HERBAL MEDICINE FOR CHRONIC INFECTIONS

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AARM
Association for the Advancement of Restorative Medicine

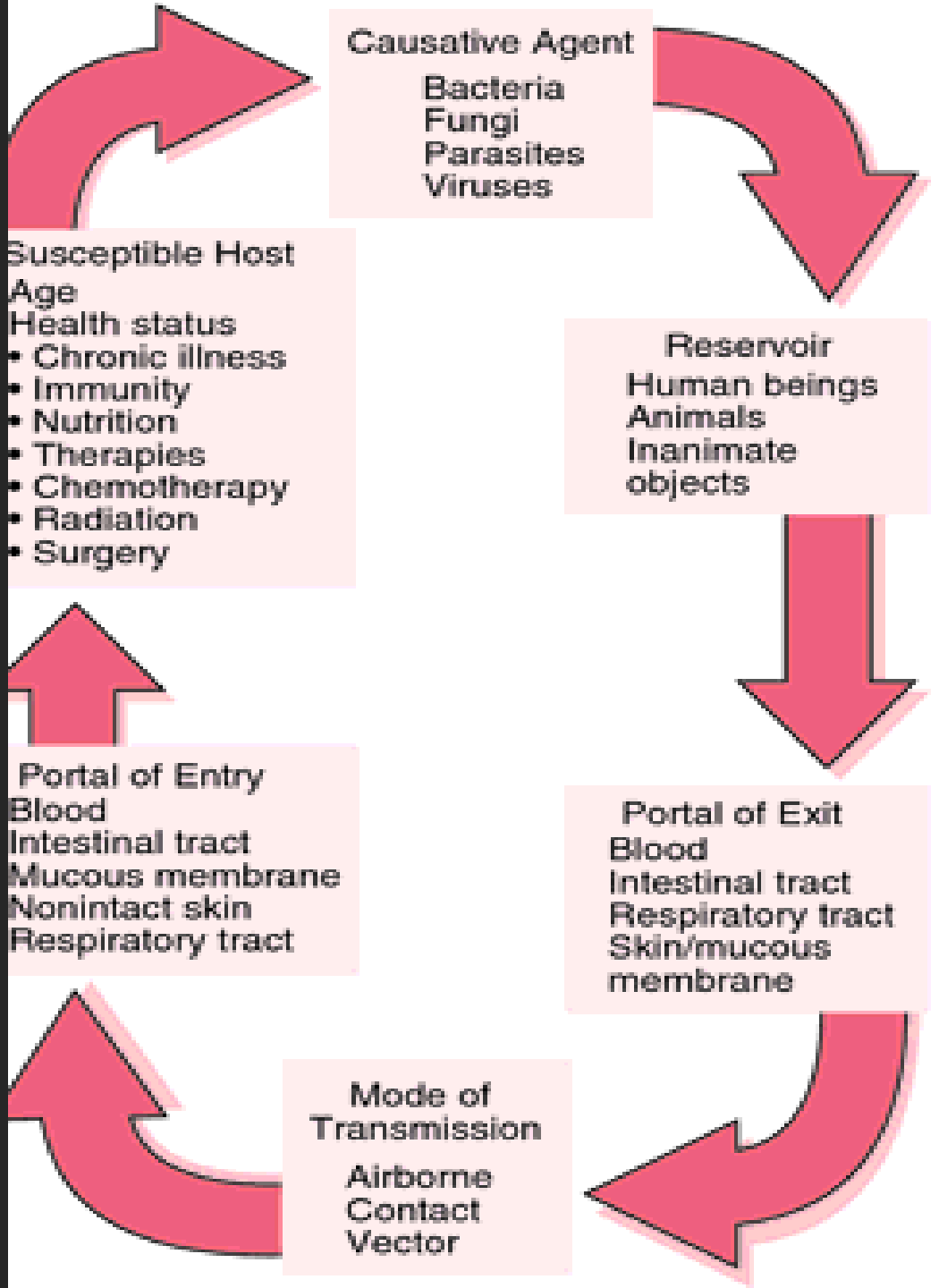
HERBS FOR INFECTIONS

This Presentation will Categorize Herbs for Infections Based On:

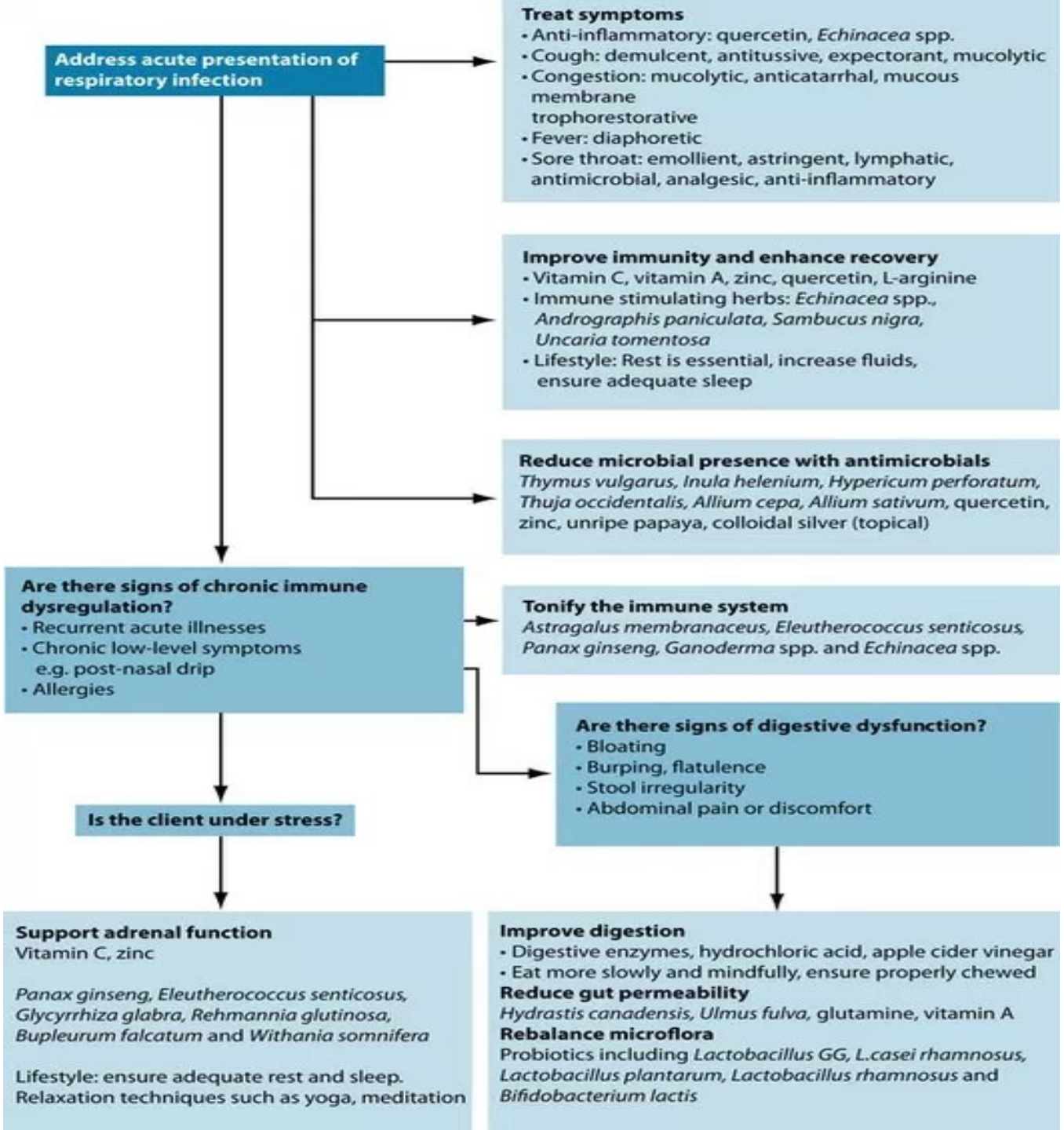
- **Adrenal Herbs and Adaptogens for Immune Support**
- **Thyroid Support Herbs for Immune Support**
- **General Herbal Support**
- **Immune Polysaccharides**
- **Herbs to Deter Biofilms**
- **Anti-Microbials**

CONTRIBUTORS TO CHRONIC INFECTIONS

- Sugar
- Poor Diet
- Stress
- Poor Sleep
- Alcohol, Smoking, Drugs
- Nutritional Deficiencies
- Meds, steroids such as Prednisone
- Intestinal Dysbiosis and Poor Digestion



TREATMENT PROTOCOLS FOR RESPIRATORY INFECTION



ADRENAL SUPPORT FOR CHRONIC INFECTIOUS ILLNESSES

Bioregional Adaptogens

	Bioregion	Adaptogen	Notable Features
	Pacific Northwest U.S., Western Canada	*Oplopanax horridum* (devil's club) root bark	Little used for this purpose. Long revered as protective medicine.
	Northern California, Northern Asia, Northeastern North America	*Aralia californica* (California spikenard), *A. elata* (Manchurian spikenard), *A. racemosa* (spikenard) root	Greatly overlooked. Quite spicy, lung affinity.
	Southeast Asia	*Panax ginseng* (Asian ginseng) root	Widely cultivated. Tends to be fairly heating and somewhat more specific to men. Relatively well researched.
	Southeast Asia	*Panax notoginseng* (tienchi ginseng) root	Also widely used to staunch bleeding.
	Southeast Asia	*Schisandra chinensis* (schisandra) fruit	Also hepatoprotective. Relatively tasty.
	Southeast Asia	*Astragalus membranaceus* (astragalus) root	Pleasant, mild taste.
	Southeast Asia	*Codonopsis pilosula* (codonopsis) root	Commonly substituted for P. ginseng in modern TCM.
	Southeast Asia	*Gynostemma pentaphylla* (jiaogulan) root	Saponins very similar to P. ginseng. Easier to cultivate. Not yet cultivated in North America.
	China, Japan	*Lentinula edodes* (shiitake) fruiting body	Cultivated.
	Siberia, Northern China	*Eleutherococcus senticosus* (eleuthero) root	Moderately heating.
	Eurasia	*Glycyrrhiza glabra* (licorice); *G. uralensis* (gan cao) root	Very tasty. Also demulcent and hepatoprotective.
	India	*Withania somniferum* (ashwagandha) root	The most calming and anxiolytic of the adaptogens.
	Siberia	*Rhodiola rosea* (goldenroot) root	Also hypotensive. Cultivated.
	Globally in temperate areas	*Ganoderma lucidum* (reishi) fruiting body	Immunomodulating effects well documented in humans.
	Eastern U.S. and Canada	*Panax quinquefolius* (American ginseng) root	Available from wild-simulated cultivation.
	Northern U.S., Southern Canada	*Dicentra formosa* or *D. canadensis* (turkey corn) tuber (low ethanol/water extract)	Tonic formerly favored by the Eclectics.
	Eastern U.S. and Canada	*Podophyllum peltatum* (mayapple) root, water extract	Not to be confused with resin extracts of the root, which are quite toxic, the Eclectics describe this as one of the best restorative tonics they had, particularly when tissue were "full."

ADRENAL HERBS

All Cultures have used herbs, now known to affect Adrenal Glands for:

Exhaustion

Reproductive Issues

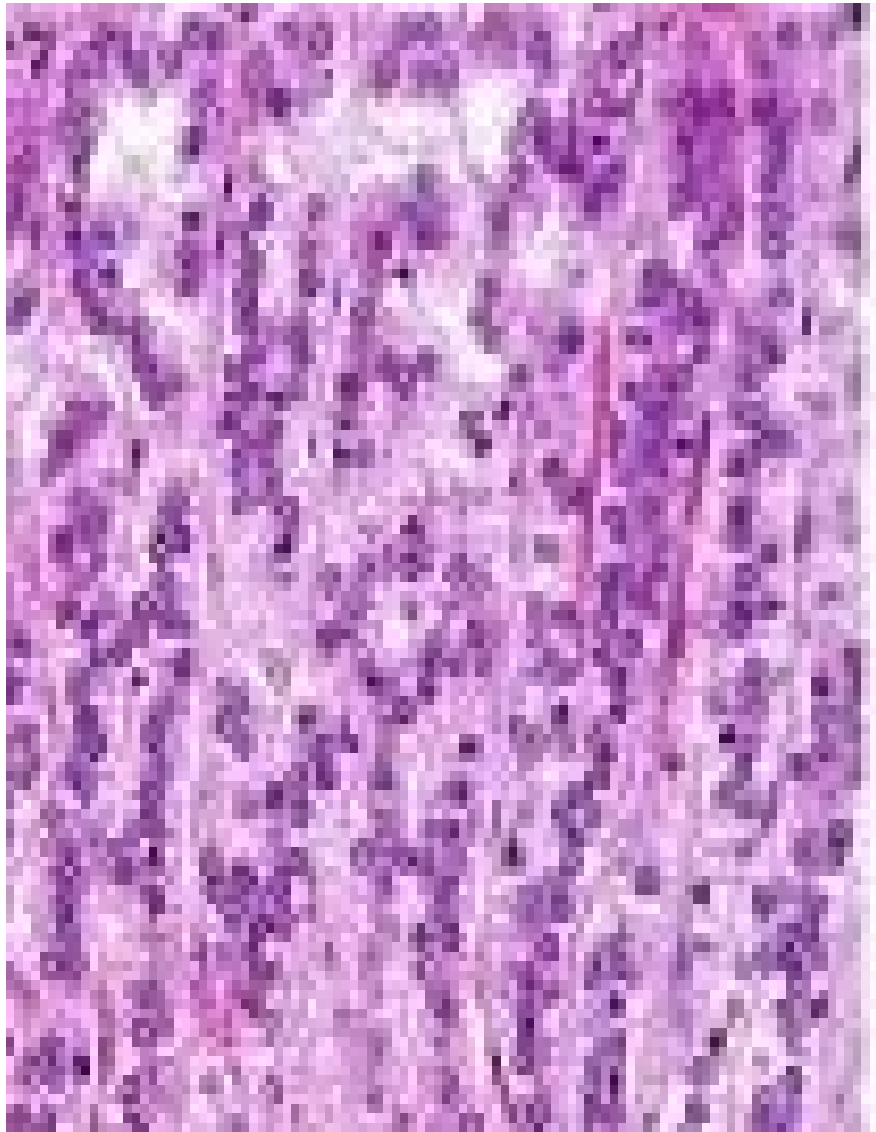
Altered Immunity

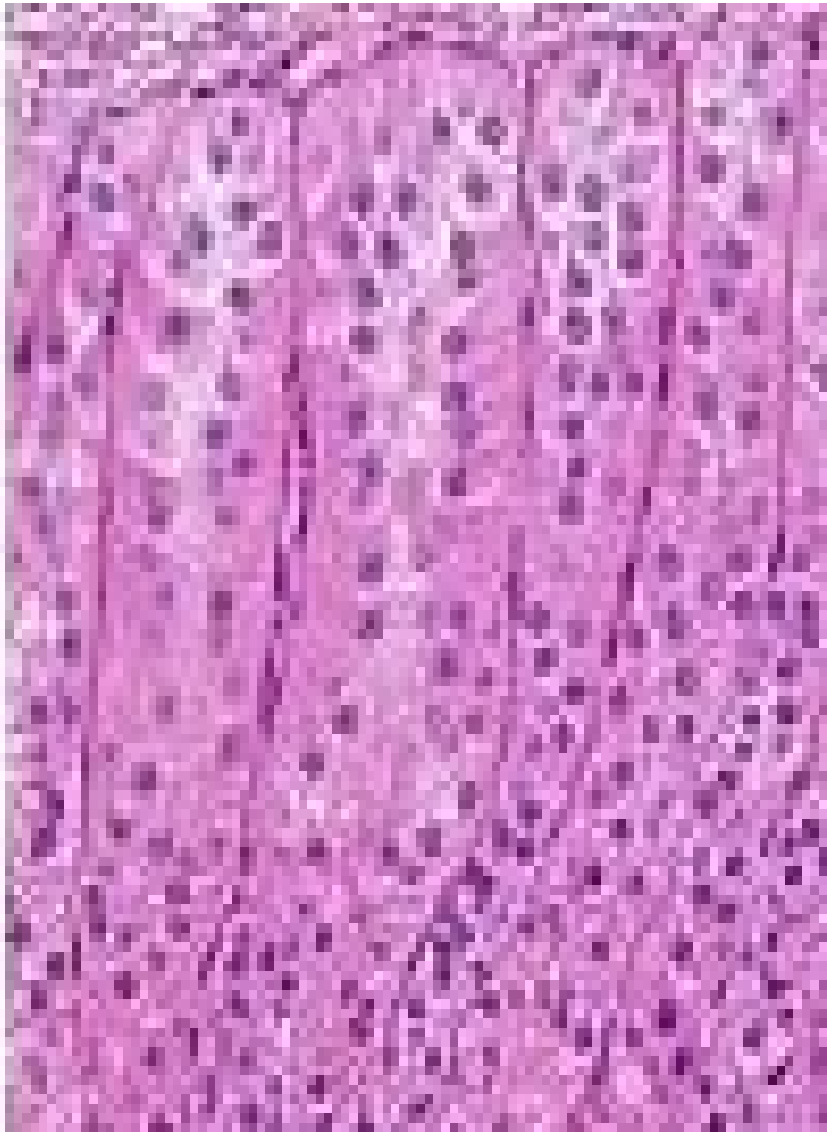
Sleep Disturbance

Stress Symptoms

ADRENAL CORTEX FEEDBACK LOOP

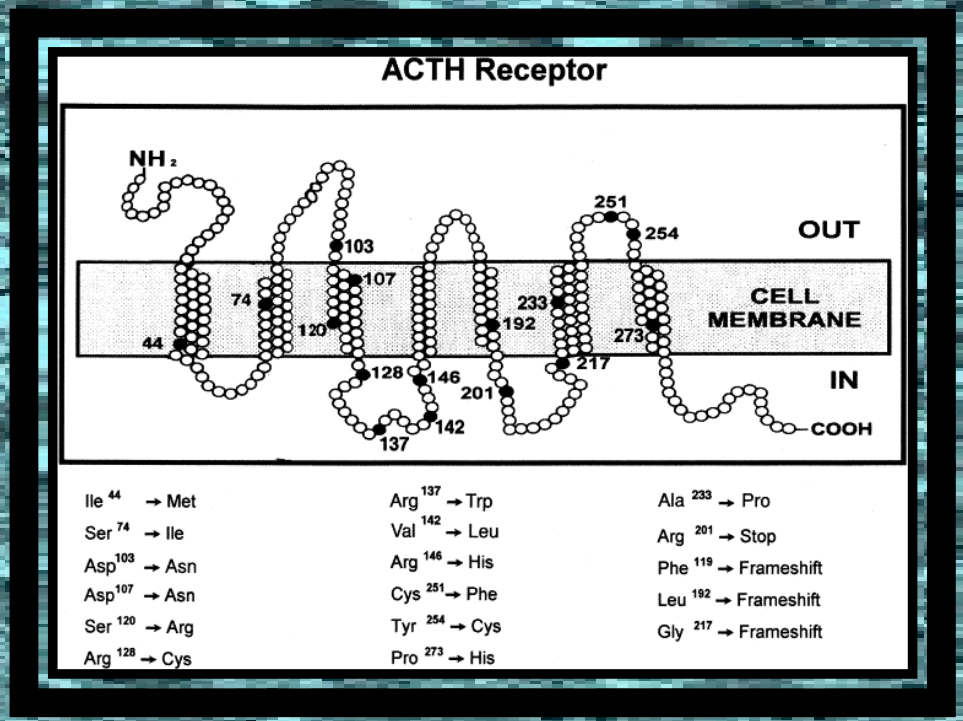
Investigations into the HPA and Stress show altered cortisol responses acutely, and down regulation of the entire adrenal gland chronically.





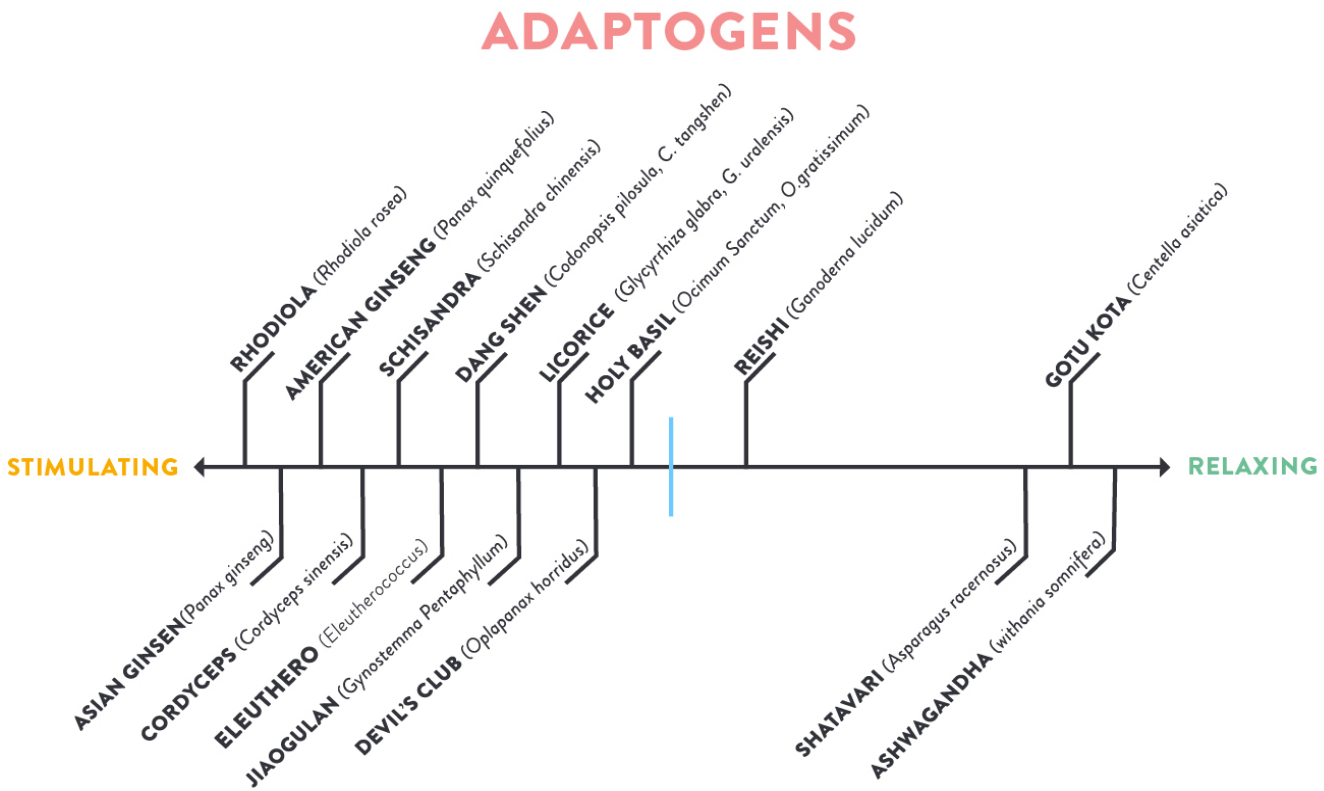
ADRENAL DOWN REGULATION

Down regulation involves a decrease in the number of cortisol receptors in tissues, or ACTH receptors on the adrenal glands themselves, and ADAPTOGENIC herbs may help restore tissue status.



