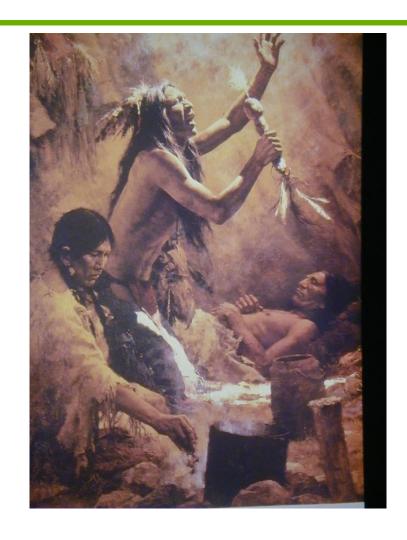
# Botanical: Scientific Validation of Herbal Medicine

Ellen Kamhi PhD, RN, AHG, AHN-BC <u>www.naturalnurse.com</u> FACEBOOK The Natural Nurse



#### Shamanic Healer

The shaman was the medicine man or woman,priest,lawyer, historian, mediator and judge, as well as the wise person of the tribe



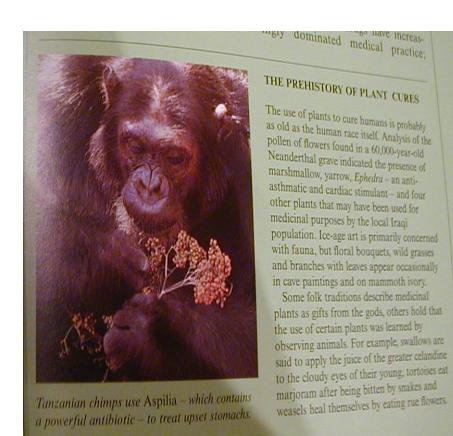
## Doctrine of Signatures

Boehme Portrait 1730 ipeg (48KB, tipo MIME: image/ipeg

- At the age of 25, Böhme claimed to have a vision in which he saw the relationship between God and man.
- He published his revelations in the book,"Signatura Rerum; The Signature of all Things"
- " REF:<u>Boehme\_Portrait\_1730.jpeg</u>
  (48KB, tipo MIME: image/jpeg



# Instinctual Dowsing Chimps caught in the act





# Doctrine of Signatures ie: Ginkgo & the Brain







#### Ginkgo Maidenhair tree/ Ginkgo biloba



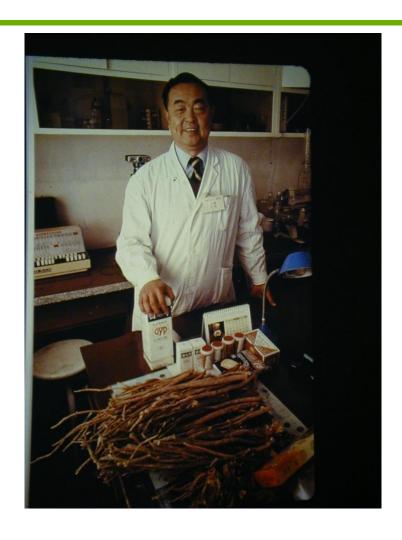
the world's oldest living tree

- ~ Age Related Cognitive Decline
- ~ Alzheimer's disease
- ~ Erectile Dysfunction
- ~ Macular Degeneration
- ~ Asthma
- -improves circulation to peripheral vasculature



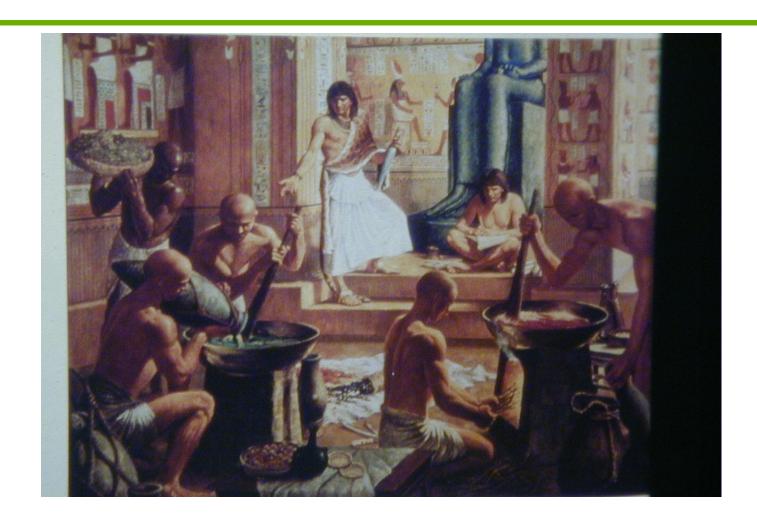


## MODERN MD IN BEJING



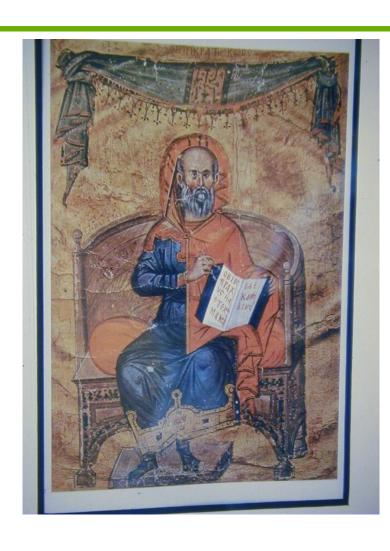
This is an oncologist with Radix Astragalas and Radix Angelica sinensis

