BOTANICAL INFLUENCES ON METABOLIC SYNDROME

Dr Jillian Stansbury
OUTLINE OF PRESENTATION

- THE DEADLY QUARTET AND EPIDEMIOLOGY
- NUTRIENTS AND THE RISK OF METABOLIC SYNDROME
- HERBAL THERAPIES FOR METABOLIC SYNDROME
THE DEADLY QUARTET

THE RISING TIDE OF DIABETES AND METABOLIC SYNDROME
Metabolic syndrome is a particularly pronounced type of insulin resistance, where insulin levels are significantly elevated, as are blood glucose and lipids, and as the condition progresses, high blood pressure ensue.

METABOLIC SYNDROME SYNONYMS

- Metabolic Syndrome is associated with a significantly increased risk for heart disease and damage.
- Metabolic Syndrome is also referred to as:
  - Metabolic Cardiovascular Syndrome
  - Metabolic Syndrome of Obesity
  - Insulin Resistance Syndrome

- The International Diabetes Federation has termed the combination of hypertension, high blood sugar, high cholesterol, and obesity as the "Deadly Quartet."
- Like diabetes, it appears that genetic predispositions do exist but that diet and lifestyle are also contributory.
Metabolic Syndrome may emerge as early as pre-puberty initiating atherosclerosis leading to coronary heart disease and stroke risk.

- Metabolic Syndrome predisposition to heart disease at an early age, certain cancers, Alzheimer's disease, and dementia.

THE DEADLY QUARTET

- High Blood Pressure
- High Blood Sugar
- High Cholesterol
- Obesity

Image from faculty.ksu
Metabolic Syndrome and Diabetes are among the significant health challenges of the modern era.

An article in the Journal of the American Medical Association reported that in 1992 22-24% of the United States general population could be diagnosed with Metabolic Syndrome with around 7% of people in their 20s being affected, up through over 40% of people in their 60s being affected.
METABOLIC SYNDROME DIAGNOSIS AND PREVALENCE

- In the US, men and women are equally affected except in African American and Mexican American populations where women are more affected.

- All in all, this shows that Metabolic Syndrome is extremely prevalent in the US population and increases the older we become.

METABOLIC SYNDROME DIAGNOSTIC CRITERIA

Central Obesity
- * Men – greater than 40 inch waist
- * Women – Greater than 35 inch waist

Fasting TGs – Over 15- mg/dl

HDL Cholesterol
- * Men – less than 40
- * Women – less than 50

Blood Pressure – 130/85 or higher

Fasting Glucose – 110 or higher

Many also calculate BMI – Body Mass Index
Metabolic Syndrome and Genetic Predisposition

- There is a strong familial occurrence of Metabolic Syndrome, especially in those from the Indian subcontinent, individuals of African, Hispanic, and American Indian descent.

- The “cause” of Metabolic Syndrome is polygenetic with numerous nutritional and lifestyle contributors.

Lifestyle factors include excessive refined carbohydrate and fat consumption, and lack of exercise.

Image from ijpm.com
METABOLIC SYNDROME
ASSOCIATED CONDITIONS

- Obesity
- Chronic Inflammatory Disorder
- Atherosclerosis
- Fatty Liver
- Blood Clots
- Gout
- Dermatitis
- Ovarian Cysts
- Dementia and Alzheimer's Disease
SIGNS AND SYMPTOMS OF METABOLIC SYNDROME

- Early and excessive weight gain during childhood, and persistent adult obesity
- Deadly Quartet: Hypertension, Hyperlipidemia, Insulin Resistance, Hyperglycemia.
- PCOS such as ovarian cysts and infertility.

OTHER ASSOCIATED CONDITIONS:
- Premature puberty
- Allergies
- Male gynecomastia
- Fat accumulation in the liver
- Early and severe development of atherosclerosis
METABOLIC SYNDROME AND INFLAMMATORY DISEASE

- Blood clotting disorders are also associated with Metabolic Syndrome due to general inflammation in the blood and blood cells.

- Chronic inflammatory disorders such as gout or skin rashes may also occur due to general body-wide increases in inflammatory molecules and processes.

- Chronic inflammation itself is associated with an increased risk of cancer, dementia and numerous chronic inflammatory disorders.

- Anti-Inflammatory herbs and diets are an important aspect of all protocols for Metabolic Syndrome.
LAB TEST FOR CV DISEASE RISK

Additional labs may be more sensitive measure of assessing the risk heart disease risk than lipid panels alone.

- **Homocysteine**
- **C Reactive Protein** – a measure of vascular inflammation. Normal values are 0.5 to 5.0. Vitamin E may reduce levels when elevated.
- **Fibrinogen** – a measure of inflammation and increased clotting potential. Proteolytic enzymes may reduce elevated levels.

Arch Gynecol Obstet. 2009 Sep 22. High sensitive serum C-reactive protein and its relationship with other cardiovascular risk factors in normoinsulinemic polycystic ovary patients without metabolic syndrome. Verit FF.


- Those with Met Women are less able to process lipids due to complex metabolic abnormalities, even with normal blood sugar.
- Even moderate lipid elevations can result in severe risks and should be taken very seriously.
- Regular laboratory testing helps assess efficacy of diet, exercise, and medical therapies.
The typical "Western" diet (i.e. processed carbohydrates and poor quality fried foods) promotes metabolic syndrome.

Animal studies show that high fat/high refined carbohydrate diets increase not only blood fats, insulin resistance, but also negatively affect key enzymes involved in cholesterol metabolism.

Infant monkeys fed a high fat diet have an increased tendency to become obese.

