Common Naturopathic Therapies for Chronic Conditions

A comprehensive introduction for allopathic providers to the various supplements used by Naturopathic doctors to treat hypertension, diabetes, and hyperlipidemia

This packet compiles information about the clinical use of each proposed supplement, including any available evidence that attests to treatment efficacy or safety of use within the targeted population

Family Medicine Clerkship Community Health Project
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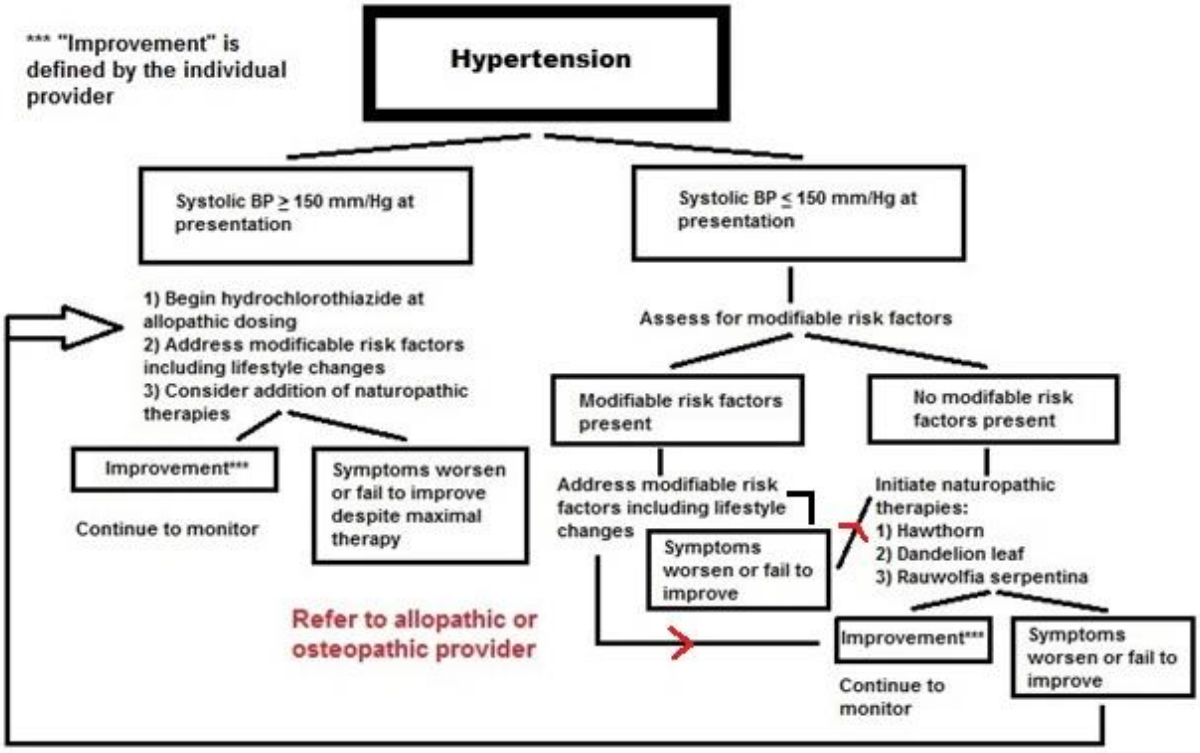
Hypertension

Naturopathic treatment protocol: *because there are no "best practice" guidelines for prescribing naturopathic remedies, each provider has complete freedom to individualize their methodologies*



Naturopathic therapies for hypertension:

***Note:** it is difficult for providers to estimate the efficacy of individual naturopathic therapies because their administration is always combined with lifestyle changes, confounding the clinical picture

1) Lifestyle changes: *whole-person centered approach*

A) Perceived efficacy: 10-15 mm/Hg decrease in systolic blood pressure[1]

2) Hawthorn

A) Dosing: 50-600mg given BID-TID[9]

B) Perceived efficacy: 5-7 mm/Hg decrease in systolic blood pressure[1]

C) Cautions: *no information available regarding absolute contraindications*

-Adverse effects: nausea, fatigue, headache, dizziness, palpitations, nosebleeds, insomnia, agitation[9]