# The Egyptian Master Pharmacist by Robert Thom



Note: all interactions are supported by studies unless noted by potential/theoretical

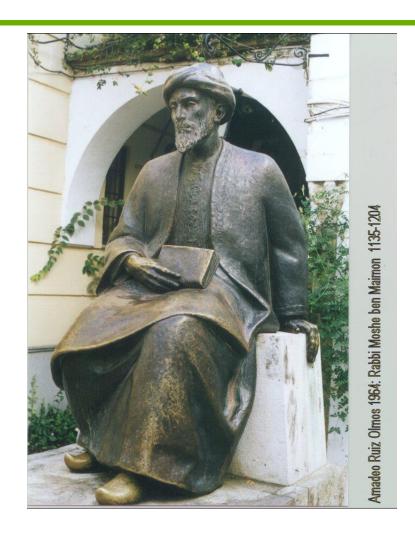
## Hippocrates of Kos (460-377BC)



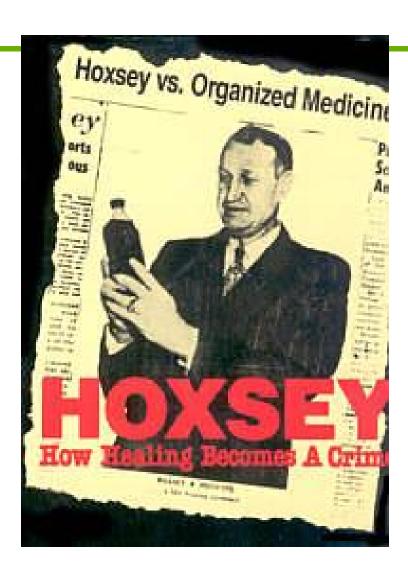
- The father of Western Medicine
- Accomplished Medical botanist
- " Developed Whe 4 humors+
- The Hippocratic school defined the field of medicine as separate from the other disciplines and made a profession of practicing medicine

## Dr./Rabbi Moses Maimonides

- Rabbi Moshe began to practice medicine, since he found it inappropriate to make money from his knowledge of the Jewish holy texts
- Rabbi Moshe was born in Cordova, Spain in 1135.
- " He was highly successful and was appointed the personal physician of Grand Vizier Alfadal and Sultan Salh'al'din.

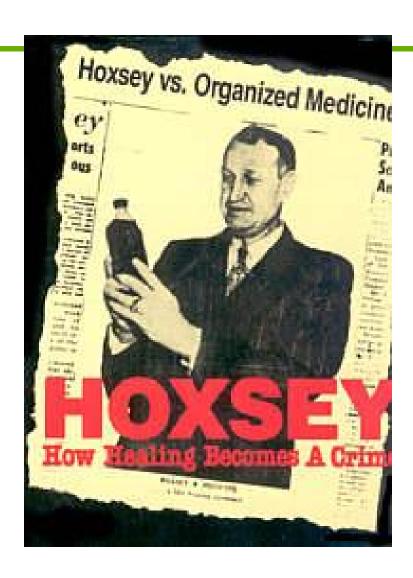


## Hoxey vs Organized Medicine



- The first Hoxsey Clinic opened in 1924 in IL
- The Battle with the AMA started after Dr. Malcolm Harris, Chief Surgeon of Alexis Bros Hospital in Chicago and secretary of the AMA, invited Hoxsey to treat a 66 y/o patient with a tumor
- In front of an audience of the AMAcs most prominent Drcs. Including Morris Fishbein, Harry administered the formula, and in three weeks, the tumor fell off of Mr. Mannix (the patient)

## Hoxey vs Organized Medicine



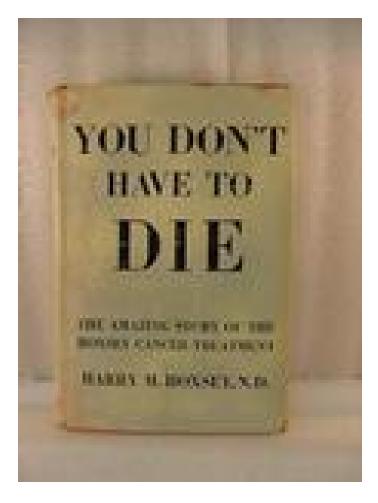
- Dr. Harris dubbed his treatment ±he eighth wonder of the worldqand Harry met with Harris and Fishbein who wanted the secret.
- Moxsey REFUSED to sign the contract, and Harris/Fishbein swore to haunt Hoxsey for as long as he lived!
- Fishbein used JAMA and other publications to attack Hoxsey, but despite this, Harry opened up 8 more clinics!
- Hoxsey sued Fishbein and got him to admit in court that his supposedly
   Brutal quack pastesqdid indeed cure cancer
- The Texas attorney general declared the 1949 state stature to practice Naturopathy to be illegal
- The FDA and FDC and USPS all conspired so that Hoxsey could not mail his medicine to patients

