Heart disease is the leading cause of death for both men and women in the United States. In 2003, 23.5 million new cases of heart disease were diagnosed and nearly 700,000 deaths were attributed to heart disease. In 2002, approximately 163,000 patients died from stroke, making it the number three leading cause of death. Combine these figures and account for unreported cardiovascular deaths, and it becomes evident that cardiovascular disease leads to nearly 1 million deaths in the U.S. per year. Atherosclerosis is the major contributor to both heart disease and stroke, making it an important target for decreasing the global burden of cardiovascular disease.

Atorvastatin (Lipitor®) and simvastatin (Zocor®) were the top two prescribed drugs in the United States in 2003, accounting for a combined total of 13.3 billion dollars in prescription drug sales. These two agents grossed roughly 43% of the revenue produced by the top ten prescribed drugs. As popular and as proven as these drugs may be, the cost of taking them as prescribed is often out of reach for many average citizens. Estimated cash prices for atorvastatin and simvastatin are $290 and $360 respectively for a 90-day supply. Even those patients with prescription drug coverage may have to pay substantial co-pays (sometimes $50 or more per month) for these drugs depending on the insurance company’s drug formulary. Furthermore, the majority of patients for whom these drugs are prescribed are elderly and may have suboptimal prescription drug coverage. While Medicare Part D is promising and has the potential to save these patients thousands of dollars, most beneficiaries will still be paying for their drug benefit. Depending on the plan, some seniors will still have to pay over $5,000 out of pocket per year, including the premiums charged, deductibles, and the gap in coverage into which many patients will fall.

When cost is analyzed from a patient’s point of view, an over the counter herbal product which promises to achieve similar results as their prescription drug at a lower cost appears attractive. In 2004, retail sales within the consumer packaged goods health and wellness industry grossed an astounding $68.6 billion in revenue. This industry is not slow-
<table>
<thead>
<tr>
<th>Herbal Product</th>
<th>Adverse Events</th>
<th>Possible Interactions</th>
<th>Warnings and Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Yeast Rice Extract</td>
<td>Headache, mild gastrointestinal upset</td>
<td>None identified. Theoretically, consider drug interactions for statins (e.g., gemfibrozil, ciclosporine, ketoconazole, erythromycin, etc.)</td>
<td>None identified. Theoretically, consider precautions for statins (e.g. pregnancy, breastfeeding, hepatic, and/or renal impairment)</td>
</tr>
<tr>
<td>Policosanol</td>
<td>Weight loss, polyuria, insomnia polyphagia, headache, dizziness</td>
<td>May have antiplatelet effect (caution with warfarin, clopidogrel, etc.)</td>
<td>None known</td>
</tr>
<tr>
<td>Guggul Extract</td>
<td>One case of rhabdomyolysis reported. Rash, abdominal discomfort, diarrhea, nausea, headache, restlessness, and hiccups</td>
<td>Decreased bioavailability of propranolol and diltiazem. Fibrinolytic activity may lead to increased risk of bleeding in patients taking anticoagulants or antiplatelet medication</td>
<td>Thyroid disorders (lowers TSH by increasing production of T3) Avoid in women who have had breast, uterine, or ovarian cancer, endometriosis, and uterine fibroids (might be an agonist on estrogen-α and progesterone receptors) Pregnancy (stimulates menstrual flow)</td>
</tr>
<tr>
<td>Fenugreek Seeds</td>
<td>Mild gastrointestinal upset (flatulence, nausea, diarrhea)</td>
<td>Might increase effects of beta-blockers, calcium channel blockers, and cardiac glycosides May have antiplatelet effect (caution with warfarin, clopidogrel, etc.) Might contribute to hypoglycemic episodes with large doses (caution with antidiabetic agents)</td>
<td>Caution use in diabetic patients (may cause hypoglycemia in large doses)</td>
</tr>
<tr>
<td>Artichoke</td>
<td>Increased flatulence, allergic reaction</td>
<td>None known</td>
<td></td>
</tr>
<tr>
<td>Garlic</td>
<td>Breath and body odor, heartburn, flatulence, nausea, vomiting, diarrhea, rhinitis, conjunctivitis, and urticaria,</td>
<td>Anticoagulant or antiplatelet drugs, contraceptive medications, ciclosporine, CYP 3A4 substrates, non-nucleoside reverse transcriptase inhibitors, and saquinavir</td>
<td>Bleeding disorders (may increase the risk of bleeding) Gastrointestinal irritation</td>
</tr>
<tr>
<td>Soy</td>
<td>Normally well tolerated Constipation, bloating, nausea, rarely supplements may cause migraine</td>
<td>Estrogen replacement therapy, tamoxifen (anti-estrogen effects) Warfarin (may decrease INR)</td>
<td>Use with caution in patients who have asthma, allergic rhinitis, estrogen sensitive cancers, venous thrombosis, cystic fibrosis, hypothyroidism, renal failure, kidney stones, or bladder cancer</td>
</tr>
<tr>
<td>English Walnut</td>
<td>Normally well tolerated Stools may become softer, mild bloating; beware of nut allergies</td>
<td>None known</td>
<td>None known</td>
</tr>
<tr>
<td>Pycnogenol</td>
<td>None reported</td>
<td>May interfere with immunosuppressant drugs because of its immunostimulant activity</td>
<td>Patients with multiple sclerosis, lupus, rheumatoid arthritis, or other autoimmune disorders due to its immunostimulant activity</td>
</tr>
<tr>
<td>Grape Seed Extract</td>
<td>Normally well tolerated Headache, abdominal pain, sore throat, nausea, and cough</td>
<td>Warfarin (may increase the INR) or any other drugs metabolized via the CYP 1A2 pathway as their plasma levels may decrease.</td>
<td>None known</td>
</tr>
</tbody>
</table>
ing down; therefore, it is important for all health care providers to familiarize themselves with these products, especially given the potential for herb-drug and herb-disease interactions. This article will analyze evidence, discuss mechanisms of action, dosing, cost, interactions, as well as decipher fact from fiction surrounding several herbal products with lipid-modifying potential.