-Drug interactions: digoxin, beta-blockers, calcium-channel blockers, phoshodiesterase-5-inhibitors, nitrates[9]

D) Antihypertensive mechanism:

1) Hawthorn extract exerts an NO-dependent vasodilatory effect at endothelial cells[2,3,4]

2) Hawthorn extract produces a dose-dependent decrease in heart rate via direct stimulation of the muscarinic receptor (M2) and possible blockade of beta receptors[5]

E) Clinical antihypertensive evidence: ***moderate clinical evidence of efficacy as antihypertensive***

1) *British Journal of General Practice,* 2006- randomized control trial demonstrating anti-hypertensive effect of hawthorn in diabetic patients taking prescription drugs[6]

2) *Phytotherapy Research,* 2002- randomized, double-blind pilot study showing anti-hypertensive effect of hawthorn in patients with mild essential hypertension[7]

3) *Phytomedicine,* 2002- randomized, controlled, cross-over study showing that hawthorn stabilizes diastolic blood pressure in patients suffering from orthostatic hypotension[8]

3) Dandelion leaf

A) Dosing: *no dosing recommendations available*

B) Perceived efficacy: 5-7 mm/Hg decrease in systolic blood pressure[1]

C) Cautions:

-Absolute contraindications: ragweed allergy

-Adverse effects: *none known*

-Drug interactions: quinolone antibiotics, lithium, CYP1A2 substrates, potassium-sparing diuretics, ACE-inhibitors

D) Antihypertensive mechanism:

1) Dandelion leaf contains potassium and sesquiterpene lactones which exert a loop diuretic-like effect leading to volume contraction[11]

E) Clinical antihypertensive evidence: ***there is no direct clinical evidence to suggest that dandelion leaf lowers blood pressure***

-Evidence of diuretic effect

1) *The Journal of Complementary and Alternative Medicine,* 2009- pilot study showing increased urinary frequency and volume in normal subjects after ingestion of dandelion extract[10]

4) Rauwolfia serpentina (Indian snakeroot)

A) Dosing: *no dosing recommendations available*

B) Perceived efficacy: 15-20 mm/Hg decrease in systolic blood pressure[1]

C) Cautions:

-Absolute contraindications: concurrent electroconvulsive therapy, gallstones, stomach or intestinal ulcers, ulcerative colitis, depression, pheochromocytoma, pregnancy[13]

-Adverse effects: **can be toxic if dosed inappropriately**, nausea, vomiting, convulsions, Parkinson's-like symptoms, slowed reaction time, coma[13]

-Drug interactions: alcohol, digoxin, levodopa, MAOIs, antipsychotics, propranolol, barbiturates, stimulant medications, TCAs, thiazide diuretics, loop diuretics[13]

D) Antihypertensive mechanism: ***based on data from reserpine, an FDA-approved antipsychotic/antihypertensive medication originally extracted from Rauwolfia serpentina***