# You Dond Have to Die A book by Harry Hoxey

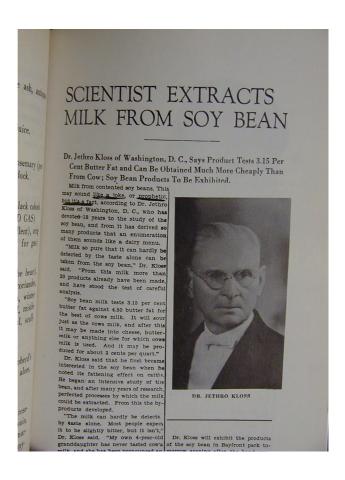
- The government was more interested in closing his clinic down than in evaluating a possible cancer cure.
- It finally succeeded in 1960. For 36 years before his clinic's closure, Hoxsey was harassed by medical boards, the AMA, and FDA.
- He was arrested 119 times between 1926-1931 for practicing medicine without a license and over 100 times between 1937-1939 after setting up a clinic in Texas.
- The doctors who worked with Hoxsey faced threats of having their own licenses revoked.
- Source: The Saga of Harry Hoxsey
  When Healing Becomes a Crime

#### **Ingredients in Hoxsey Remedy:**

Red Clover Flower, Pau D' Arco, Echinacea Root, Buchu Leaf, Astragalus, Chaparral Leaf, Blood Root



#### Jethro Kloss 1863-1946



- É Born in Wisconsin
- É Wrote Back to Edenøin 1939→His book was banned by the Tennessee medical establishment
- É Famous for his book and perfecting the Japanese extraction of milk from soy and promoting it to the masses
- É Formed the Benevolent Food Association
- É Studied with Kellogg

#### REGULATION- DOES IT LEAD TO SAFETY????????

## Incidence of Adverse Drug Reactions in Hospitalized Patients A Meta-analysis of Prospective Studies

Jason Lazarou, et. al. **JAMA**. 1998;279:1200-1205.

**Conclusions.**— The incidence of serious and fatal ADRs in US hospitals was found to be extremely high.

one hundred and six thousand deaths (106,000) from properly prescribed drugs during 1997, plus hundreds of thousands more of dangerous adverse effects

#### Deaths from consumer use of herbs: 37/year

According to the FDA, between 1993 and 1998, federal, state and local agencies reported a total of 184 deaths, most of which were associated with weight-loss formulas.

184 Deaths/5 Years = 37 Deaths/Year

Reference:

Mortality From Herbs:

http://www.emedicine.com/EMERG/topic449.htm

Author: Jon Mark Hirshon, MD, MPH

Mortality/Morbidity: The FDA noted 2621 adverse herb-drug reactions and 184 deaths due to herbal products over a 5-year period (1993-1998).

## Natural Herbs and Supplements have a MUCH BETTER SAFETY PROFILE than Pharmaceutical Drugs!

The American Association of Poison Control Centers released statistics in 2009 after an exhaustive 174 page study found that not even one death was caused by any dietary supplement in 2008. The data was published in the journal Clinical Toxicology

The use of antibiotics is associated with an increased risk of fatal breast cancer (JAMA, Feb 4, 2004).

Regular use of painkillers such as ibuprofen and acetaminophen increases the risk of chronic kidney failure. (New Engl Jour Med Dec 20, 2001)

1.9 million adverse drug events occurring each year, and up to 180,000 of these are life threatening or fatal (JAMA, Mar 5, 2003)

#### DSHEA REGULATION

Dietary supplements, including herbal products, are regulated under the Dietary Supplement Health and Education Act (DSHEA) of 1994 as a food product. The Food and Drug Administration (FDA) may prohibit sales of herbal products containing pharmaceutical agents. The FDA also may prohibit sale of an herbal product proven to have serious or unreasonable risk under conditions of use on the label or as commonly consumed; prohibition of an herbal product generally occurs after marketing and extensive distribution to the public. The burden of proof lies with the FDA and consumer reporting.

Herbal products may contain:

- ~ ingredients not listed on the label
- ~quantities of ingredients listed on the label can vary greatly
- ~ incorrect substitutions . ie- *Aristolochia* mistakenly substituted for *Stephania* in a weight loss product caused kidney damage

Note: all interactions are supported by studies unless noted by potential/theoretical

#### Mechanisms of Herb- Drug Interactions

Pharmacodynamic Interaction- herbal product causes additive, synergistic or antagonistic activity in relation to a conventional drug

**Additive:** coumadin- anticoagulant, ginkgo- anticoagulant- causes excessive bleeding

**Synergistic:** metforin- lowers blood sugar- gymnema- lowers blood sugar

**Antagonistic**: xanax- sedative hypnotic- guarana- stimulant- offsets relaxation response

Pharmacokinetic Interaction- herbal product changes the absorption, distribution, metabolism protein binding, or excretion- thus changing blood level of drug

Eg. Milk thistle up-regulates the action of P 450 liver enzymes, thus breaking drugs down more efficiently- thus lowers blood level of drug

# Immune Support Herbs













ACTIVE ANTIMICROBIAL

INCREASES PRODUCTION & ACTIVITY OF WHITE BLOOD CELLS

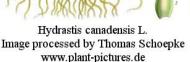
INTERFERES
WITH VIRAL
REPLICATION

NATURE'S ANSWERS

## GOLDENSEAL (Hydrastis canadensis)

- Endangered species
- Root most medicinal
- Watch for leaf capsules at lower prices

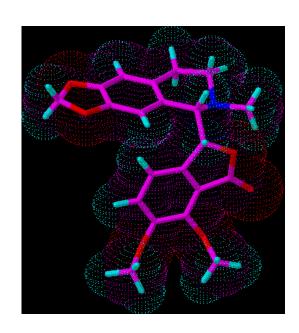






#### GOLDENSEAL

- Berberine
- Berberastine
- Hydrastine





Hydrastine, a strong antibacterial & fungicide

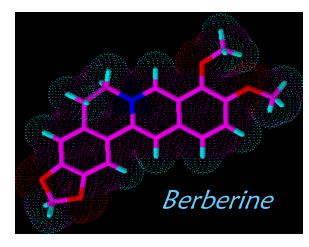
#### OREGON GRAPE (Mahonia aquafolium)