**Red Yeast Rice Extract**

Red yeast rice has been used in Asia for centuries as a food preservative, food colorant, and for medicinal purposes. It is made by fermenting rice with red yeast (*Monascus purpureus*). During this process, ten different monacolins, all of which are naturally occurring hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors, are formed. Merck & Co isolated monacolin K and patented it as Mevacor® (lovastatin). Other active ingredients include sterols, isoflavones, and monounsaturated fatty acids.

The proposed mechanism of action is similar to the HMG-CoA reductase inhibitors: blocking the synthesis of cholesterol in hepatic cells. There have been several clinical trials performed testing the lipid-lowering effects of red yeast rice extract. All of these randomized trials discovered significant reductions in total cholesterol of 16% to 31%, low-density lipoprotein (LDL) of 21%-32%, and triglycerides of 16%-34% when compared with baseline, placebo, or control. Furthermore, an increase in high-density lipoprotein (HDL) of 15%-20% was shown in three of the studies. While these studies seem promising, none of the human trials were conducted for longer than three months, and almost all of them simultaneously implemented a regimented low fat, low cholesterol diet.

Although larger, longer randomized controlled trials are needed to ensure a low toxicity profile, current evidence has not revealed toxicity concerns. Studies conducted in animals for as long as four months report no adverse events or toxicities while being administered red yeast rice extract. Studies conducted in humans have failed to show elevations in liver enzymes or renal impairment; potential side effects documented by researchers have been limited to gastrointestinal discomfort and headaches. Supplementation of Coenzyme Q10 may be considered if a patient plans to take the red yeast rice extract long term, because HMG-CoA reductase inhibitors can reduce its production, though the ability of this strategy to prevent toxicity is unclear.

