohimbe		0.7	-43	17
Total Mass Market sales (all herbs)		289	+7.2	
Total all channels sales (estimated)		4,800	+0.9	

The above figures include only sales from food stores, drug stores, and mass market retailers but with Wal-Mart figures not included. It does not include warehouse buying clubs (Costco), convenience stores, natural foods stores, multilevel marketers, health professional sales, mail order or internet sales.

Grape Seed Extract

- Botany
  - Seeds from Vitis vinifera
- History
  - Relatively recent use as an antioxidant
- Chemistry
  - seeds contain olygemeric proanthocyanidins (OPC)
  - OPC s are oligomeric or polymeric flavonoid like polyphenolic compounds
  - OPC s have strong antioxidant and free radical scavanging activities
  - OPC s are also high in marine pine bark (pycnogenol) and green tea



Proanthocyanidin oligomer

Pharmacology

- In vitro will prevent destruction of elastin, collagen and hyaluronic acid
- In animal models will reduce capillary permeability and decrease swelling and inflammation
- Action due to the ability of OPC s to block free radical damage and otherwise protect against oxidative damage

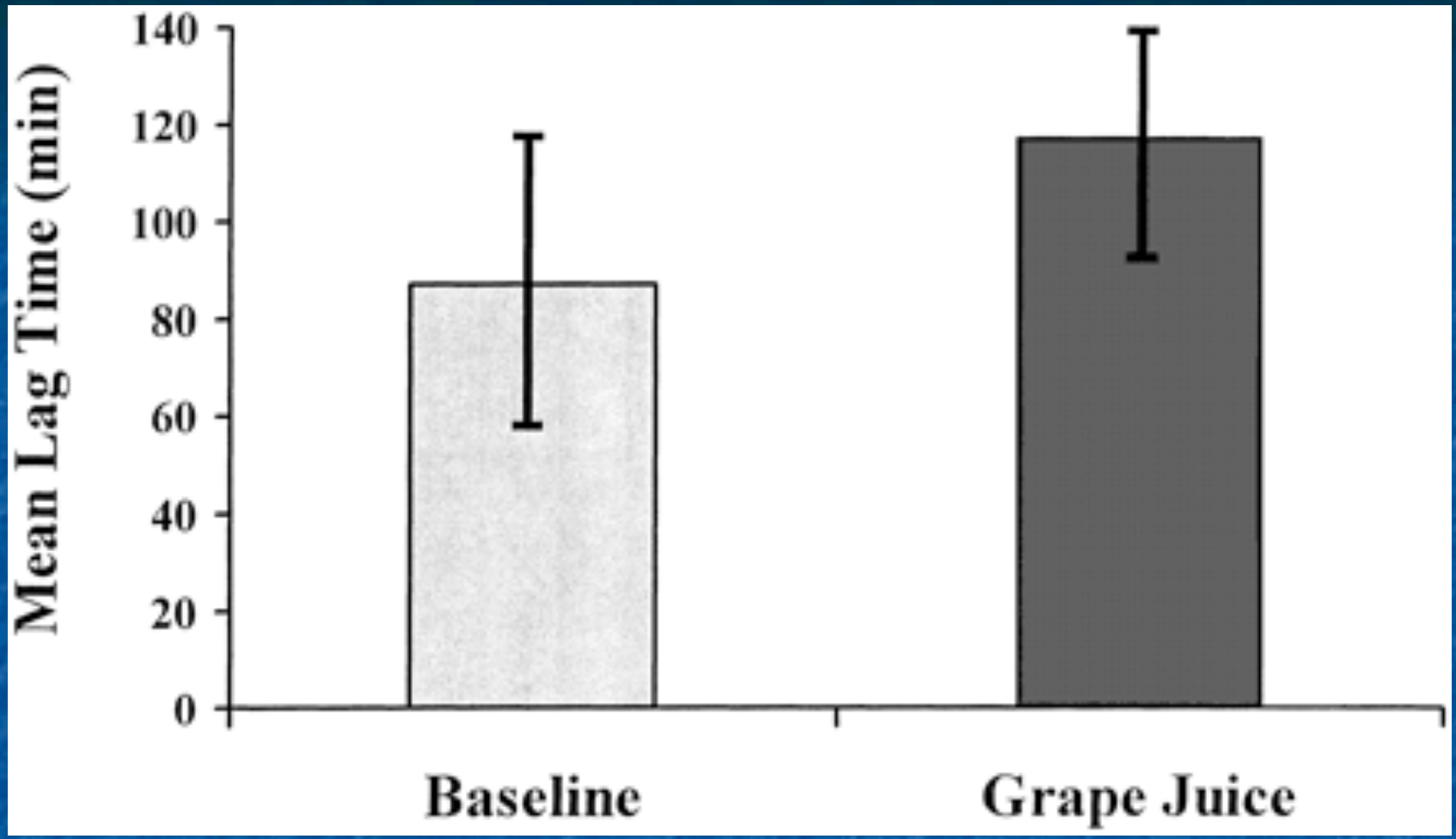
Uses

- Treatment of varicose veins and chronic venous insufficiency
- Reduce swelling due to surgery or injury
- Treat and prevent macular degeneration
- To reduce the risk for cancer and heart disease
- Treat diabetic retinopathy and neuropathy
- other