#### OREGON GRAPE

- Berberine & relatives predominate
- Some hydrastine
- Actions very similar to Goldenseal





LG

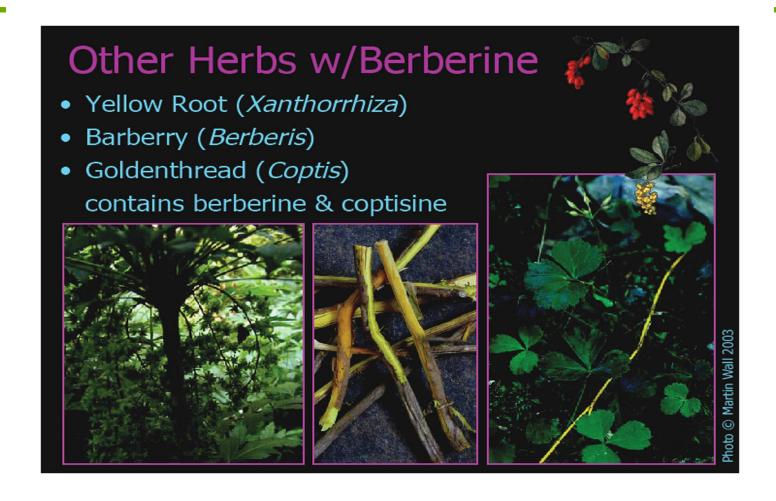
## BERBERINE

#### Goldenseal & Oregon Grape





- Contain berberine & related alkaloids: antibacterial, antifungal; antibiotic alternative
- Tonic for mucous membranes
- Useful for upper respiratory conditions & UTI's



#### BERBERINE

- Found in 23 genera
- Important sources:

Golden Seal (Hydrastis canadensis) Phellodendron (Phellodendron amurense)

Oregon Grape Root (Mahonia Aquafolium) Bloodroot (Sanguinaria canadensis)

Barberry (Berberis spec) Chinese Goldenseal (Coptis chinenesis)

# Protoberberines: Berberine • Antiprotozoal (Leishmania)

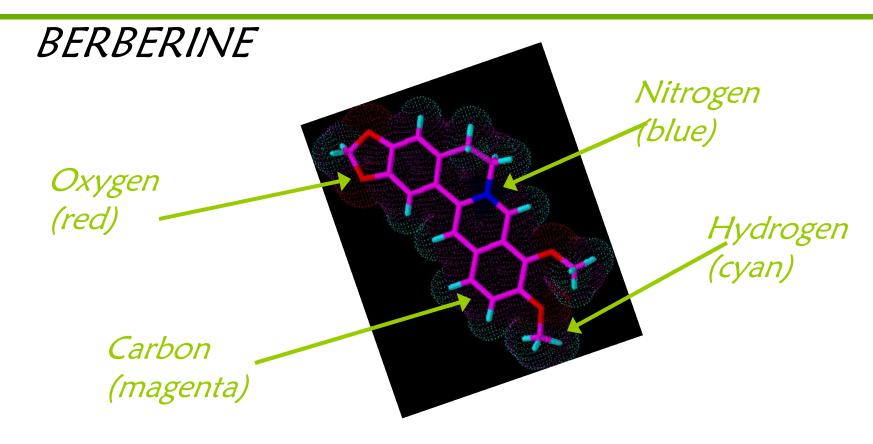
- Antimicrobial, antiseptic
- Anti-inflammatory, antispasmodic
- Astringent, hemostatic
- Tones mucous membranes
- Bitter digestive tonic



LG

#### BERBERINE

- Yellow in color
- Soluble in ETOH
- Highest concentration in Root bark
- Amoebicidal
- Antibacterial (Swap on tonsils for strep throat)
- fungal
- antitumor
- bitter
- hepatic
- Mucus membrane support



antimicrobial molecule in Oregon Grape

#### BERBERINE

MDR Pump: Multi Drug Resistant Pump Biological mechanism used by a cell to rid itself of chemicals

PGP: P-glycoprotein efflux pump

Study on mechanism of action of 5'-MHC-D & pheophorbide-A

http://www.ncbi.nlm.nih.gov/pubmed/12842327

#### BERBERINE

Exophysiological Synergy



- Antibacterial: Staphylococcus aureus
- MDR pump (PGP) ejects the berberine
- 5'-MHC-D & pheophorbide-A inhibit PGP
- Berberine stays inside bacteria, kills it

#### Early Study on Synergy

# Synergy in a medicinal plant: Antimicrobial action of berberine potentiated by 5'-methoxyhydnocarpin, a multidrug pump inhibitor

Frank R. Stermitz\*, Peter Lorenz\*, Jeanne N. Tawara\*, Lauren A. Zenewicz†, and Kim Lewis†‡

\*Department of Chemistry, Colorado State University, Fort Collins, CO 80523; and †Biotechnology Center, Tufts University, Medford, MA 02155

Communicated by Arnold L. Demain, Massachusetts Institute of Technology, Cambridge, MA, December 13, 1999 (received for review October 6, 1999)