In conclusion, red yeast rice can significantly lower total and LDL cholesterol levels, as well as lower triglycerides when used for 8-12 weeks. The dose most commonly used is 2.4 grams per day; however, a dose of 1.2 grams per day provides some benefit. Red yeast rice should be used cautiously in patients with known contraindications to HMG-CoA reductase inhibitors.

**Policosanol**

Policosanol is a mixture of eight cyclic alcohols derived from sugar cane wax and beeswax. Octacosanol is the prominent alcohol found in the herbal product, comprising approximately 63% of the compound; triacontanol (13%) and hexacosanol (6%) are the other two major components. The combination of these alcohols has demonstrated cholesterol-lowering abilities equal to statin drugs. Policosanol may also reduce platelet aggregation, endothelial damage and foam cell formation, as well as lower total and LDL cholesterol.

The exact mechanism of action is yet to be determined. It appears that policosanol lowers LDL and total cholesterol synthesis prior to the formation of mevalonate. Furthermore, it increases the binding, uptake, and degradation of LDL in the endoplasmic reticulum, which is independent of its effect on cholesterol synthesis. Policosanols’s antiplatelet effects are exhibited through its ability to decrease levels of thromboxane A2 and increase levels of prostacyclin. Numerous policosanol studies have been conducted in recent years. All of them, both short-term and long-term, have shown statistically significant lipid lowering effects when taken in doses of 5 mg to 10 mg per day. In two short-term studies (eight and six weeks), the cholesterol lowering effect of taking 5 mg per day and 5 mg twice daily was 17.7% and 21.5% for LDL and 13.1% and 16.2% for total cholesterol respectively. Long-term studies show even more promise, especially with respect to increasing HDL levels. In two such studies (52 and 104 weeks), 5 mg twice daily lowered total cholesterol and LDL by a range of 16.3% to 18.3%, and 24.8% to 27.5%, respectively. Furthermore, policosanol raised HDL cholesterol by 11.2% to 25.9%.

Head-to-head stud-
ies with policosanol versus statin drugs have also been completed. A meta-analysis that reviewed thirty policosanol trials found that overall, there was a 23.7% reduction in LDL level and 10.6% increase in HDL levels. These findings are similar to those observed with other lipid lowering drug therapies, and this analysis cites policosanol as slightly more effective than fibric acid derivatives and similar in efficacy to low-dose statins.16 One specific trial compared policosanol 10 mg daily to lovastatin 20 mg daily in fifty-three patients for twelve weeks.17 Policosanol lowered LDL and total cholesterol by 20.4% and 14.2% ($p < 0.0001$), respectively, while lovastatin lowered LDL and total cholesterol by 16.8% ($p < 0.01$) and 14.0% ($p < 0.001$), respectively. Policosanol increased HDL by 7.5% ($p < 0.01$), and lovastatin lowered HDL 2.8% (not significant).17 Similar results were obtained during a trial that compared policosanol 10 mg daily to pravastatin 10 mg daily for eight weeks.18 With findings such as these, more studies should be performed to assess its safety in the general population.

In summary, policosanol taken in doses of 5 to 10 mg per day seems to significantly decrease total and LDL cholesterol, and increase HDL cholesterol. Products should be used with caution in patients who are taking anti-platelet or anticoagulant drugs, as this product may have additive effects. Since the exact mechanism of action of policosanol is unknown, it should not be given concurrently with statins. Furthermore, its safety and efficacy has not been studied in pregnant and lactating women.8

### Guggul Extract

Guggul is made from the oleogum resin of the Camphiphora mukul tree which is native to India. It has been credited with impacting the lipid profile, possibly due to the guggulsterone content. It has also been promoted for use in obesity, osteoarthritis, and nodulocystic acne. Several mechanisms have been theorized for the effects of this herbal agent. Guggul may increase the breakdown of LDL by decreasing hepatic steroid production.23 A second proposed mechanism of action is that guggulsterones E and Z may increase hepatic binding sites for LDL, leading to increased LDL clearance. A recent review suggested that guggulsterones act as antagonists at the farnesoid X receptor and the bile acid receptor, two key hormone receptors involved in the regulation of bile acid production and cholesterol metabolism. By antagonizing this receptor, 7α-hydroxylase is released, activating the catabolism and subsequent excretion of cholesterol.19