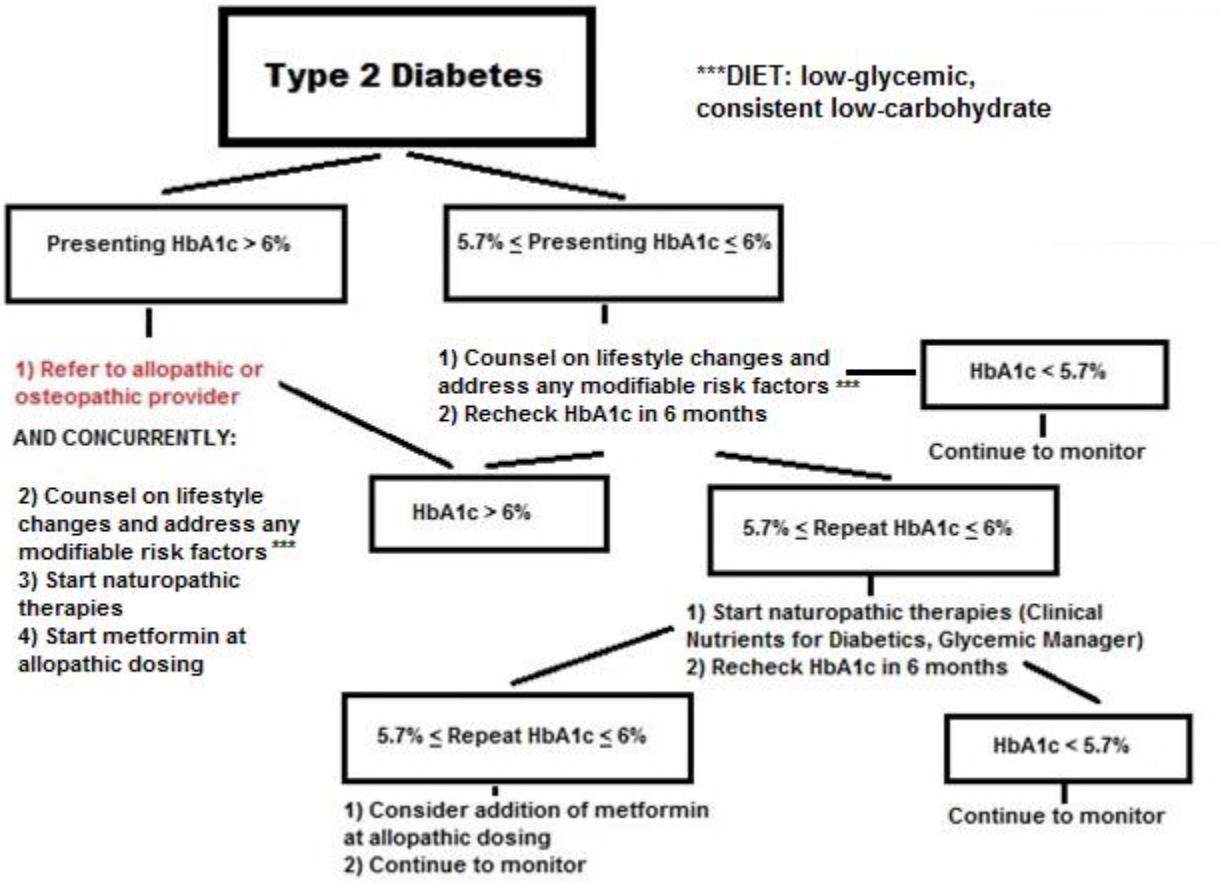
1) Rauwolfia serpentina likely irreversibly blocks the uptake (and storage) of norepinephrine and dopamine into synaptic vesicles by inhibiting vesicular monoamine transporters[14]

E) Clinical antihypertensive evidence: ***only available for use of reserpine; strong clinical evidence of efficacy as antihypertensive***

1) *The Cochrane Database of Systematic Reviews,* 2009- the overall pooled effect from 4 randomized control trials demonstrates a statistically significant reduction in systolic blood pressure in patients taking reserpine compared to placebo[12]

Type 2 Diabetes Mellitus

Naturopathic treatment protocol: *because there are no "best practice" guidelines for prescribing naturopathic remedies, each provider has complete freedom to individualize their methodologies*



Naturopathic therapies for type 2 diabetes mellitus:

***Note:** it is difficult for providers to estimate the efficacy of individual naturopathic therapies because their administration is always combined with lifestyle changes, confounding the clinical picture

1) Lifestyle changes: *whole-person centered approach*
-Diet should be low-glycemic, low-carbohydrate
A) Perceived efficacy: variable and dependent on modifiable risk factors
2) Clinical Nutrients for Diabetics supplement (Integrative Therapeutics) ***
***Representative management supplement used by Naturopathic doctors**
A) Dosing: 2 tablets QD - BID
B) Perceived efficacy: 0.3% decrease in HbA1c[1]
C) Clinical evaluation of "anti-diabetic" ingredients:
1) Selenium: ***no clinical evidence for supplementation in T2DM***

-*Endocrine,* 2014- review of randomized clinical trials from 1990-2013 does not demonstrate any appreciable anti-diabetic effect of selenium in type 2 diabetics[15]

-Adverse effects: affects sperm motility, increased risk of prostate cancer, increased risk of skin cancer, worsening of hypothyroidism[15]