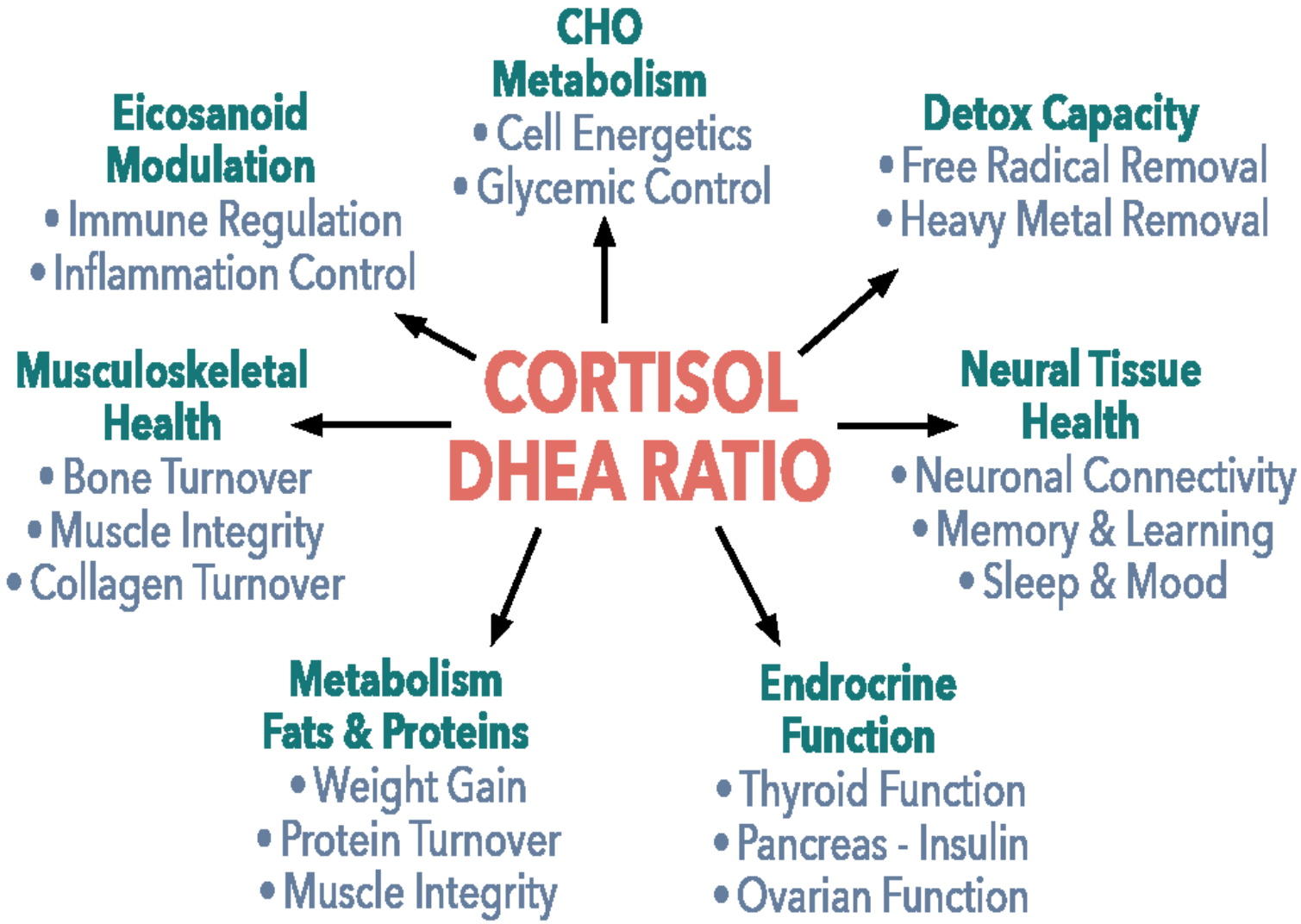
ADRENAL SUPPORT FOR CHRONIC INFECTIONS

- **Stress and High Cortisol can suppress WBCs and other immune factors**
- **Low cortisol may also increase infection susceptibility**
- **Licorice is an example of an herb to support adrenal function, and is also shown to have anti-viral effects**
- ***Eleutherococcus* and all of the Adaptogenic herbs have substantial research regarding resisting and treating chronic infections.**



INDICATIONS FOR ADAPTOGENS AND LICORICE

Subtle signs of adrenal weakness, or blunting of the HPA axis include easy fatigue, poor stamina, poor memory, depression, irritability, and frequent infections – the same symptoms that indicate the use of adaptogenic herbs.



STRESS, HIGH CORTISOL, AND INFECTIONS

- **Stress and High Cortisol can suppress WBCs and other immune factors.**
- **Flu virus symptoms are exacerbated by stress.**
- **Herpes simplex cold sores may flare with stress.**
- **High cortisol can suppress wound healing, allow fungal growth.**

<u>Immunosuppression Mechanisms</u>

Neural and Endocrine Responses

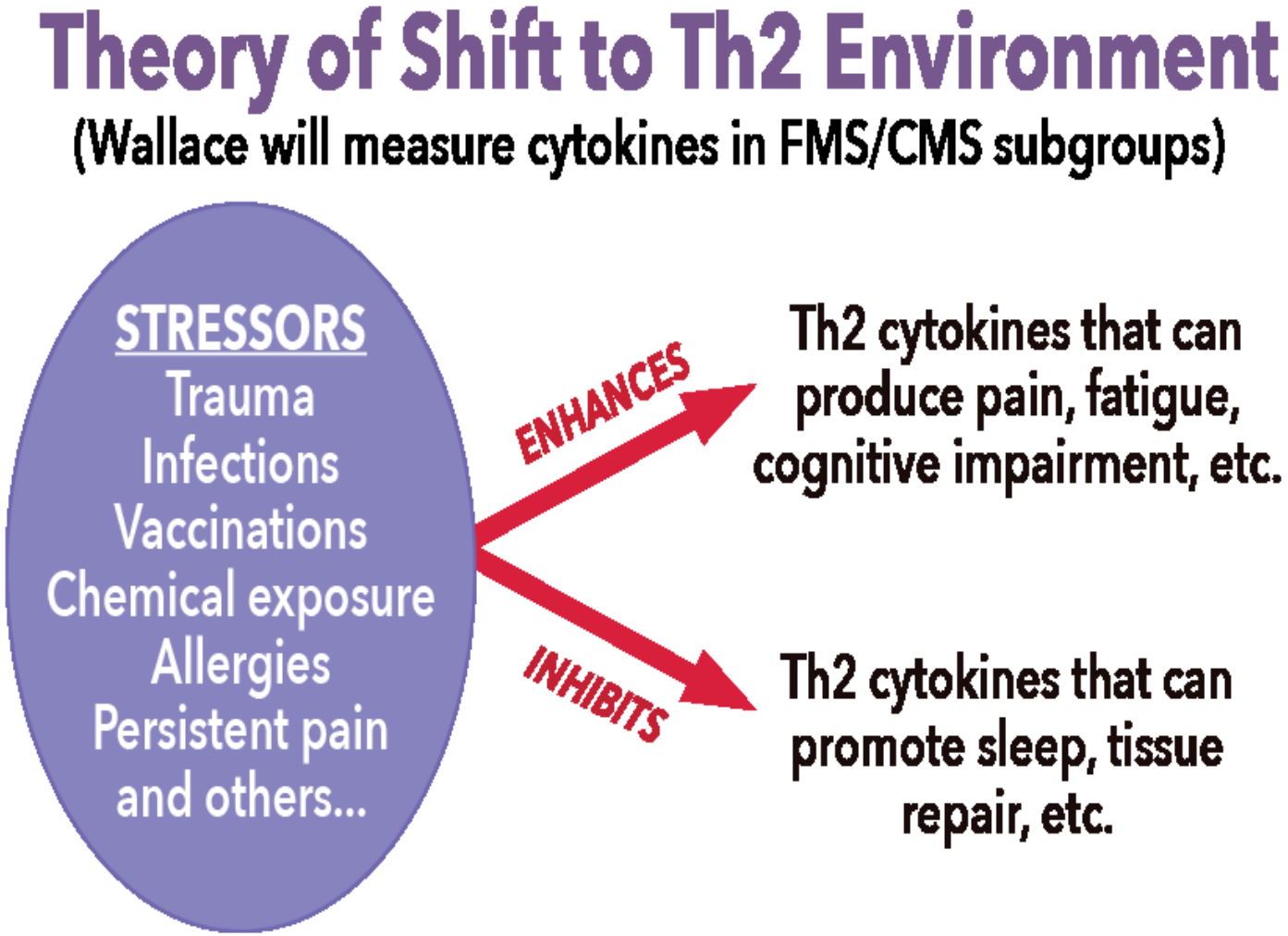
- **Autonomic nervous system changes**
- **Release of Neuropeptides**
- **Alterations in Th1 and Th2 Ratios**

HIGH CORTISOL SYMPTOMS

- Anxiety
- Mood Swings
- Poor Sleep
- Food Cravings
- Increase Abdominal Fat
- Brain Fog
- Irritability
- Insulin Resistance
- Blood Sugar Dysregulation
- Frequent Infections
- Auto-immune Phenomena
- Hypertension
- Depression
- Muscle Loss
- Bone Loss
- Premature Aging
- Hair Loss
- Skin Disorders
- Allergic Phenomena
- Eczema

ADRENAL FUNCTION

Allergies and infections can increase as a result of adrenal disorders, as cortisol suppresses WBCs and alters cytokine response.



Eksp Klin Farmakol. 1998 Sep-Oct;61(5):37-41. *A comparative study of the mechanisms of the immunosuppressive action of morphine and adrenaline in leukocytes in vitro*. Dolmatova LS, Romashina VV

Image from afsafund.org.

ADAPTOGENS IMPROVE ADRENAL RESPONSE

Glycyrrhiza glabra

LICORICE

Panax ginseng

GINSENG

Eleutherococcus

SIBERIAN GINSENG

Rhodiola rosea

ARCTIC ROSE

Withania somnifera

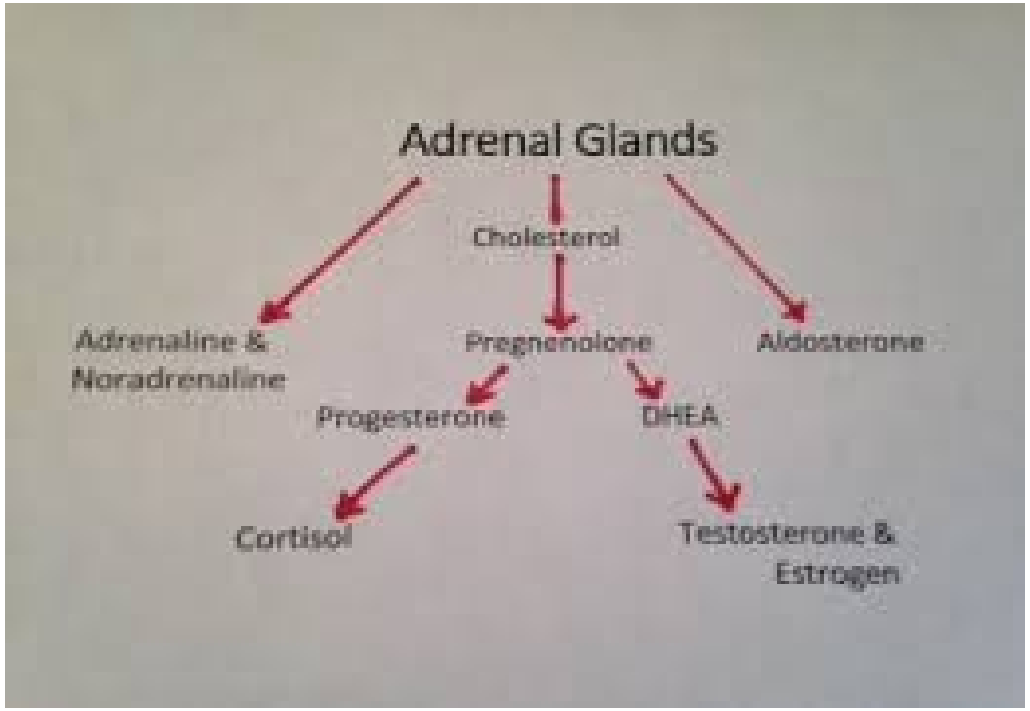
ASHWAGHANDA

Ocimum sanctum

HOLY BASIL

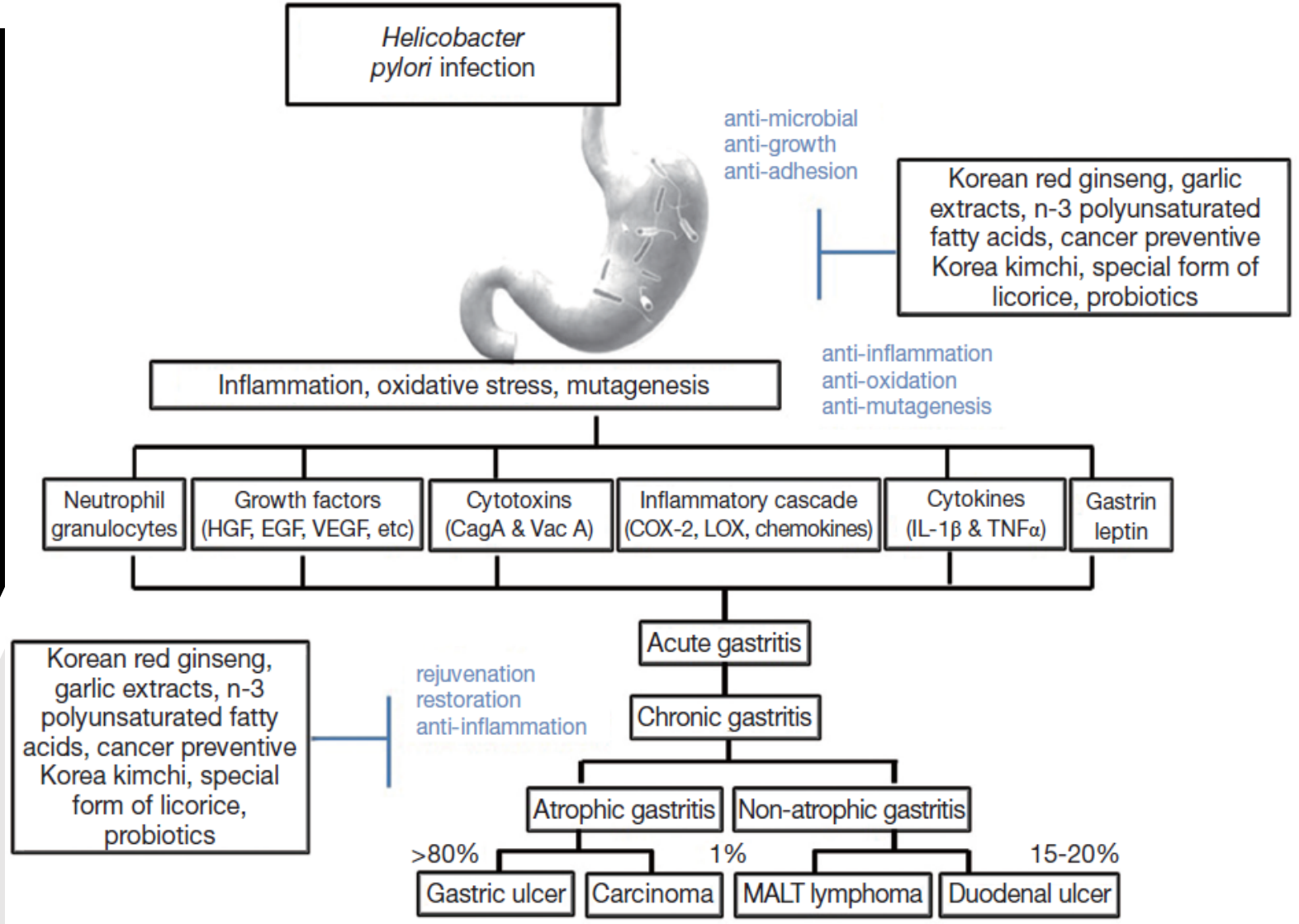
INDICATIONS FOR ADAPTOGENS AND LICORICE

Subtle signs of adrenal weakness, or blunting of the HPA axis include easy fatigue, poor stamina, poor memory, depression, irritability, and frequent infections – the same set up symptoms that indicate the need for adaptogenic herbs



LICORICE
Glycyrrhiza glabra

- Licorice supports adrenal function and hormone balance
- Licorice is especially indicated for H. pylori and enteric infections.



LICORICE FOR INFECTIONS

Glycyrrhiza glabra

A multi-purpose herb with adaptogenic effects on the HPA Axis.

Anti-Viral
Immune Modulator
Anti-Ulcer
Anti-Inflammatory

LICORICE and CORTISOL RESEARCH

Licorice supports adrenal function, in part, by effecting cortisol metabolizing dehydrogenase enzymes.

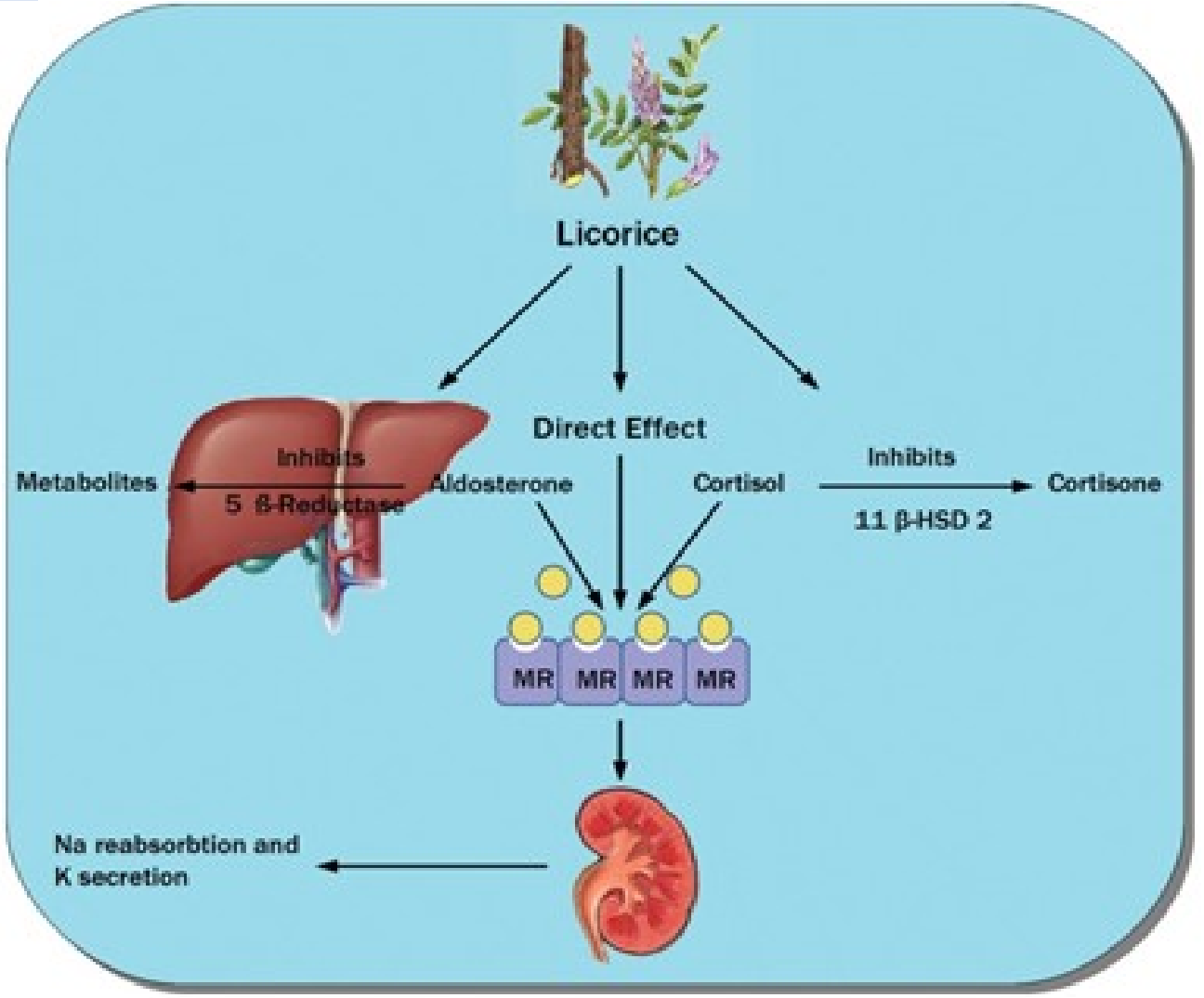
Licorice increases blood levels of cortisol and decreases urinary cortisol excretion in both animal and human studies.

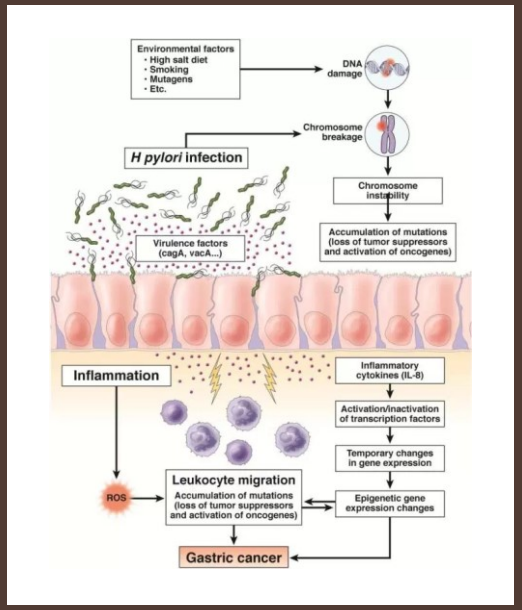
J Hypertens. 2000 Mar;18(3):241-8. *The role of the 11beta-hydroxysteroid dehydrogenase type 2 in human hypertension.* Ferrari P1, Lovati E, Frey FJ.

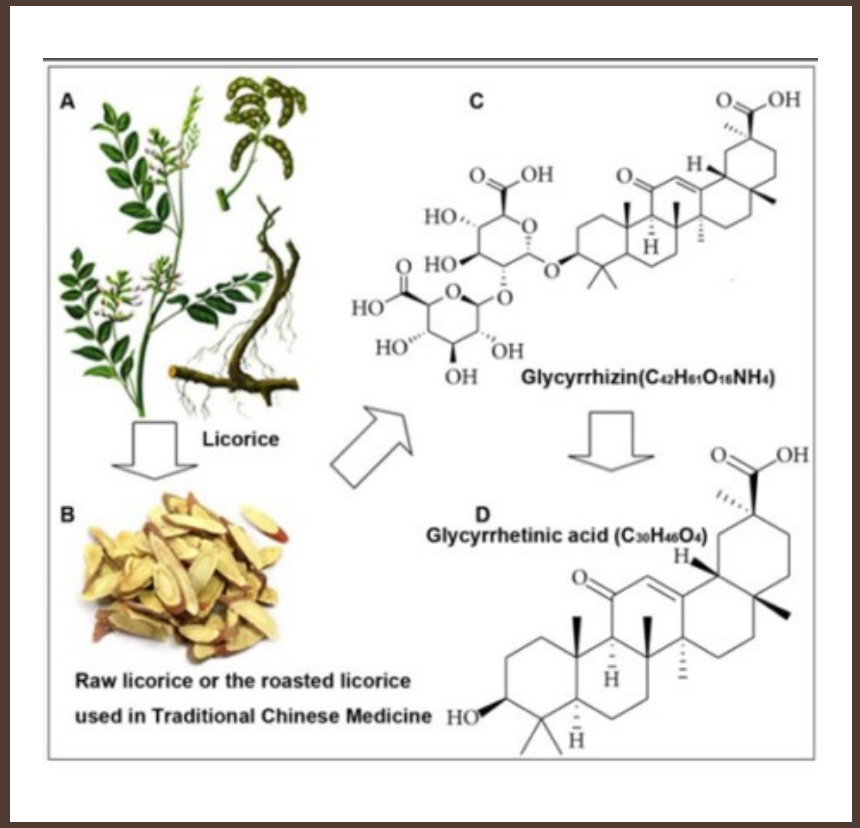
LICORICE CORTISOL RESEARCH

- **Blunting of responsiveness to glucocorticoids and the circadian rhythm of cortisol and DHEA occurs in various diseases, as well as in general aging.**

- **Weakness in the HPA axis amplifies age-related changes in the neuroendocrine system.**







LICORICE CONTAINS STEROID-LIKE MOLECULES – SUCH AS GLYCYRRHIZIN

LICORICE GLYCYRRZINATES

Doses of 500 mg or less of glycyrrhetinic acid inhibit dehydrogenase enzymes only transiently, while 1000 and 1550 mg may cause long lasting cortisone-like effects.