There have been several trials testing the lipid-lowering effects of guggulipid. Most of these studies, however, were too small and not well designed or reported. Clinical studies conducted in India have shown that a standardized extract of guggul can lower total, LDL and triglycerides, as well as raise HDL in both healthy and hyperlipidemic subjects. Many of these studies also placed subjects on fruit- and vegetable-enriched diets, and the results between guggul and placebo were often not statistically significant.9 In a recent trial, guggul did not appear to improve cholesterol levels; in fact, LDL increased by 9% to 10% during the eight week trial period.20 This discrepancy might be caused by differences in the diet of the subjects studied. Although this seemingly provides evidence against the efficacy of guggul for hypercholesterolemia, due to the precedent of prior research and historical use, further study is necessary before a definitive conclusion can be reached. More rigorous studies need to be conducted in larger patient populations in order to prove both its safety and efficacy.

Guggul extract in doses of 3 to 6 grams per day seems to lower total cholesterol, LDL, and triglycerides in Indian populations. However, in the studies that have been conducted in populations eating Western diets, guggul does not seem to lower total cholesterol or triglycerides, or raise HDL cho-

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**Table 2: Safety vs. Efficacy of Natural Products**

<table>
<thead>
<tr>
<th>Safety</th>
<th>Efficacy</th>
<th>Likely Safe</th>
<th>Possibly Safe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely Effective</td>
<td>- Soy</td>
<td>- Red Yeast Rice</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Walnuts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Possibly Effective</td>
<td>- Garlic</td>
<td>- Artichoke</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Policosanol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insufficient Evidence</td>
<td>- Grape Seed</td>
<td>- Pycnogenol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Guggul</td>
<td>- Fenugreek</td>
<td></td>
</tr>
</tbody>
</table>

*Adapted from The Natural Medicines Database*
lesterol. Guggul should be used with caution in pa-
tients with thyroid disord ers, women who have had
hormone sensitive cancers, and women who are
pregnant.8

Fenugreek Seeds
Fenugreek (Trigonella foenum graecum), grown originally in Asia, is now widely cultivated in
India, Argentina, Egypt and the Mediterranean. Of-
ten referred to as ‘Methi,’ it is commonly used as a
cooking condiment in India. The seeds contain many
nutrients including protein, carbohydrates, polyun-
saturated fats, vitamins and minerals, fiber, trigonel-
line, 4-hydroxyisoleucine, sotolon, saponin, and
other constituents. Fiber and saponin have been the
components of greatest interest in this herbal product,
as these have been shown to have the most choles-
terol-lowering activity.21

Several different mechanisms of action have
been theorized for fenugreek’s hypocholesterolemic
effect. It is thought to lower cholesterol by enhancing
the excretion of bile acids and neutral sterols, while
simultaneously decreasing cholesterol stores in the
liver (by converting the cholesterol into bile salts).
The fiber component of fenugreek potentially re-
duces the rate of diffusion of glucose and cholesterol
towards the mucosal surface of the gut. Fiber has
also been shown to increase the viscosity of food,
thereby inhibiting uptake of cholesterol and bile ac-
ids.21 Of note, about 80% of the amino acids present
in the seeds are 4-hydroxyisoleucine, which appears
to directly stimulate insulin. This action, combined
with the decrease in glucose absorption stimulated by
fiber may cause patients with diabetes mellitus who
are treated with oral hypoglycemics or insulin to ex-
perience episodes of hypoglycemia.8

The quality of most of the clinical trials that
have been performed to evaluate the efficacy of
fenugreek have been poor. Five fenugreek seed stud-
ies reviewed in a meta-analysis showed statistically
significant reductions in total cholesterol of 15% to
33% compared with baseline. Similar to the guggl
trials, all but one of these studies was conducted in
India; therefore, it is unknown how much diet and
other confounders may have contributed to these re-
sults.9