Drug interactions: antiplatelet drugs, statins, niacin, barbiturates, warfarin[15]

2) Chromium: ***no clinical evidence for supplementation in T2DM***

-*World Journal of Diabetes,* 2014- review of randomized clinical trials demonstrated that chromium supplementation did not improve fasting plasma glucose levels or have any relevant effects on body weight in individuals with type 2 diabetes[16]

-Absolute contraindications: chromate or leather allergy[16]

-Adverse effects: skin irritation, headaches, nausea, impaired thinking, judgment, and coordination, liver problems, kidney problems, worsening of psychiatric conditions[16]

-Drug interactions: levothyroxine[16]

3) Bitter melon fruit extract: ***mild clinical evidence for supplementation in T2DM***

-*Journal of Ethnopharmacology,* 2011- bitter melon had a modest hypoglycemic effect and significantly reduced fructosamine levels in type 2 diabetics at a dose of 2000 mg/day. The hypoglycemic effect of bitter melon was less than metformin at 1000 mg/day[17]

4) Gymnema leaf extract: ***extremely limited and flawed clinical evidence for supplementation in T2DM***

-*Journal of Dietary Supplements,* 2011- preliminary evidence from small, flawed human trials suggests hypoglycemic effects of a long-term oral gymnema regimen when used as an adjunct to insulin or oral hypoglycemic drug. Gymena has not been thoroughly evaluated as a safe or effective alternative to current anti-diabetic medications[18]

5) Fenugreek Trigonella seed extract: ***mild but flawed clinical evidence for supplementation in T2DM***

-*Nutrition Journal*, 2014- significant effects on fasting and 2-hour postprandial glucose levels were only found for studies that administered high doses of fenugreek to persons with type 2 diabetes. Most of the trials were of low methodological quality[20]

6) Bilberry fruit extract: ***no clinical evidence for supplementation in T2DM – only available trial combined bilberry with fermented oatmeal and used healthy subjects***

-*Nutrition Journal,* 2011- in healthy subjects, bilberries added to a fermented oatmeal drink induced a lower insulin response than the fermented oatmeal drink alone. The mechanism for the lowered acute insulin demand is unclear[22]

-Drug interactions: antiplatelet medications[22]

7) Vanadium: ***no clinical evidence for supplementation in T2DM – may even increase triglycerides***

-*Monthly Journal of the Association of Physicians*, 2008- 151 clinical studies reviewed for benefit of vanadium supplementation in type 2 diabetic patients – none even met original inclusion criteria – and though there were significant treatment effects, they must be interpreted with caution due to extremely poor experimental quality[23]

-*Annals of Nutrition & Metabolism*, 2008- vanadium administration in patients with impaired glucose tolerance increased triglyceride concentrations with changes in insulin sensitivity[24]

-Adverse effects: increased triglycerides, kidney problems[23]

-Drug interactions: antiplatelet drugs[23]

2) Glycemic Manager (Integrative Therapeutics) ***

*****Representative management supplement used by Naturopathic doctors**

A) Dosing: 2 tablets QD

B) Perceived efficacy: 0.3% decrease in HbA1c[1]

C) Clinical evaluation of "anti-diabetic" ingredients:

1) Myricetin: ***never been trialed alone in T2DM, but moderate clinical evidence of anti-diabetic effect when given with chlorogenic acid and quercetin***

-*Journal of Medicinal Food,* 2013- blend of chlorogenic acid, quercetin, and Myricetin has shown efficacy in reducing fasting blood glucose, 2-hour postprandial glucose, and post-50g OGTT in type 2 diabetic patients. Effect was equivalent to that of metformin alone[27]