Multidrug resistance pumps (MDRs) protect microbial cells from both synthetic and natural antimicrobials. Amphipathic cations are preferred substrates of MDRs. Berberine alkaloids, which are cationic antimicrobials produced by a variety of plants, are readily extruded by MDRs. Several Berberis medicinal plants producing berberine were found also to synthesize an inhibitor of the NorA MDR pump of a human pathogen Staphylococcus aureus. The inhibitor was identified as 5'-methoxyhydnocarpin (5'-MHC), previously reported as a minor component of chaulmoogra oil, a traditional therapy for leprosy. 5'-MHC is an amphipathic weak acid and is distinctly different from the cationic substrates of NorA. 5'-MHC had no antimicrobial activity alone but strongly potentiated the action of berberine and other NorA substrates against S. aureus. MDR-dependent efflux of ethidium bromide and berberine from S. aureus cells was completely inhibited by 5'-MHC. The level of accumulation of berberine in the cells was increased strongly in the presence of 5'-MHC, indicating that this plant compound effectively disabled the bacterial resistance mechanism against the berberine antimicrobial.

bation at 37°C. Growth was assayed with a microtiter plate reader (Bio-Rad) by absorption at 600 nm.

Measurement of Active Transport. Cells were cultured with aeration at 37°C to an OD<sub>600</sub> of 1.8, pelleted, and washed twice with 20 mM Hepes/NaOH (pH 7.0) buffer. Cells then were resuspended in 1 ml of Hepes buffer at an OD<sub>600</sub> of 0.3 containing 10  $\mu$ M CCCP and 10  $\mu$ g/ml ethidium bromide followed by incubation at 37°C for 30 min (6). The cells were centrifuged, washed, and resuspended at an OD<sub>600</sub> of 0.15 in Hepes buffer, and fluorescence was measured with a Perkin–Elmer LS-5B luminescence spectrometer at 530-nm excitation and 600-nm emission wavelengths. Measurement of berberine efflux was performed by following a similar procedure with excitation at 355 nm and emission at 517 nm. The concentration of berberine for cell loading was 30  $\mu$ g/ml.

**Isolation of MDR Inhibitors and Structure Determination.** Dried, ground leaves (188 g) of *B. fremontii* were submerged in 1,200 ml

### Goldenseal

- Paclitaxel: An in vitro study reported that a constituent contained in goldenseal root/rhizome (berberine) may decrease the effectiveness of this medication. Use with caution.
- Benzodiazepines: Human studies have reported that goldenseal inhibited human CYP3A activity in vivo when taken with midazolam. These agents should not be taken together without close medical supervision.
  - . These drugs include alprazolam, diazepam, lorazepam, clorazepate dipotassium, chlordiazepoxide, oxazepam, buspirone, doxepin, hydroxyzine, meprobamate, midazolam.

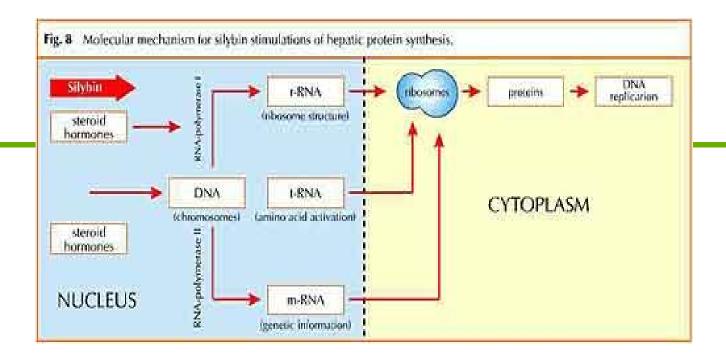




# Milk Thistle (Silybum marianum)



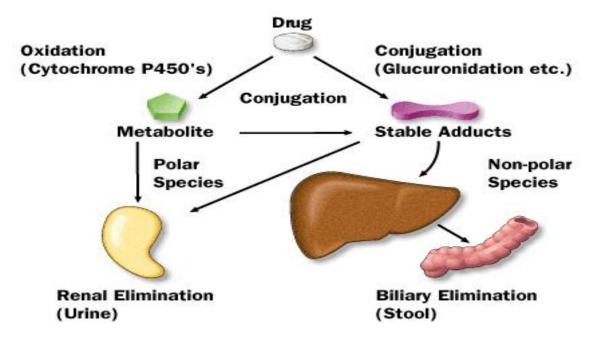
Medications metabolized by CYP-3A4: Until further research is performed, caution should be considered for the individuals who are on medications metabolized in the liver, especially when on multiple drug regimens or taking medications with narrow therapeutic windows. Milk thistle has been reported to reduce the activity of CYP3A4 enzyme and to increase Phase II detoxification, which may alter the hepatic metabolism of certain pharmaceutical drugs and therefore potentially alter drug dosages. Potential/Theoretical



This graph shows the mechanism by which silybin has been clinically shown to stimulate protein synthesis in liver cells. This process leads to the regeneration of healthy liver cells.