Our diets early in life and even in utero influences affect our metabolism for remainder of our lives.


Rats fed a high fructose diet develop insulin resistance and high triglycerides.

A high intake of concentrated fructose and sweetened fruit juices have been shown to impair glucose tolerance in genetically susceptible individuals, but eating fresh fruit appears free of such consequences.

Significant damage to the heart and blood vessels occurs when a 10% fructose solution replaces plain water in animal studies.

Foods containing high fructose corn syrup should be banned from the diet.


HYPERLIPIDEMIA
NATURAL THERAPIES
BOTANICALS FOR IMPROVING BLOOD LIPIDS
DIETARY CHOICES TO HELP LOWER LIPIDS

- Have Hand-outs Ready to Help Patients
  Eat more Fiber, Fish, Nuts, Veggies.

Top 5 Foods to Lower Cholesterol

Here are the Top 5 foods or food groups that can lower your cholesterol and protect your heart, as suggested by the experts at Mayo Clinic.

1. Oatmeal, oat bran and high-fiber foods (5-10 grams/day)
2. Fish and Omega-3 fatty acids (2 servings/week)
3. Walnuts, almonds and other nuts (1.5 ounces/day)
4. Olive Oil (23 grams/day)
5. Foods with added plant sterols or stanols (2 grams/day)
**THERAPEUTIC FATS AND OILS TO IMPROVE BLOOD LIPIDS**

- Fish oil - ingestion of fish oils and eating fish reduce the risk of heart disease and improve lipoprotein ratios. 5-10 g/day may lower total cholesterol and improve lipid ratios.

- Essential Fatty Acids – The ingestion Alpha linolenic acid and linoleic acid may reduce diastolic blood pressure and increase serum triacylclycerol concentration in hypercholesterolemic subjects.

- Nuts – Walnuts in particular are rich in polyunsaturated fatty acids and may benefit the heart. Some studies have shown walnut oils to have a positive impact on plasma fatty acid and lipoprotein ratios.

- Vegetable Oils – Olive oil, walnut, and Coconut oil may improve lipid levels, while others such as corn oil may challenge healthy lipid ratios in the blood.

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Shekelle RB, et al, "Diet, serum cholesterol, and death from coronary heart disease." The Western Electric Study NEJM 1981;304;65


INGESTION OF FIBER TO IMPROVE BLOOD LIPIDS

- Plant fibers such as oat bran, wheat bran, pectins and vegetable fibers may lower total cholesterol and improve glycemic control.

- Fiber may lower blood lipids by a simple mechanical trapping of some fats within a food bolus, limiting its absorption.

- Fiber optimizes digestive transit time and favors aerobic conditions within the intestines, encouraging the growth of beneficial intestinal microbes, enhancing lipid elimination.
Garlic improves lipid profiles
- Reduces in blood pressure
- Improves platelet aggregation
- Improves endothelial protection

Garlic lowers cholesterol and triglycerides by inhibiting biosynthesis in the liver, and inhibiting oxidation of LDL.

A dose of 3 cloves, a gram of crude garlic powder, 5 or more Mg of “garlic oil”, 5-10 mg allicin show positive results in various clinical trials.

Several sulfur containing constituents in garlic bulbs, \textit{allyl propyl disulfide} or APDS and \textit{diallyldisulfide oxide} or allicin, are believed to contribute many of the medicinal effects.

Animal models of diabetes show garlic to reduce blood glucose, improve insulin sensitivity, and reduce oxidative stress in animals fed a high fructose diet.

\textbf{Image from pubs.rsc.org}

Animal studies also suggest that garlic may help protect the heart from the damage that occurs in diabetes.


GARLIC TO TREAT METABOLIC DISORDERS

- Garlic may reduce the protein glycation and build up in the tissues of AGEs.
- Animal studies suggest garlic oil to improve glucose tolerance and ameliorate proteinuria, more so than isolated diallyl disulfide.


GARLIC CLINICAL TRIAL ON DIABETIC PATIENTS

- One RCT dosed diabetic patients with either garlic and Metformin or placebo and Metformin to evaluate the effect on serum lipids and glucose.
- Lab values were run at 0, 12 and 24 week.
- Total cholesterol and LDL cholesterol reduced to a greater amount in those taking the garlic, and HDL levels increased, compared to the control.

Garlic consumption may slow atherosclerotic plaque formation.

A pilot study evaluating coronary artery calcification in patients on statin drugs showed adding garlic had incremental benefits compared to statin drugs alone.

One RCT evaluated the effects of daily raw red onion consumption compared to a low “liliaceous vegetable diet in women with PCOS.

Women in the onion group consumed 40-60 grams of raw red onions 2 times per day 8 weeks.

Body mass index and metabolic parameters (fasting blood sugar, triglycerides, total cholesterol, HDL and LDL were evaluated in the follicular phase of the menstrual cycle at baseline and after 8 weeks.

Onion consumption significantly decreased total cholesterol

Dong Quai is thought to be a “Blood Mover” in TCM.

*Angelica sinensis* is a vasodilator in part due to *Nicotinic acid* content.

*Angelica* “moves” the blood via many mechanisms and compound including:

- *Ferulic acid*
- *Lugistilide*
- *Coumarins*

Zhu, David, Dong Quai, Am J Chinese Med
ANGELICA’S ACTIONS

- These compounds give Angelica antihistamine, anticholine, antiserotonin, and platelet anti-aggregation effects.


- These compounds also give Angelica anti-inflammatory and anti-allergy effects, helping to reduce damage and inflammation to the blood vessels and tissues.