2) Cinnamon: ***no clinical evidence for supplementation in T2DM***

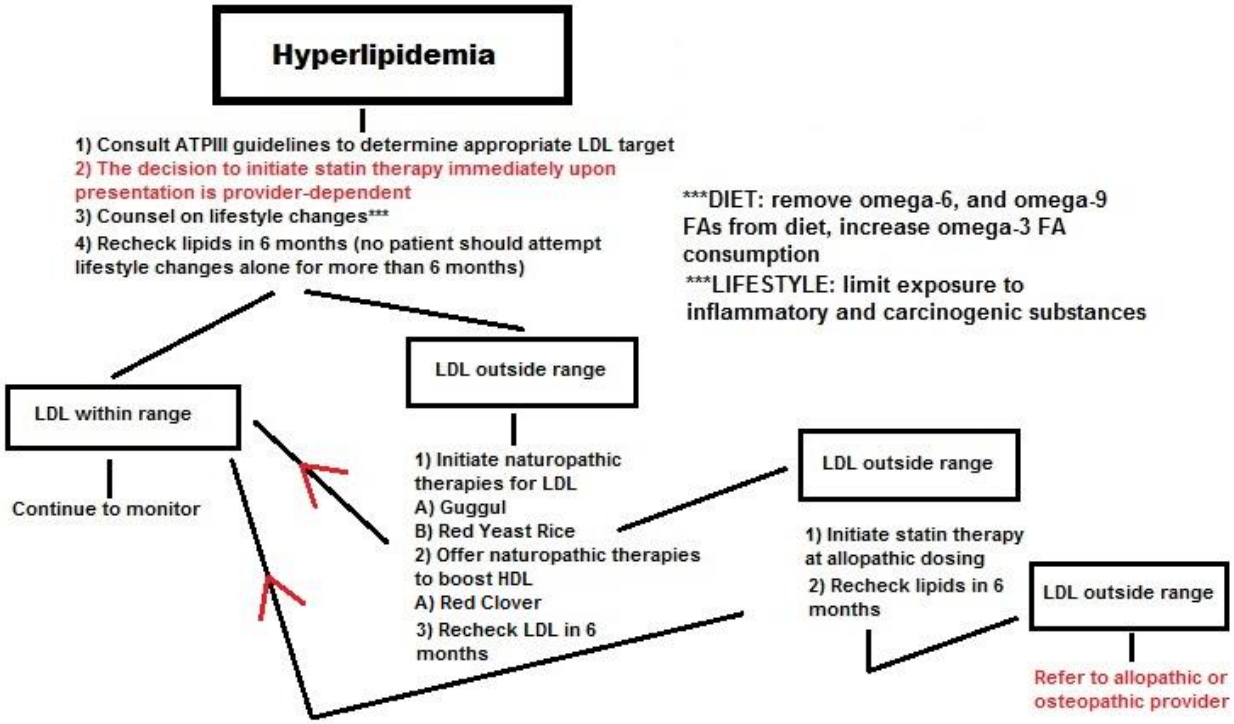
-*Journal of Traditional and Complementary Medicine,* 2013- randomized clinical trial in which patients were given either cinnamon or placebo in addition to their routine type 2 diabetes treatment for 60 days. There was no significant difference in either fasting blood sugar or glycosylated hemoglobin levels before and after administration of cinnamon. There was no significant difference in either fasting blood sugar or glycosylated hemoglobin levels between treatment groups[25]

-Adverse effects: cassia cinnamon hepatotoxic in high doses[25]

-Drug interactions: use cautiously with other potentially hepatotoxic medications[25]

Hyperlipidemia

Naturopathic treatment protocol: *because there are no "best practice" guidelines for prescribing naturopathic remedies, each provider has complete freedom to individualize their methodologies. It seems that most naturopathic doctors use the ATPIII guidelines for LDL classification. HDL is targeted on patient-specific basis*



Naturopathic therapies for hyperlipidemia:

*****Note:** it is difficult for providers to estimate the efficacy of individual naturopathic therapies because their administration is always combined with lifestyle changes, confounding the clinical picture

1) Lifestyle changes: *whole-person centered approach*
-Diet should limit omega-6 and omega-9 fatty acids while increasing consumption of omega-3 fatty acids
-Avoid exposure to carcinogenic and inflammatory substances (e.g. tobacco)
A) Perceived efficacy: minimal effect on LDL[35]

2) Guggul
A) Dosing: 500-1000mg BID-TID
B) Perceived efficacy: *unable to assess; no patients encountered using this supplement*
C) Cautions:
-Absolute contraindications: hormone-sensitive conditions, pregnancy, hyperthyroidism, hypothyroidism
-Adverse effects: headache, nausea/vomiting, loose stools, hiccups, skin rash