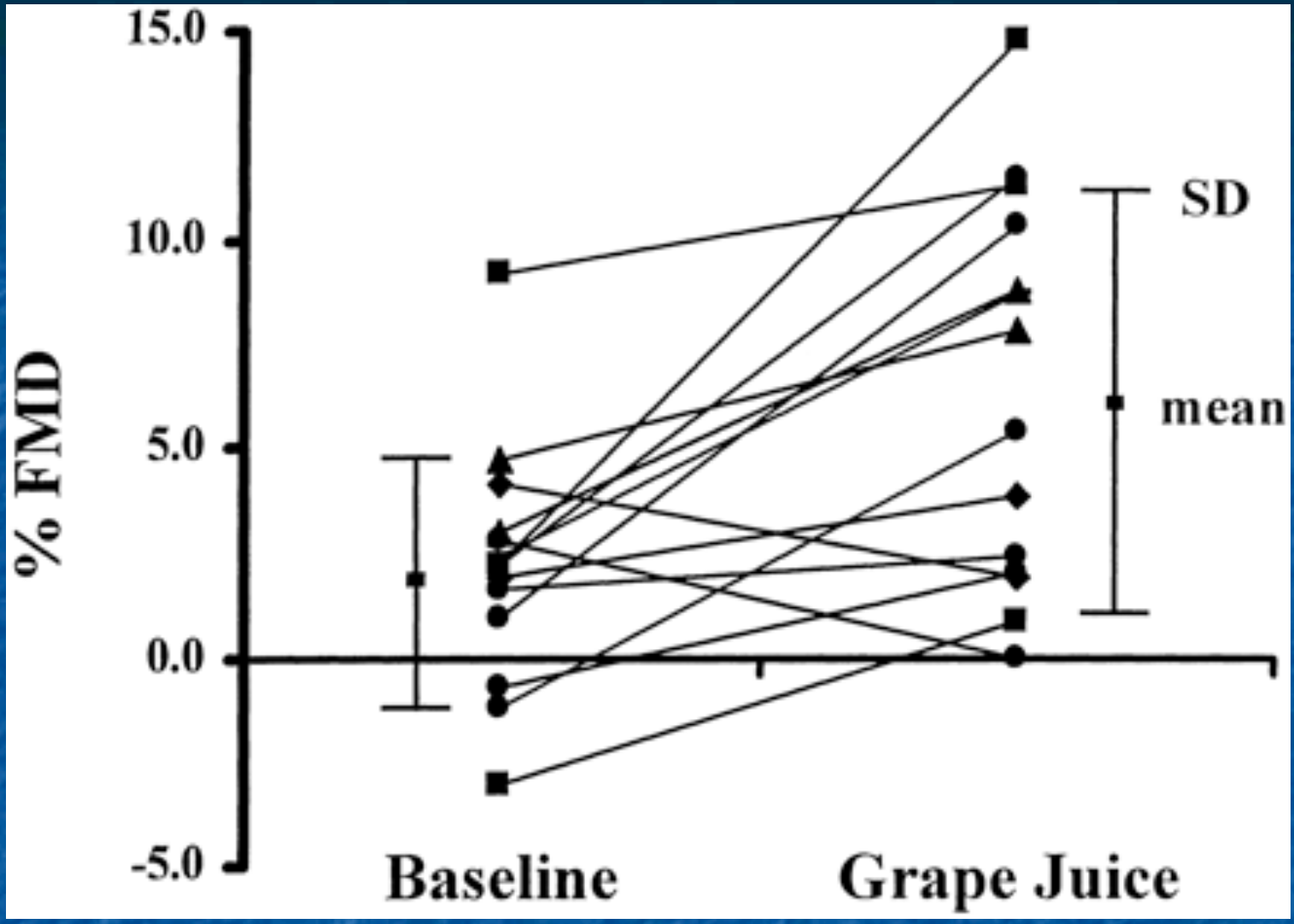
Evidence

- Varicose veins
  - Reasonable evidence based on placebo controlled trials. Trials published in French and Italian thus not readily evaluated by all
- Reduce pain and swelling due to injury/surgery
  - Three controlled studies (in French)
- Vision - one study
- Heart Disease – some evidence for potential

Other – limited evidence from animal or in vitro studies; may lower cholesterol in combination with chromium



LDL oxidation; N=15 with CAD; grape juice x14d; Stein et al. Circulation 1999;100:1050-1055.



Flow mediated vasodilation; N=15 with CAD; grape juice x14d; Stein et al. Circulation 1999;100:1050-1055.

Safety

Considered nontoxic

Interactions

OPCs have antiplatelet adhesion properties so that an anticoagulant effect could be noted at higher doses; avoid concurrent use with warfarin and other anticoagulants

Products

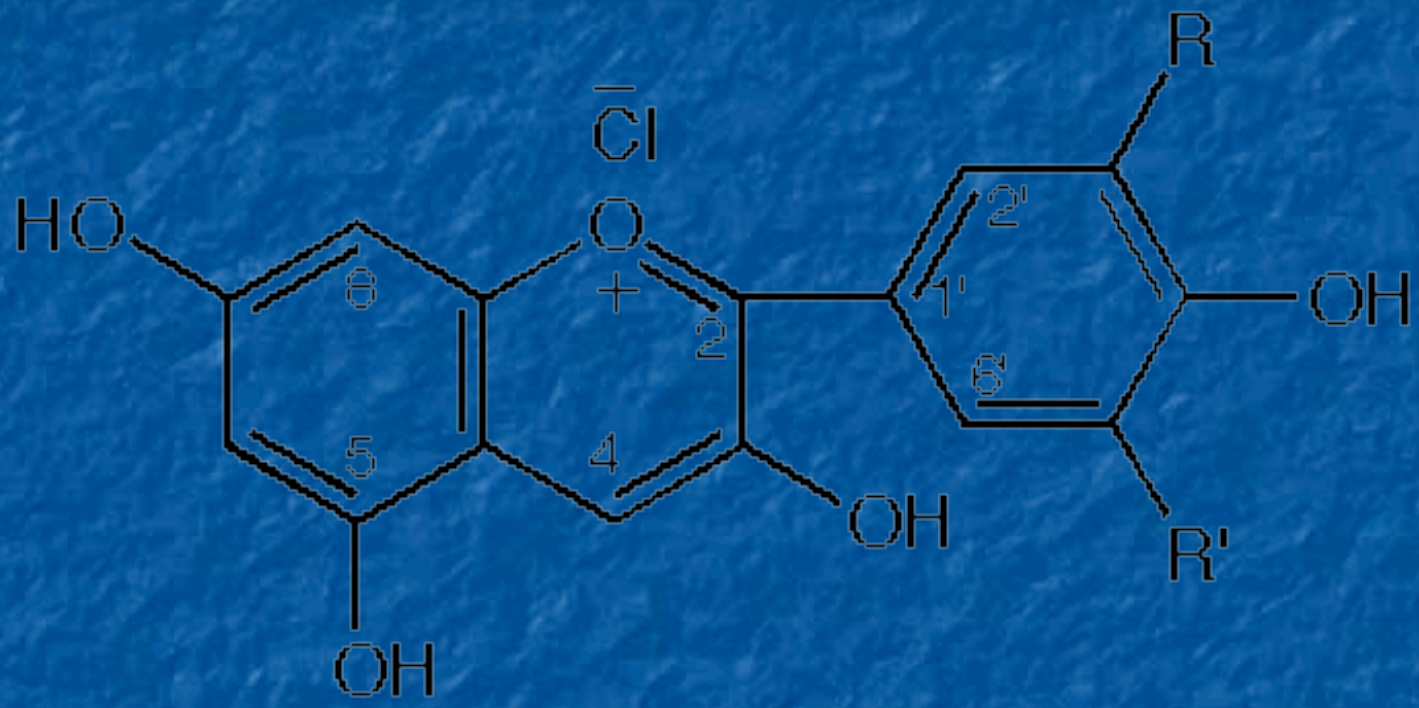
Grape seed extract products contain 100mg of extract per capsule. Dose: 100mg TID

Grape Seed Extract

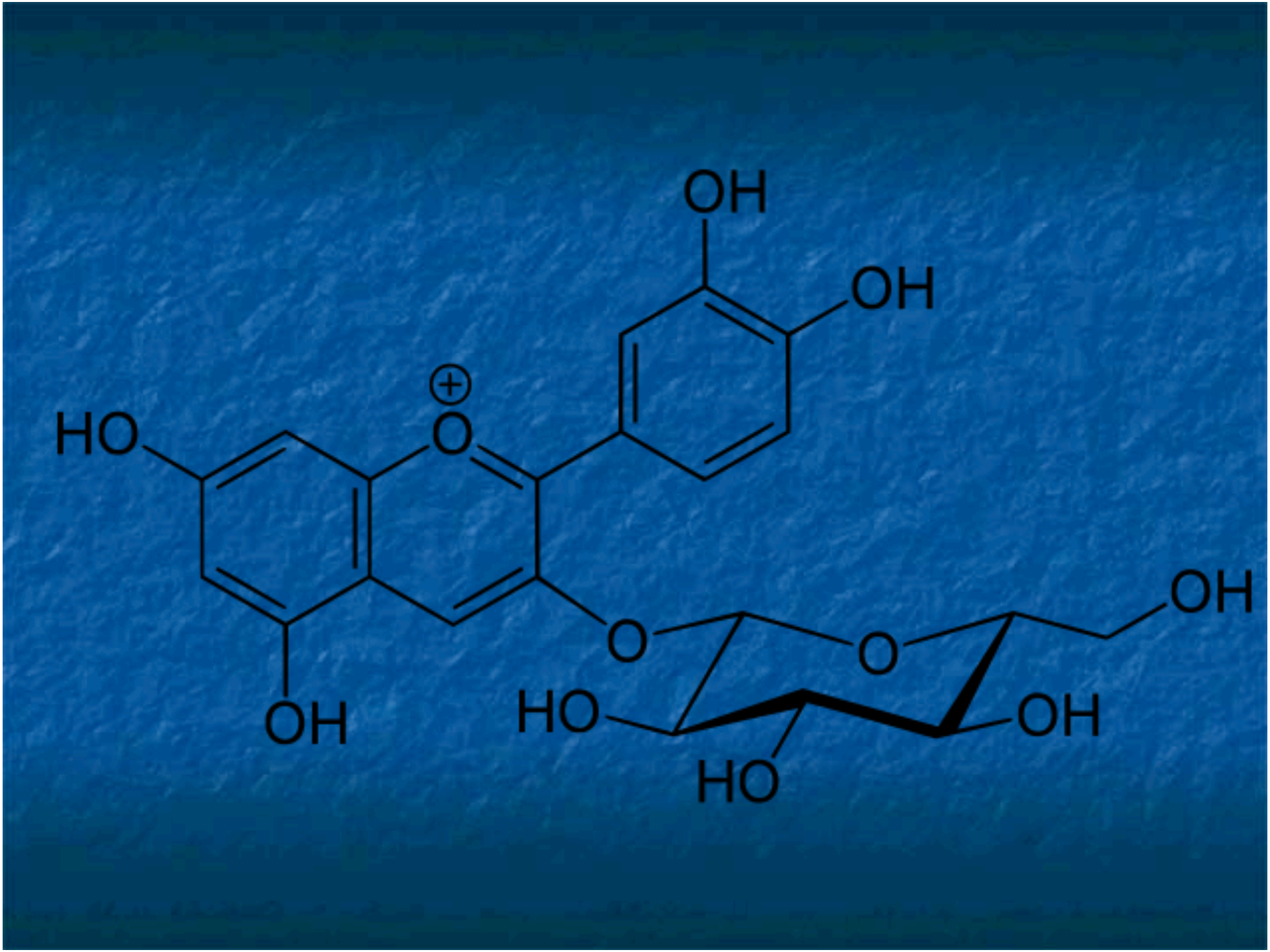
- **Summary**
  - **Efficacy: probably effective for varicose veins and venous insufficiency. May help vision and macular degeneration. Other uses need more work.**
  - **Safety: good**
  - **Drug interactions: careful with anticoagulants**
  - **Product selection: ? Most are not standardized to OPCs**
  - **Dose: 100mg TID**
  - **Questions remaining include**
    - ***Will grape seed extract help in vascular diseases other than varicose veins? What about coronary disease?***