Glycyrrhizinates may also reduce new releases of cortisol by inhibiting conjugation of metabolic precursors, deoxycorticosterone and dehydroepiandrosterone, in the adrenal gland.

J Clin Endocrinol Metab. 1994 Mar;78(3):581-5. *Kinetics and dynamics of orally administered 18 beta-glycyrrhetinic acid in humans.* Krähenbühl S1, Hasler F, Frey BM, Frey FJ, Brenneisen R, Krapf R.
Mol Cell Endocrinol. 2011 Apr 10;336(1-2):102-9. *Liquorice and glycyrrhetinic acid increase DHEA and deoxycorticosterone levels in vivo and in vitro by inhibiting adrenal SULT2A1 activity*. Al-Dujaili EA1, Kenyon CJ, Nicol MR, Mason JI.

ADAPTOGENIC AND AMPHOTERIC EFFECTS OF LICORICE

These polar effects of raising serum cortisol in Addison's patients and lowering it in other populations is evidence of the ability of licorice's adaptogenic action.

Licorice may normalize HPA axis and optimize cortisol regardless of where the baseline cortisol lies – deficient or excess.

LICORICE CORTISOL RESEARCH

A small pilot study showed serum cortisol levels in Addison's disease patients on prescription cortisone acetate to increase when licorice is added, and cortisol delivery to all tissues improves.

Herbs with Anti-Microbial Effects Via Mitochondrial Membrane Disruption

- **Glabridin is a polyphenolic flavonoid found *Glycyrrhiza glabra* roots.**
- **It has been shown to be active against the malaria-causing plasmodium organism via affects on its mitochondrial membrane.**

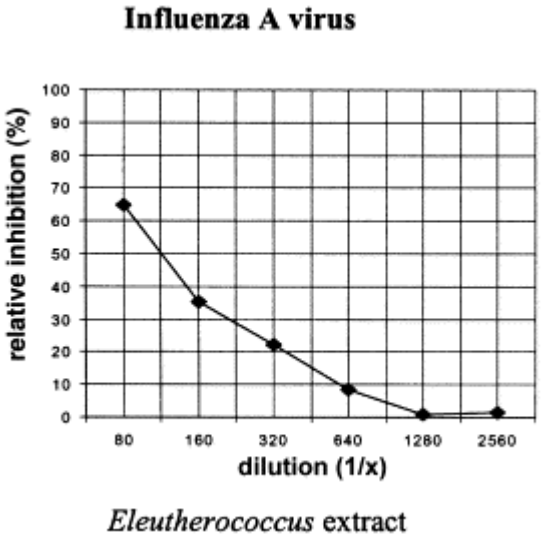
Eleutherococcus senticosis
Siberian Ginseng

- **Eleutherococcus is one of the northern hemisphere's primary adaptogens that has been researched for many decades.**

- **Listed in the USP as early as the 1800s for fatigue, stress, and infections**

Eleutherococcus Traditional Uses

- *Eleutherococcus senticosus*, Siberian Ginseng or Eleuthero.
- The plant is known as Shigoka in Japan and Ciwujia in China where is has been widely used to invigorate qi/chi, meaning general energy and vitality.



ELEUTHEROCOCCUS

Traditional uses emphasis Eleuthero for fatigue, poor stamina and stress intolerance.

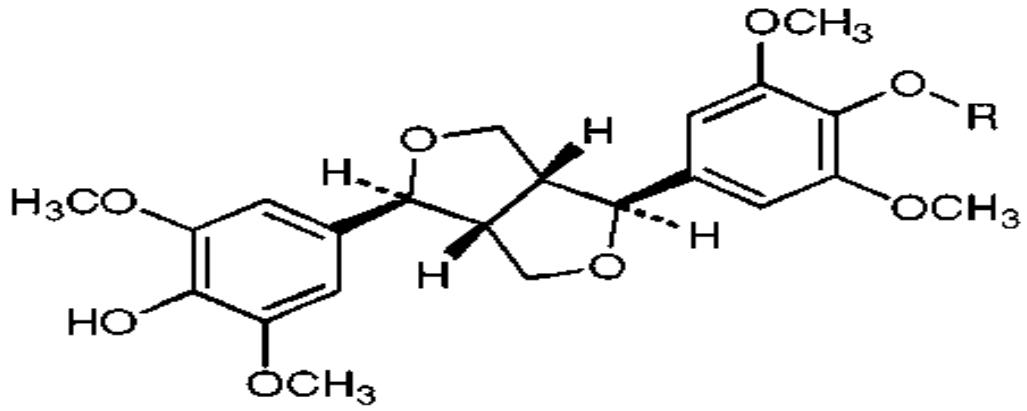
Eleuthero is also used for nervous and mood disorders such as depression, mental fatigue, and poor concentration.

Eleuthero is helpful to treat chronic and acute infections, improve immune function, protect against toxins including hepatotoxins, neurotoxins, and cerebral vascular inflammation.

Eleuthero may improve cardiovascular inflammation, treat ischemic disorders, hypertension, and hepatitis.

ELEUTHERO

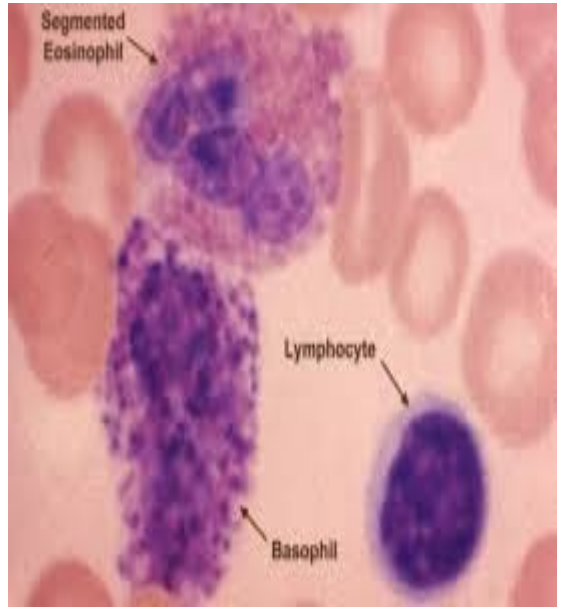
Eleuthero has fairly extensive molecular, animal and human research demonstrating anti-stress, antiulcer, anticancer, anti-oxidant, and anti-inflammatory activity.



Int J Biol Macromol 2013 Aug;59:290-4. *Ultrasound extraction optimization of Acanthopanax senticosus polysaccharides and its antioxidant activity.* Zhao Z1, Xu X, Ye Q, Dong L.

Toxicol In Vitro. 2007 Dec;21(8):1530-7. *(+)-Syringaresinol-di-O-beta-D-glucoside, a phenolic compound from Acanthopanax senticosus Harms, suppresses proinflammatory mediators in SW982 human synovial sarcoma cells by inhibiting activating protein-1 and/or nuclear factor-kappaB activities.* Yamazaki T1,

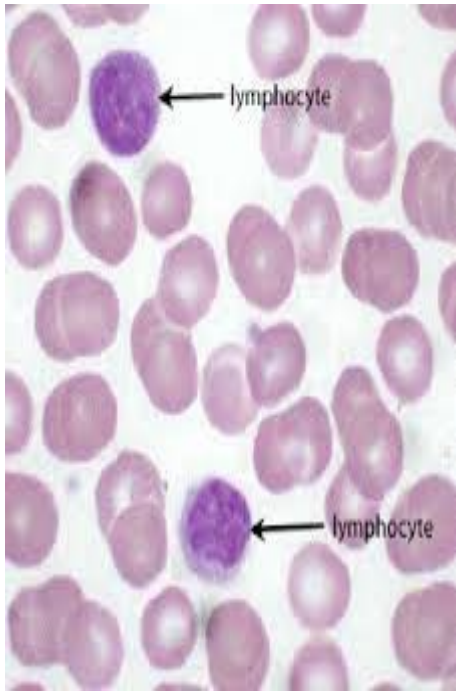
ELEUTHERO & IMMUNE MODULATION



Eleuthero **improves basic immune status and has immune modulating effects.**

A human placebo controlled study evaluated the effects of 10 ml of *Eleuthero* tincture 3 times a day for 4 weeks on immune parameters in healthy subjects.

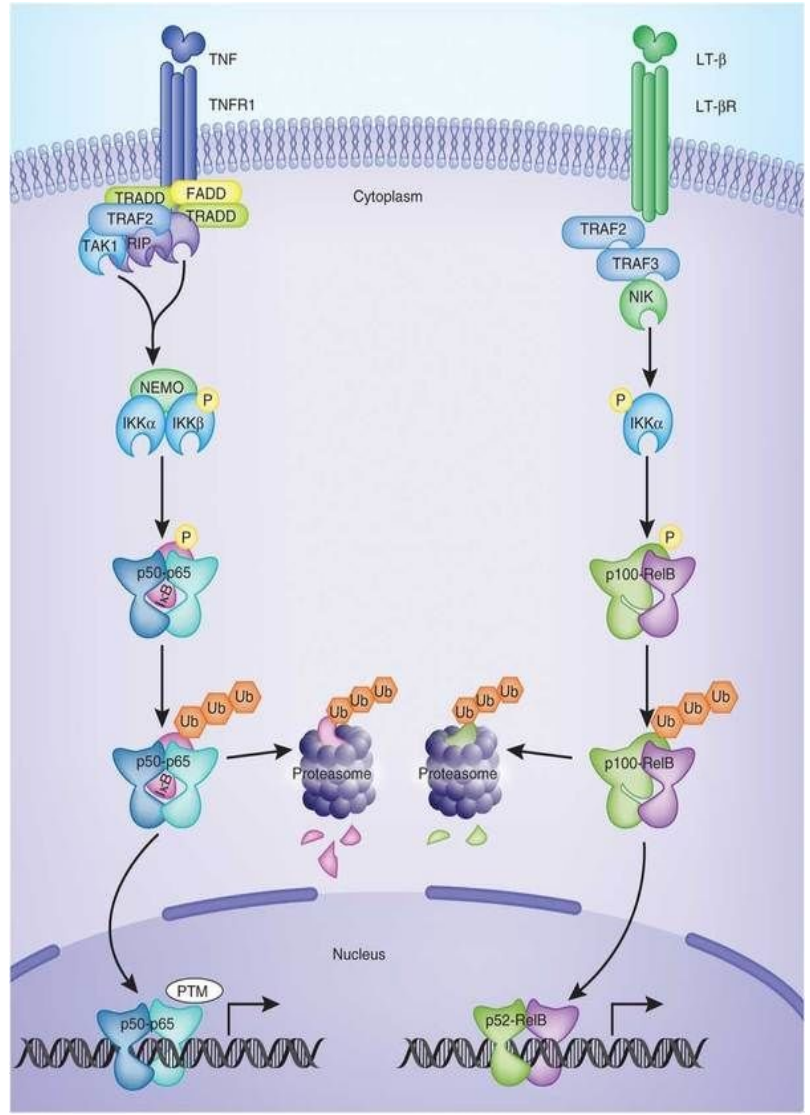
Eleuthero **significantly increased the number of immune competent cells, particularly T Helper lymphocytes, as well as cytotoxic and natural killer cells.**



Arzneimittelforschung. 1987 Oct;37(10):1193-6. *Flow-cytometric studies with eleutherococcus senticosus extract as an immunomodulatory agent*. Bohn B1, Nebe CT, Birr C.

ELEUTHERO & IMMUNOPROTECTION

Animal studies show Eleuthero to restore macrophage and B and T lymphocyte levels when suppressed due to cadmium toxicity, enhance survival following parathion exposure, and protect animals from endotoxic shock, reducing production of inflammatory mediators, NF-kappaB activation, preventing the infiltration of inflammatory cells into the heart, liver and lung.



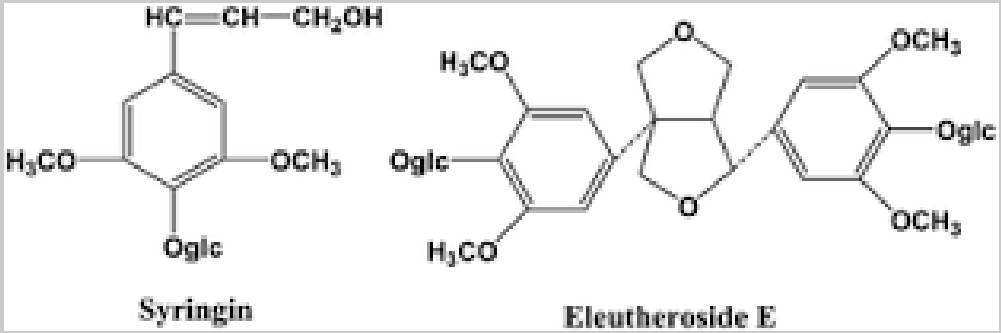
J Toxicol Environ Health A. 2014;77(21):1311-8. *Effect of Acanthopanax senticosus on the accumulation of cadmium and on the immune response of spleen cells.* Smalinskiene A1, Savickiene N, Zitkevicius V, Pangonyte D, Sadauskiene I, Kasauskas A, Ivanov L, Lesauskaite V, Savickas A, Rodovičius H
Zhongguo Yao Li Xue Bao. 1984 Dec;5(4):278-81. *Effect of aqueous extracts of Acanthopanax senticosus on parathion toxicity in mice*. Ferguson PW, Medon PJ, Watson CF.
J Ethnopharmacol. 2008 Aug 13;118(3):495-502. *Protective effect of Acanthopanax senticosus extract against endotoxic shock in mice.* Lin QY1, Jin LJ, Cao ZH, Li HQ, Xu YP.

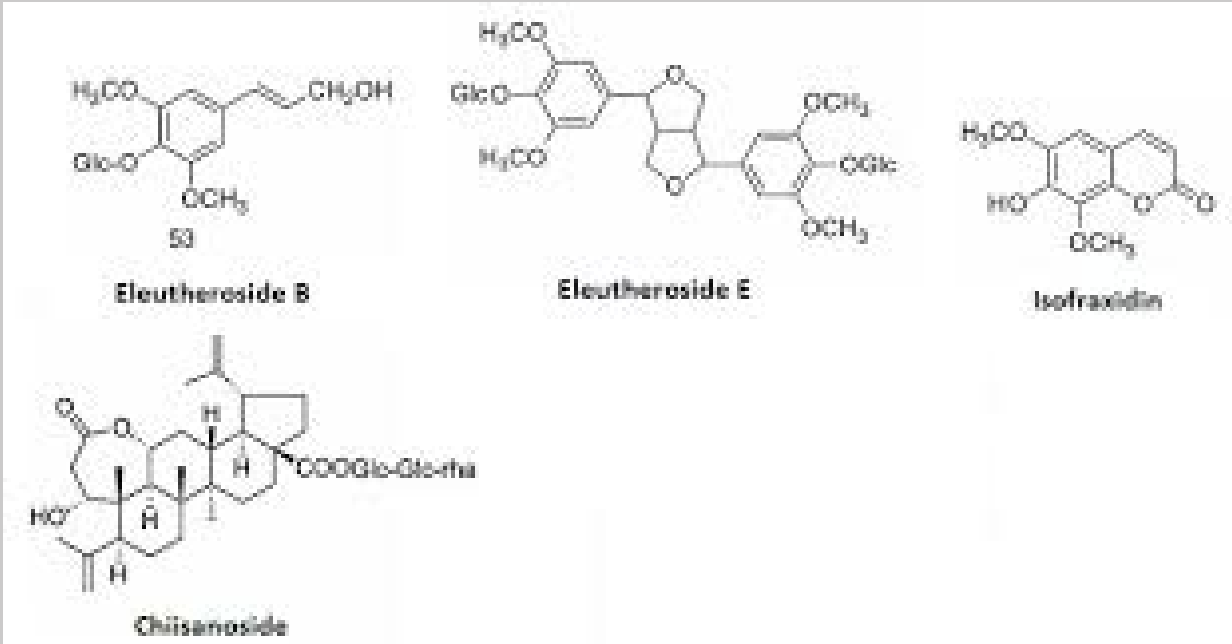
ELEUTHERO MECHANISMS

Eleuthero's medicinal actions are credited to the Eleutherosides, a group of phenylpropanoid and lignin glycosides in the roots and stems, including syringin (eleutheroside B) and syringaresinol (eleutheroside E), schisandrin and sesamin.

Appl Microbiol Biotechnol. 2014 Sep;98(17):7319-29. *Bio-technological production of eleutherosides: current state and perspectives.* Murthy HN1, et al.

Nat Prod Res. 2010 Oct;24 (16):1523-7. *A new 3,4-seco-lupane-type triterpenoid from the pulp of Acanthopanax senticosus (Rupr. et Maxim) Harms.* Yan ZW1, et al

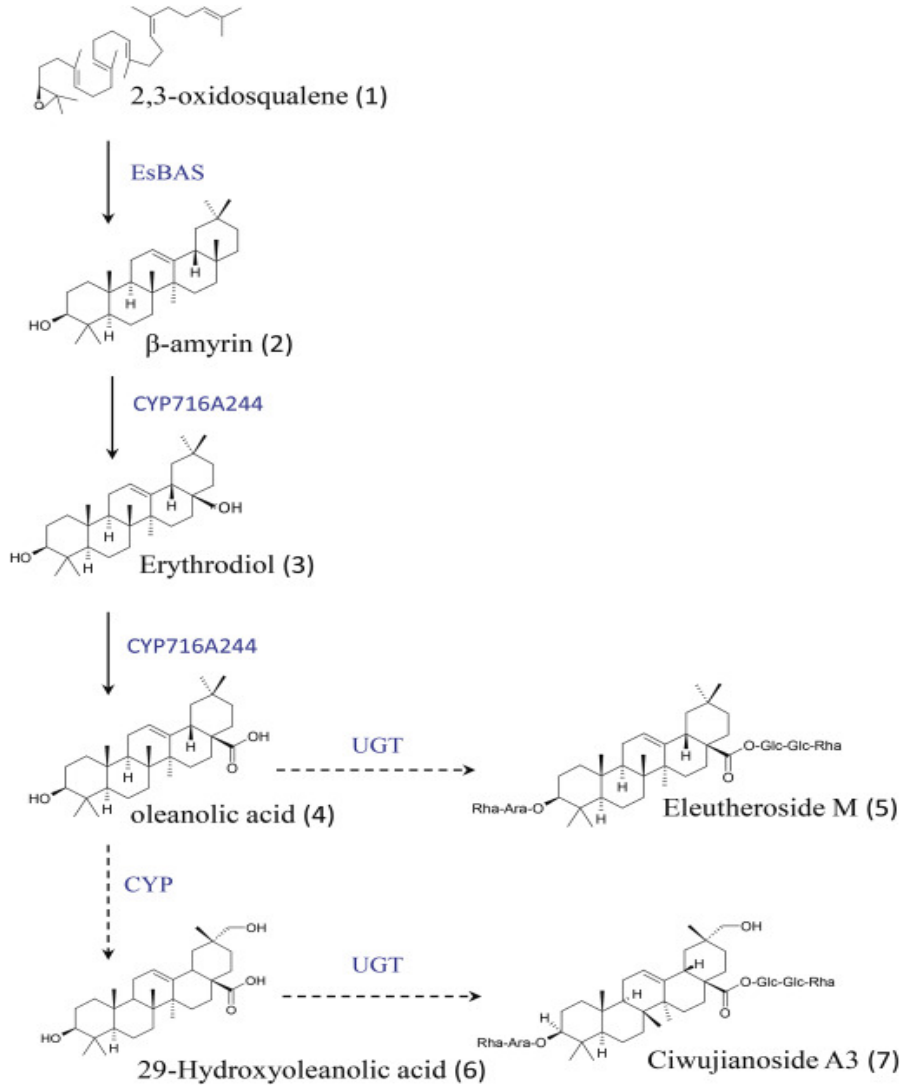




ELEUTHERO CONSTITUENTS

Ciwujianosides are mast cell stabilizers, reducing histamine release provoked by immunoglobulins.
One study reported the anti-histamine effects to be approximately 6800 times stronger than that of disodium cromoglycate at a similar dosage.

J Pharm Sci. 1992 Jul;81(7):661-2.*Ciwujianosides D1 and C1: powerful inhibitors of histamine release induced by anti-immunoglobulin E from rat peritoneal mast cells.*
Umeyama A1, Shoji N, Takei M, Endo K, Arihara S.