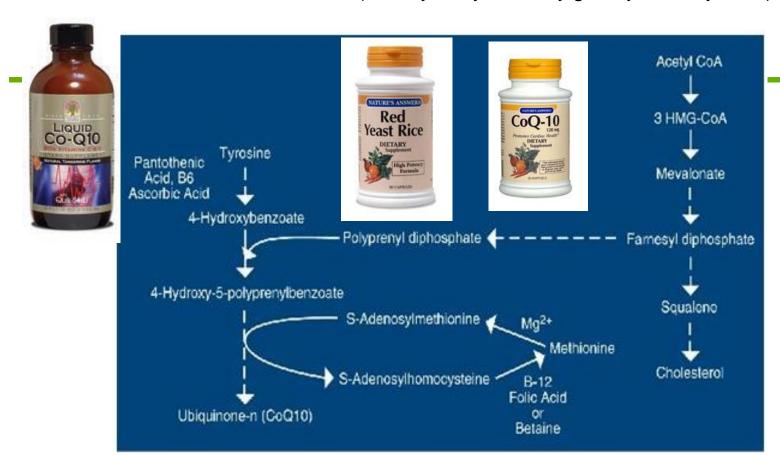
http://www.maximummilkthistle.com/charts-and-graphs.htm

#### Liver Detoxification Pathways



http://extremeliversupport.com/Graphics/Cytocrhome%20P450%20Diagram\_lg.jpg

**HMG-CoA** (or 3-hydroxy-3-methylglutaryl-coenzyme A)



As in the case of prescription medications that inhibit HMG-CoA, it is advisable that persons using Red Yeast Rice products also supplement 30 - 60 mg of CoEnzyme-Q10 daily.

#### August 6, 1999



Special on St John's Wort

Changed the demographics Of the Health Food Industry

## St Johns Wort Hypericum Perforatum







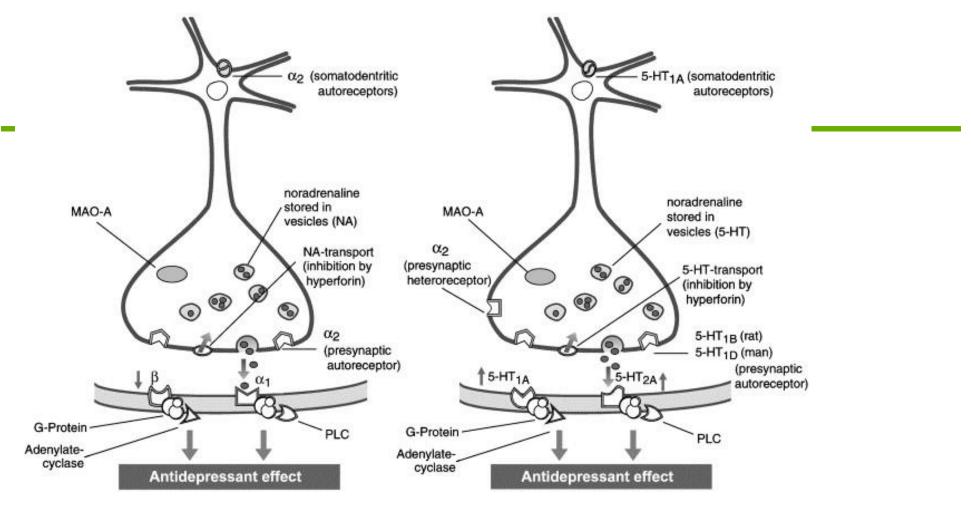
Carpenter, C., Crigger, N., Kugler, R., & Loya, A. Hypericum and nurses.

Journal of Holistic Nursing. 26(3): 200-207. (September 1, 2008).

Conclusions: The compounds in St. John's wort herbal preparations are more effective than placebo and, in several studies, more effective than common antidepressant medications in treating minor depression.

Cochrane Systematic Review 2008, Issue 4. Art. No.: CD000448. doi: 10.1002/14651858.CD000448.pub3.

Conclusion: % John's wort for major depression+, K. Linde, et. al. Overall, we found that the St. John's wort extracts tested in the trials were superior to placebos and as effective as standard antidepressants, with fewer side effects."



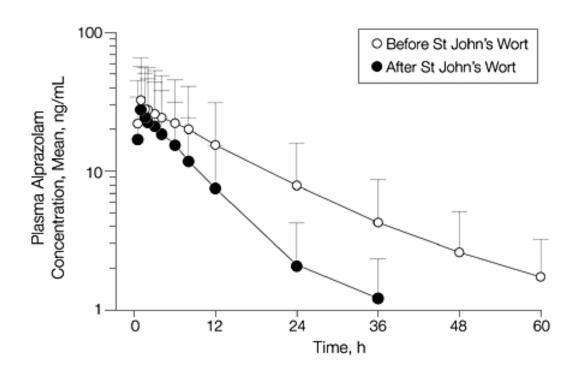
Inhibits the synaptosomal uptake of serotonin, dopamine and noradrenaline (norepinephrine) with approximately equal affinity. However, other in vitro binding assays carried out using St John's wort extract demonstrated significant affinity for adenosine, GABA(A), GABA(B) and glutamate receptors. In vivo St John's wort extract leads to a downregulation of beta-adrenergic receptors and an upregulation of serotonin 5-HT(2) (CNS Drugs. 2003;17(8):539-62. Mechanism of action of St John's wort in depression: what is known? Butterweck V.)

http://www.ncbi.nlm.nih.gov/pubmed/12775192

Image from: http://www.sciencedirect.com/science/article/pii/S1043661802002669

#### Effect of St John's Wort on Drug Metabolism by Induction of Cytochrome P450 3A4 Enzyme John S. Markowitz, et. al JAMA. 2003;290:1500-1504.