Elderberry

- Botany: Sambucus sp. , usually S. niger
- Chemistry: anthocyanadin glycosides, e.g. cyanidin-3-glucoside
- Pharmacology: elderberry anthocyanidins inhibit influenza viruses in vitro (also H1N1) and have immune stimulation and antiinflammatory properties



Anthocyanidin structure


OH
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Elderberry

- Uses: influenza, sciatica, immune stimulant, asthma and other uses
- Efficacy: shown to have some activity in relieving symptoms of influenza
  - Zakay-Rones et al. J Altern Complement Med 1995;1:361-9. (Israel study against influenza B). 2-3d vs 6d end of symptoms, n=27)

- Zakay-Rones et al. J Int Med Res 2004;32:132-40. (Influenza A and B)
  N=60, 15ml of syrup QID x 5d starting within 48h of onset. Study done in Oslo Norway. Difference in time to end of symptoms was 4d shorter in elderberry vs placebo ($p<0.001$). Reduced use of pain and other cold meds in elderberry group.

- Kong F. Online Journal of Pharmacology and Pharmacokinetics 2009;5:32-43. (lozenge) n=64 relief of symptoms faster compared to placebo

TABLE 4:
Number of patients with influenza using rescue medication in the placebo and elderberry syrup-treated groups

Type of medication	Placebo group	Elderberry group
Nasal spray	21	5
Painkiller	26	7

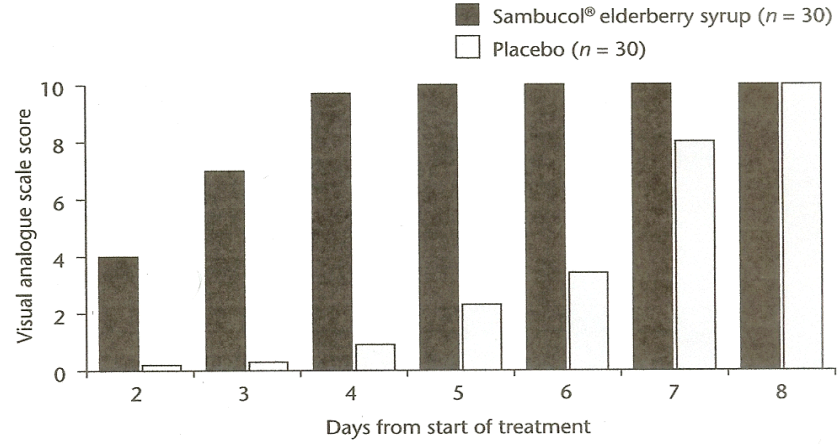
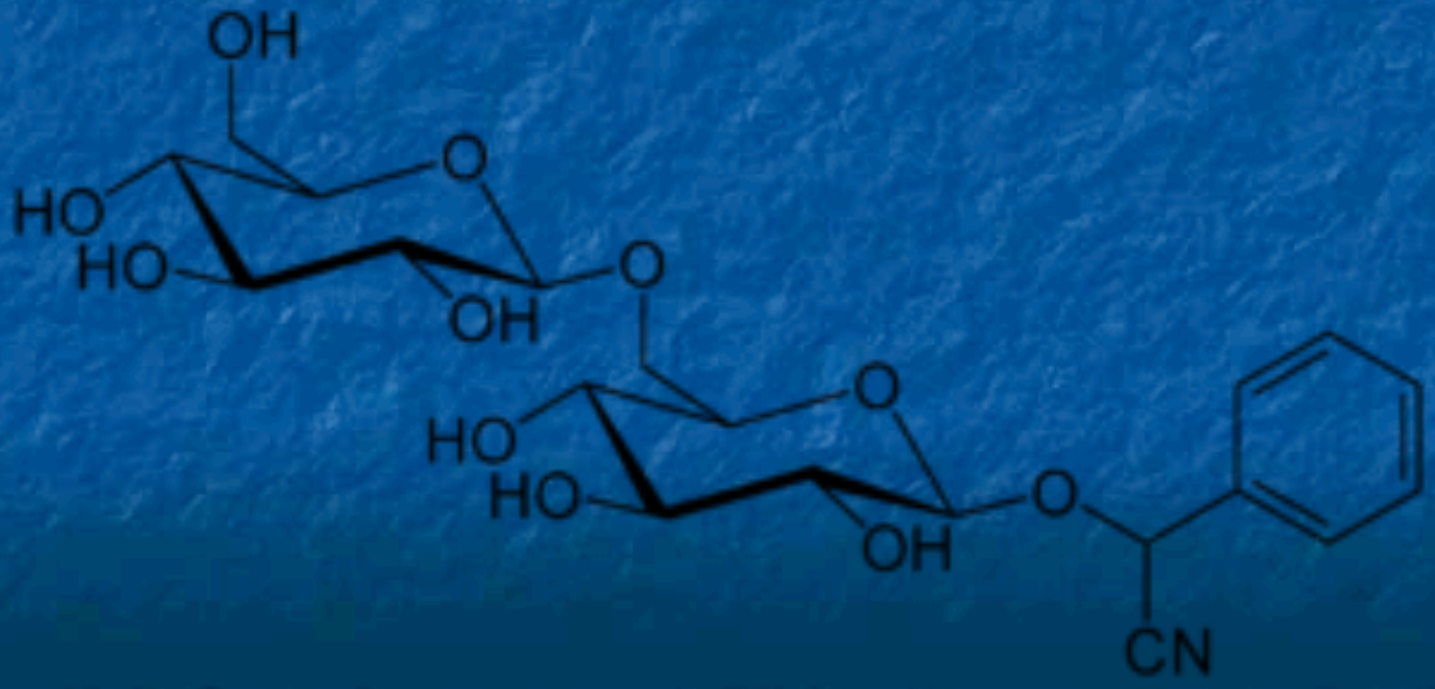