There is conflicting evidence regarding the
use of fenugreek for use as a cholesterol-lowering
agent. Doses of 0.6 to 2.5 grams of fenugreek 2 twice
daily with meals has been used in an effort to lower
lipids. Fenugreek should be used cautiously in pa-
tients who are taking medications for diabetes, be-
cause this herbal product might cause hypoglycemia.
Counsel patients taking this herbal product to sepa-
rate its ingestion by two to four hours from other
medications, since fenugreek could affect their ab-
sorption.8

There are many other alternative medicinal
agents which are being used to lower cholesterol;
however, due to either their extensive review else-
where or insufficient evidence, they will only be
mentioned briefly below.

Artichoke Extract
Artichoke, Cynara Scolymus, has been used
as an ancient herbal remedy for a variety of diseases;
it has been used mainly for the treatment of dyspep-
sia, but in recent years, artichoke extract has also
been used for the treatment of hyperlipidemia. In ani-
mal studies, it seems to increase bile flow and inhibit
hepatocyte cholesterol biosynthesis. During studies
conducted in humans, a moderate hypocholes-
terolemic effect has been shown. It also seems to
possess antioxidant properties in endothelial cells
and monocytes, and contributes to the antagonism of
lipid peroxidation.22 There is a small body of evi-
dence that supports the theory that artichoke extract,
when taken in divided doses of 1800 mg to 1920 mg
per day, seems to modestly reduce total and LDL
cholesterol over six to twelve weeks of treatment.
Artichoke extract looks promising, but further study
is warranted before recommending it for most pa-
tients. Artichoke should be used cautiously in pa-
tients that have gallstones or bile duct obstruction.8

Garlic
Garlic has been studied thoroughly, and
there is significant controversy surrounding its effi-
cacy. Many different trials have tried to either prove
or disprove garlic’s effectiveness in the treatment of
hyperlipidemia. Many of the pharmacological effects
of garlic are attributed to allicin. Bulbs contain an
odorless sulfur-containing amino acid derivative
called alliin. When the bulbs are crushed, the enzyme
alliinase is released; allinase converts alliin to allicin.
Garlic’s proposed mechanism of action in lowering
cholesterol is by acting similarly to an HMG-CoA
reductase inhibitor. There is also some evidence that
S-allyl-L-cysteine (a component in garlic) might be
an inhibitor of hepatic cholesterol synthesis.

There is disagreement over the effectiveness of taking garlic orally for hyperlipidemia. Doses of 900 mg per day seem to slow the development of atherosclerosis in both aortic and femoral arteries when ingested over a four-year period. Conversely, studies have also shown no significant benefit when used for 6 months or longer. Products should be used with caution in patients that have bleeding disorders, those who have had recent surgery (garlic may increase the risk of bleeding), or those who have gastrointestinal irritation. There are potential drug interactions in patients taking anticoagulant or antiplatelet drugs, contraceptive medications, cyclosporine, CYP 3A4 substrates (e.g. calcium channel blockers, chemotherapeutic agents, ketoconazole, itraconazole, glucocorticoids, cisapride, fentanyl, lidocaine, losartan, fexofenadine, midazolam, and others), nonnucleoside reverse transcriptase inhibitors, or saquinavir. Concomitant use of garlic and saquinavir has been shown to decrease saquinavir concentrations by up to 50%.

### Soy

Soy protein preparations reduce total cholesterol and LDL levels in both hypercholesterolemic and normocholesterolemic men and women. Replacement of dietary animal protein with soy protein decreases total cholesterol by 9%, LDL cholesterol by 13%, and triglycerides by 11% after one to two months; the effect on HDL is inconsistent. Soy products should be used with caution in patients who are

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**Table 3: Comparison of Lipid Lowering Agents.**