**Context** St John's wort is used to treat depression but it has been implicated in drug interactions. **Conclusions** A 14-day course of St John's wort administration significantly induced the activity of CYP 3A4 as measured by changes in alprazolam (Xanax) pharmacokinetics. This suggests that long-term administration of St John's wort may result in diminished clinical effectiveness or increased dosage requirements for all CYP 3A4 substrates, which represent at least 50% of all marketed medications.



### St. John's Wort

#### **Interactions**

- Antidepressants:
- " Reserpine
- " Digoxin
- " Theophylline
- " <u>Immunosuppressants</u>
- " Warfarin
- <u>Antiarrhythmic medications</u>
- " Protease inhibitors
- Drugs metabolized by the cytochrome P-450 pathway
- Oral contraceptives
- " Anesthetic agents
- " Hormone replacement therapy (HRT)

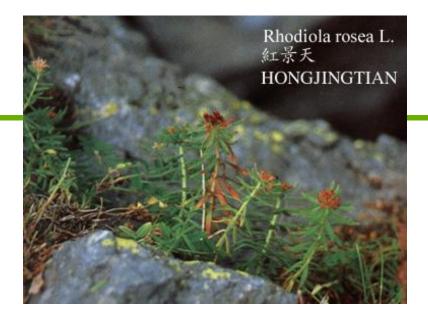








Also called Golden Root and Arctic Root



## Rhodiola has been used in traditional folk medicine in China and Siberia :

Édecreases fatigue Éncreases natural resistance Éstress management Ésupports nervous system Écardiovascular health Éenhances energy Éelevates mood

In Siberia, it is said that, "those who drink rhodiola tea regularly will live more than 100 years."

- Imagine the skin as a trampoline, which has to rebound after every stretch and strain.
- The dermis is the second of three layers of skin, sitting just below the epidermis consists of connective tissues.
- Connective Tissue: elastin and collagen support the skin and provide its flexibility.
- When in good supply, elastin and collagen prevent sagging and wrinkling.
- Rhodiola extract increases collagen synthesis and skin cell proliferation.
- Rhodiola elevates the number of hydroxyproline and hexosamine molecules, which are necessary for the body to make collagen.



Sun damage is the chief culprit in pre-mature aging of the skin.

- Study published in June 2008 issue of "Journal of Cosmetic Dermatology" showed extracts of Rhodiola rosea improved the skin's defensive barrier functions against the stress of ultra violet rays.
- It is highly effective in retarding the signs of photo-aging and protecting the skin from UV damage.

Journal of Cosmetic Dermatology. 2008 Jun;7(2):112-9

Neuroimmunomodulatory compound for sensitive skin care: in vitro and clinical assessment.

<u>Dieamant Gde C, Velazquez Pereda Mdel C, Eberlin S, Nogueira C, Werka RM, Queiroz ML.</u>

Department of Pharmacology/Hemocenter, Faculty of Medical Science, State University of Campinas, Campinas, São Paulo, Brazil.

http://www.ncbi.nlm.nih.gov/pubmed/18482014

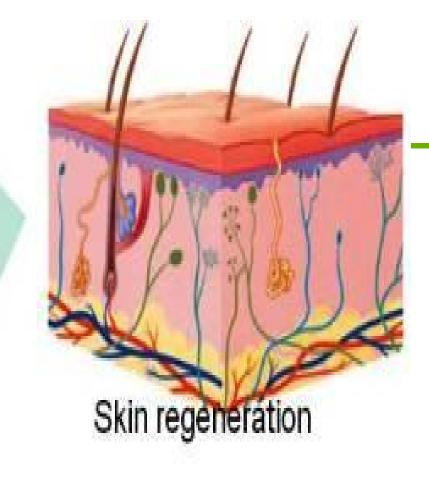
# Rhodiola Chemical Compounds

- Phenylpropanoids: rosavin, rosin, rosarin (specific *R. rosea*)
- Phenylethanol derivatives: salidroside (rhodioloside), tyrosol
- Flavanoids: rodiolin, rodionin, rodiosin, acetylrodalgin, tricin
- Monoterpernes: rosiridol, rosaridin
- Triterpenes: daucosterol, beta-sitosterol
- Phenolic acids: chlorogenic and hydroxycinnamic, gallic acids

1. DNA & Protein

2. Hydroxyproline

3. Hexosamine



DNA 8 protein increase

DNA & Protein Increase

hydronyproline





hexosamine.