FIGURE 1: The development of self-evaluation scores in global well-being in the 60 patients with influenza who received either elderberry syrup or placebo (15 ml, four times daily with meals, for 5 days)

Elderberry

- Safety: seems OK but leaves and unripe berries contain cyanogenic glycosides that can release HCN



Summary

- Evidence: A few human studies support use to decrease influenza symptoms
- Safety: a quality product is recommended due to risk of cyanide poisoning if contaminated with leaves or unripe fruit.
- Drug Interactions: possibly not with immunosuppressants
- Products: syrup
- GWE:.worth a try to relieve flu symptoms. Start ASAP and take for 5d. Nature's Way Sambucus product is suggested

Bilberry

- Botany- extract of the fruit of the "European Blueberry" which has a white inside. Vaccinium myrtillus. Common blueberries are other Vaccinium sp.
- History-used by English pilots in WWII to improve night vision
- Chemistry-contains anthocyanosides (glycosides of anthocyanidins); these like OPCs (see grape seed extract) are powerful antioxidants
- Pharmacology- antioxidant and free radical scavanging activities with maybe special action in the eye
- Use-poor night vision, cataracts,macular degeneration,diabetic retinopathy

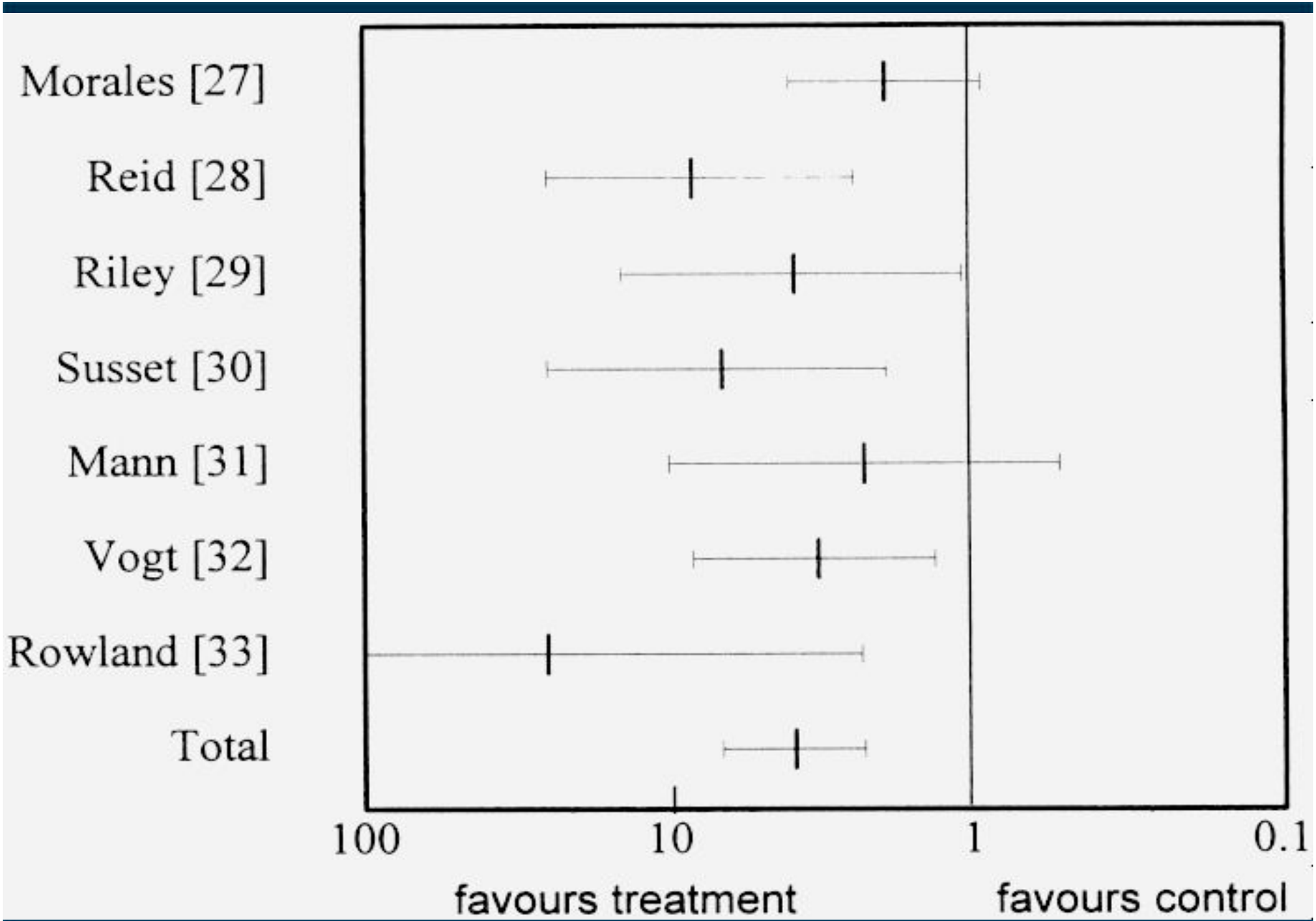
- Evidence-
  - conflicting small studies. More work needs to be done; study by the US Navy showed no benefit in night vision (Muth et al. Alter Med Rev 2000;5:164-173) in a small placebo controlled study (n=13) in men with normal vision
  - Retinopathy. Diabetic and hypertensive retinopathy improvement in 2 small studies.
- Safety-OK Interactions-none
- Products-look for extracts standardized to 25% anthocyanosides; 100mg qd or BID
- Summary-safe but unproven product for vision problems

Yohimbe

- Botany:
  - W. African tree (Pausinystalia yohimbe)
  - bark used
- Chemistry:
  - about 6% alkaloids
  - 2-4% yohimbine (Rx only, 5.4mg TID)
- Pharmacology:
  - alpha adrenergic receptor blocker
  - increase excitability in sacral region of spinal cord
  - MAOI
    vasodilation

Yohimbe

- Adverse
  - CNS stimulation (lower doses)
  - hypertension (lower doses), insomnia
  - activation of psychoses
  - Hypotension (higher doses)
  - Cardiac depression (higher doses)
- Herbal/Drug interactions
  - MAOI
  - additive problems with adrenergic and other MAOI