-Drug interactions: estrogens, birth control pills, diltiazem, CYP3A4 substrates, antiplatelet drugs, propranolol, tamoxifen, levothyroxine

D) Mechanism of action:

1) Decreases hepatic steroid production, ultimately increasing the catabolism of plasma LDL cholesterol[28]

2) Increases hepatic binding sites for LDL cholesterol, this increasing LDL clearance[28]

E) Clinical evidence of lipid effect: ***no clinical evidence for supplementation in hyperlipidemia – may even increase LDL***

-*Complementary Therapies in Medicine,* 2009- double-blind, randomized control trial of healthy adults with moderately increased cholesterol demonstrating a significant decrease in LDL from baseline with 2160mg guggul extract QD. There were a significant number of adverse effects reported by the experimental group, several of which resulting in withdrawal from the trial[28]

-*JAMA,* 2003- double-blind, randomized, placebo-controlled trial of healthy adults with hyperlipidemia showing no significant decrease in LDL cholesterol using either 1000mg or 2000mg guggul daily from that of placebo. LDL was actually increased in the experimental groups. Guggul also appeared to cause a dermatologic hypersensitivity reaction in several patients[29]

-*Complementary Therapies in Medicine*, 2005- at this time there is not enough scientific evidence to support the use of guggul for any medical condition. Guggul may cause stomach discomfort or allergic rash as well as other serious side effects and interactions. It should be avoided in pregnant or breast-feeding women and in children. Safety of use beyond 4 months has not been well studied[30]

3) Red Yeast Rice

A) Dosing: 1200-2400mg BID-TID

B) Perceived efficacy: 20-25 point decrease in LDL[35]

C) Cautions:

-Absolute contraindications: kidney disease, liver disease, allergies to yeast or fungus[31]

-Adverse effects: headache, stomach upset, muscle pain, liver injury[31]

-Drug interactions: immune suppressive medications, antifungals, protease inhibitors[32]

D) Mechanism of action:

1) Forms naturally occurring HMG-CoA reductase inhibitors called monacolins which lower LDL[32]

E) Clinical evidence of lipid effect: ***strong clinical evidence for supplementation in hyperlipidemia- lowers LDL and raises HDL***

-*PLoS One,* 2014- a review of 13 randomized, placebo-controlled trials showing that red yeast rice significantly lowers LDL and triglycerides, and significantly raises HDL in healthy adults with hyperlipidemia. Red Yeast Rice appears to be a safe approach to dyslipidemia[31]

-*BMC Complementary and Alternative Medicine*, 2013- double-blind, randomized, placebo-controlled trial demonstrating that red yeast rice significantly lowers LDL in healthy adults with hyperlipidemia

4) Red Clover

A) Dosing: 40-80mg QD[34]

B) Perceived efficacy: 5 point increase in HDL[35]

C) Cautions:

-Absolute contraindications: bleeding disorder, hormone-sensitive conditions, protein S deficiency[34]
-Adverse effects: rash, muscle pain, headache, nausea, vaginal bleeding[34]
-Drug interactions: estrogens, birth control pills, CYP1A2 substrates, CYP2C19 substrates, CYP2C9 substrates, CYP3A4 substrates, antiplatelet drugs, tamoxifen[33]

D) Mechanism of action:

1) Isoflavones in Red Clover act like estrogens[33]

E) Clinical evidence of lipid effect: ***strong clinical evidence for supplementation in postmenopausal women- raises HDL—****no research conducted in men or premenopausal women*

-*Menopause,* 2001- double-blind clinical trial conducted in healthy postmenopausal women showing that Red Clover significantly increases HDL, and significantly decreases apolipoprotein B as compared to placebo[33]
-*Journal of Obstetrics and Gynecology Research,* 2009- double-blind clinical trial conducted in healthy postmenopausal women demonstrating that Red Clover significantly lowers LDL and triglycerides, and significantly raises HDL. There were no adverse effects reported[34]

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Hypertension

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Hyperlipidemia

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