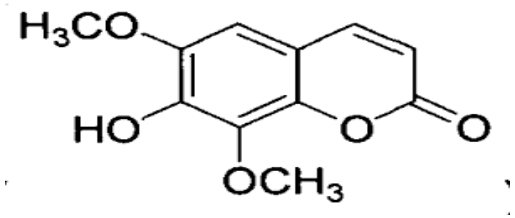


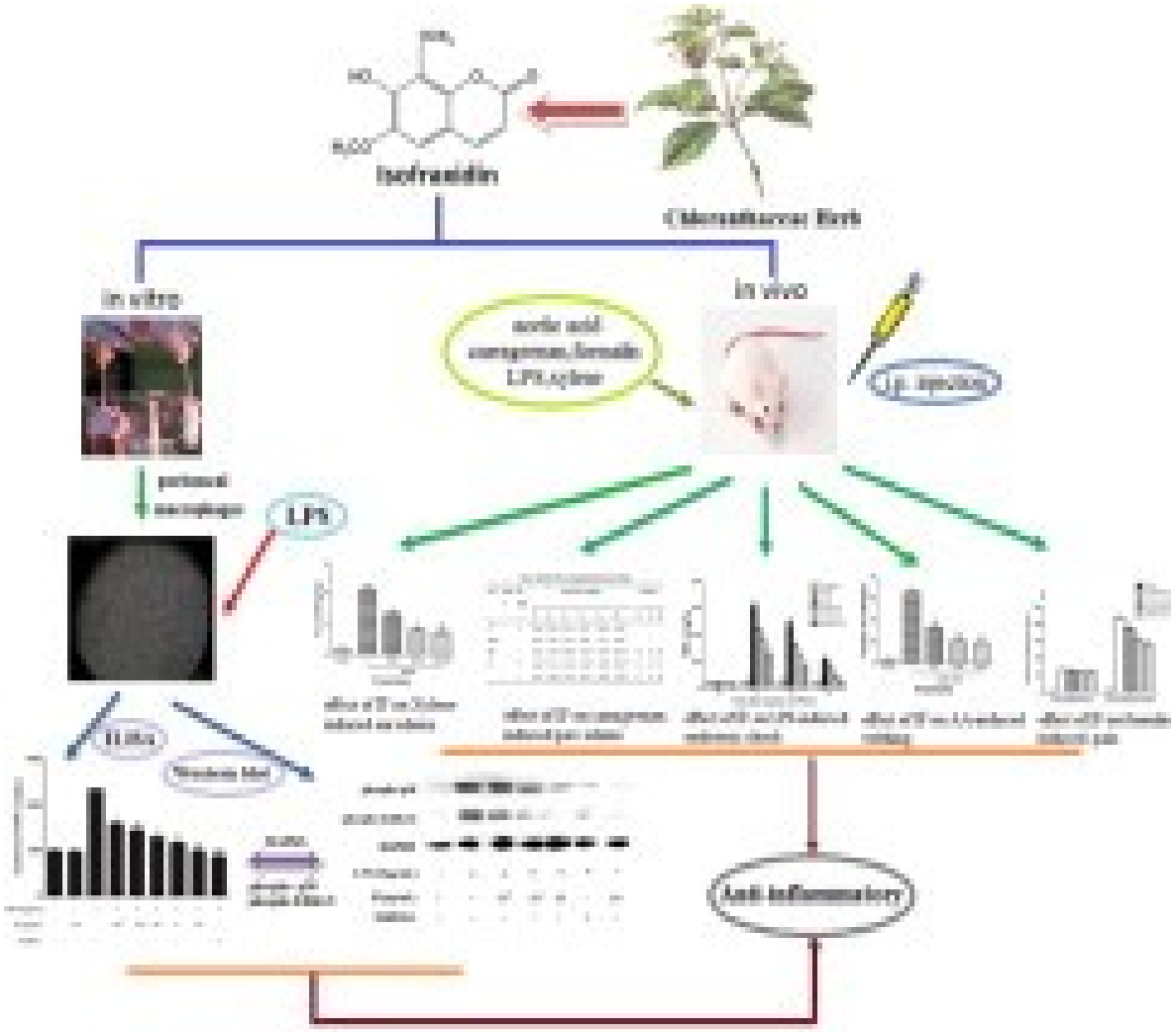
ELEUTHERO CONSTITUENTS

Eleuthero also contains coumarins including isofraxidin, and flavones.

The coumarin, isofraxidin is credited with anti-oxidant, anti-inflammatory activities, and immune modulating actions.

Isofraxidin inhibits cyclooxygenase expression in the lungs which regulates the production of prostaglandins, and inhibits NF Kappa B pathways offering tissue protective effects.





ELEUTHERO'S IMMUNE POLYSACCHARIDES

Eleuthero also contains immune polysaccharides with significant immuno-stimulatory activities as demonstrated by granulocyte and carbon clearance tests, and may help protect against other pathogens and toxins.

One mouse investigation showed the polysaccharide fraction to suppress tuberculosis from propagating the lungs.

Another animal study showed the polysaccharides to inhibit tumor growth.

Arzneimittelforschung. 1985;35(7):1069-75.*Immunostimulating action of polysaccharides (heteroglycans) from higher plants*.Wagner H, Proksch A, Riess-Maurer I, Vollmar A, Odenthal S, Stuppner H, Jurcic K, Le Turdu M, Fang JN.
Int J Immunopharmacol. 1991;13(5):549-54. *Immunomopharmacological effects of polysaccharides from Acanthopanax senticosus on experimental animals.* Shen ML1, Zhai SK, Chen HL, Luo YD, Tu GR, Ou DW.
Zhonghua Zhong Liu Za Zhi. 1989 Sep;11(5):338-40. *Immunoregulatory effect of polysaccharide of Acanthopanax senticosus (PAS). I. Immunological mechanism of PAS against cancer].* Xie SS1.

ELEUTHERO DOSAGE & DELIVERY

Traditional medicines include teas, syrups, and powders at a wide variety of dosages depending on whether Eleuthero is a lead or supportive herb in various formulas. Encapsulations and Solid Extracts also available in the modern era.

Treatment Dosage: Modern encapsulations will use 250 to 1000 mg in a single dose that is repeated several times a day.

1:1 to 1:4 Tinctures are dispensed at a dose of ½ to 1 tsp 2 to 4 times daily.

ELEUTHERO SIDE EFFECTS

Side effects:

There are no commonly reported side effects.

Human trials have not shown adverse events or significant side effects with the use of 300 mg/day for several months' time.

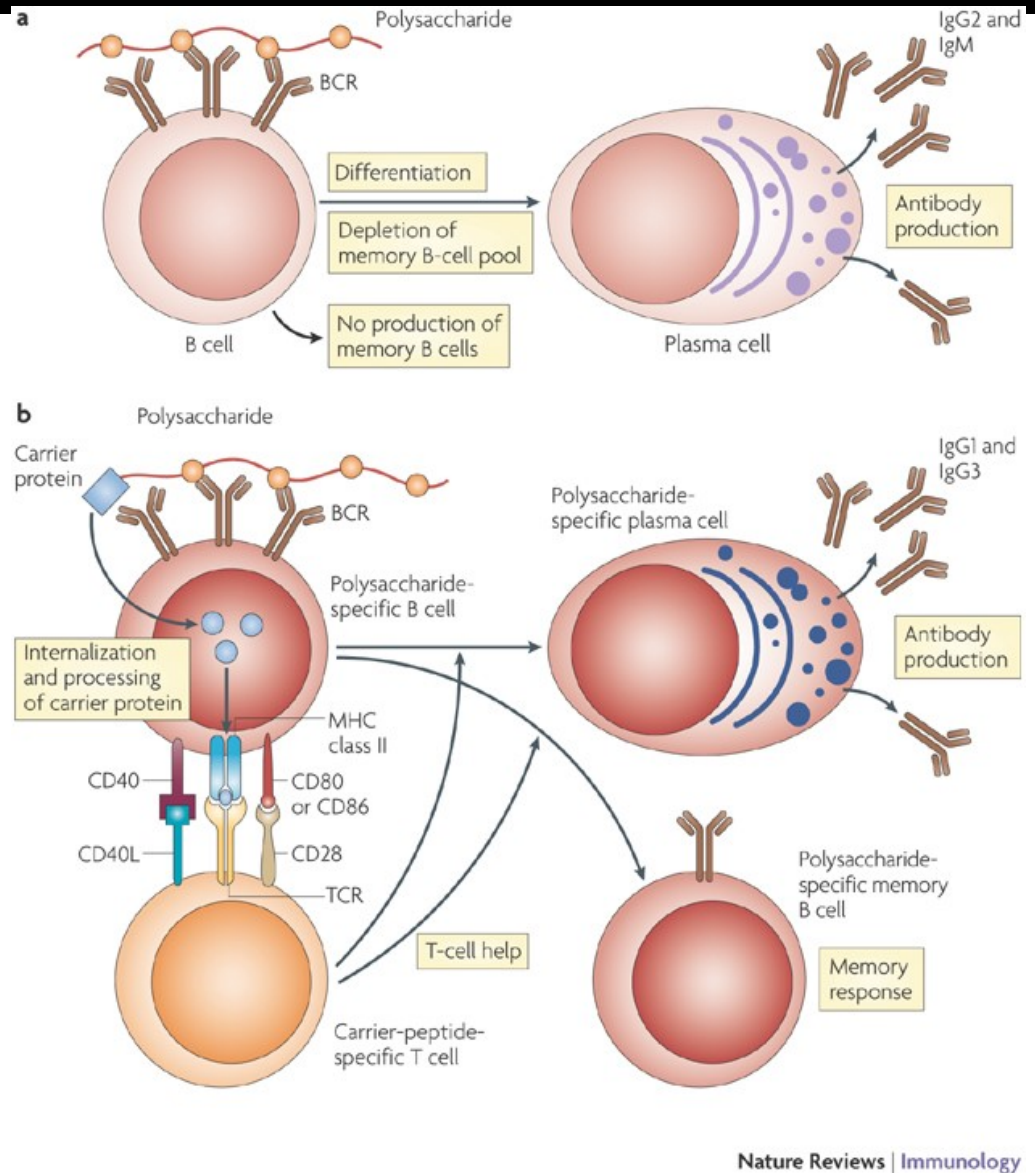
Arch Gerontol Geriatr Suppl. 2004;(9):69-73. *Effects of Siberian ginseng (Eleutherococcus senticosus maxim.) on elderly quality of life: a randomized clinical trial.* Cicero AF et al.

Arzneimittelforschung. 1987 Oct;37(10):1193-6. *Flow-cytometric studies with eleutherococcus senticosus extract as an immunomodulatory agent*. Bohn B, et al

IMMUNE POLYSACCHARIDES

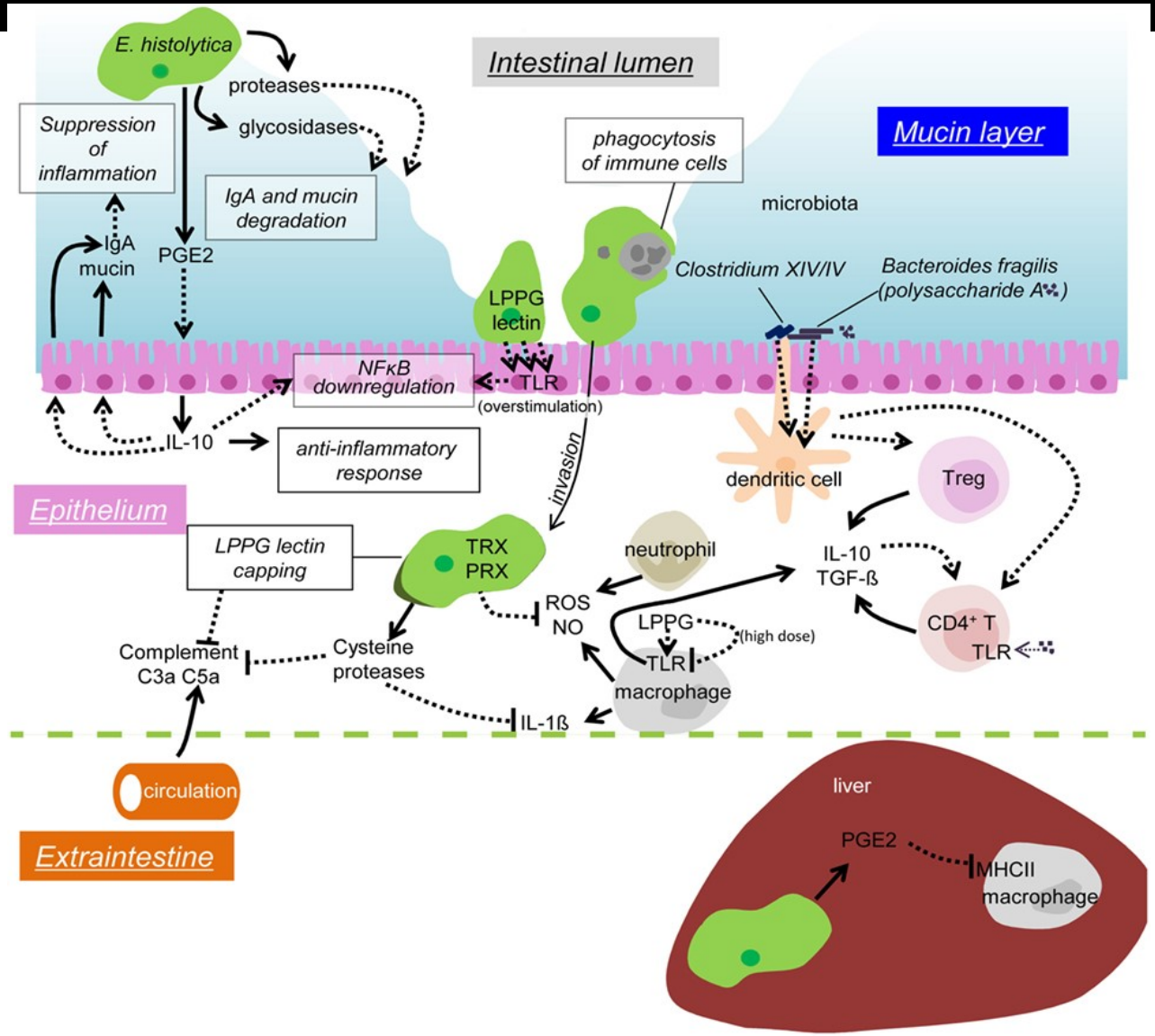
IMMUNE POLYSACCARHIDES

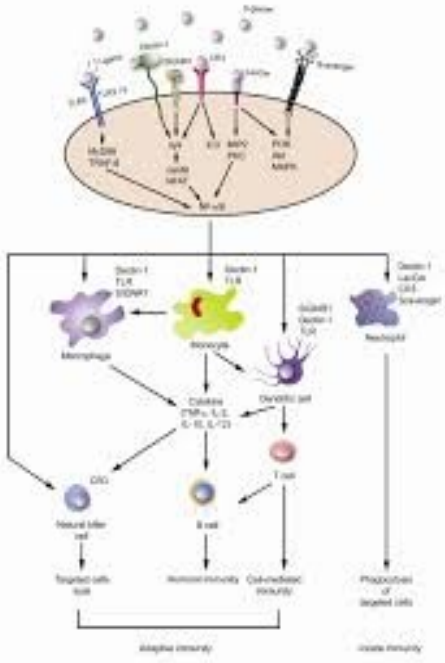
- **"Immune Polysaccarides" are large molecules known to enhance immune responses.**
- **One mechanism may be via local effects in the gut that triggers immune response via the carbohydrate aspect of the cytoskeleton.**



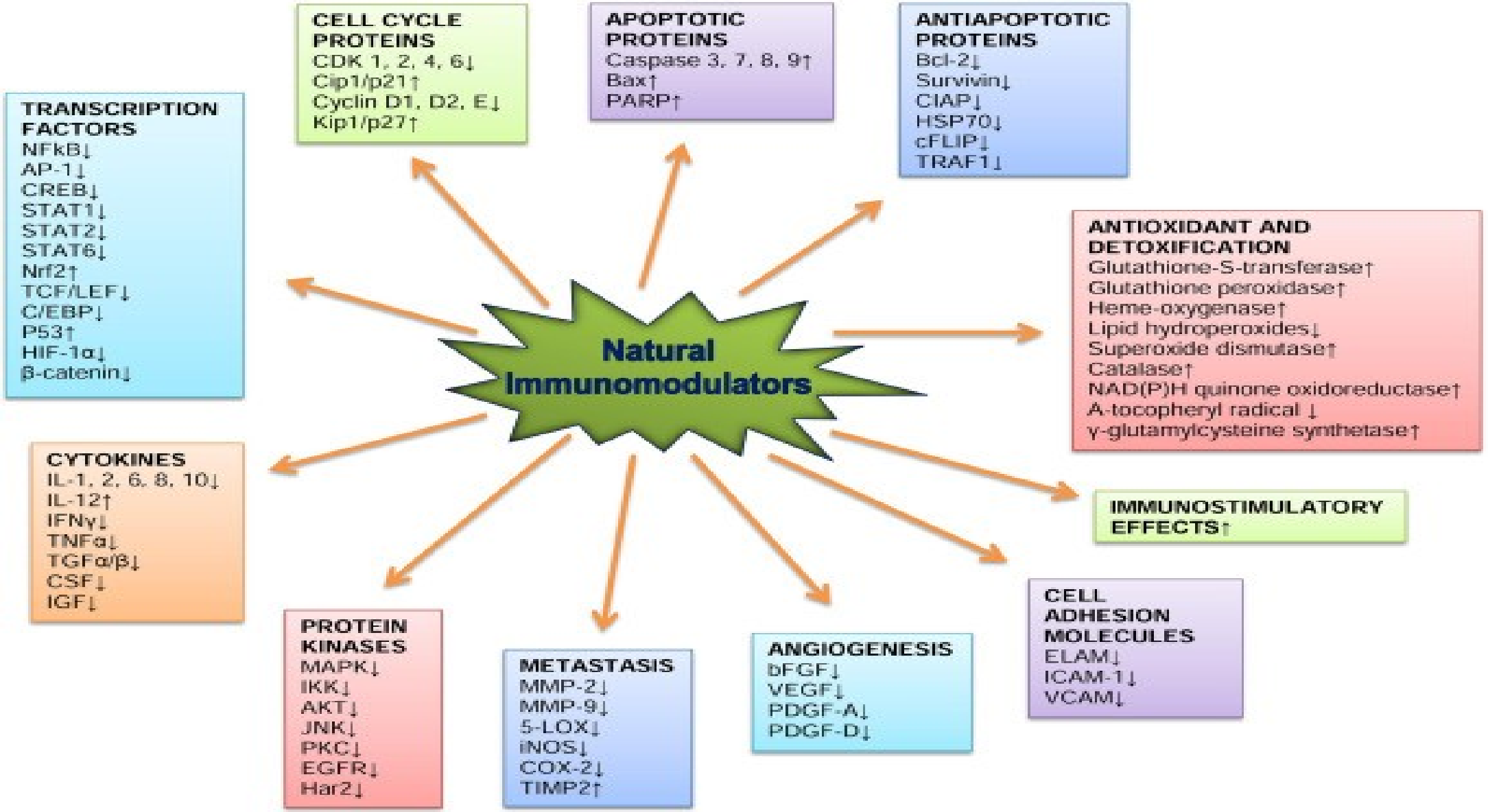
HERBS WITH IMMUNE POLYSACCARHIDES

- Echinacea
- Astragalus
- Glycyrrhiza
- Ganoderma
- Lentinula
- Baptisia
- Seaweed
- Panax ginseng
- Aloe vera





VARIED EFFECTS OF IMMUNE MODULATORS



MEDICINAL MUSHROOMS FOR CHRONIC INFECTIONS

MUSHROOMS CONTAIN IMMUNE POLYSACCHARIDES

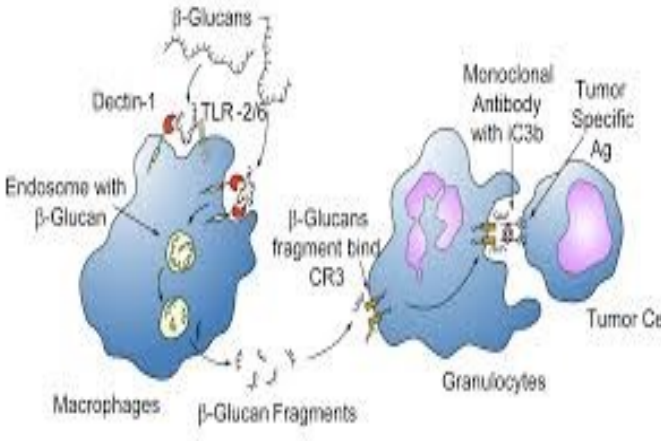
REISHI MUSHROOM

- **The Reishi mushroom, *Ganoderma lucidum* contains Immune Polysaccharides**
- **One Prime Area of Reishi Research Involves its Effects on the HPA Axis.**

BETA GLUCAN

Many medicinal mushrooms may contain beta glucans.

Polyporus umbellatus contains beta glucans shown to be a potent activator of B cells, macrophages and dendritic cells.

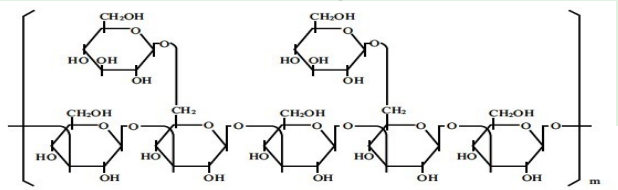


The Five Key Immune Responses Targeted By Beta Glucan

1. Production of white blood cells
2. Cellular mobilization
3. Phagocytic capacity
4. Production of reactive oxygen intermediates
5. Help shift from an overstimulated TH2 to a TH1 cell mediated immune response.

BETA GLUCANS

Shitake mushrooms, *Lentinus edodes* also contains the beta glucan lentinan thought to contribute the immune potentiating properties of this



THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 286, NO. 36, pp. 31194–31198, September 9, 2011

Immunomodulatory β-Glucan from *Lentinus edodes* Activates Mitogen-activated Protein Kinases and Nuclear Factor-κB in Murine RAW 264.7 Macrophages*

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Lentinan, a cell wall β-glucan from the fruiting bodies of *Lentinus edodes*, is well known to be a biological defense modifier, but the signal transduction pathway(s) induced by Lentinan have not been elucidated. In this study, we extracted Lentinan (LNT-S) by ultrasonication from *Lentinus edodes* and report that, in murine RAW 264.7 macrophages, LNT-S glucan activated NF-κB p65 and triggered its nuclear translocation as determined by Western blotting. Moreover, LNT-S enhanced NF-κB-luciferase activity in the Dual-Luciferase gene system assay. Its upstream signaling molecules, MAPKs such as ERK1/2 and JNK1/2, were shown to be activated by assessing the level of phosphorylation in a time- and concentration-dependent manner, but its downstream proinflammatory enzyme, inducible NOS, was not observed. The data evaluated using a TNF-α ELISA kit and Griess reagent further demonstrated that no proinflammatory mediators such as TNF-α and NO were produced by LNT-S stimulation in RAW 264.7 cells. In contrast, LPS significantly induced inducible NOS expression and increased NO and TNF-α production, which are associated with activation of the NF-κB p65/p50 heterodimer complex. It is possible that LNT-S did not activate NF-κB p65/p50, and the activation of NF-κB p65 was not sufficient to stimulate cytokine production. These data demonstrate that LNT-S glucan carries out its immunomodulating activity by activating MAPK signaling pathways without secretion of TNF-α and NO.

β-Glucans are known to possess significant biological and physiological activities, including antitumor activity (1, 2), antiviral activity (3, 4), antibacterial activity (5–7), antifungal activity (8), and immunomodulating activity (9–12). In addition, β-glucans are effective in wound healing (3) and in lowering blood cholesterol (13) and glucose (14) concentrations. Therefore, β-glucan is a promising product in biochemical and medical applications.

Among the numerous β-glucans derived from different sources such as plants, animals, and microbials, Lentinan from *Lentinus edodes* is especially remarkable for its anticancer and immunomodulating activities (15–17) and is a β-(1,3)-glucan with one β-(1,6)-glucose branch every five glucose residues. Lentinan is currently used clinically as an antitumor agent (18, 19). It has been shown to stimulate natural killer cell activity (20–22), macrophage/monocyte functions (secreting IL-1 and superoxide anion), phagocytosis, and cytotoxicity (23–28). Lentinan was found to elevate the cytotoxic activity and TNF secretion of macrophages *in vitro* and *in vivo* (16, 29). Pretreatment of bone marrow macrophages with Lentinan results in increased production of NO *in vitro* (16). However, Masihi *et al.* (30) demonstrated that pretreatment of Lentinan before LPS administration induces a striking inhibition of up to 89% of circulating TNF-α in bacillus Calmette-Guérin-primed mice. It is possible that the different immunomodulatory reaction was highly dependent on the genotype of the host. To our knowledge, most of the research has focused on secretion of proinflammatory cytokines or mediators such as TNF-α, IL-12, IFN-γ, and NO and on inflammatory mRNA expression from Lentinan-stimulated macrophages or monocytes (16, 29–31), and there have been few studies involved in the signal transduction for macrophage activation by Lentinan. In contrast, the signal transduction of β-glucans, in particular water-insoluble zymosan or yeast glucan from *Saccharomyces cerevisiae* as a model of immunomodulatory glucans, has been partly elucidated (32, 33). It has been reported that, after activation of receptor dectin-1 by zymosan, spleen tyrosine kinase (Syk) is recruited and induces the assembly of a scaffold consisting of the Card9 (caspase recruitment domain 9) protein and the adaptor proteins Bcl10 and Malt1; the Card9-Bcl10-Malt1 scaffold then couples dectin-1 to the canonical NF-κB pathway by activation of the IκB kinase complex, leading to nuclear translocation of NF-κB subunit p65 (32). Yan and co-workers have demonstrated that yeast glucan particles amplify phagocyte killing of iC3b-opsonized tumor cells via the complement receptor 3-Syk-PI3K pathway (33) and activate murine resident macrophages to secrete proinflammatory cytokines, including TNF-α, MCP-1 (monocyte chemotactic protein-1), and IL-6, through MyD88- and Syk-dependent pathways (34). Therefore, in this study, we explored activation of RAW 264.7 macrophages induced by Lentinan to clarify the signal transduction pathways used by Lentinan.