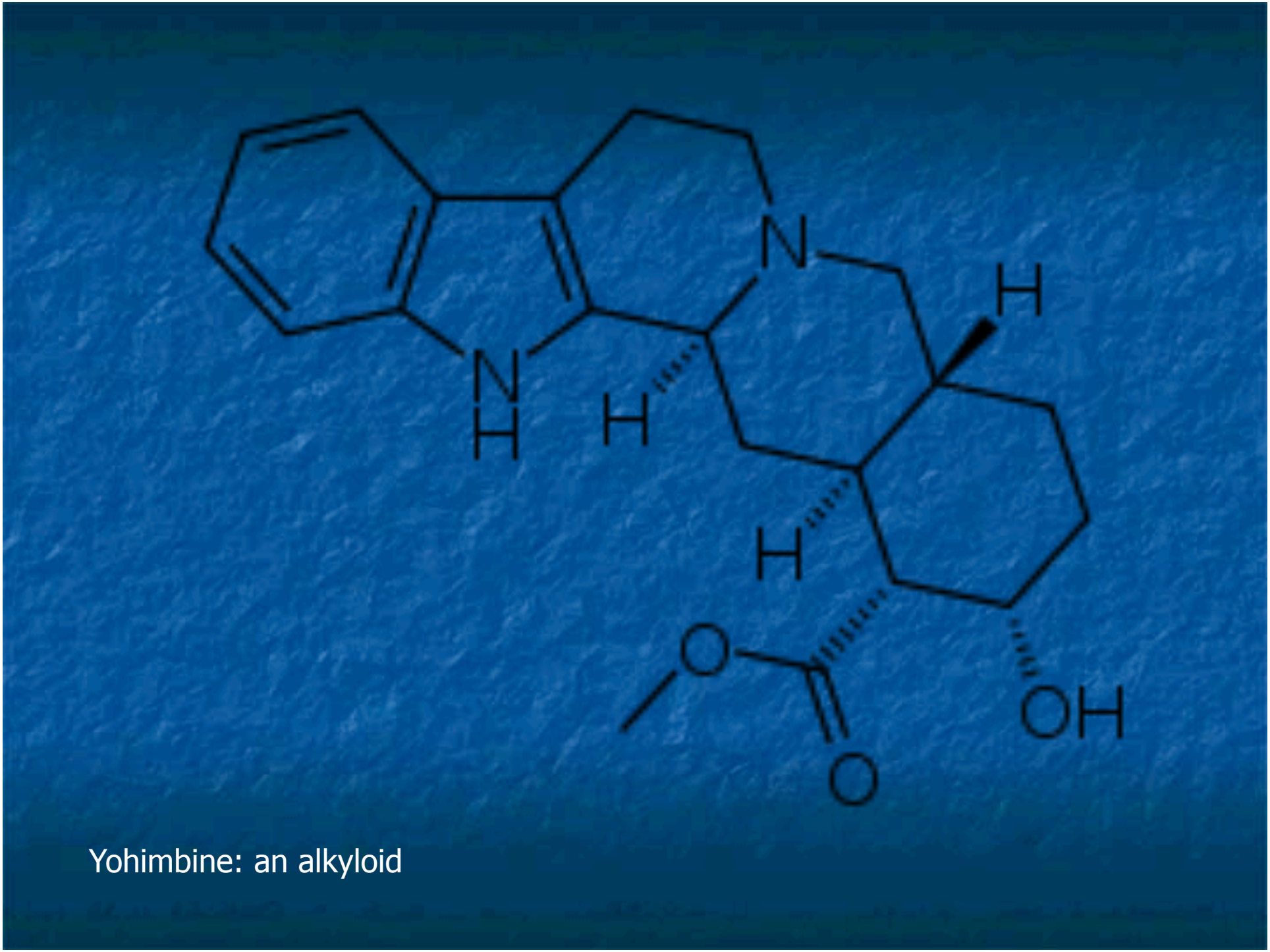
Ernst and Pittler, J. Urology 159:433-436,1998

Yohimbine-Bottom line

- Adverse effects could be significant but warnings in the literature may be exaggerated
- Reasonable evidence for some improvement in ED and sexual dysfunction associated with SSRI therapy
- Studies needed to compare with Viagra etc
- Rx drug, usually 15-30mg/d used; avoid >30mg/d

Yohimbe-Bottom line

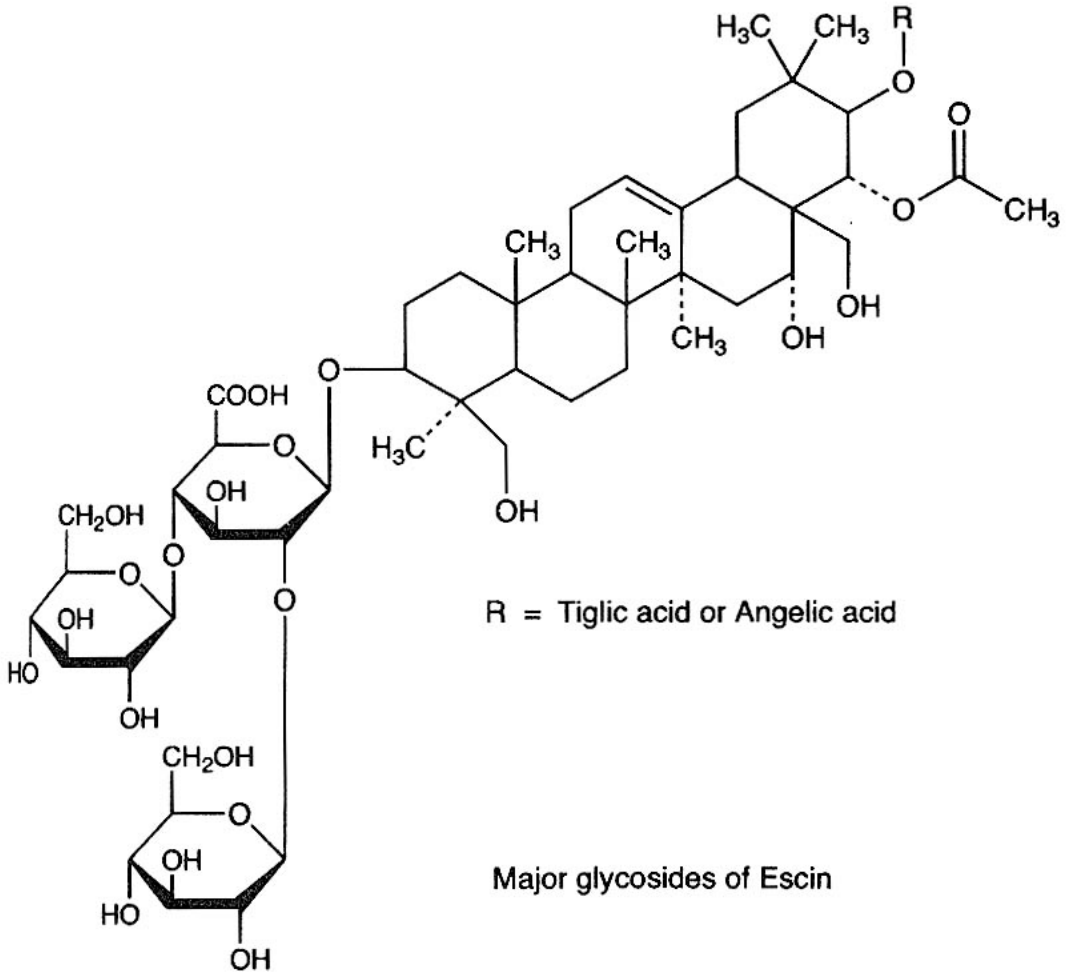
- May work but adverse effects exist and other drugs are probably better
- Quality control problems
- Most dietary supplement products have subtherapeutic amounts of yohimbine
- If 6% yohimbine, then 250-500mg/d would be the dose