<table>
<thead>
<tr>
<th></th>
<th>LDL</th>
<th>HDL</th>
<th>TGs</th>
<th>Dose</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins</strong></td>
<td>↓ up to 55%</td>
<td>↑ 6% to 14%</td>
<td>↓ 15% to 35%</td>
<td>Variable depending on product</td>
<td>$90-$120/mo</td>
</tr>
<tr>
<td><strong>Bile acid sequestrants</strong></td>
<td>↓ 10% to 30%</td>
<td>-</td>
<td>Variable; sometimes ↑</td>
<td>Variable depending on product</td>
<td>$60-$180/mo</td>
</tr>
<tr>
<td><strong>Ezetimibe</strong></td>
<td>↓ 18% to 24%</td>
<td>-</td>
<td>↓ 10%</td>
<td>10mg/day</td>
<td>$75.00/mo</td>
</tr>
<tr>
<td><strong>Niacin</strong></td>
<td>↓ 10% to 15%</td>
<td>↑ 35%</td>
<td>↓ 20% to 50%</td>
<td>50mg-1000mg/day</td>
<td>$12-$80/mo</td>
</tr>
<tr>
<td><strong>Fibrates</strong></td>
<td>Variable; sometimes ↑</td>
<td>↑ 5% to 15%</td>
<td>-</td>
<td>Variable depending on product</td>
<td>$20-$100/mo</td>
</tr>
<tr>
<td><strong>Red Yeast Rice</strong></td>
<td>↓ 21% to 32%</td>
<td>↑ 15% to 20%</td>
<td>↓ 16% to 34%</td>
<td>1.2 – 2.4g/day</td>
<td>$22.00/mo</td>
</tr>
<tr>
<td><strong>Policosanol</strong></td>
<td>↓ 11% to 31%</td>
<td>↑ 7% to 9%</td>
<td>-</td>
<td>5-10mg/day</td>
<td>$20.00/2mo</td>
</tr>
<tr>
<td><strong>Guggul Extract</strong></td>
<td>Variable, sometimes ↑</td>
<td>-</td>
<td>-</td>
<td>3 – 6g/d</td>
<td>$22.00/mo</td>
</tr>
<tr>
<td><strong>Fenugreek</strong></td>
<td>↓ up to 38%</td>
<td>↓ 4% to 7%</td>
<td>-</td>
<td>0.6 – 2.5g/day</td>
<td>$8.50/mo</td>
</tr>
<tr>
<td><strong>Aritchoke Extract</strong></td>
<td>↓ up to 23%</td>
<td>-</td>
<td>-</td>
<td>1.8 – 1.9g/day</td>
<td>$11.00/2mo</td>
</tr>
<tr>
<td><strong>Garlic</strong></td>
<td>↓ 4% to 12%</td>
<td>-</td>
<td>-</td>
<td>900mg/day</td>
<td>$15.00/2mo</td>
</tr>
<tr>
<td><strong>Soy</strong></td>
<td>↓ 13%</td>
<td>-</td>
<td>↓ 11%</td>
<td>Variable (use based on diet)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Walnuts</strong></td>
<td>↓ 8% to 16%</td>
<td>-</td>
<td>-</td>
<td>Variable (use based on diet)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Pycnogenol</strong></td>
<td>‡</td>
<td>‡</td>
<td>‡</td>
<td>360mg/d</td>
<td>$100.00/mo</td>
</tr>
<tr>
<td><strong>Grape Seed Extract</strong></td>
<td>↓ 1% to 3%</td>
<td>-</td>
<td>-</td>
<td>40 – 300mg/d</td>
<td>$15.00/mo</td>
</tr>
</tbody>
</table>

*Adapted from The Natural Medicines Database. †: Cost varies according to manufacturer and quality and purity of the component. ‡: To date, studies have not concluded range of effects on lipid profiles.
taking antibiotics, estrogen replacement therapy, tamoxifen, or warfarin. Also use with caution in patients that have the following disease states: asthma (inhaled soy dust can trigger symptoms), allergic rhinitis, estrogen sensitive cancers, cystic fibrosis, hypothyroidism, renal failure, kidney stones, or bladder cancer.8,23