EXPERIMENTAL PROCEDURES

Sample Preparation—The dried fruiting bodies of *L. edodes*, a commercial product cultivated in the Fujian Province of

* This work was supported by Japan Society for the Promotion of Science Postdoctoral Fellowship 20.08431 (to X. X.), National Natural Science Foundation Grant 20874078, and Youth Technology Chenguang Project of Wuhan 200950431193.

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BETA GLUCANS

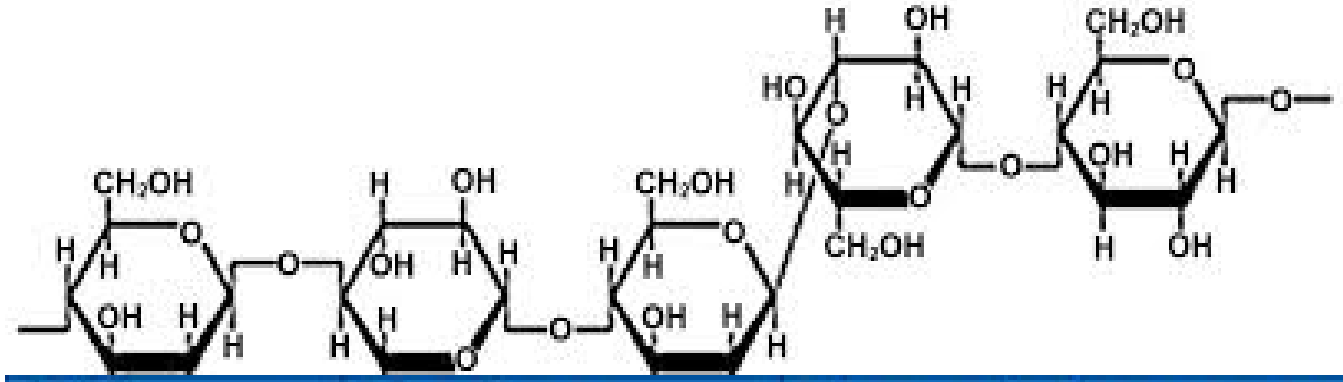
- Glucans are natural occurring plant carbohydrates that stimulate immunity.
- Glucans are taken into cells such as macrophages due to the pattern recognition receptor, Dectin-1.
- Once taken up glucans colocalize with endosomes within minutes, and in the golgi appartus in minutes to hours.
- Clathrins support the uptake of Glucans, and caveolin inhibit uptake.

BETA GLUCANS

Beta glucans contribute greatly to water holding properties in plants and have many anti-cancer and immunomodulating effects, and anti-inflammatory effects on the GI.

Beta glucans may help lower cholesterol.

Beta glucans also occur in brewer's yeast, *Saccharomyces cerevisiae*, contributing to immune-modulating effects.



Origin	Beta glucan	Effect on the immune system
Brewer's yeast (Baker's yeast)	Long 1,3/1,6 branches	★★★★★
Mushroom, fungus, seaweed	Short 1,3/1,6 branches	★★★
Barley, oat	1,3/1,4 branches	★
Bacteria	1,3 (no branches)	—

SULFATED POLYSACCARHIDES IN SEAWEEDS

- Seaweeds are some of the richest sources of sulfated polysaccharides.
- Sulfated glycans may interact with cellular polysaccharides in a manner that enhances immune response.

Mar. Drugs **2011**, *9*, 2605-2621; doi:10.3390/md9122605

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Article

Fucose-Containing Sulfated Polysaccharides from Brown Seaweeds Inhibit Proliferation of Melanoma Cells and Induce Apoptosis by Activation of Caspase-3 *in Vitro*

Marcel Tutor Ale [1], Hiroko Maruyama [2], Hidekazu Tamauchi [3], Jørn D. Mikkelsen [1] and Anne S. Meyer [1,*]

[1] Center for Bioprocess Engineering, Department of Chemical and Biochemical Engineering,

Fucose-Containing Sulfated Polysaccharides from Brown Seaweeds Inhibit Proliferation of Melanoma Cells and Induce Apoptosis by Activation of Caspase-3 in Vitro

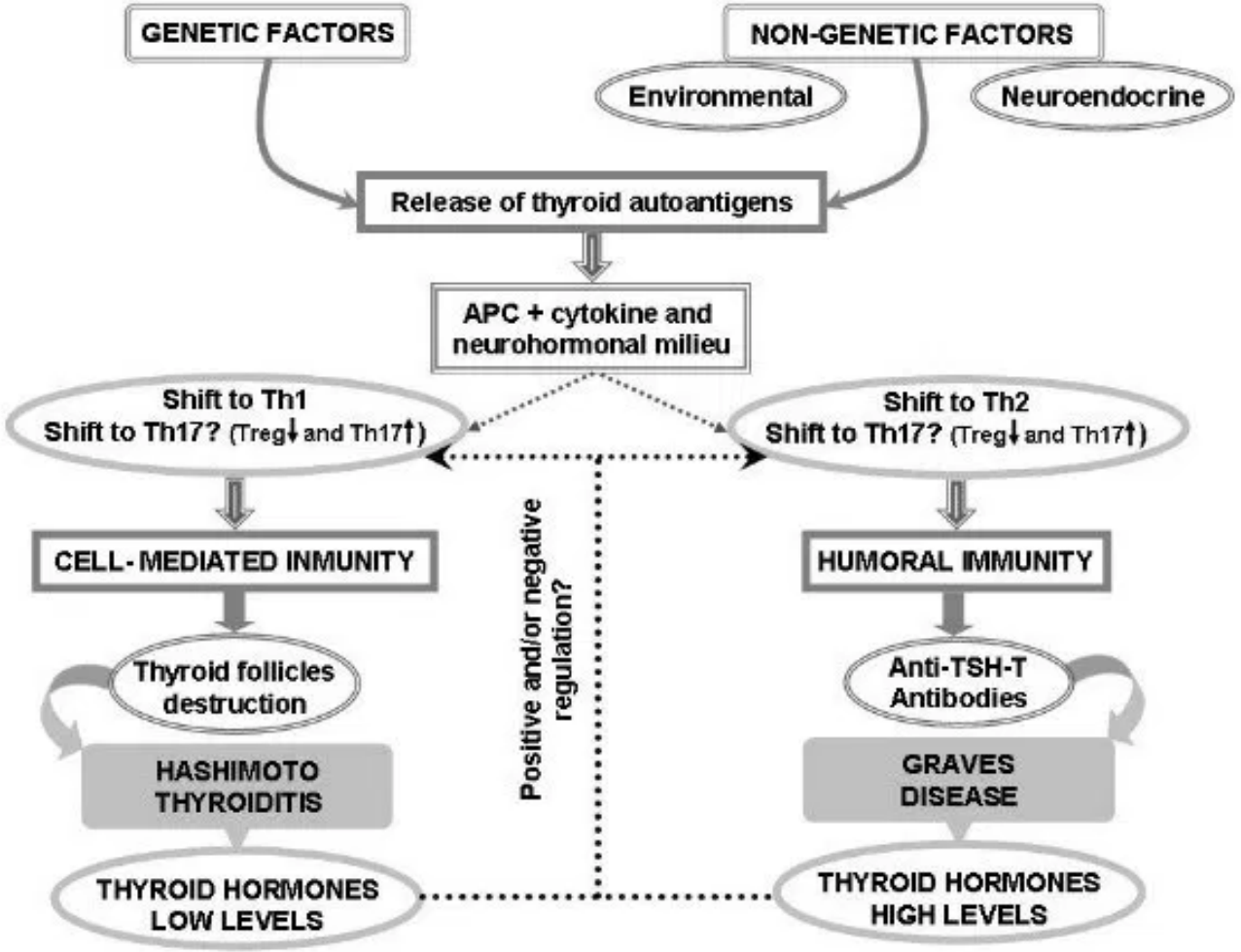
especially brown macro-algae, are known to possess essential bioactive properties, notably growth inhibitory effects on tumor cells. In this work, we conducted a series of *in vitro* studies to examine the influence of FCSPs products from *Sargassum henslowianum* C. Agardh (FSAR) and *Fucus vesiculosus* (FVES), respectively, on proliferation of melanoma B16 cells and to investigate the underlying apoptosis promoting mechanisms. Cell viability analysis showed that both FCSPs products, *i.e.*, FSAR and FVES, decreased the proliferation of the melanoma cells in a dose-response fashion, with FSAR being more potent at lower dosages, and FVES being relatively more anti-proliferative than FSAR at higher dosages. Flow cytometric analysis by Annexin V staining of the melanoma cells exposed to the FCSPs products confirmed that both FSAR and FVES induced apoptosis. The FCSPs-induced apoptosis was evidenced by loss of plasma membrane asymmetry and translocation of the cell membrane phospholipids and was accompanied by the activation of caspase-3. The FCSPs bioactivity is proposed to be attributable to distinct structural features of the FCSPs, particularly the presence of sulfated galactofucans (notably in

THYROID SUPPORT FOR CHRONIC INFECTIOUS ILLNESSES

Thyroid Support for Chronic Infections:

- **Low thyroid increases susceptibility to infections, low body temperature allow opportunistic infections.**
- **High thyroid suppresses WBCs and increases allergic reactivity and infections.**

*** Supporting thyroid function may help those with Lyme dz, intestinal dysbiosis, chronic URIs, and other infections**



OUR UNDERSTANDING OF THYROID HORMONES IS RAPIDLY EVOLVING

- Recent clinical research is advancing our understanding of thyroid hormone signaling defects and syndromes of hormone resistance.
- Mental retardation, obesity, metabolic disorders, and a number of cancers are affected by thyroid hormones.
- Our new understanding is beginning to be translated into therapeutic strategies for treating hyperlipidemia and obesity, cardiac disease, cancer, and cognitive function

Thyroid Hormone Resistance Syndromes

- **Two forms of resistance to thyroid hormones are recognized:**
  - Generalized resistance to thyroid hormones (GRTH)
    - 75% of reported cases are familial
    - mutations in the thyroid hormone receptor
  - Selective pituitary resistance to thyroid hormones (PRTH)
    - mutations in the thyroid hormone receptor

J Clin Invest. 2012 Sep 4;122(9):3035-43. 2012 Sep 4. *Mechanisms of thyroid hormone action*. Brent, GA

SEAWEED FOR HYPOTHRYOIDISM

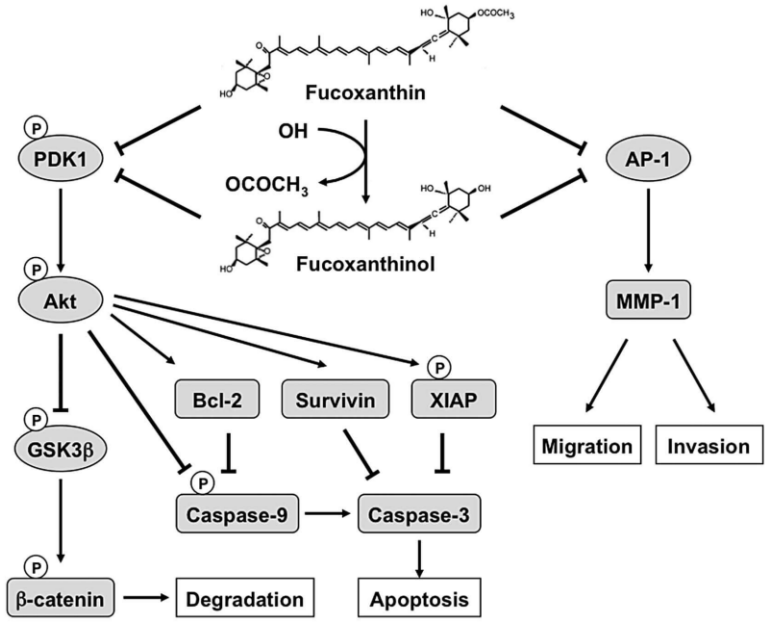
- **Seaweeds are high in numerous highly bioavailable minerals and halides including iodine.**

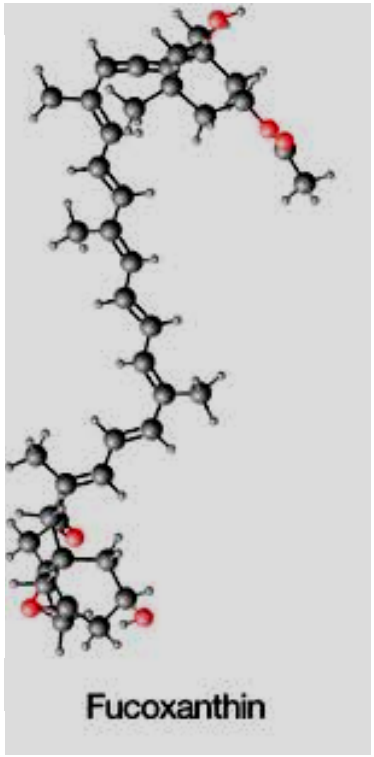
- **Seaweeds also contain sulfated polysaccharides and Beta Glucans with immune modulating and anti-inflammatory affects.**

Cell Mol Biol 2002 Jul;48(5):563-9. *Bioavailability of seaweed iodine in human beings.*

FUCUS VESICULOSUS - Bladderwrack

Fucus vesiculosus **contains the flavonoid fucoxanthin reported to have the greatest antioxidant activity of all the edible seaweeds tested. This may contribute to stabilizing effects in thyroiditis.**





Bioscience, Biotechnology and Biochemistry, 63(3): 605-607 (1999) *Fucoxanthin as the major antioxidant in Hijikia fusiformis, a common edible seaweed.* Yan, X.J., Y. Chuda, M. Suzuki and T. Nagata

Journal of the science of food and agriculture. 81 (5): 530-534. (2001) *Antioxidant activity of fresh and processed edible seaweeds*. Jimenez-Escrig A., I. Jimenez-Jimenez, R. Pulido and F. Saura-Calixto

KELP FORMS AND DELIVERY

Kelp may be consumed as a food, a tincture, and in encapsulations.

The fishy flavor and gummy texture make kelp less suitable to consume as a tea.

There is no officially approved or standardized dosage, however most herbalists recommend 4-6 grams of the crude dried seaweed to treat metabolic function, which would deliver roughly 400 to 500 micrograms of iodine.

HERBS WITH ANTIMICROBIAL EFFECTS

HERBAL ANTIMICROBIAL MECHANISMS

Naturally Occurring Molecules can Affect:

- **Viral and bacterial adhesion to cell membranes**
- **Cellular Entry**
- **Mitochondrial Take Over**
- **Golgi Protein Manufacture**
- **And other cellular replication Affects**

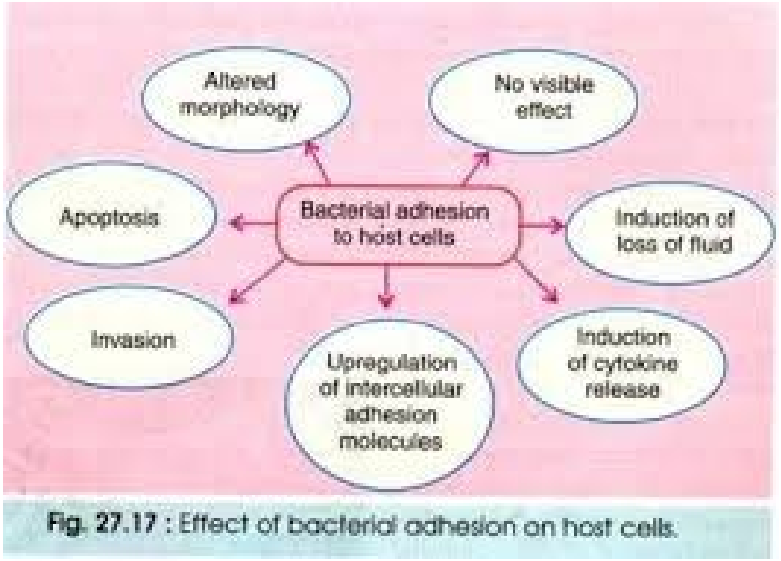
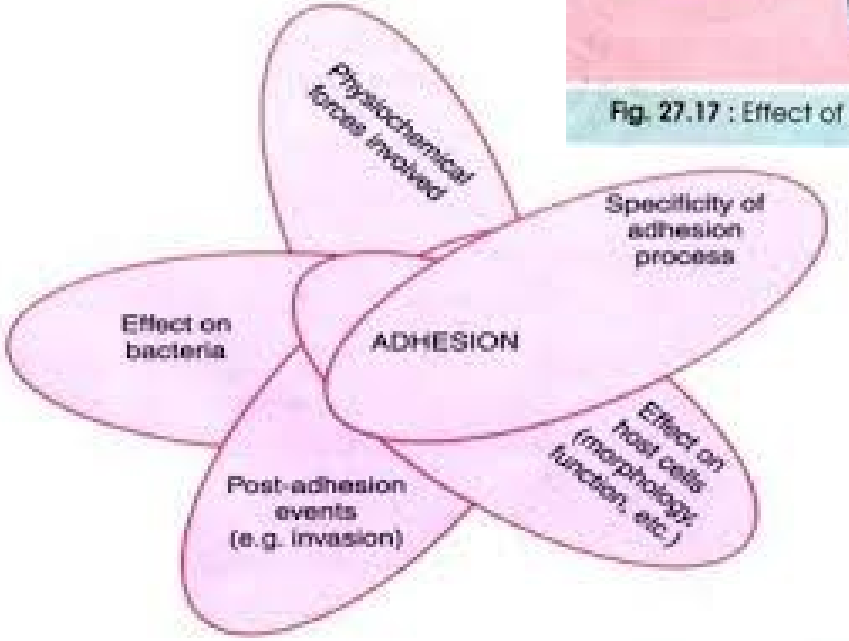


Fig. 27.17 : Effect of bacterial adhesion on host cells.



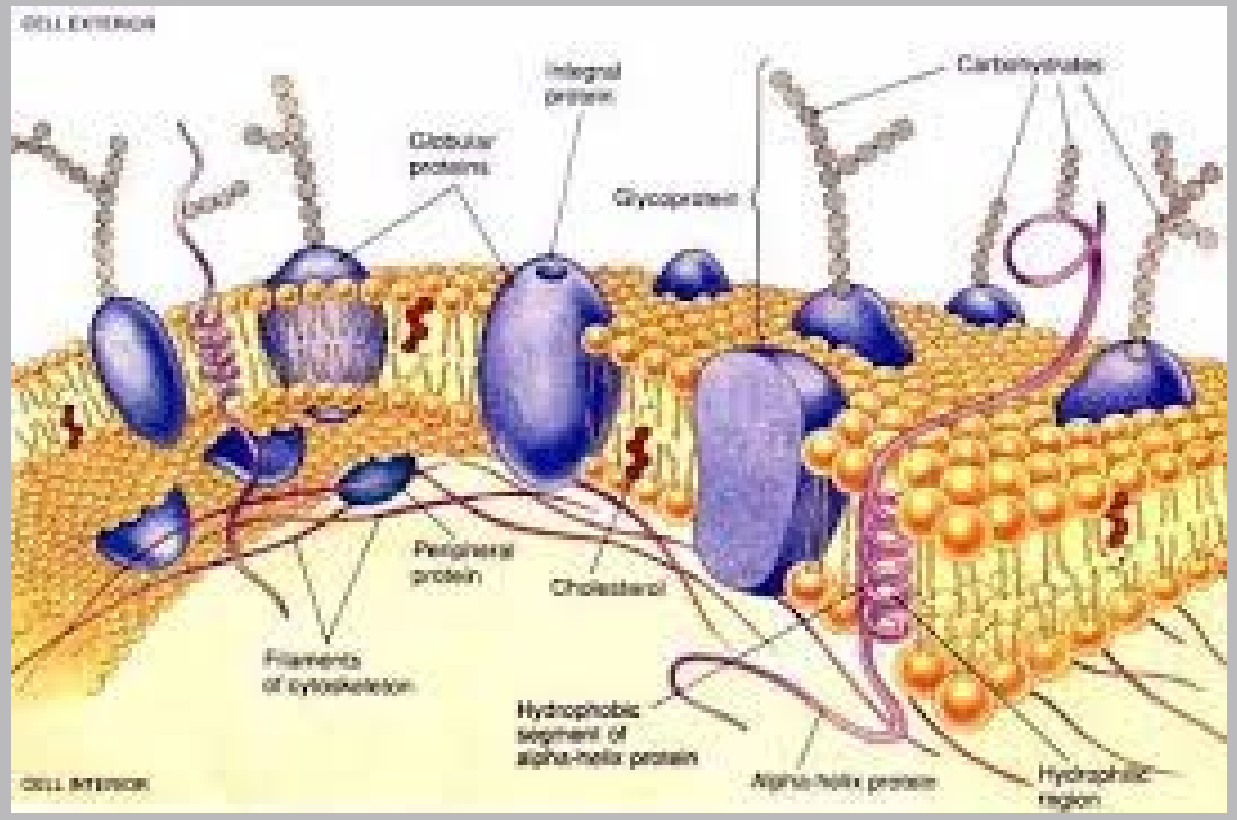
HERBS THAT AFFECT MICROBIAL ATTACHMENT AND CELLULAR DISRUPTION

CELL MEMBRANE, MITOCHONDRIAL, AND REPLICATIONS AFFECTS

Glycoprotein Receptors

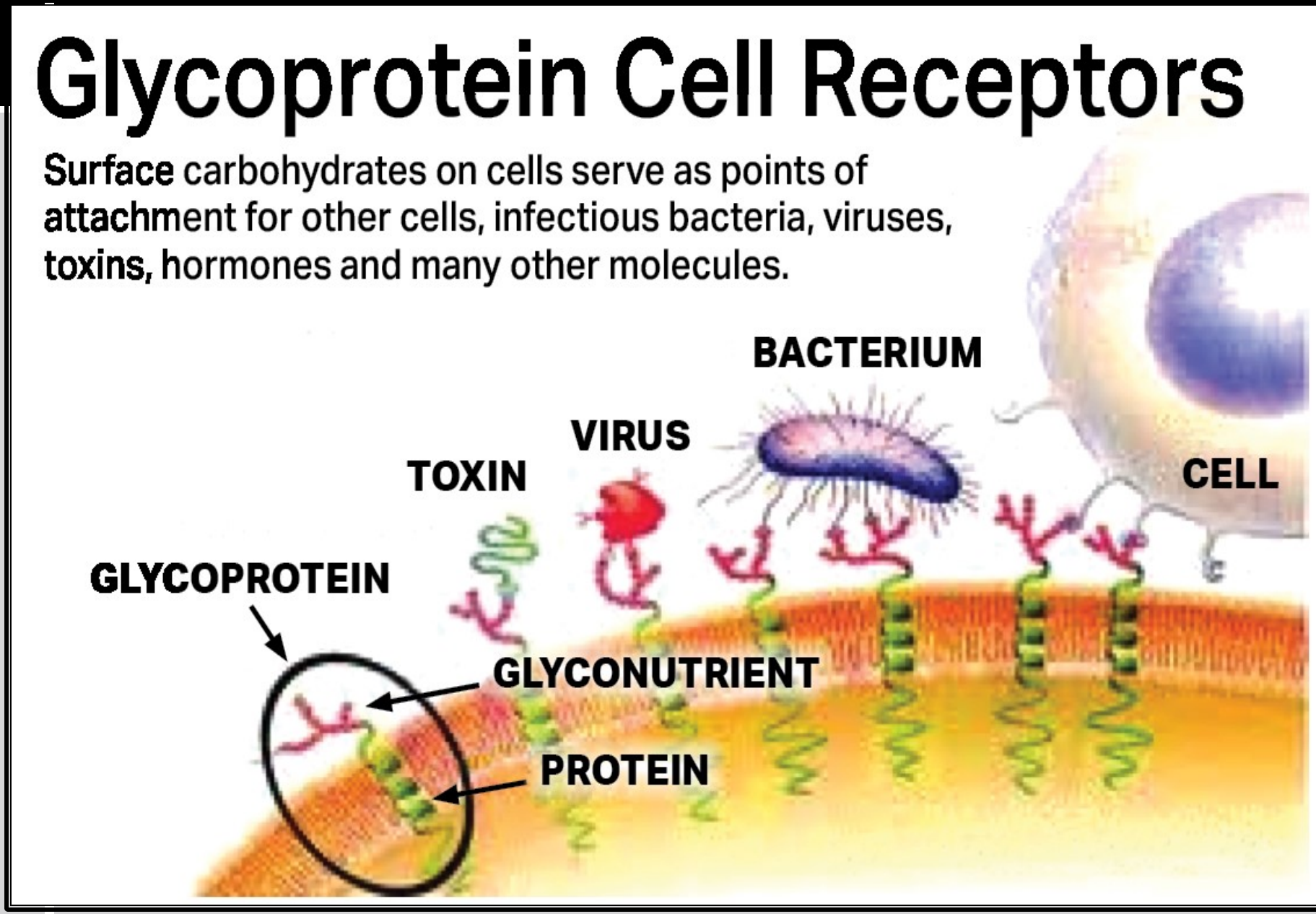
GLYCOPROTEIN RECEPTORS

- Glycoprotein receptors extend outward from the cell surface like whiskers.
- Glycoprotein receptors help direct immune responses, cell adherence, apoptosis, and the ability to discern SELF FROM NON-SELF.