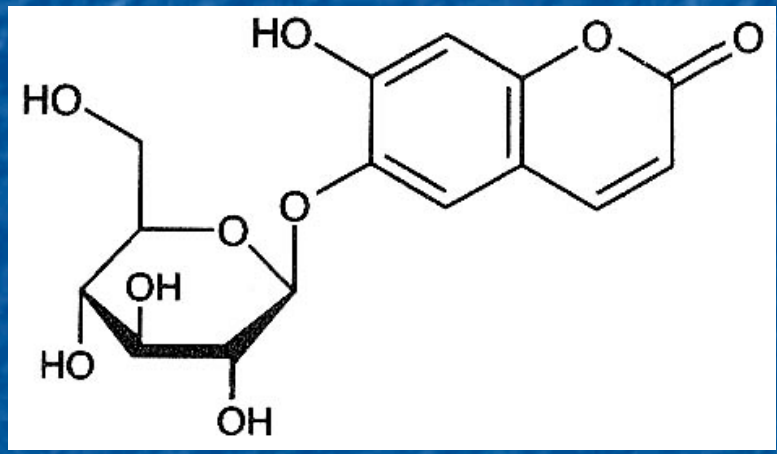
Yohimbine: an alkyloid

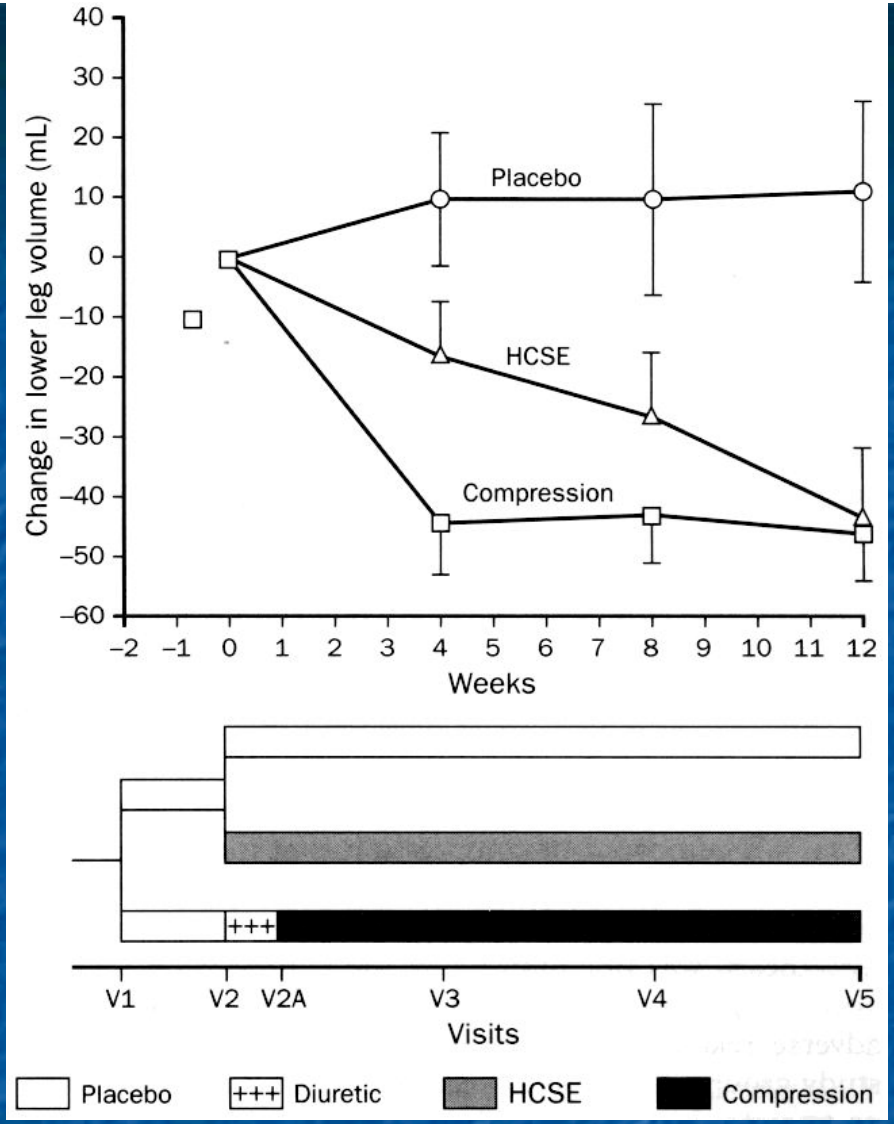
Horse Chestnut

- Botany — Aesculus hippocastanum
- History — Long used but in recent years seed extract has been tested in human studies
- Chemistry — the triterpine glycoside escin is thought to be the active
- Pharmacology — Escin inhibits hyaluronidase and elastase which are involved in increased capillary permeability.
- Use — horse chestnut seed and leaf are used for the treatment of varicose veins, hemorrhoids, and phlebitis. Horse chestnut seed is used for diarrhea, fever, and enlarged prostate.
  Seed extract used for venous insufficiency and varicose veins



Major glycosides of Escin





Diehm et al. Lancet 1996;347:292-294; n=240; extract containing 50mg escin BID

Horse Chestnut

- **Horse chestnut seed extract for chronic venous insufficiency.**
- Pittler MH, Ernst E Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003230.

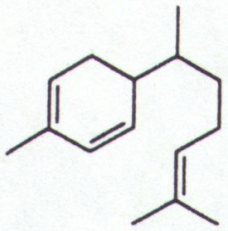
- Authors' conclusions
- "The evidence presented implies that HCSE is an efficacious and safe short-term treatment for CVI. However, several caveats exist and more rigorous RCTs are required to confirm the efficacy of this treatment option."

Horse Chestnut

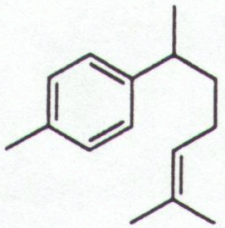
- Evidence: human studies support use of the seed extract in varicose veins
- Safety:the raw seed contains the toxic esculin which can cause bleeding and other adverse events. The extract does not and is safe.
- Drug Interactions: anticoagulants
- Products:seed extract only
- Summary:reasonable evidence for varicose veins and is recommended. Use seed extract standardized to 16-24% escin (aescin).

Ginger

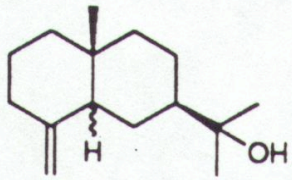
- Zingiber officinale
- History-long used for food and medicine
- Pharmacology
  - **digestive aid**
  - **flavor**
  - **nausea and vomiting treatment-effect is on the stomach and less on the CNS**
  - **For pain**
- Chemistry
  - **volatile compounds**
  - **non volatile compounds**
    - **gingerol**
    - **shogaol**



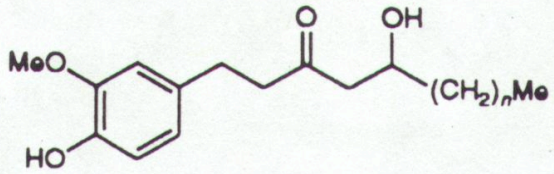
Zingiberene



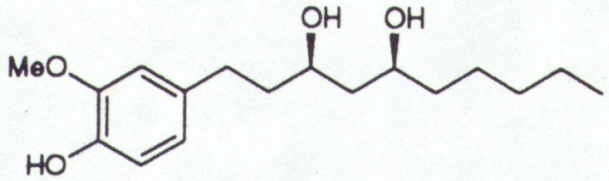
ar-Curcumene



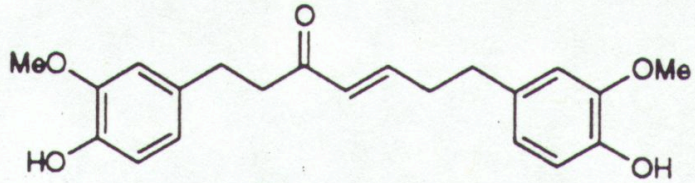
Zingiberol



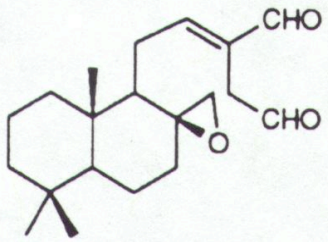
Gingerols
[6]-Gingerol, (n = 4)
[8]-Gingerol, (n = 6)
[10]-Gingerol, (n = 8)



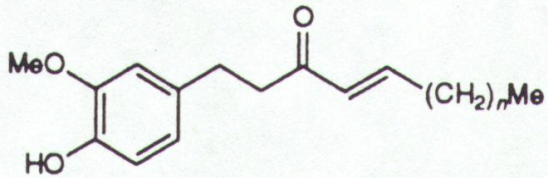
[6]-Gingerdiol
(Acetylation of one or two of the three hydroxyls gives rise to a further range of compounds)



Gingerenone A



A dialdehyde
[(E)-8β,17-epoxylabd-12-ene-15,16-dial]



Shogaols
[6]-Shogaol, (n = 4)
[8]-Shogaol, (n = 6)
[10]-Shogaol, (n = 8)

Fig. 21.18. Constituents of ginger.