**ANGELICA’S FERULIC ACID**

- *Ferulic acid* reduces blood cholesterol and triglycerides and improve blood viscosity.
- *Ferulic acid* is antioxidant
- Gamma oryzanol also occurs naturally in plants as esters of ferulic acid.
- Gamma oryzanol metabolizes into *Ferulic acid* in the body
- Rice bran is presently used as a source of gamma oryzanol for therapeutic use.
Angelica coumarins inhibit platelet aggregation.

Angelica coumarins inhibit platelet aggregation.

INTRODUCTION

The Angelica dahurica ( Umbelliferae) root has not been used as a medicinal plant in traditional medicine as an analgesic (Kim et al., 1998). To date, only twenty coumarins have been isolated from this plant (Fujimura et al., 1982; Kim et al., 1992; Kuwabara et al., 1997). We were interested in the chemical constituents of A. dahurica root. Repeated column chromatography of the CHCl3-soluble fraction led to the isolation of four compounds. This paper deals with their isolation and the elucidation of their structure.

MATERIALS AND METHODS

Instruments and reagents

Melting points were determined on a Fisher-Johns melting-point apparatus and were uncorrected. Optical rotations were measured with a JASCO DIP-1000 instrument. Nuclear magnetic resonance spectra (1H and 13C) were recorded at 300 and 75 MHz on a Varian Gemini 200 and Bruker AMX-500 spectrometers using deuterated solvents as the internal standard. The IR (KBr pellet) and UV spectra were determined using a Perkin-Elmer 457 spectrometer. NMR and UV spectra are deposited in the Biological Microscopic Library, Kyushu University. Each fraction was evaporated in vacuo to yield the residues of n-hexane fraction (f), CH2Cl2 (f), CHCl3 (f), MeOH (f), and Me2CO (f).

The CH2Cl2-soluble fraction (0.3 g) was subjected to column chromatography on a silica gel (230-400 mesh, 15 = 50 cm) using n-hexane-petroleum ether (PE) (1:1, v/v) as eluent to yield 15 fractions (F1 to F15).

The above fractions were then subjected to preparative HPLC using a semipreparative column (ODS, 10 µm, 10 × 250 mm) and eluted with a gradient elution with a u-HPLC (40,21,1.1, v/v) system to obtain pure compounds

Correspondence to: Chang-Min Kim, College of Pharmacy, Kyung Hee University, Seoul 134-719, Korea. E-mail: kim@coughahn.ac.kr

A small pilot study investigated the effects of Angelica on platelets in UC patients.

*Angelica* improved thromboxane levels, platelet aggregation, and other measures of platelet reactivity, compared to controls.

Researchers concluded that *Angelica* significantly inhibit platelet activation, relieved vascular endothelial cell injury, and improved microcirculation.

Angelica is commonly combined with Astragalus, or with *Salvia miltiorrhiza* to treat chronic renal diseases (chronic glomerulonephritis, chronic renal tubulointerstitial disease, hypertensive renal damage).

One RCT reported improved renal function from and *Angelica* and *Astragalus* combination in treating advance renal diseases.

Hibiscus has been shown to improve lipid profiles in patients with dyslipidemia including total Cholesterol and HDL/LDL levels.

Commiphora mukul
Guggul

- Guggul is a traditional herb from India used for obesity, inflammation, and sluggish metabolic rate.

- Modern research has shown benefits for lipid metabolism, general metabolic rate, and thyroid function.
Commiphora mukul
Guggul

- Guggul improve blood lipids, including increasing HDL and reducing LDL and VLDL.
- Guggul acts on bile acid receptors promoting hepatic degradation of LDL and may reduce atherosclerotic processes.
- Guggul helps prevent and treat arterial plaques.
COMMIPHORA’S GUGGULSTERONES

- Guggul contains a group of steroidal molecules referred to as guggulsterones.

- Guggulsterones may interfere with lipoprotein synthesis by inhibiting the production of cholesterol in the liver.


Animal studies show guggulsterones to inhibit the development and maturation of fat storing cells, the adipocytes.

**Guggulsterones exert direct inhibitory effect on adipocytes by:**

- Reducing synthesis of new cells,
- Decreasing fat accumulation in existing cells,
- Increasing apoptotic destruction of fat cells,
- Suppressing adipocyte regulatory proteins.


Guggulsterones are shown to have the following actions:

- Antagonism of farnesoid x receptor (FXR), a key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis, contributing to hypolipidemic action.

- Upregulation of the bile salt export pump (BSEP), an efflux transporter responsible for removal of cholesterol metabolites, bile acids from the liver, promoting cholesterol metabolism into bile acids, another hypolipidemic activity.

- Potent inhibition of NF-kappaB activation contributing to the antiinflammatory effect.

Curcuma longa
Turmeric

- Turmeric, a relative of ginger and an important ingredient in curry powder, is a powerful antioxidant and anti-inflammatory compound.

- The yellow pigmented flavonoid curcumin is credited with these anti-inflammatory actions, as well as cholesterol-lowering, and liver supportive activities.
Curcumin, a flavonoid in Turmeric, may improve lipids by several mechanisms:

- Reduces intestinal absorption of cholesterol from the intestines.
- Promotes the transformation of cholesterol into beneficial bile acids.
- Promotes, as well as promote biliary excretion of cholesterol.
- Promotes prostaglandin processing enzymes reducing vasoconstrictive and pro-inflammatory thromboxanes.
- Promotes synthesis of inflammatory modulating prostacyclins.
Curcuma longa
Turmeric

A review of the last decades’ research on Curcumin revealed the following MOA that may benefit diabetics and/or reduce inflammatory burden in obesity and metabolic syndrome:

- Interaction with specific proteins in adipocytes, pancreatic cells, hepatic stellate cells, macrophages, and muscle cells
- Suppression of cellular proteins NF-κB, STAT-3, Wnt/β-catenin and
- Activates PPAR-γ, Nrf2 cell signaling pathway.
- Downregulation of inflammatory cytokines, resistin and leptin,
- Upregulates adiponectin and associated proteins.