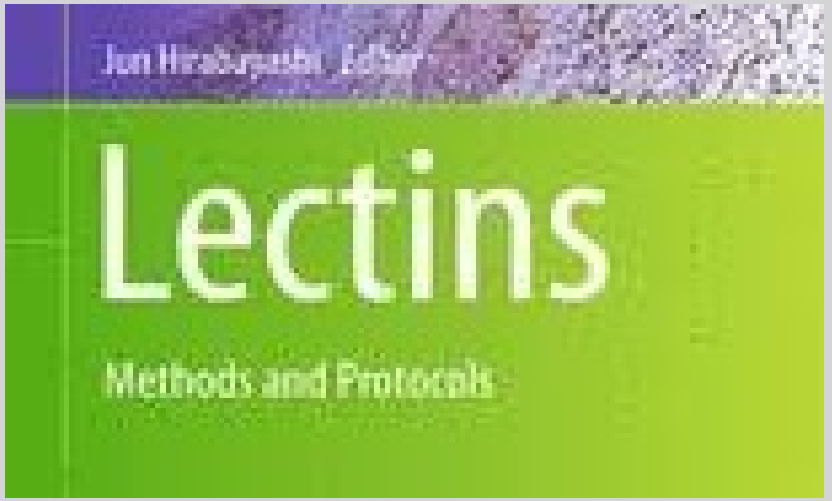
GLYCOPROTEIN RECEPTORS

- Glycoprotein receptors are comprise of proteoglycans – simple carbohydrates combined with amino acids.
- Bacteria and viruses can attach to and enter cells via glycoprotein receptors.
- Our immune system can recognize proteoglycan combinations as being foreign.



LECTINS ARE NOT ALL BAD!

- Many allergenic foods such as soy, nut, and shellfish trigger immune reactions due to the lectins they contain.
- However, many immune supportive and anti-cancer plants, such as *Phytolacca*, *Viscum*, and Castor oil, support immune and white blood cell activities due to the lectins they contain.



Lectin name/ Symbol	Source	Specificity
N-acetylglucosamine binding lectins		
Wheat Germ Agglutinin (WGA)	*Triticum vulgaris*	GlcNAcβ1-4GlcNAcβ1-4GlcNAc, Neu5Ac (sialic acid)
Elderberry lectin (SNA)	*Sambucus nigra*	Neu5Acα2-6Gal(NAc)-R
Maackia Amurensis Lectin (MAL)	*Maackia amurensis*	Neu5Ac/Gcα2-3Galβ1-4GlcNAcβ1-R
Galactose and N-acetylgalactosamine binding lectins		
Ricinus communis Agglutinin, ricine, RCA120 (RCA)	*Ricinus communis*	Galβ1-4GlcNAcβ1-R
Peanut Agglutinin (PNA)	*Arachis hypogaea*	Galβ1-3GalNAcα1-Ser/Thr (T-Antigen)
Jacalin (AIL)	*Artocarpus integrifolia*	(Sia)Galβ1-3GalNAcα1-Ser/Thr (T-Antigen)
Hairy vetch lectin (VVL)	*Vicia villosa*	GalNAcα-Ser/Thr (Tn-Antigen)
Mannose binding lectins		
Concanavalin A (ConA)	*Canavalia ensiformis*	Branched α-mannosidic structures; high α-mannose type, hybrid type and biantennary complex type N-Glycans
Lentil lectin (LCH)	*Lens culinaris*	Fucosylated core region of bi- and triantennary complex type N-glycans
Snowdrop lectin (GNA)	*Galanthus nivalis*	α-1-3 and α 1-6 linked high mannose structures
Fucose binding lectins		
Ulex europaeus agglutinin (UEA)	*Ulex europaeus*	Fucα1-2Gal-R
Aleuria Aurantia Lectin (AAL)	*Aleuria aurantia*	Fucα1-2Galβ1-4(Fucα1-3/4)Galβ1-4GlcNAc, R2-GlcNAcβ1-4 (Fucα1-6)GlcNAc-R1

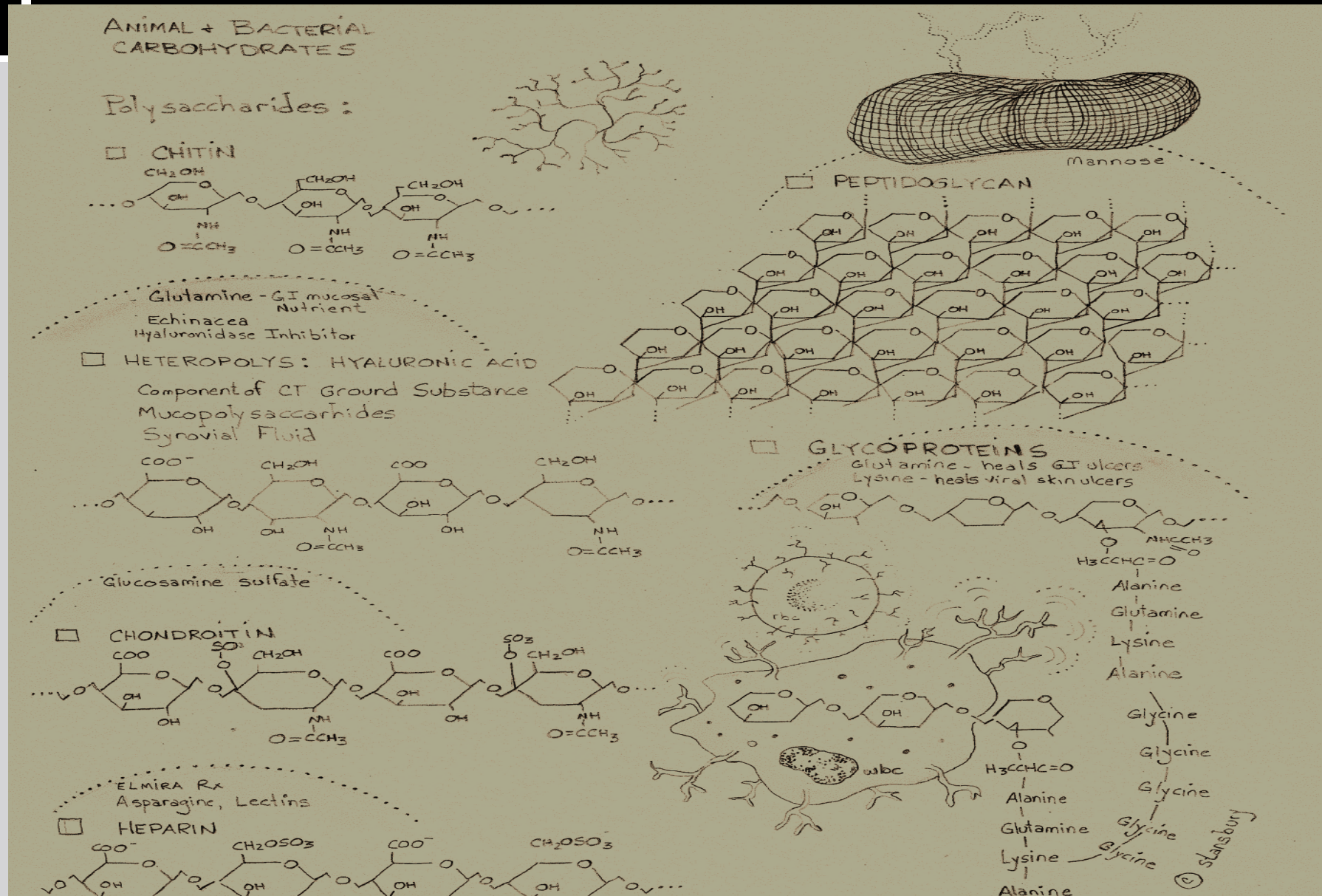
GLYCOPROTEINS AND CARBOHYDRATE CHAINS

BACTERIAL CARBOHYDRATE
- Peptidoglycan

INSECTOID CARBOHYDRATE
- Chitin

CRUSTACEAN GLYCOPROTEIN
- Glucosamine

MAMMALIAN GLYCOPROTEIN
- Chondroitin
- Mucopolysaccarhides
- Lectin
- Heparin



Herbs with Anti-Microbial Effects Via Mitochondrial Membrane Disruption

- **Many essential oils disrupt fungal and bacterial mitochondrial membranes, including Oregano, Fennel, Tea Tree and others.**
- **Some antimicrobial plants lyse bacteria by inhibiting mitochondrial efflux-pumps.**
- ***Hydrastis canadensis* acts in this manner along with other antimicrobial mechanisms.**

Herbs with Anti-Microbial Effects Via Mitochondrial Membrane Disruption

- ***Mahonia/Berberis***
- ***Azadirhata* (Neem)**
- ***Tricosanthes***
- ***Achillea* (Yarrow)**
- ***Coptis* (Gold Thread)**

OREGON HOLLYGRAPE
Berberis aquifolium Pursh
Barberry Family

NUTRIENTS THAT SUPPORT MITOCHONDRIAL HEALTH

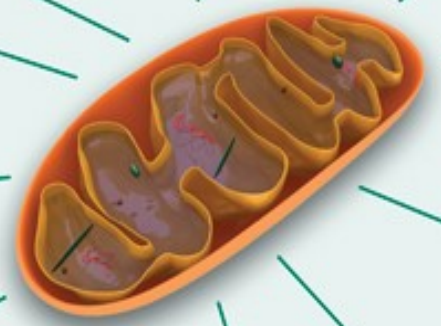
COENZYME Q10
Acts as an electron carrier between complexes I, II, and III of the mitochondrial respiratory chain. Deficiency causes a decline in activities of complex II + III, complex III and complex IV, reduced expression of mitochondrial proteins involved in oxidative phosphorylation, decreased mitochondrial membrane potential, increased production of reactive oxygen species, increased mitophagy of dysfunctional mitochondria, and reduced growth rates.

QUERCETIN
Restores mitochondrial membrane potential and enhances ATP levels.

ALPHA-LIPOIC ACID
Significantly improves mitochondrial content and size in the liver during animal studies.

GREEN TEA (EPICATECHIN)
Protects the cardiac mitochondria from damage.

OMEGA-3 FATTY ACIDS
Rats with mitochondrial heart damage fed omega-3 fatty acids experienced significant restoration of the respiration rate of mitochondria.



NICOTINAMIDE RIBOSIDE
Oral administration of nicotinamide riboside increases NAD+ levels in mice and stimulates mitochondrial biogenesis. Delays early- and late-stage mitochondrial myopathy disease progression in mice.

GLUCOSAMINE
A preliminary study in nematodes and aging mice indicates glucosamine stimulates mitochondrial biogenesis and extends lifespan.

ACETYL L-CARNITINE
Improves mitochondrial content and size in the liver. Acetyl L-carnitine given to old rats promotes the development of new mitochondria in the liver, which can contribute to the reduction of cellular oxidative stress. Protects against mitochondrial dysfunction in models of stroke, ischemia, and neurodegenerative disorders.

N-ACETYL CYSTEINE (NAC)
Significantly improves compromised total mitochondrial bioenergetics in a dose-dependent manner in a rat model of spinal cord injury. Inhibits the inflammatory response that occurs in cultured human synoviocytes due to mitochondrial damage.

RESVERATROL
In fibroblasts from early-onset Parkinson's disease, increases complex I activities and mitochondrial ATP production. Stops the development of diabetic cardiomyopathy in diabetic rats, partially through beneficial effects on the mitochondria.

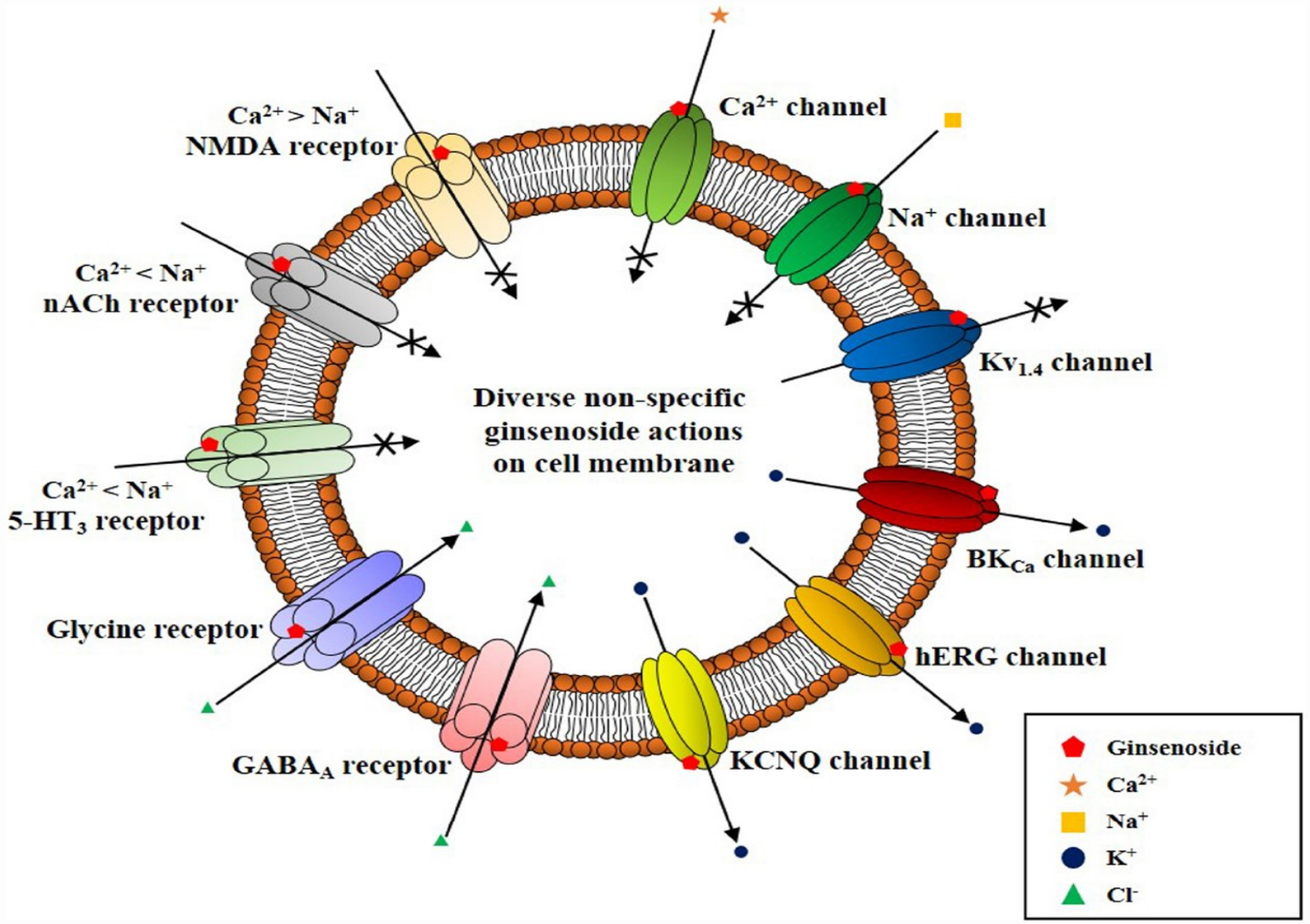
CREATINE MONOHYDRATE
Together with coenzyme Q10 and alpha-lipoic acid improves the health of patients who have mitochondrial cytopathies by reducing lactate and markers of oxidative stress. In people who have mitochondrial encephalomyopathies, creatine improves aerobic oxidative function of the mitochondria.

Mitochondrial Membrane Toxins

Sanguinarine from *Sanguinaria canadensis* affects external mitochondrial membranes and interferes with the negative charges usually held, and inhibits oxidative phosphorylation and ATP synthesis

Herbs with Immune Modulating Effects Via Cell Membrane Activity

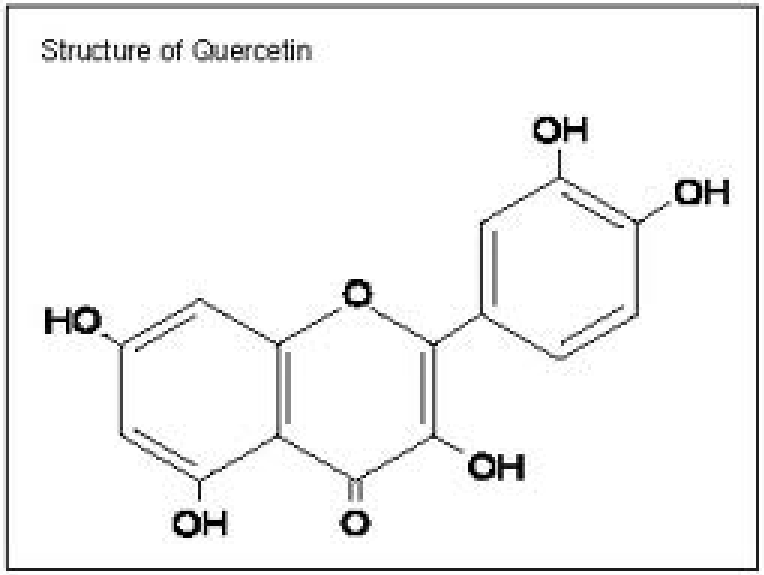
Ginsenosides may induce apoptosis of cancer cells via altering mitochondrial membrane potentials in cancer cells.



FATTY ACID SYNTHESIS DISRUPTORS

- **Fatty acid synthase is involved in cell membrane synthesis and fungal growth and agents that inhibit FAS may have antifungal effects by disrupting the fungal cell membranes.**

- **Quercetin, trans-chalcone, ellagic acid, luteolin, galangin, and genistein may all inhibit fatty acid synthase.**



BACTERIAL ADHERENCE DISRUPTORS
An Apple a Day

Phloretin, an antioxidant flavonoid found abundantly in apples is reported to deter E coli from forming a biofilm in the gut.

Iranian Journal of Pharmaceutical Sciences
Spring 2011: 7(2): 89-97
ijps.sums.ac.ir

Original Article

Hepatoprotective activity of phloretin and hydroxychalcones against Acetaminophen Induced hepatotoxicity in mice

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Abstract

Polyphenolics form a major part of the dietary antioxidant capacity of fruits and vegetables have been identified as chemopreventive or anticancer agents. Hydroxychalcones are polyphenols abundantly distributed throughout the plant kingdom and are compounds with two aromatic rings (benzene or phenol) and an unsaturated side chain. In the present study, effect of phloretin (apple major flavonoid), 4-hydroxychalcone and 4'-hydroxy-chalcone were investigated against acetaminophen-induced acute liver damage. The study was designed as multiple dose pre- and post-treatments. Mice were administrated acetaminophen (1g/kg and 640 mg/kg for mortality and acute toxicity experiments, respectively). Mortality rate, serum transaminases (SGOT and SGPT) and histological examination were applied. Acetaminophen produced 100% mortality at the dose of 1 g/kg in mice, while pre-treatment and post-treatment (i.p., twice daily for 48 hrs) of animals with phloretin and 4-hydroxychalcone (50 mg/kg) and 4'-hydroxychalcone (25 mg/kg) significantly reduced the mortality rate. Acetaminophen produced acute toxicity at the dose of 640 mg/kg in mice, while pre- and post-treatments of animals with phloretin and hydroxychalcones significantly lowered the rise in SGOT and SGPT. Liver sections collected for histological examination showed cellular changes including centrilobular necrosis, extensive portal inflammation, and micro and macro vesicular structures in the acetaminophen group. These cellular changes were reduced following treatment of mice with Phloretin and hydroxychalcones. Taken collectively, from the results of this study it may be suggested that phloretin and hydroxychalcones have hepatoprotective activity against acetaminophen liver injury in mice.

Key words: Phloretin, Hydroxychalcones, Hepatoprotection, Acetaminophen, SGOT, SGPT

*Corresponding autour: Prof. Omid Sabzevari, Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, P.O. Box 14155/6451, Tehran, Iran.
Tel: +9821 6412 2121, Fax: +9821 6412 2161;
Email: omid@tums.ac.ir

1. Introduction

Daily diet of human contains approximately 1 g of herbal phenols which can also be found in many traditional medicines. Most of antioxidant capability of fruits and vegetables

E COLI ADHESION

- ***Vaccinium*** **species deter bacteria via inhibiting their adherence to cells and inhibiting bacterial enzymes.**

BETA GLUCANS AND FUNGAL CELL MEMBRANES

β-glucans are a particular group of cell wall carbohydrates occurring in some mushrooms, seaweeds cereals grains including barley and oats.

All β-glucans are glucose polymers but have slightly differing molecular structures depending on the source.