Ginger

Efficacy Studies

- motion sickness
  - most studies "in the field" show some benefit but those in a spinning chair are equivocal
- Nausea and vomiting of pregnancy
  - Seems helpful with little risk
- post operative nausea and vomiting
  - most studies, but not, all support benefit

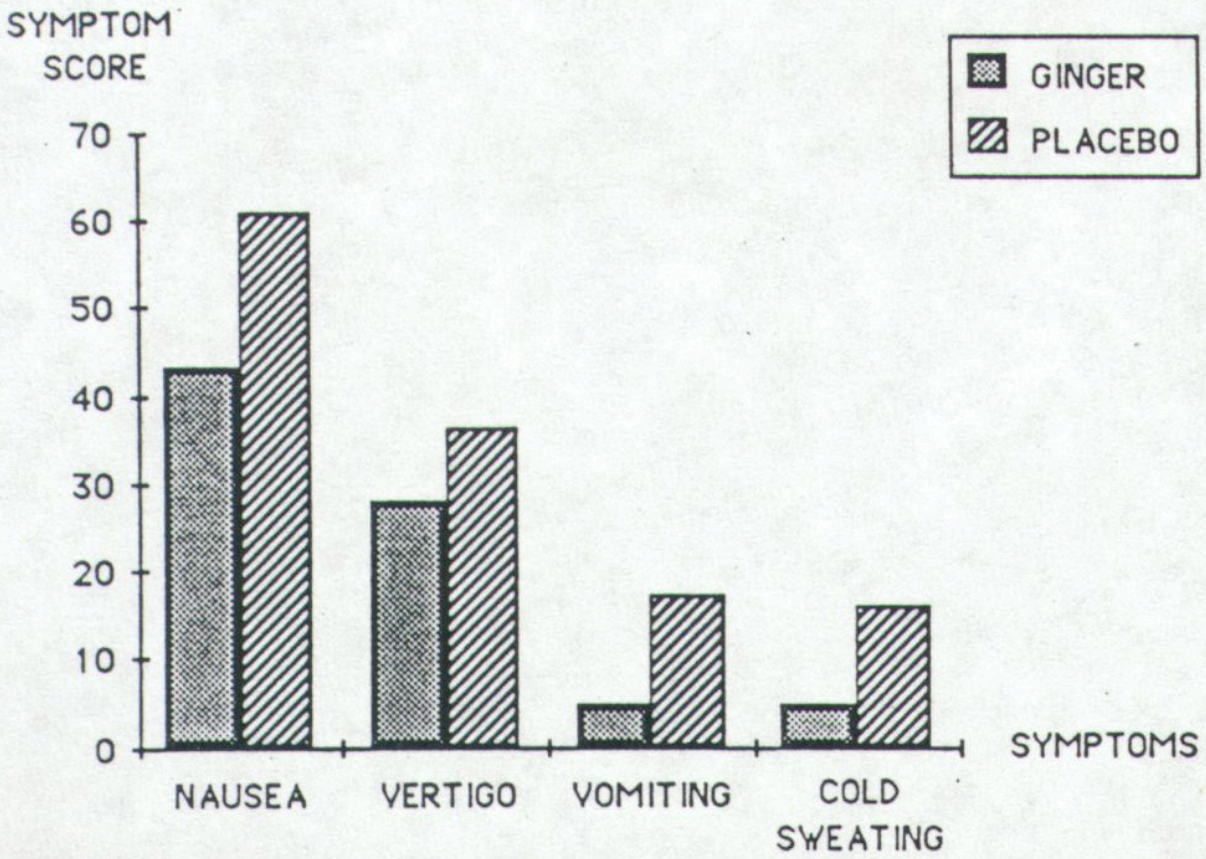


Fig. 1. The total sum of symptom scores arranged according to the category of symptom.

Grontved A, Brask T, Kambskard J, Hentzer E. Ginger root against seasickness: a controlled trial on the open sea. Acta Otolaryngol 1998;105:45-9. n=80

Pregnancy nausea scores (difference from baseline at day 4); 1g ginger/d; n=67; p=.005

From Vutyavanich et al. Obstet Gynecol 2001;97:577-582.