A small study investigated the effects of 6 grams of *Curcuma* of plasma glucose, insulin level, and glycemic index in health subjects following GTT.

The ingestion of 6 g *C. longa* had no significant effect on the glucose response, while postprandial insulin levels were increased.

A meta-analysis reviewed 6 eligible clinical trials on curcuminoids and reported strong evidence that the flavonoids could significantly reduce circulating levels of C reactive protein.


Curcuma has been shown to reduce inflammatory cytokines, particularly interleukins in renal disease patients, reducing inflammation and improving antioxidant capacity.

- Soy and other legumes contain isoflavones known to act as weak estrogen receptor agonists as well as exert mild lipid lowering effects.
- Aim to eat beans at least once a day
- Offer Patients Recipes, including breakfast ideas.

Image from www.lakshyanatural.com
One RCT investigated the effects of substituting meat for legumes of cardiovascular risk factors in Type 2 diabetics.

Specific diets were followed for 8 wks, and then subjects were crossed-over to a legume free control diet.

The Legume-based diet significantly decreased fasting glucose, insulin, TGs, and LDL.

Monascus purpureus
Red Rice Yeast

- Monascus is a type of red yeast used in traditional Chinese medicine as early as the Tang Dynasty to promote circulation.
- The traditional preparation fermented rice with this yeast and used the resulting food in the diet.
- Modern investigation has shown Monascus to act as a natural HMG-CoA reductase inhibitor.
- HMG-CoA reductase inhibitors deplete CoQ10 so this should be taken in tandem.
**CULINARY “BLOOD MOVERS’**

- Many common culinary herbs support circulation and reduce the tendency to clot formation.
- Use as medicines and help patients to work these spices into your daily cooking such that they might have a protective effect against circulatory diseases and risk factors.

- Garlic (*Allium sativum*)
- Onions (*Allium cepa*)
- Ginger (*Zingiber officinalis*)
- Cayenne (*Capsicum species*)
- Cinnamon (*Cinnamomum species*)
Ginger has broad anti-inflammatory and immune modulating effects. Ginger can be used in capsules, tinctures, teas, and as a medicinal foods.

Ginger’s effect on Lipids include:

- Promoting cholesterol transformation into bile salts
- Promoting biliary excretion of excess cholesterol.
- Improving blood viscosity by reducing platelet aggregation, and
- Reducing inflammatory and oxidative damage to vascular endothelium by reducing thromboxane synthesis and favoring series 2 prostaglandins.
Those with metabolic syndrome are at an increased risk of clot formation due to vascular inflammation and hyper-reactivity.

Botanical agents improve blood viscosity benefitting ischemic disease, poor perfusion, and tendency to clots or thrombi.

Garlic, Onions, Ginger, and Cayenne are all credited with the ability to keep blood fluid and prevent pathologic platelet aggregation.


Bordia, AK et al. 'Effect of garlic oil on fibrinolytic activity in patients with CHD', Athersclerosis, 1977, 28, pp 155-9

LIPOTROPIC AGENTS FOR HYPERLIPIDEMIA

- *Lipotropic* means fat mover and lipotropic agents and refers to agents that assist the liver to move or process lipids.

Traditional categories of herbs that may have a lipotropic effect include:
- Cholagogues
- Alteratives

These herbs make valuable components of an protocol for hyperlipidemia and Metabolic Syndrome

LIPOTROPIC NUTRIENTS

- Choline
- Methionine
- Inositol
- Betaine

Choline deficiency in rats has been shown to impair VLDL synthesis, and since choline is a component of phosphotidycholine, this is impaired as well. Choline may be synthesized from methionine. Lecithin contains a form of choline.
**ALTERATIVES AND CHOLAGOGUES**

- **Taraxicum** – Dandelion Roots
- **Arctium** – Burdock
- **Rumex** – Yellow Dock
- **Curcuma** – Turmeric
- **Silybum** – Milk Thistle
- **Cynara** – Blessed Thistle
- **Hydrastis** – Goldenseal
- **Mahonia** – Oregon Grape
- **Chelidonium** – Celendine
**Mahonia vulgaris** and **Hydrastis canadensis**
Oregon Grape and Goldenseal

- **Mahonia vulgaris** (formerly *Berberis vulgaris*) and *Hydrastis canadensis* are two alterative and cholagogue herbs.

- Both of these bitter roots improve digestive and liver function and help process fats and sugars.

- Both *Mahonia* and *Hydrastis* contain the isoquinoline alkaloid berberine. Berberine has been shown to improve insulin resistance in human investigations.

Human clinical trials with insulin resistant diabetics have shown significant reductions in blood glucose, fats, and insulin as evidence of improved insulin response and general metabolism with berberine.

Researchers in China report berberine to lower blood lipids by numerous complex effects on cellular enzymes, insulin signals inside cells, and other direct effects on adipocytes.
A small RCT evaluated the effect of berberine on insulin sensitivity and secretion in patients with metabolic syndrome.

Either 500 mg of berberine or placebo were dosed TID ac X 3 months

Berberine led to remission of metabolic syndrome, a decrease in waist circumference, Systolic BP, triglycerides, total insulin secretion, and improvement in insulin sensitivity.