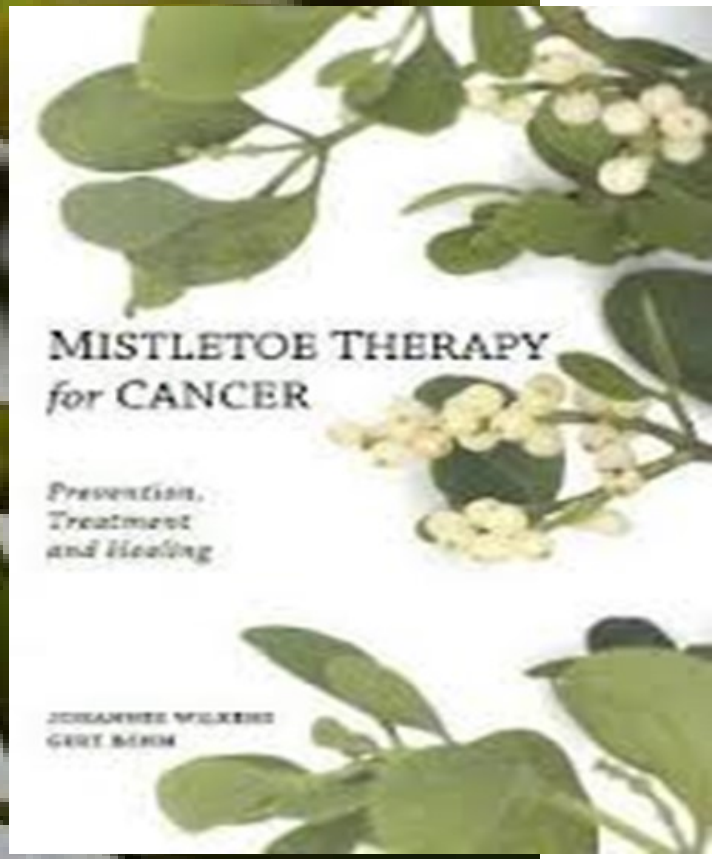
β-glucans have immunomodulatory and anticancer properties via binding to lectins on human cells.


VISCUM
AND CELL
ADHESION

VISCUM AND CANCER

Viscum **affects cell to cell adhesion and can induce apoptosis in cancer cells.**

Lectins are credited with cell adhesion effects.



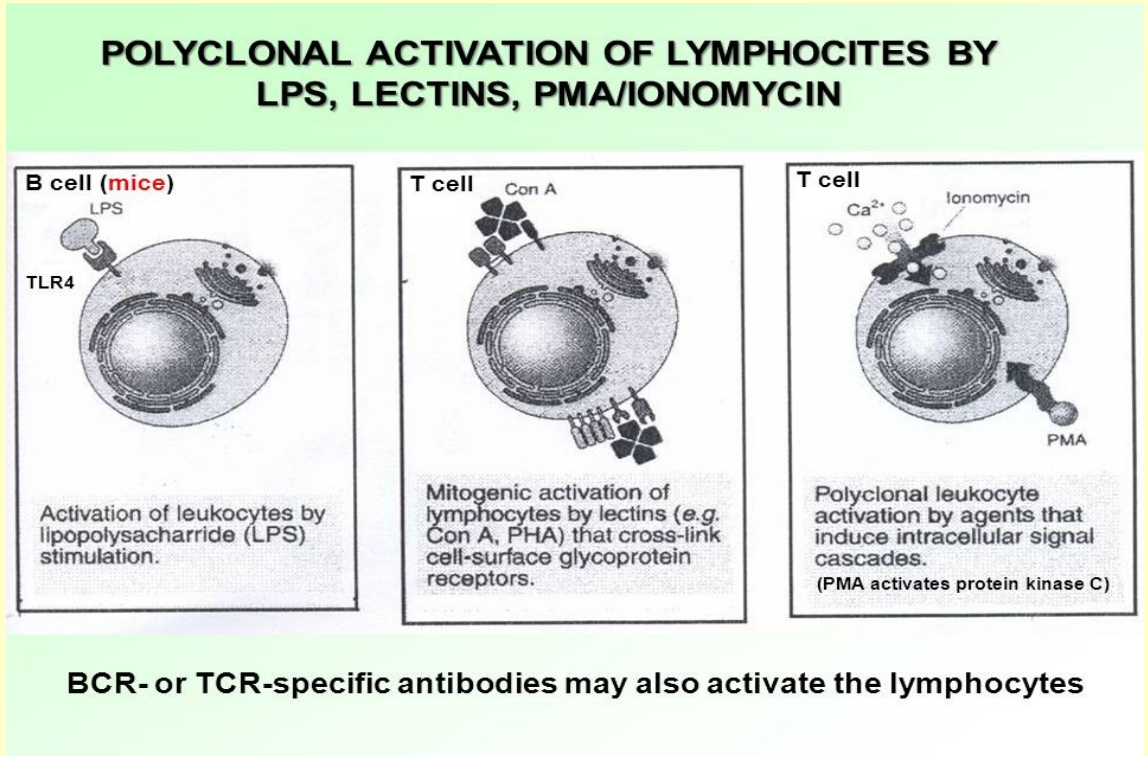
H1N1 AND FLU VIRUS ADHERENCE

- ***Sambucus*** **berries limit the ability of respiratory and influenza viruses to enter cells.**
- **Elderberry syrup is a classic cold and flu remedy.**

PHYTOLACCA SPECIES

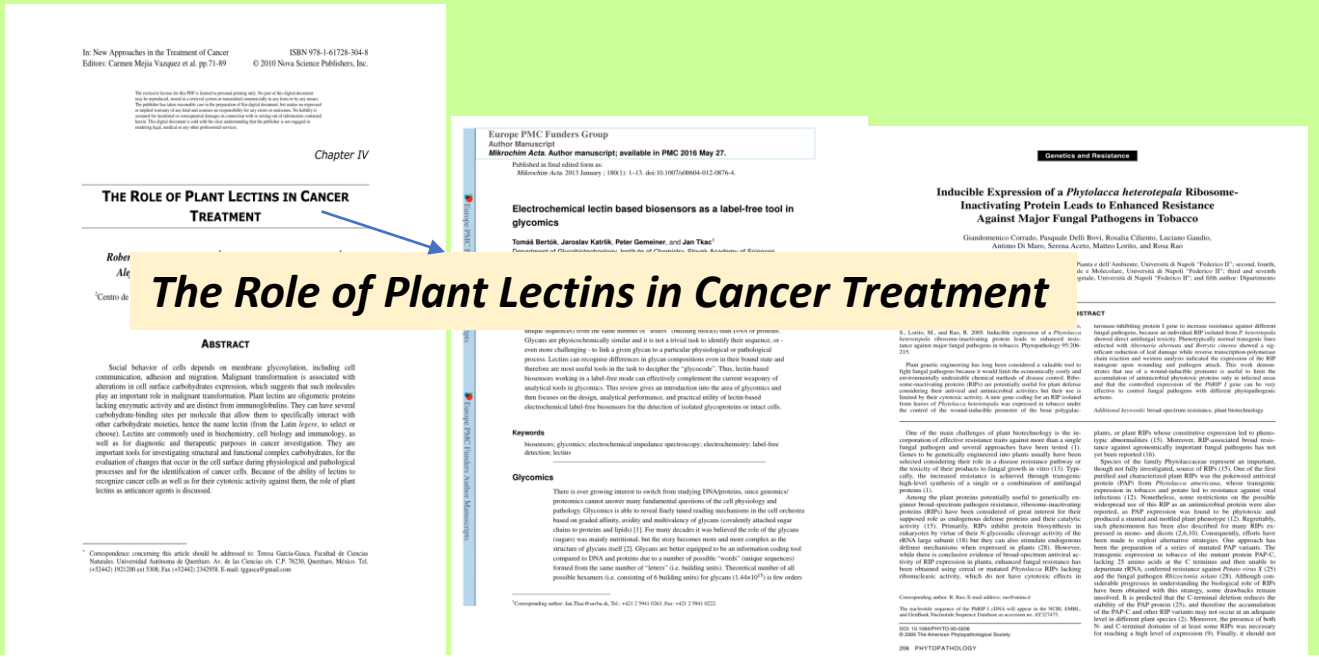
COMMON POKEBERRY
Phytolacca americana L.
POKEBERRY FAMILY

- **Lectins in *Phytolacca* can affect cell to cell adhesion, communication and white blood cell activity.**



PHYTOLACCA

- ***Phytolacca*** **lectins have historically been used topically on the breast and cystic masses, suggesting an ability to penetrate the skin or otherwise affect underlying lymphatic, cancer and fluid flow.**



In: New Approaches in the Treatment of Cancer
Editors: Carmen Mejia Vazquez et al. pp.71-89

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Chapter IV

THE ROLE OF PLANT LECTINS IN CANCER TREATMENT

ABSTRACT

Social behavior of cells depends on membrane glycosylation, including cell communication, adhesion and migration. Malignant transformation is associated with alterations in cell surface carbohydrates expression, which suggests that such molecules play an important role in malignant transformation. Plant lectins are oligomeric proteins lacking enzymatic activity and are distinct from immunoglobulins. They can have several carbohydrate-binding sites per molecule that allow them to specifically interact with other carbohydrate moieties, hence the name lectin (from the Latin *legere*, to select or choose). Lectins are commonly used in biochemistry, cell biology and immunology, as well as for diagnostic and therapeutic purposes in cancer investigation. They are important tools for investigating structural and functional complex carbohydrates, for the evaluation of changes that occur in the cell surface during physiological and pathological processes and for the identification of cancer cells. Because of the ability of lectins to recognize cancer cells as well as for their cytotoxic activity against them, the role of plant lectins as anticancer agents is discussed.

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Electrochemical lectin based biosensors as a label-free tool in glycomics

Tomáš Bertok, Jaroslav Katrlik, Peter Gemeiner, and Jan Tkac

Keywords

biosensors; glycomics; electrochemical impedance spectroscopy; electrochemistry; label-free detection; lectins

Glycomics

Genetics and Resistance

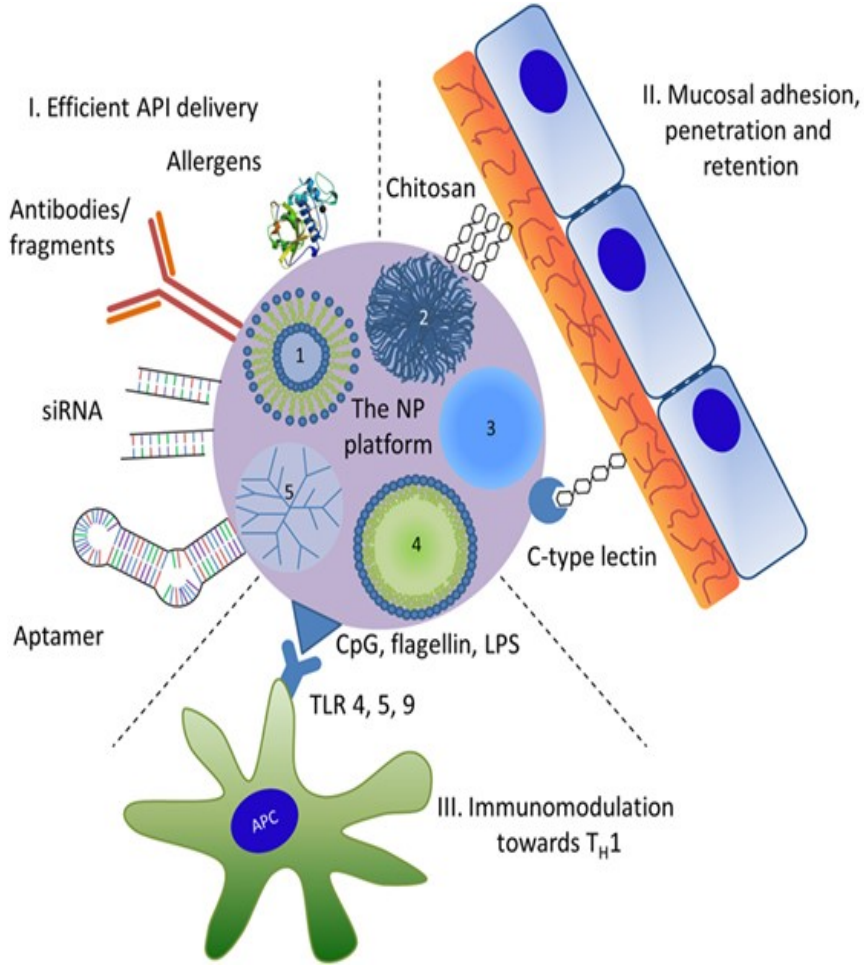
Inducible Expression of a *Phytolacca heterotepala* Ribosome-Inactivating Protein Leads to Enhanced Resistance Against Major Fungal Pathogens in Tobacco

Giandomenico Corrado, Pasquale Delli Bovi, Rosalia Cilliento, Luciano Gaudio, Antimo Di Maro, Serena Aceto, Matteo Lorito, and Rosa Rao

ABSTRACT

Keywords: broad-spectrum resistance, plant biotechnology.

RICINIS CASTORIS
TOPICALLY FOR IMMUNE-MODULATING EFFECTS

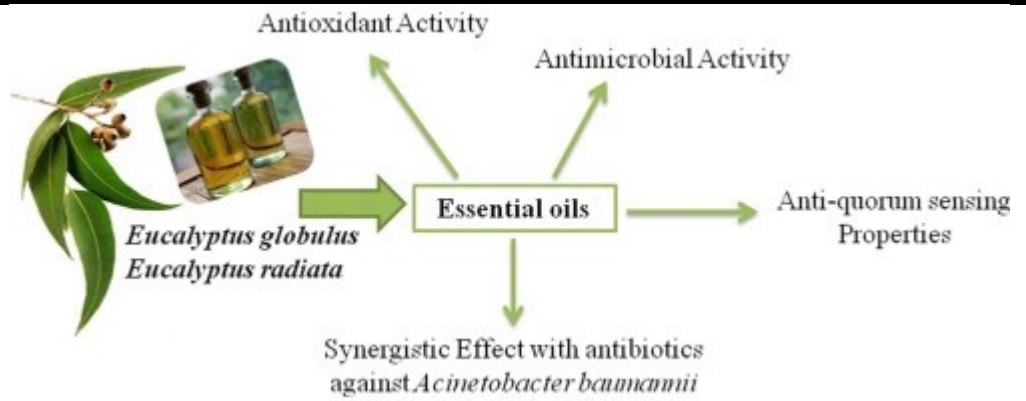


ESSENTIAL OILS FOR ACUTE & CHRONIC INFECTIONS

ESSENTIAL OILS AS ANTI-MICROBIAL AGENTS

All essential oils are anti-microbial with Tea Tree, Oregano and Lavender essential oils being popular in natural products.

Individual aromatic molecules such as carvacrol, thymol, and cinnamaldehydes have been shown to disintegrate the outer membranes of bacterial cell walls and reduce ATP resources intracellularly.



ESSENTIAL OILS AS ANTI-MICROBIAL AGENTS

Eugenol, an aromatic component of clove oil has antifungal activity via inhibition of fungal wall proteins necessary to transport amino acids through fungal membranes.

RESEARCH ON THE ANTIMICROBIAL EFFECTS OF ESSENTIAL OIL

Journal of Medicinal Plants Research Vol. 5(15), pp. 3453-3456, 4 August, 2011
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Full Length Research Paper

Antimicrobial activity of essential oil extract of *Ocimum basilicum* L. leaves on a variety of pathogenic bacteria

Amir Mohammad Daneshian Moghaddam[1]*, Jalal Shayegh[2], Peyman Mikaili[3] and Jalil Dolghari Sharaf[2]

slamic Azad University,

lamic Azad University,

es, Urmia, Iran.

Volume 8 · Number 3 · 2003
HELICOBACTER

Antimicrobial Activity of Essential Oils against *Helicobacter pylori*

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ABSTRACT

Background. *Helicobacter pylori* is an important pathogen responsible for gastroduodenal diseases in humans. Although the eradication of *H. pylori* using antibiotics often improves gastroduodenal diseases, resistance to the antibiotics is emerging.
Materials and Methods. The antimicrobial effect of essential oils and the development of resistance to the essential oils were evaluated in vitro and in vivo.
Results. Thirteen essential oils used in this study completely inhibited the growth of *H. pylori* in vitro at a concentration of 0.1% (v/v). *Cymbopogon citratus* (lemongrass) and *Lippia citriodora* (lemon verbena) were bactericidal against *H. pylori* at 0.01% at pH and 5.0. Resistance to lemongrass did not develop after 10 sequential passages, whereas resistance clarithromycin developed under the same conditi In in vivo studies, the density of *H. pylori* in stomach of mice treated with lemongrass was signi antly reduced compared with untreated mice.
Conclusions. These results demonstrate that essential oils are bactericidal against *H. pylori* with the development of acquired resistance, suggest that essential oils may have potential as new and agents for inclusion in anti-*H. pylori* regimens.

Helicobacter pylori is now recognized as an important causal agent in gastroduodenal diseases, such as chronic gastritis, peptic ulceration, gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma (MALToma) [1–6]. Infection can be cured in > 80% of *H. pylori*-infected patients using standard therapies [7,8]. However, emerging resistance of *H. pylori* to antibiotics, especially metronidazole and clarithromycin, limits the use of these antibiotics in the treatment of *H. pylori* infection [9–12].

Antimicrobial substances other than antibiotics would be very useful in the treatment of *H. pylori* infection if they were shown to be effective against both antibiotic-resistant and -susceptible *H. pylori* strains. In fact, a number of drugs and natural substance such as ecabet sodium, tea cathechins, garlic extracts and honey have been shown to have an antibacterial effect against *H. pylori* in vitro [13–16]. Essential oils, which are extracted from plants (e.g. leaves, peels) have also been used for many years to treat a vari of medical ailments, although the mechani of their action is generally not clarified [1 Recently, the antimicrobial activity of natu compounds has been reported [18,19], includi a few reports on the effects of essential against *H. pylori* [20,21], however, no anir experimentation was reported.

In the present study, we investigated the ar bacterial activity of essential oils against *H. py* both in vitro and in vivo. We also investiga the development of *H. pylori* resistance to essential oils in vitro.

Reprint requests to: Tomoyuki Ohno MD, Mailing address: Third Department of Internal Medicine, Kyoto Prefec-

Antimicrobial Effect of Some Essential Oils

Flora V. Romeo, Serena De Luca, Amalia Piscopo and Marco Poiana*
BIOMAA - Department of Biotechnologies for Agricultural Food and Environmental Monitoring, Mediterranean University of Reggio Calabria, Feo di Vito 89060 (RC), Italy

Abstract

Commercially available oils of lavender (*Lavandula angustifolia* Mill.), lemon-balm (*Melissa officinalis* L.), juniper berry (*Juniperus communis* L.), lemon verbena (*Lippia citriodora* Kunth), rosemary (*Rosmarinus officinalis* L.) and cypress (*Cupressus sempervirens* L.) were evaluated for their antimicrobial activity. Analyses of the oils by GC-FID and GC/MS revealed that the major constituents of these oils were linalool (23.1%) and linalyl acetate (23.1%) in lavender, citronellal (23.8%) and geranial (11.6%) in lemon-balm, α-pinene (29.2%) in juniper berry, neral (36.2%) and geranial (41.9%) in lemon verbena, 1,8-cineole (24.4%) and camphor (17.1%) in rosemary, α-pinene (31.1%) and δ-3-carene (18.8%) in cypress oil.

The antimicrobial activity of the essential oils was evaluated on survival and growth of some microorganisms potentially dangerous to the safety of foods (*Escherichia coli*, *Staphylococcus aureus*, *Listeria innocua*). The antimicrobial tests were carried out both in solid and in liquid media. *E. coli* was the most sensitive organism among the tested ones to the inhibition effect of the oils.

Key Word Index

Lavandula angustifolia, *Rosmarinus officinalis*, *Melissa officinalis*, Lamiaceae, *Aloysia citriodora*, Verbenaceae, *Juniperus communis*, *Cupressus sempervirens*, Cupressaceae, essential oil composition, linalool, linalyl acetate, citronellal, geranial, α-pinene, neral, 1,8-cineole, camphor, δ-3-carene, antimicrobial activity.

Introduction

Currently, there is a strong debate about the safety aspects of chemical preservatives since they are considered responsible for many carcinogenic and teratogenic attributes as well as residual toxicity. For these reasons, consumers tend to be suspicious of chemical additives and thus the demand for natural and socially more acceptable preservatives has been intensified.

Due to the increasing interest of consumers in natural ingredients and their desire to adopt more natural alternatives for the maintenance of product shelf-life, there is a great interest in the potential use of essential oils isolated from many spices and herbs as antimicrobial additives. Phenolic components present in the oils have been known to possess antimicrobial activity and some are classified as Generally Recognized as Safe (GRAS) substances and therefore could be used to prevent post-harvest growth of native and contaminant bacteria. Recent studies suggest that this mechanism of action may be more complex: the spice oils can inhibit enzyme activity and some of these disrupt cell membranes (1). Their action depends on the type, composition and concentration of the oils, the type and concentration of the target micro-organism, the

Phenolic components of oils have been to sensitize the phospholipid bilayer of the cell membrane, causing an increase of permeability and leakage of vital intracellular constitutes or an impairment of bacteria enzyme systems (4).

The minimum inhibitory concentration (MIC) is defined as the minimum level of essential oil concentration that produces a 90% reduction in the growth of microbial colonies. The minimum bactericidal concentration (MBC) is defined as the minimum level of essential oil concentration that produces at least a 99.9% reduction in the growth of microbial colonies (5). As the different MIC and MBC, the substances are classified as more or less effective.

Micro-organisms cause many diseases and also cause deterioration of many types of products. Particularly, *E. coli* infections are disseminated by foods, water and person to person contact (4). *E. coli* O157:H7 (recognized as a pathogen in 1982) is considered to be the main cause of hemorrhagic and of haemolytic uraemic syndrome (6). Among these pathogens, *S. aureus* and *L. monocytogenes* are of great importance. *Listeria monocytogenes* has also been established as an important foodborne pathogen, due to the severity of infection and a mortality rate

Research Titles:

- *Antimicrobial Activity of Essential Oil extract of Ocimum basilicum L. Leaves on a Variety of Pathogenic Bacteria*
- *Antimicrobial Activity of Essential Oils Against Helicobacter pylori*
- *Antimicrobial Effect of Some Essential Oils*

RESEARCH ON THE ANTIMICROBIAL EFFECTS OF ESSENTIAL OIL

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Review

Antimicrobial activity of essential oils extracted from medicinal plants against the pathogenic microorganisms:

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[2]Department of Plant Science, College of Agriculture and Veterinary Sciences, Ambo University, Ambo 19, Ethiopia.

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Tel: +251-923793757;
Fax: +251-471-112-214

INTRODUCTION

Medicinal plants have the ability
wide range of pathogenic microor
of essential oils. The antimicrobi
and its various components ex
plants has been well documente
Hood et al., 2003; Duschatzky et
have been extracted from com
molecules produced by the se
medicinal plants. Hammer et al.,
essential oils extracted from n
approximately 20-60 compone
concentrations.

Essential oils are natural,
compounds characterized by a str
soluble in lipid and organic solven
by all plant organs, i.e. buds, flow
seeds, fruits, roots, wood or b
secretary cells, cavities, canals, ep

Malaysian Journal of Pharmacy 2012; 1(10):111-115 *Research article*

Chemical Composition and Antimicrobial Activity of *Eucalyptus camaldulensis* Dehnh Essential Oil from Malaysia

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Institute of Biological Sciences, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia.