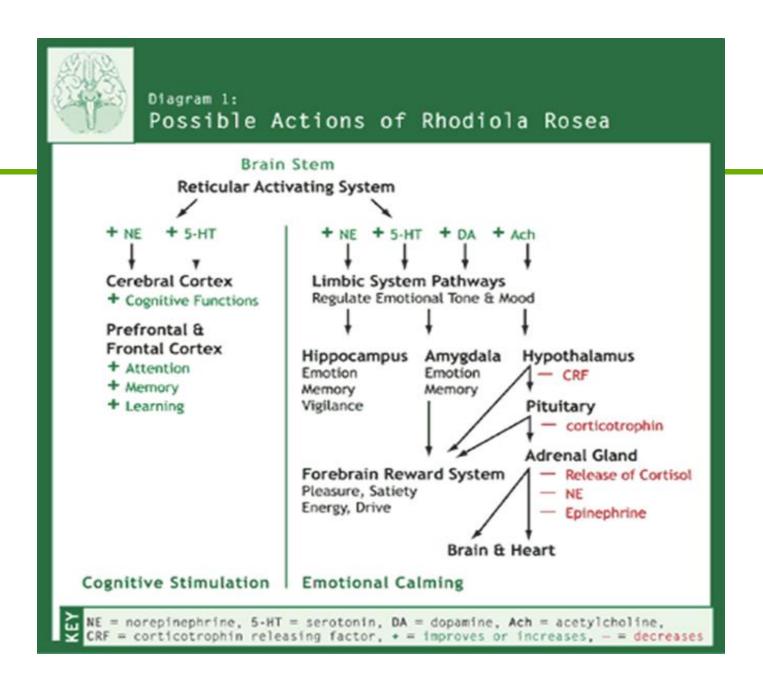




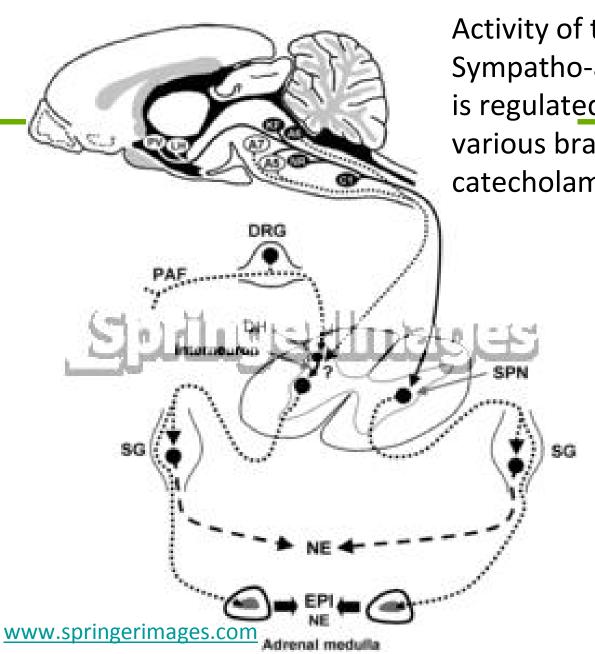
UVradiation absortion







http://www.p2life.com/article/rhodiola-rosea-a-phytomedicinal-overview



Activity of the Sympatho-adrenal system (SAS) is regulated and modulated by various brain areas including catecholaminergic cell groups





**ANTISTRESS** 

UV PROTECTION

#### **Rhodiola Studies**

Richard P. Brown, M.D., Patricia L. Gerbarg, M.D., and Zakir Ramazanov, Ph.D., D.S., **Rhodiola rosea: A Phytomedicinal Overview**, *HerbalGram*. 2002;56:40-52

Wu XL, Zeng WZ, Wang PL, et al., Effect of compound rhodiola sachalinensis A Bor on CCI4-induced liver fibrosis in rats and its probable molecular mechanisms. *World J Gastroenterol.* 2003 Jul;9(7):1559-62.

Nan JX, Jiang YZ, Park EJ. Protective effect of Rhodiola sachalinensis extract on carbon tetrachloride-induced liver injury in rats. *J Ethnopharmacol.* 2003 Feb;84(2-3):143-8.

Kelly GS. Rhodiola rosea: a possible plant adaptogen., *Altern Med Rev.* 2001 Jun;6(3):293-302.

Seo WG, Pae HO, Oh GS, et al., **The aqueous extract of Rhodiola** sachalinensis root enhances the expression of inducible nitric oxide synthase gene in RAW264.7 macrophages. *J Ethnopharmacol.* 2001 Jun;76(1):119-23.

Maslov LN, et al. **Mechanism of The Anti-arrhythmic Effect of Rhodiola rosea Extract.** *Biull Eksp Biol Med.* Apr1998;125(4):424-26.

#### **Rhodiola Cautions**

Adrenergic blocking agents: (beta-blockers, slow heart rate) rhodiola may have similar action to these medications, which may alter the effects and dose of the medications (atenolol, esmolol, betaxolol, penbutolol, carteolol, bisoprolol, pindolol, metoprolol, timolol, sotalol, acebutolol, nadolol, propranolol, labetalol, carvedilol, methyldopa, clonidine, guanfacine, guanabenz, brimonidine tartrate, dipiprazole, levobunolol, levobetaxolol, metipranolol.)

Antiarrhythmic medication: rhodiola may have similar action to these medications, which may alter the effects and dose of the medications (amiodarone, bretylium tosylate, adenosine, dofetilide, propafenone, lidocaine, tocainide, flecainide, ibutilide fumarate, moricizine, quinidine, disopyramide, procainamide, mexiletine, verapamil, digoxin, propranolol, sotalol, esmolol, acebutolol)

## Alkaloids: ISOQUINOLONE

#### OREGON GRAPE

#### Oregon Grape Medicinal Use:

http://www.vitaminshoppe.com/content/en/healthguide/hncontent.jsp? resource=%2fassets%2fnutritional-supplement%2foregongrape%2f%7edefault

#### Herb-Drug Interaction Sources

#### Natural Medicine Comprehensive Database

www.naturaldatabase.com

Scientific Gold Standard for Evidence-Based, Clinical Information on Natural Medicines

#### Natural Standard

www.naturalstandard.com

Compilation of evidence-based information about complementary and alternative therapies from contributors at 100+ academic institutions using validated rating scales. Information is incorporated into comprehensive monographs that undergo blinded editorial and peer review designed to facilitate clinical decision making.

**Healthnotes-** info can be found on several websites: www.vitaminshoppe.com under ARTICLES

## Ellen Kamhi, PhD, RN, AHG, AHN-BC

" www.naturalnurse.com

#### " FACEBOOK The Natural Nurse