Silybum marianum, the Milk Thistle plant reduces hyperlipidemia.

One placebo controlled double blinded trial used 420 mg of Silymarin, a component of Silybum for a duration of 3 months.

Total Cholesterol and HDL levels were noted to be slightly reduced in those receiving Milk Thistle compared to placebo.
Silybum marianum
Milk Thistle
BOTANICAL THERAPIES FOR HYPERTENSION

Natural Beta Blockers, Calcium Channel Blockers and Other Mechanisms
High blood pressure is common in the adult population affecting over 1 in 5 Americans.

Physical fitness is associated with lower blood pressure.

Vegetarians generally have less hypertension than non-vegetarians do, and an inadequate consumption of fiber is associated with a greater risk of developing hypertension.

Murray M, Pizzorna J, Encyclopedia of Natural Medicine, 1990 Prima Pub Rocklin, CA Chapter 48


Kaplan NM, “Non drug treatment of hypertension” Annals of Internal Medicine, 1985, 102, pp 359-73
Garlic promotes nitric oxide and improves blood viscosity.

Garlic may improve blood pressure with dosages from 1800mg fresh garlic to 18mg-garlic oil to 900 mg dry garlic powder standardized to 1.3% alliin.

Some patients may have digestive SA and tolerate “aged” garlic best.

- Rotzch, E, “Postprandial lipidemia under treatment with Allium sativum. Controlled double-blind study in healthy volunteers with reduced HDL2-cholesterol levels” J Arznheim Forsch 1992 42(10), pp 1223-7
GARLIC CLINICAL TRIALS

- One RCT evaluated the effects of garlic at various dosages on BP in hypertension patients, compare to both atenolol and placebo.

- Garlic reduced BP in both a dose and duration manner compared to placebo, and similar to atenolol at the higher dosage range of 1200 and 1500 mg/day.

CRATAEGUS OXYCANTHA, MONOGYNA
Hawthorne Berry

- Hawthorn is in the Rose Family and like rose hips, apples, cherries, plums and other fruits of the same family, bears fruits that are high in flavonoids with many antioxidant and anti-inflammatory effects.

- Proanthocyanidins in Hawthorn berries have been the subject of much research.
**Crataegus PCOs**

- **Procyanidolic oligomers (PCO) or “pycnogenol”** are small dimers of epicatechin, a tannin derivative.
- PCOs are also extracted from grape seeds and pine bark, hazel leaves, and lime flower bracts.
- PCOs are flavonoids that stabilize capillaries when taken at a dosage of 150 to 300 mg per day, and serve to reduce vascular permeability and fragility.

Hawthorn - *Crataegus* PCOs

- *Crataegus* products are standardized to 10-28% PCO content, and/or 1.8% vitexin-4-rhamnoside.
- Hawthorne’s PCOs have a positive ionotropic action, promote diuresis but do not deplete minerals, and normalize blood pressure.
- Hawthorne enhances myocardial contractility, yet coronary arteries are dilated rather than contracted.

Rewerski VW et al Some pharmacologic properties of oligomeric procyanidin isolated from hawthorne (*Crategus oxyacantha*) *Arzneim Forsch*, 17:490-1, 1967
Hawthorn - *Crataegus* PCOs

- *Crataegus* PCOs have a stabilizing effect on capillaries serving to reduce vascular permeability and fragility.
- *Crataegus* may be included in formulas for both hyper- and hypotension, elevated cholesterol levels, angina pectoris, and atherosclerosis.
- Clinical trials using Hawthorne extracts in patients with CHF showing significant improvements in symptoms and heart function.


Hawthorne PCOs have ACE inhibiting effects.

Hawthorn is a natural Calcium Channel Blocker due to Phosphodiesterase Inhibition.

One RCT investigated the effects of hawthorn for hypertension in patients with type 2 diabetes taking prescribed drugs.

No herb-drug interaction was found and minor health complaints were reduced from baseline in both groups.

Gingko biloba
The Maidenhair Tree

- Gingko is a traditional medicine for heart Dz, Allergies, Asthma, and Inflammation.
- Gingko leaves have vasodilating effects, reducing blood pressure, and enhancing peripheral, coronary, and cerebral perfusion.
- Gingko flavonoids are antioxidant, reduce lipid peroxidation, and free radical damage.

Ginkgo contains physiologically active flavonoids called heterosides.

Ginkgo products are often standardized to 24% flavonoids also known as heterosides.

GINKGO FLAVONOIDS INCLUDE:
- Heterosides
- Quercitin
- Kaemferol
- Isorhamnetin
- Proanthocyanindins (Cyanidin, Delphinidin)
- Carotenoids (Zeaxanthin, Lutein)
Ginkgo Terpenes

- Terpene constituents in Ginkgo include the gingkolides, a group of bitter diterpenes unique to Gingko and numerous other sesquiterpenes.
As early as the 1970s, clinical research reported *Gingko* to be useful in cases of arterial insufficiency, intermittent claudication, ischemic heart disease, and other cases of tissue hypoxia.

*JAMA*, 1975, 231; 1162
Ginkgo biloba

Gingko is a plant helpful for supporting circulation

➤ to the brain,
➤ to the extremities,
➤ to the microcirculatory blood vessels,
➤ and to the heart muscle itself.


- Beta receptors promote stimulation of the heart, vasculature, and uterus, thus many classic botanical uterine antispasmodics are also vasodilators.