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ABSTRACT

An investigation of the oil constituents of *E. camaldulensis* Dehnh (River Red Gum) grown in Malaysia was carried out. The oil was extracted by hydrodistillation and the chemical composition was analyzed by GC-MS. The essential oil yield was 1.33% of dried weight, a relatively higher content of essential oil. The main 20 chemical components were identified. The oil was highly rich in monoterpenes. four major compounds were dominated in the oil. γ-terpinene is the main component of the essential oil. It's relative content was 63.8% followed by *o*-Cymene, Terpinen-4-ol and Terpinolene (22.5%, 9.5% and 1.3%, respectively). However, other *Eucalyptus* oil components such as 1,8-cineole, α-pinene and α-phellandrene were found to be in very low concentrations in the oil (0.71%, 0.44% and 0.02%, respectively). Antibacterial screening tests of *E. camaldulensis* Dehnh essential oil against different bacterial species showed inhibitive effects against the tested microorganisms.

Keywords: essential oil, γ-terpinene, relative content, chemical components

INTRODUCTION

Essential oils, the volatile compounds from aromatic plants, are used in perfumery, aromatherapy, and for flavoring. They have been shown to possess various biological activities.

Eucalyptus are important plants containing

Chemical composition and biological activity of essential oils are determined by a number of genetic factors, climate, time of harvesting, the plant age and others. To identify the chemical coposition of *Eucalyptus camaldulensis Dehnh* essential oil grown in Malaysian enviroment and test *in-vitro* antimicrobial effects against some bacterial species.

Arch. Biol. Sci., Belgrade, 67(2), 455-466, 2015 DOI:10.2298/ABS1412030101

COMPOSITION AND ANTIMICROBIAL ACTIVITY OF ESSENTIAL OILS OF *ARTEMISIA JUDAICA*, *A. HERBA-ALBA* AND *A. ARBORESCENS* FROM LIBYA

Peđa Janaćković[1,*] Jelica Novaković[1], Marina Soković[2], Ljubodrag Vujisić[3],
a Dajić Stevanović[5] and Petar D. Marin[1]

Institute of Botany and Botanical Garden "Jevremovac", Studentski

ical Research "Siniša Stanković", Mycological Laboratory, Bulevar bia

ry, Studentski trg 16, 11000 Belgrade, Serbia

lty of Science, Department of Botany, Zintan, Libya

ıde, Nemanjina 6, 11080 Belgrade, Serbia

;ac.rs

odistillation from the aerial parts of *Artemisia judaica* L., *Artemisia herba-* ivated) from Libya, were analyzed by GC and GC-MS. The antimicrobial nicrodilution method against eight bacterial species: *Bacillus cereus* (clinical *isteria monocytogenes* (NCTC7973), *Staphylococcus aureus* (ATCC6538), *aeruginosa* (ATCC27853), *Salmonella typhimurium* (ATCC13311), *Entero-* ngal species: *Aspergillus niger* (ATCC6275), *A. ochraceus* (ATCC12066), (ATCC1022), *Penicillium ochrochloron* (ATCC9112), *P. funiculosum* 61) and *Candida albicans* (human isolate). The major constituents of *A.* ons (47.4%). Oxygenated monoterpenes were the dominant constituents !% and 77.3%, respectively). Camphor (24.7%) and chamazulene (20.9%) oil of *A. arborescens*, chrysanthenone (20.8%), *cis*-chrysanthenyl acetate n the *A. herba-alba* oil, and the major constituents in the *A. judaica* oil were 9.1%). The best antimicrobial activity was obtained for *A. judaica* oil and *is* oil. The effect of the tested oils was higher against Gram (+) than Gram ntibacterial activity against *Listeria monocytogenes* and the lowest against *terobacter cloacae,* compared to streptomycin and ampicillin. All three oils conazole, except *A. arborescens* oil against *Aspergillus niger*.

erba-alba; *Artemisia arborescens*; essential oils; antimicrobial activity

ruary 3, 2015; **Accepted** February 5, 2015

Research Titles:

- *Antimicrobial activity of essential oils extracted from medicinal plants against the pathogenic microorganisms*
- *Chemical composition and antimicrobial activity of Eucalyptus camaldulensis Dehnh essential oil from Malaysia*
- *Composition and antimicrobial activity of essential oils of Artemisia Judaica, A Herba-alba and A. Arboescens from Libya*

Table 3 - (Table 2 continued). Antimicrobial activity of the evaluated essential oils against food-related microorganisms, as detected in the agar disc-diffusion test (mm) [a].

	Mint	Pennyroyal	Orange [b]	Oregano	Rosemary	Ampicilin	Chlor. [c]
S.aureus	25.1 ± 1.4 ^{de}	16.0 ± 0.4 ^{i}	21.5 ± 1.1 ^{f}	22.9 ± 1.0 ^{ef}	28.2 ± 0.9 ^{c}	36.4 ± 1.8 ^{b}	26.1 ± 0.5 ^{cd}
E.faecalis	14.1 ± 0.5 ^{f}	13.7 ± 0.6 ^{f}	17.1 ± 0.5 ^{d}	16.0 ± 0.7 ^{de}	14.9 ± 0.7 ^{ef}	27.0 ± 0.4 ^{a}	23.6 ± 0.2 ^{b}
L.monocytogenes	15.4 ± 1.3 ^{f}	13.9 ± 0.6 ^{fg}	21.2 ± 2.7 ^{e}	25.4 ± 1.3 ^{d}	26.5 ± 1.4 ^{cd}	31.1 ± 0.9 ^{b}	28.4 ± 1.0 ^{bc}
L.plantarum	19.6 ± 0.9 ^{ef}	24.0 ± 2.3 ^{cd}	14.1 ± 0.6 ^{hi}	17.4 ± 1.1 ^{fg}	12.1 ± 0.5 ^{i}	32.0 ± 0.9 ^{a}	29.2 ± 1.0 ^{ab}
B.cereus	21.4 ± 1.7 ^{d}	17.1 ± 0.2 ^{e}	33.1 ± 1.2 b	26.2 ± 0.6 ^{c}	26.4 ± 0.5 ^{c}	12.1 ± 0.2 ^{g}	27.9 ± 0.7 ^{c}
B.subtilis	21.1 ± 0.8 ^{e}	17.7 ± 0.9 ^{fg}	85.0 ± 0.0 ^{a}	18.0 ± 1.7 ^{efg}	36.0 ± 0.6 ^{c}	31.1 ± 1.8 ^{d}	29.9 ± 0.5 ^{d}
Y.enterocolitica	24.7 ± 1.8 ^{d}	0.0 ± 0.0 ^{h}	26.7 ± 1.5 ^{cd}	18.9 ± 1.2 ^{f}	16.7 ± 0.5 ^{f}	21.7 ± 0.5 ^{e}	28.1 ± 0.5 ^{bc}
E.coli	0.0 ± 0.0 ^{h}	0.0 ± 0.0 ^{h}	0.0 ± 0.0 ^{h}	14.5 ± 0.4 ^{f}	12.2 ± 0.3 ^{g}	18.9 ± 0.5 ^{d}	26.1 ± 0.6 ^{a}
S. Typhimurium	0.0 ± 0.0 ^{f}	0.0 ± 0.0 ^{f}	0.0 ± 0.0 ^{f}	12.0 ± 0.8 ^{d}	10.5 ± 0.0 ^{e}	27.1 ± 0.5 ^{a}	24.4 ± 0.5 ^{b}
E.aerogenes	0.0 ± 0.0 ^{d}	0.0 ± 0.0 ^{d}	0.0 ± 0.0 ^{d}	11.4 ± 0.5 ^{c}	10.2 ± 0.3 ^{c}	0.0 ± 0.0 ^{d}	23.0 ± 0.7 ^{a}
P.vulgaris	41.5 ± 2.1 ^{a}	0.0 ± 0.0 ^{h}	27.7 ± 3.0 ^{c}	23.7 ± 0.6 ^{d}	14.9 ± 2.3 ^{g}	21.1 ± 1.0 ^{de}	22.4 ± 0.8 ^{de}
P.aeruginosa	0.0 ± 0.0 ^{c}	0.0 ± 0.0 ^{c}	0.0 ± 0.0 ^{c}	12.7 ± 0.5 ^{b}	0.0 ± 0.0 ^{c}	0.0 ± 0.0 ^{c}	0.0 ± 0.0 ^{c}

[a] Inhibition area including 9mm disc diameter, expressed as the mean of four replicates ± SD. Inhibition degrees: 10 -13,9mm: weak; 14-18mm: moderate; >18mm: strong. Means followed by the same letter in the same row are not significantly different ($P<0.05$).

[b] Orange oil were obtained from the plant leaves.

[c] Chloranphenicol.

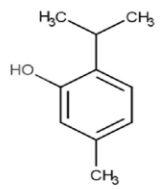
ANTIMICROBIAL EFFECTS OF OREGANO OIL

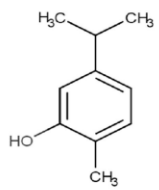
Table 2 - *In vitro* antimicrobial activities of oregano essential oil on some microorganisms

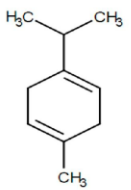
Microorganism	Minimum inhibitory concentration	Minimum lethal concentration
Escherichia coli	0.5 mg/mL	-[1]
Salmonella typhimurium	0.5 mg/mL	0.5 mg/mL
Shigella dysenteriae	0.5 mg/mL	1.0 mg/mL
Clostridium perfringens	0.5 mg/mL	0.5 mg/mL
Staphylococcus aureus	0.5 mg/mL	2.5 mg/mL
Bacilus cereus	0.5 mg/mL	-[1]

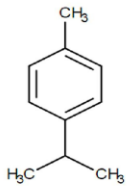
[1] Not determined.

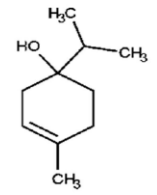
- **Oregano Oil contains Borneol, Thymol, and Carvacrol, among other individual essential oils, each having potent antimicrobial action.**


Carvacrol


Thymol


γ-Terpinene


p-Cymene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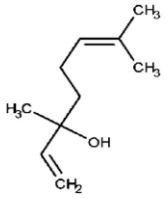
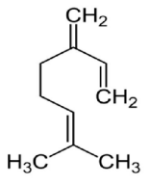

Linalool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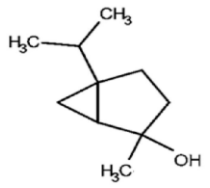
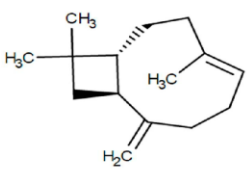
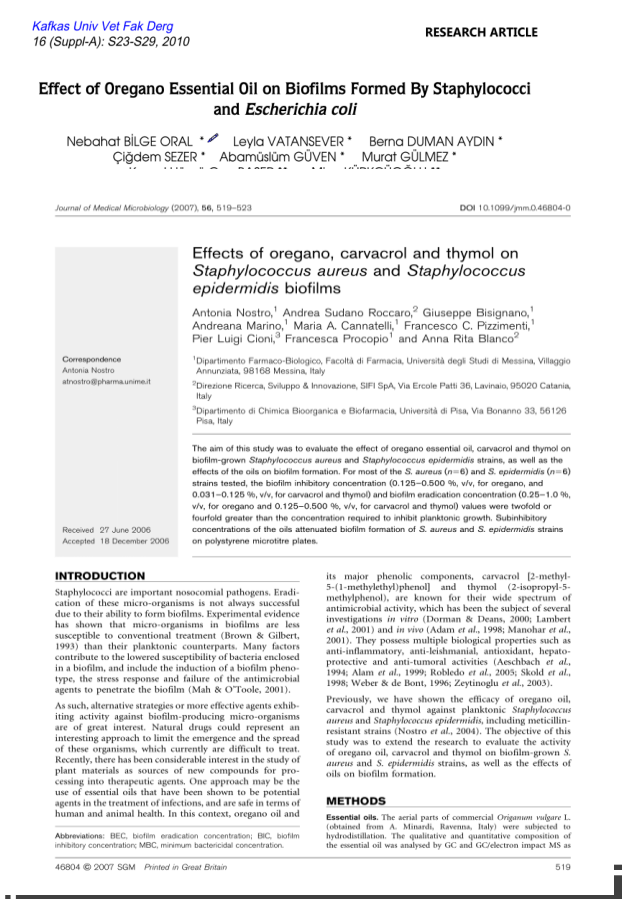

trans-Sabinene hydrate


β-Caryophyllene



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RESEARCH ARTICLE

Effect of Oregano Essential Oil on Biofilms Formed By Staphylococci and *Escherichia coli*

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Effects of oregano, carvacrol and thymol on *Staphylococcus aureus* and *Staphylococcus epidermidis* biofilms

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The aim of this study was to evaluate the effect of oregano essential oil, carvacrol and thymol on biofilm-grown *Staphylococcus aureus* and *Staphylococcus epidermidis* strains, as well as the effects of the oils on biofilm formation. For most of the *S. aureus* (n=6) and *S. epidermidis* (n=6) strains tested, the biofilm inhibitory concentration (0.125–0.500 %, v/v, for oregano, and 0.031–0.125 %, v/v, for carvacrol and thymol) and biofilm eradication concentration (0.25–1.0 %, v/v, for oregano and 0.125–0.500 %, v/v, for carvacrol and thymol) values were twofold or fourfold greater than the concentration required to inhibit planktonic growth. Subinhibitory concentrations of the oils attenuated biofilm formation of *S. aureus* and *S. epidermidis* strains on polystyrene microtitre plates.

INTRODUCTION

Staphylococci are important nosocomial pathogens. Eradication of these micro-organisms is not always successful due to their ability to form biofilms. Experimental evidence has shown that micro-organisms in biofilms are less susceptible to conventional treatment (Brown & Gilbert, 1993) than their planktonic counterparts. Many factors contribute to the lowered susceptibility of bacteria enclosed in a biofilm, and include the induction of a biofilm phenotype, the stress response and failure of the antimicrobial agents to penetrate the biofilm (Mah & O'Toole, 2001).

As such, alternative strategies or more effective agents exhibiting activity against biofilm-producing micro-organisms are of great interest. Natural drugs could represent an interesting approach to limit the emergence and the spread of these organisms, which currently are difficult to treat. Recently, there has been considerable interest in the study of plant materials as sources of new compounds for processing into therapeutic agents. One approach may be the use of essential oils that have been shown to be potential agents in the treatment of infections, and are safe in terms of human and animal health. In this context, oregano oil and its major phenolic components, carvacrol [2-methyl-5-(1-methylethyl)phenol] and thymol (2-isopropyl-5-methylphenol), are known for their wide spectrum of antimicrobial activity, which has been the subject of several investigations *in vitro* (Dorman & Deans, 2000; Lambert *et al.*, 2001) and *in vivo* (Adam *et al.*, 1998; Manohar *et al.*, 2001). They possess multiple biological properties such as anti-inflammatory, anti-leishmanial, antioxidant, hepatoprotective and anti-tumoral activities (Aeschbach *et al.*, 1994; Alam *et al.*, 1999; Robledo *et al.*, 2005; Skold *et al.*, 1998; Weber & de Bont, 1996; Zeytinoglu *et al.*, 2003).

Previously, we have shown the efficacy of oregano oil, carvacrol and thymol against planktonic *Staphylococcus aureus* and *Staphylococcus epidermidis*, including meticillin-resistant strains (Nostro *et al.*, 2004). The objective of this study was to extend the research to evaluate the activity of oregano oil, carvacrol and thymol on biofilm-grown *S. aureus* and *S. epidermidis* strains, as well as the effects of oils on biofilm formation.

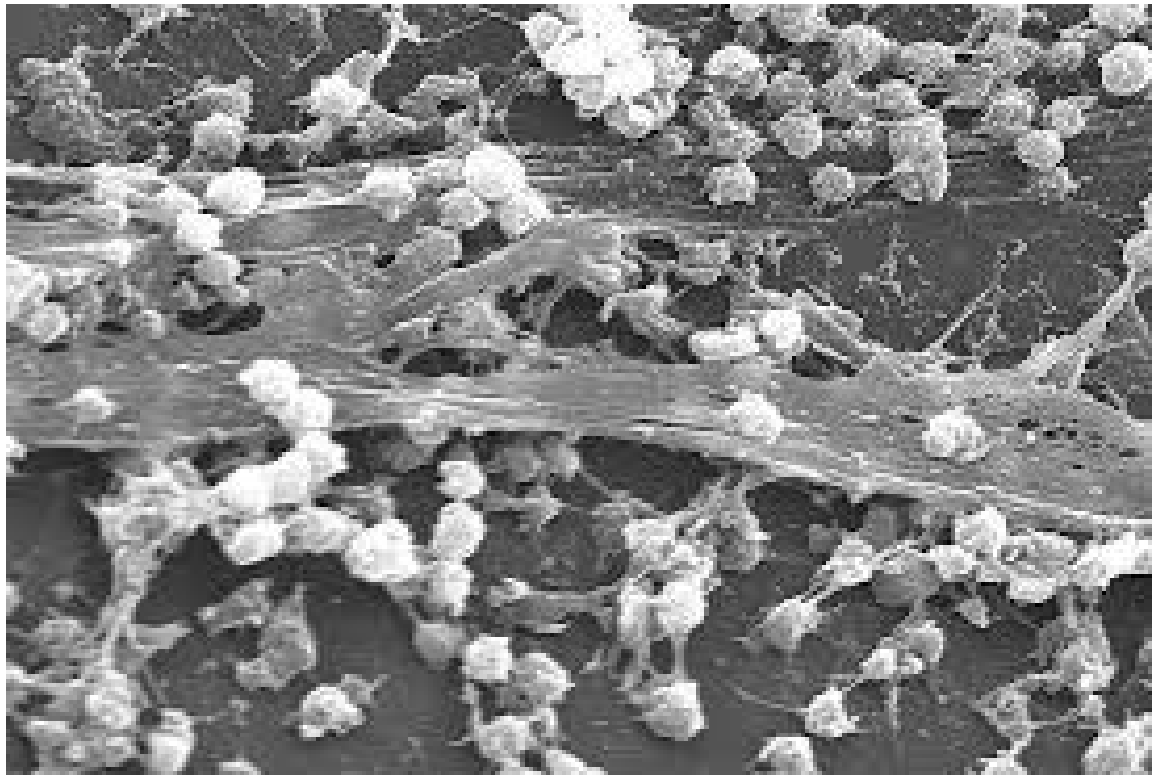
METHODS

Essential oils. The aerial parts of commercial *Origanum vulgare* L. (obtained from A. Minardi, Ravenna, Italy) were subjected to hydrodistillation. The qualitative and quantitative composition of the essential oil was analysed by GC and GC/electron impact MS as

Abbreviations: BEC, biofilm eradication concentration; BIC, biofilm inhibitory concentration; MBC, minimum bactericidal concentration.

Research Titles:

- *Effect of Oregano Essential Oil on Biofilms Formed by Staphylococci and E. coli*
- *Effects of Oregano, Carvacrol, and Thymol on S. aureus and S. epidermis Biofilms*



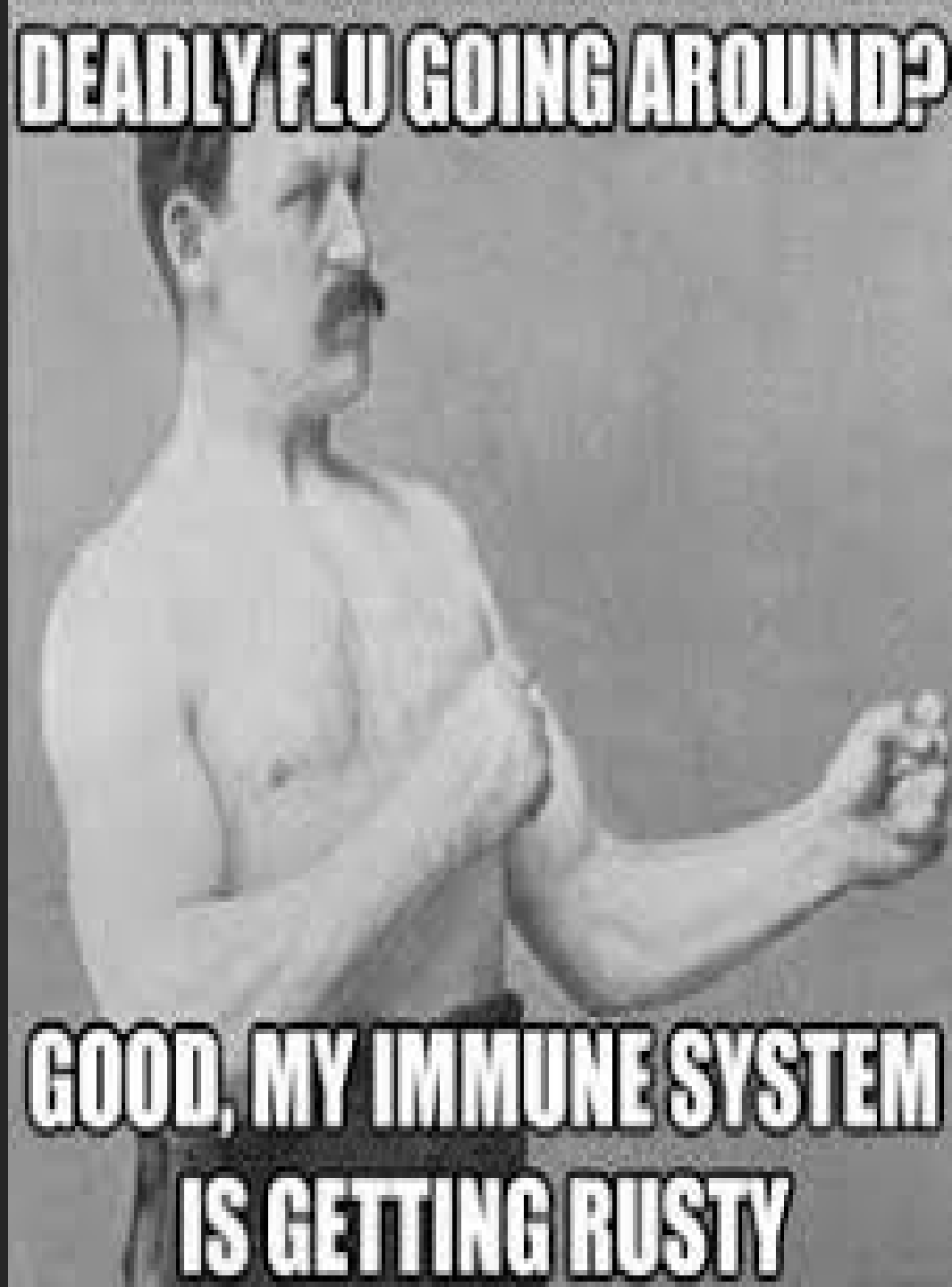
OREGANO OIL CAN PENETRATE AND CLEAR BIOFILMS

OREGANO OIL IS SAFE TO CONSUME ORALLY

- Thymol, Eugenol, Carvacol are on the FDA's GRAS list
- Oral capsules are useful for intestinal infections.
- Steam inhalations are useful for respiratory infection.
- Topical salve and washes are useful for skin infections.

SUMMARY OF AVOIDING ANTIBIOTICS AND BUILDING IMMUNE RESISTANCE

- Address Lifestyle factors
- Optimize Nutrition
- Get Adequate Sleep
- Offer Adapogens Where Needed
- Offer Thyroid Suport Where Needed
- Offer Specific Antimicrobial Herbs to Treat Acute Situations
- Offer Deep Immune Support to Resolve Chronic Infections



THANK YOU!!!