**English Walnut**

English walnuts contain high amounts of the polyunsaturated fatty acids, linoleic acid and alpha-linolenic acid. It also contains significant amounts of fiber, phosphorus, potassium, and folate. Theoretically, other constituents such as fiber, vitamin E, and folate might contribute to the seemingly beneficial effect on cardiovascular disease risk. Clinical research also suggests walnuts might improve endothelial function, which might be beneficial in preventing atherosclerosis. In addition to alpha-linolenic acid, walnuts contain significant amounts of arginine, a precursor amino acid of the endogenous vasodilator nitric oxide.8 When English walnuts are added to a low fat diet in doses of approximately 8-11 walnuts per meal24 (substituted for other dietary fats), total cholesterol may be decreased by 4% to 12% and LDL may be decreased by 8% to 16%. There are no known disease or drug interactions when using this product; however, warn against using this substitution when the patient has an allergy to nuts.8

**Pycnogenol**

Pycnogenol is found in the extract from the bark of the French maritime pine tree. Pycnogenol contains several active constituents including flavonoid monomers such as catechin, epicatechin, and taxifolin. It also contains condensed flavonoids or proanthocyanidins.26 As far as hyperlipidemia is concerned, there is some evidence that pycnogenol 120 mg three times daily lowers LDL. Pycnogenol is used for a variety of other disorders for which there is greater evidence to support its use: asthma, enhanced athletic performance, chronic venous insufficiency, hypertension, and retinopathy. Interestingly, pycnogenol inhibits the oxidation of LDL, inhibits epinephrine induced platelet aggregation, and also inhibits angiotensin converting enzyme.26 It might also increase nitric oxide production from vascular endothelial cells. It should be used with caution in patients who are taking immunosuppressants or patients who have autoimmune diseases.8

**Grape Seed Extract**

Grape flavonoids have a wide variety of effects including antioxidant, vasodilating, antilipoperoxidant activity, and antiplatelet properties that might prevent heart disease. Ingestion of purple grape products, such as purple grape juice, grape seed extract, and red wine, might improve endothelium-dependent vasodilation, prevent LDL oxidation, and suppress platelet-mediated thrombosis.27 Theoretically, consumption of these products long-term might reduce the risk of cardiovascular disease. It has been suggested that initially, patients would take grape seed extract in doses between 75-300 mg daily for three weeks followed by a maintenance dose of 40-80 mg daily. Use with caution in patients taking warfarin (may increase the INR) or any other drugs metabolized via the CYP 1A2 pathway (e.g. amitriptyline, chlordiazepoxide, clopidogrel, cyclobenzaprine, diazepam, estradiol, mirtazapine, naproxen, propranolol, theophylline, verapamil, etc.), as their plasma levels may decrease.8

**Summary**

Of the herbal preparations discussed, the safest and most likely to be effective are soy products or walnuts substituted for fats in the diet. These can be recommended for the majority of patients initiating therapeutic lifestyle changes. Red yeast rice is likely effective at lowering LDL cholesterol. While garlic is likely safe, and possibly effective, there is controversy surrounding garlic and its efficacy; therefore, its use is not recommended. Both artichoke extract and policosanol are possibly safe and effective. Pycnogenol and grape seed extract are well tolerated but there is insufficient evidence to support recommending its use. Guggul and fenugreek seeds have are possibly ineffective at treating hyperlipidemia. Their use cannot be recommended.

A major drawback for the vast majority of herbal preparations is the inconsistency of the product from one bottle to the next. There is currently no regulation over the companies who create and market these products.

There is conflicting data on herbals and hyperlipidemia. Many of the trials cited were not methodologically sound. Even more were conducted in foreign countries, where the diet is considerably different than that of an American. While there is little doubt that some of these agents exhibit beneficial
effects on lipid parameters, their efficacy is tempered by the lack of long term studies, variable product quality, and difficulties extrapolating the data to other populations. More studies conducted in larger, more diverse populations are needed to prove the safety and efficacy of all of these agents.

References