- Botanicals the Antagonize Beta Adrenergic Receptors Include:
  - *Leonurus cardiaca*
  - *Tilia europea*
  - *Viburnum opulus*
  - *Lobelia inflata*
Viburnum opulus
Crampbark

- Crampbark is primarily a B2 antagonist, with action primarily on the uterus.
- Crampbark is also relaxing to the bronchi, intestines, skeletal muscle, and vasculature to a lesser degree.
- The smooth muscle relaxing activity of Viburnum provides a hypotensive effect when included in herbal formula.

Leonurus cardiaca
Motherwort

- *Leonurus* cardiac is a Mint Family plant traditionally for nervous heart conditions and digestive disorders, bronchial asthma, climacteric symptoms, and ammenorrhoea, as well as externally in wounds and skin inflammations.

- *Leonurus* has mild negative chronotropic, hypotonic and sedative effects

- *Leonurus cardiaca* has demonstrated many activities that reduce CV risk factors including antioxidant, anticoagulant, and anti-apoptotic effects in vascular cells.
Leonurus cardiaca
Motherwort

- Leonurus is a natural beta blocker with an affinity for the uterus and vasculature.
- Leonurus has a hypotensive effect.
- In the folkloric literature, Leonurus is specific for pelvic pain with concomitant heart palpitations, anxiety attacks, and stress.

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<th>Leonurus cardiaca</th>
<th>Motherwort</th>
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<tr>
<td><strong>Leonurus Flavonoids Include:</strong></td>
<td><strong>Leonurus Also Contains:</strong></td>
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<tr>
<td>- Chlorogenic acid</td>
<td>- Terpenes: monoterpenes, diterpenes, triterpenes</td>
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<td>- Orientin</td>
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Leonurus cardiaca
Motherwort

- *Leonurus* injections improve blood viscosity by decreasing platelet aggregation, fibrinogen content, and erythrocyte deformation.

Leonurus cardiaca
Motherwort

MODERN RESEARCH SHOWS MECHANISMS INVOLVING:

- Down-regulation of TNF-α, IL-1, IL-6, IL-8, KIM-1 expression and by the
- Inhibition of the phosphorylation of IκBa and p65 translocalization. These results suggest that LEO may
- Suppression of NF-κB activation
- Inhibition of pro-inflammatory cytokine production

- L. cardiaca can significantly reduce phosphorylation activities involved with mitochondrial oxidative respiratory chains generated by free radicals.
- Leonurus may offer cardioprotection via this and other mechanisms.

Leonurus cardiaca
Motherwort

- Animal studies suggest protective effects on the renal vasculature.
- One pilot study evaluated the effects of Leonurus on patients with hypertension associated with anxiety and sleep disorder.
- After one month on 1200 mg/day, a significant improvement in the symptoms of anxiety and depression was observed in 32% of patients, a moderate improvement in 48% and a weak effect in 8%; 12% of patients did not respond to therapy.
- Side effects were minimal.


**Leonurus cardiaca**

**Motherwort**

- *Leonurus* may deter endocarditis due to inhibition of bacterial adherence and biofilm formation.

Leonurus cardiaca
Motherwort Clinical Trial

- One pilot study evaluated the effects of Leonurus on patients with hypertension associated with anxiety and sleep disorder.
- After one month on 1200 mg/day, a significant improvement in the symptoms of anxiety and depression was observed in 32% of patients, a moderate improvement in 48% and a weak effect in 8%; 12% of patients did not respond to therapy.
- Side effects were minimal in all groups.

Lobelia inflata

- Lobelia is vasorelaxing via B Adrenergic blockade.

- Lobelia is a traditional remedy for cough, asthma, hypertension, angina, and tachycardia.
Botanicals that may affect Calcium Channels on cardiac muscle include:

- *Angelica sinensis*
- *Mentha piperita*
- *Crataegus* species
- *Daucus carota* and relatives
- *Tussilago farfara*
Angelica may have calcium channel blocking ability.

Angelica contains Ferulic acid which may calm cardiac arrhythmias.

Angelica also contains nicotinic acid with vasodilating action.

Angelica’s traditional indications include stagnant circulation, pelvic congestion, and uterine cramps.

Mint is a calcium antagonist to smooth muscle, but less so cardiac muscle.

Mint may help angina following meals when digestive spasm triggers angina, arrhythmia, and tightness in the chest.

Peppermint oil was included in the “Glyconda Formula” of 1800s used for angina, arrhythmia, and cardiovascular symptoms accompanied by indigestion, and gastric and intestinal ailments.

**Tussilago farfara**

Coltsfoot

- Tussilago or Coltsfoot is also a Ca channel blocker and PAF inhibitor.
- Animal studies have noted Tussilago to have calcium channel blocking activity in rat aorta.
- Tussilago has been used historically for asthma, chronic cough, hypertension and tightness in the chest.

Botanical Diuretics may complement vasodilating, calcium channel blocking, and ACE inhibiting herbs.

Botanical Diuretics do not deplete K, Mg or other minerals as pharmaceutical diuretics do.

**Botanical Diuretics Include:**
- *Equisetum* (Horsetail)
- *Medicago* (Alfalfa)
- *Taraxicum* (Dandelion)
- *Urtica* (Nettles)
- *Petroselinum* (Parsley)
- *Apium* (Celery Seeds)
Other botanical agents that improve hypertension include sedative muscle relaxing herbs.

Sedative herbs are palliative and useful to include in formulas for hypertension, but may not slow pathology or protect the vasculature the way flavonoids and metabolic correctives agents can.

Herbal Sedatives and Vasorelaxers Include:
- Rauwolfia serpentina
- Viscum
- Tilia europea
- Valerian officinalis stichensis
- Passiflora incarnata
Native to India, *Rauwolfia* has been used as a traditional Ayurvedic medicine for many ailments, including anxiety, headaches, snakebites, and as a general sedative for over 1000 years.