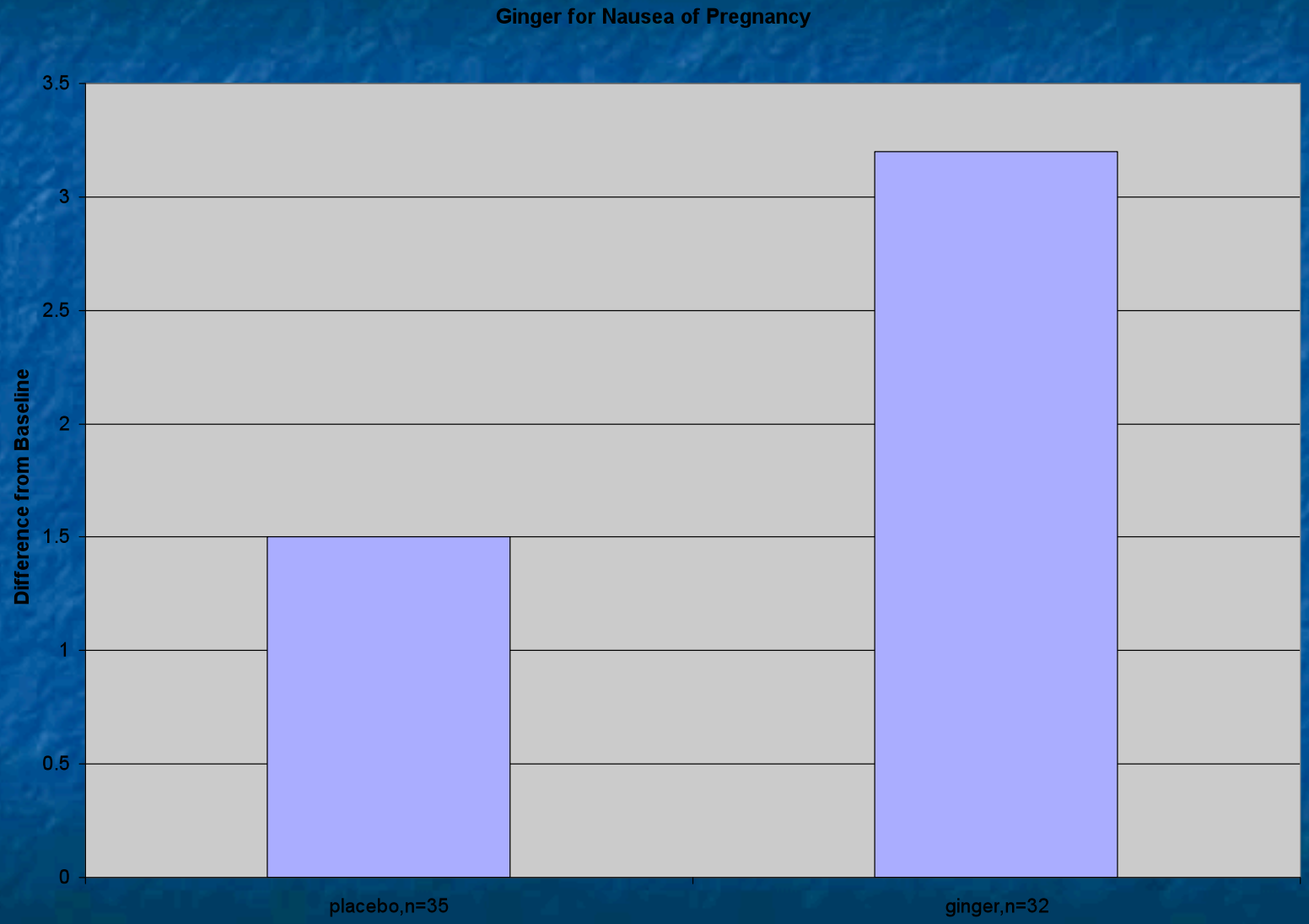
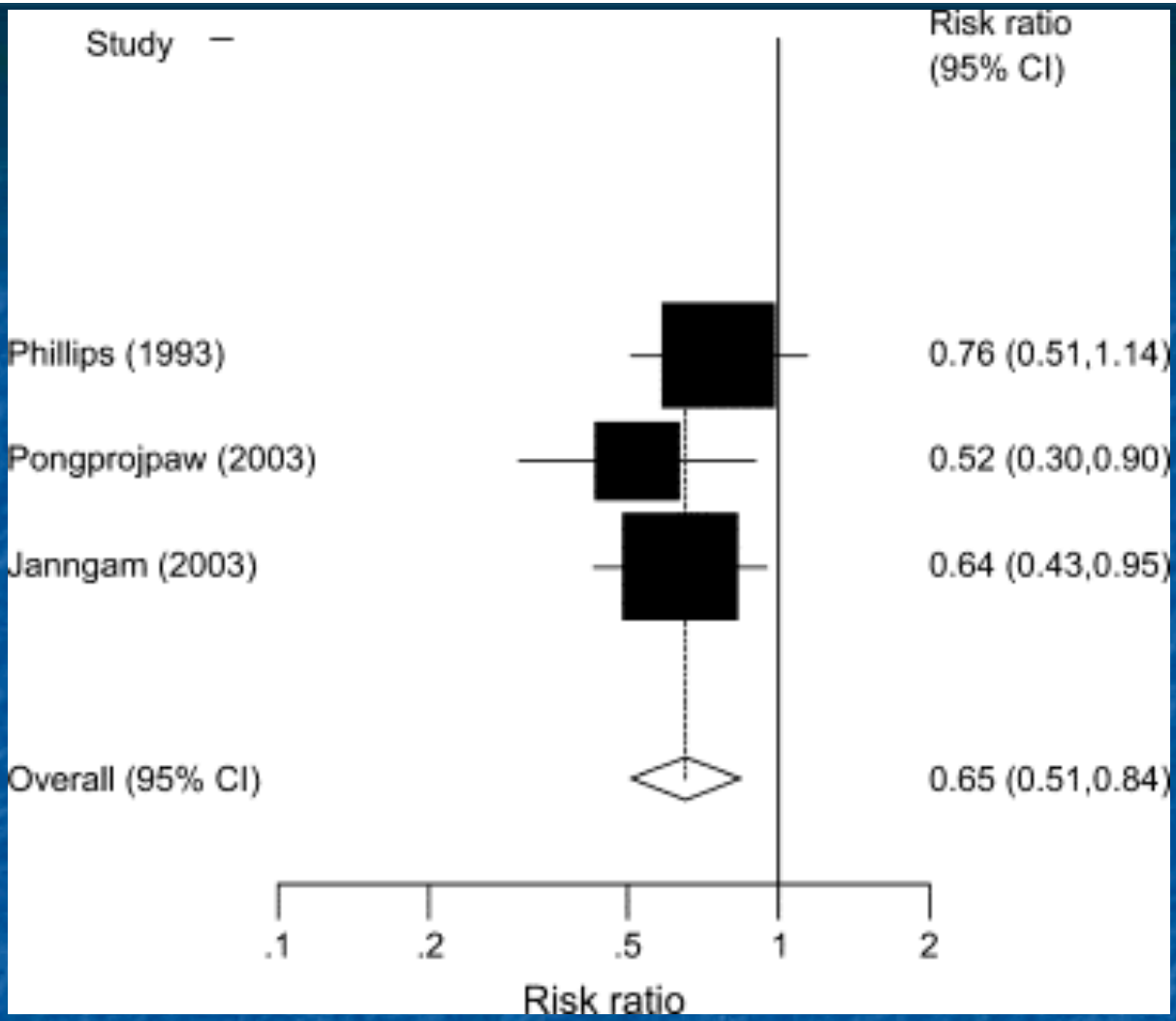


Table 2. Change in Nausea, Dry Retching, and Vomiting From Baseline (Averaged Over Time)

Change in symptoms	Ginger		Vitamin B6		Difference of means (90% confidence interval)	*P*
	Change in score	Standard error	Change in score	Standard error		
Nausea	−3.6	0.2	−3.9	0.2	0.2 (−0.3, 0.8)	< .001
Dry retching	−0.5	0.1	−0.7	0.1	0.3 (−0.0, 0.6)	< .001
Vomiting	−0.9	0.2	−1.4	0.2	0.5 (0.0, 0.9)	< .001

P values are for equivalence testing, and a difference in means > +2 indicates nonequivalence.

N=291 <16 weeks pregnant; assessed at 7, 14, 21d
Smith et al. Obstet Gynecol. 2004 Apr;103(4):639-45



Chaiyakunapruk et al. Am J Obstet Gynecol. 2006;194:95-9

Postoperative nausea and vomiting

Other uses:

- **Pain/osteoarthritis – possible mild effects based on a few studies but ginger takes weeks to see benefit**
- **Nausea asociated with cancer chemotherapy- studies are not in agreement**

European Journal of Obstetrics & Gynecology and Reproductive Biology, 42 (1991) 163–164

EUROBS 01250

Letter to the Editor

Ginger in preventing nausea and vomiting of pregnancy: a caveat due to its thromboxane synthetase activity and effect on testosterone binding

It was recently reported that ginger root diminishes or eliminates the symptoms of hyperemesis gravidarum [1] and that this is due to its aromatic, carminative and absorbent properties.

ger inhibit platelet aggregation and alter arachidonic acid metabolism. Biomed Biochem Acta 1984;43:335–346.
3 Backon J. Ginger: inhibition of thromboxane synthetase and stimulation of prostacyclin: relevance for medicine and psychiatry. Med Hypoth 1986;20:271–278.
4 Backon J. Antidepressant activity of cimetidine: relevance of thromboxane inhibition. Med Sci Res 1987;15:1078.
5 Bone ME, Wilkinson DJ, Young JR, McNeil J, Charlton S. Ginger root – a new antiemetic: the effect of ginger root on postoperative nausea and vomiting after major gynaecological surgey. Anaesthesia 1990;45:669–671.

Since ginger is a potent thromboxane synthetase inhibitor [2,3], as is cimetidine [4], it may affect testosterone receptor binding in the fetus possibly affecting sex steroid differentiation of the fetal brain. Ginger has recently been found to significantly reduce postoperative emetic sequelae [5].

Our group has had extensive therapeutic experience with ginger. We have suggested numerous uses for it [3,6] including: preventing liver damage [7], in burns [8], in treating peptide ulceration [9], as an antidepressant [4], and in preventing aging penile vascular changes and impotence [10].

We carried out toxicological tests on ginger using the SOS Chromotest but could find no evidence of toxicity (Backon J, unpublished data). However, until the effects of ginger on testosterone receptor binding in the fetus are thoroughly investigated, I would be hesitant in recommending its use in pregnant women.

References

1 Fischer-Rasmussen W, Kjaer SK, Dahl C, Asping U. Ginger treatment of hyperemesis gravidarum. Eur J Obstet Gynecol Reprod Biol 1990;38:19–24.

2 Srivastava KC. Aqueous extracts of onion, garlic and gin-

Summary for Ginger

- **Efficacy: possibly worthwhile in preventing motion sickness; worthwhile in treating and preventing nausea of pregnancy; possibly worthwhile in treating postop nausea**
- **Safety: good; abdominal discomfort for some**
- **Drug interactions: caution with warfarin**
- **Product selection: ?**
- **Dose: for pregnancy, use 250mg QID (or more); to prevent motion sickness use 1g 1-4h before travel and 250mg QID during; to prevent postop nausea use 1g 1h prior to anesthesia**
- **Questions remaining:**
  - ***How much benefit and how best used***