The whole plant extract 1:4 may be dosed at ml at a time, increasing to building to two and three times a day if necessary. Do not exceed 5-6 mg of whole extract/day.

*Rauwolfia* has potential side affects of muscle weakness, fatigue, impotence, and depression, so this is not a first choice therapy.
**Rauwolfia serpentina**
Indian Snake Root

**Rauwolfia’s Actions Include:**
- Decreases myocardial excitability,
- Inhibition of AV conduction, and
- Extension of the refractory period of the heart rhythm.

- Although *Rauwolfia* will reduce blood pressure, its effects are more pronounced on the CNS, than the peripheral nervous system through activity at the diencephalon.
- The alkaloid reserpine decreases the release and accumulation of noradrenaline.
- Another alkaloid, *ajamaline* is thought to be antiarrhythmic.
- *Rauwolfia* blocks adrenergic activity.
Viscum album
Mistletoe

- *Viscum* is a strong hypotensive with toxic potential.

- *Viscum* is specifically indicated for the hypertensive patient who has a weak feeble pulse, dyspnea, and restlessness.

- *Viscum* is also indicated for sudden rushes of blood to the head causing frequent headaches with flushed face, and tearing intense pain.

- *Viscum* is also indicated for CHF where there is enlargement of the heart.
Viscum album
Mistletoe

- *Viscum* contains a choline derivative similar to acetylcholine with a vasodilating properties via parasympathetic mechanisms.

- *Viscum* also contains a vasodilating nitrates that promote vascular relaxation as endogenous Nitric oxide itself does.

- Endogenous and exogenous nitrates stimulate cGMP promoting vascular smooth muscle relaxation.

- Nitrates such as amylNitrate and Nitroglycerine have been used for anginal pain since the late 1800s.
OTHER HERBS TO SUPPORT THE VASCULATURE

FLAVONOIDS, PHYTOSTEROLS AND TONICS
Phytosterols inhibit intestinal cholesterol absorption.

Plant sterols attenuate gene expression reducing cholesterol uptake and lowering the cholesterol esterification.

Phytosterols have potent antioxidant effects reducing oxidative stress in the body.

Consumption of phytosterols in oils, nuts, and plants are associated with healthier blood lipids and inflammatory markers.

Chart from quickanddirtytips.com
Beta sitosterol is a common phytosterols

Certain protein kinases help regulate metabolism of intracellular lipids and glucose.

Beta-sitosterol has been shown to regulate these kinases.

Beta-sitosterol increases glucose uptake and reduces intracellular triglycerides and cholesterol.

Cholesterol, Phytosterol, and Tocopherol Content of Food Products and Animal Tissues

MILLY LANGE, Chemical Division, The Proctor and Gamble Company, Cincinnati, Ohio

Atherosclerosis. Many myths have been created concerning the causes and treatment of atherosclerosis, a disease in which fatty deposits collect in the inner lining of the arteries. These deposits may eventually block the flow of blood, causing heart attacks, strokes, and other serious medical problems. The disease is thought to be caused by a combination of factors, including high blood pressure, high cholesterol levels, cigarette smoking, and a poor diet. The main treatment for atherosclerosis is to reduce the risk factors that contribute to its development. This can be done by making lifestyle changes, such as eating a healthy diet, getting regular exercise, and avoiding smoking. In addition, medications may be prescribed to lower cholesterol levels or to treat other conditions that contribute to the development of atherosclerosis.

Beta-sitosterol has been shown to regulate these kinases. Beta-sitosterol increases glucose uptake and reduces intracellular triglycerides and cholesterol.
Resveratrol, a naturally occurring polyphenol with numerous health benefits including anti-oxidant, anti-inflammatory, anti-aging, cardioprotective and neuroprotective activities.

Resveratrol has antioxidant and apoptotic action.

STEROLS IN NUTS

- Almonds, Sesame seeds, Walnuts, Peanuts and other nuts are high in phytosterols.
- Including nuts and nut oils in the diet has been shown to lower total cholesterol and improve lipid profiles.
- Epidemiologic studies show that those with the highest nut consumption displayed intake reduced risk of CHD incidence based on lipid profiles.
- Nuts are rich in Phytosterols and anti-inflammatory sterols such as resveratrol.
- Proanthocyanidins are found in almonds, cashews, hazelnuts, pecans, pistachios, peanuts, and walnuts, with concentrations varying from 9-494 mg/100 g.
- An inverse relationship has been shown between nut consumption and cardiovascular disease.
Phytoestrogens act as specific ER modulators and improve the actions of estrogen in the aging blood vessels.

Genistein, the most common phytosterols, reduces vascular inflammation and exerts a positive effects on endothelial cells.

Isoflavones activate Nitric Oxide synthesis in endothelial cells and protect against cell damage.

Genistein inhibits angiotensin-converting enzyme offering a hypotensive effect.


Image from algaecal.com
Licorice is a medicinal plant used for thousands of years.

Its most common side effect is hypokalemic hypertension, which is secondary to a block of 11beta-hydroxysteroid dehydrogenase type 2 at the level of the kidney, leading to an enhanced mineralocorticoid effect of cortisol.

This effect is due to glycyrrhetinic acid, which is the main constituent of the root, but other components are also present, including isoflavans, which have estrogen-like activity, and are thus involved in the modulation of bone metabolism.
Abnormal cortisol metabolism plays a role in the pathogenesis of hypertension.

11beta-hydroxysteroid dehydrogenase (11beta-HSD) isozymes catalyze interconversion of cortisol and cortisone, playing an important role in the regulation of the effects of cortisol.

Activity of 11beta-HSD type 2, converting active cortisol in inactive cortisone, is crucial in preventing access of cortisol to the renal mineralocorticoid receptors (MRs).

Decreased activity of this isozyme in the kidney, either congenitally in Apparent Mineralocorticoid Excess syndrome or acquired following licorice consumption, allows cortisol access to the MRs, resulting in hypokalemic hypertension.
BIOFLAVINOIDS CONTAINING BOTANICALS

- For all Vascular Issues, use high bioflavonoid containing herbs and foods.
- Bioflavonoids have antioxidant and anti-inflammatory actions and support integrity of the blood vessels themselves.
- The carotenoids, the procyanadin oligomers, the anthocyanosides, rutin, querticin, and hesperitnin are all common in brightly colored frutis, veggies, and herbs.
Vaccinium myrtillis
Blueberry, Bilberry

- Blueberry leaves and fruit have long been a folk remedy for diabetes.
- Animal studies shown blueberries to reduce blood glucose and enhance insulin sensitivity in type 2 diabetic mice.
- Blueberries promote the intracellular "second messenger" cyclic AMP and associated protein kinases.

Human studies on *Vaccinium*’s glucose regulation are sparse, but one study on overweight and obese women with Metabolic Syndrome reported the consumption of blueberries to have a slight but statistically significant effect of total weight and waist circumference compared to other berries and isolated chemical concentrates from berries.

Vaccinium myrtillus
Blueberry, Bilberry

- Anthocyanins (also called anthocyanosides) are a group of bluish-purple pigmented flavonoids found in Vaccinium species that have a protective effect on capillaries and blood vessel walls.

- Anthocyanins are powerful antioxidants and reduce the inflammatory damage to blood vessels inflicted by the many inflammatory and abnormal metabolic processes seen with diabetes, high cholesterol, and Metabolic Syndrome.

Vaccinium myrtillus
Blueberry, Bilberry

- Blueberries enhance circulation and are both a preventative and therapy for diabetic retinopathy, peripheral neuropathy, and circulatory insufficiency.

- Many commercial products exist, often standardized to deliver 160 mg anthocyanins per day.

- Eating whole blueberries is highly recommended for diabetics and those with Metabolic Syndrome.
HERBS TO IMPROVE METABOLIC FUNCTION

BOTANICAL AGENTS THAT IMPROVE CARBOHYDRATE AND LIPID METABOLISM
Botanical Agents may improve basic metabolic function via:

- Thyroid Support (Guggul, Fucus)
- Insulin Reception (Opuntia, Stevia)
- Liver Support (Cholagogues, Alteratives)
Opuntia
Prickly Pear Cactus

- **Opuntia** optimizes basic metabolism
- **Opuntia** normalizes blood glucose and cholesterol in animal models of diabetes.
- **Opuntia** juice lowers elevated blood sugar.
- **Opuntia** normalized carbohydrate metabolism in diabetic animals.

Stevia redbudiana
Stevia or Sweet Leaf

- Stevia, a sweet tasting herb from the South American Andes, improves insulin resistance.
- The sweet steviosides have no calories and a glycemic index of zero.
- Stevia is naturally high in chromium, a mineral that supports insulin signal transduction.
- Animals suggest Stevia may improve insulin output from the pancreas for Type I diabetes, as well as improve insulin resistance in Type II diabetes.


Lepidium meyenii
Maca

- Maca contains linoleic and linolenic essential fatty acids and is noted to improve blood fats when included in animal feed.

- Animal studies shown Maca to reduce high blood pressure.

- Maca may enhance kidney clearance of Na, K, and Cl in a manner that helps reduce blood pressure.

- Lepidium may also improve blood flow in the heart.


Maca improves metabolic syndrome when induced in rats are fed a high sucrose diet, abolishing the tendency to cholesterol and glucose elevations.

General hypoglycemic effects have also been reported.

Maca may increase the urinary excretion of glucose.

Maca is available as a flour-like powder that may also be stirred into juices, milks, and fruit purees to enhance the medicinal value of the daily diet.

THE LEGUME FAMILY
All Types of Beans and Legume Family Herbs

- Legumes offer many health benefits for blood sugar, obesity, and metabolic syndrome.
- Legumes in the diet and medicinal herbs in the legume family are beneficial for insulin resistance, hormonal balance, and lowering blood sugar and cholesterol.
- Legumes contain fiber, choline, magnesium, lecithin, saponins and other beneficial compounds which have been investigated together and individually.

DIETARY LEGUMES

- The legume family of plants may be eaten in the form of hummus, bean soup, a side of lentils or a soy smoothie, garbanzo flour substituted for wheat flour, etc.
- Legume family herbs may be consumed as herbal teas, tinctures, or in encapsulated products.
Legumes contain *Pinnitol* and the *D-Chiro-Inositol*, both known to support insulin reception.

*Pinnitol* from soy has been shown to support HDL ("good") cholesterol and promote antioxidant enzymes in the liver.

*Pinnitol* and *D-Chiro-Inositol* improve insulin resistance by improving signal transduction.

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**Chart from pcosinfo.wordpress.com**

Many Herbaceous Legume Family Plants may also improve insulin reception and signal transduction including:

- *Pueraria mirifica, lobata* Kudzu
- *Astragalus membranaceous* Milk Vetch
- *Medicago sativa* Alfalfa
- *Glycyrrhiza glabra* Licorice
- *Trigonella foenum-graecum* Fenugreek
QUESTIONS