Patented Blend of Citrus Polymethoxylated Flavones + Palm Tocotrienols

Targets endogenous cholesterol synthesis to maintain cholesterol and triglyceride levels already within a healthy range*
Introducing Sytrinol

Maintaining cholesterol and triglyceride levels within the normal range is essential to heart health, and there are many natural ingredients available for this purpose. Unfortunately, not all of them are effective. Others create unpleasant side effects or have safety issues. Consumers concerned with cholesterol need a practical solution — something that’s strong enough to work, yet gentle enough to do no harm.

Soft Gel Technologies is pleased to offer Sytrinol — a patented blend of polymethoxylated flavones (PMFs) from citrus and tocotrienols from Malaysia red palm oil — in a convenient softgel form. Clinical research has shown that not only does Sytrinol help maintain blood lipid levels already within a healthy range, but when provided in softgel form, its bioavailability increases dramatically.*

Understanding Blood Lipids

Cholesterol is a lipid, or fat, found in the blood. This waxy substance is the primary component of cell membranes. It is also used to synthesize hormones, bile acids, and vitamin D. About two-thirds of bodily cholesterol is manufactured endogenously (within the body) by the liver and one third comes from dietary sources. While cholesterol is essential to function, many Americans exceed a healthy level caused by poor dietary decisions.

There are two types of cholesterol: low-density lipoprotein (LDL-C), referred to as “bad cholesterol,” and high-density lipoprotein (HDL-C), often called “good cholesterol.” When too much LDL-C circulates in the blood, it can build up inside the arteries causing them to narrow and resulting in decreased flexibility. HDL-C supports cardiovascular health by carrying cholesterol away from the arteries and back to the liver where it is eliminated from the body.

Triglycerides are another type of lipid found in the blood. Like LDL-C, they are associated with narrowing of the arteries. Those who eat high-carbohydrate diets often have high triglyceride levels.

The American Heart Association has established the following targets for blood lipids:

- Total cholesterol: 200mg/dL or lower
- LDL: 100mg/dL or lower
- HDL: 40mg/dL or higher for men, 50mg/dL or higher for women
- Triglycerides: 150mg/dL or lower

Sytrinol can help maintain lipid levels that are already within the normal range.*

What is Sytrinol?

Developed at the University of Western Ontario, Sytrinol is a patented blend of citrus PMFs, extracted from immature citrus fruits and peels, and concentrated tocotrienols (as Tocomax™ 30%), derived from sustainably sourced virgin red Malaysian palm oil. PMFs are a distinct type of citrus bioflavonoid. Sytrinol provides a blend of PMFs, standardized to specific levels of nobiletin and tangeretin. Tocotrienols, like tocopherols, are isomers of vitamin E. Sytrinol provides all four tocotrienols: alpha, beta, gamma, and delta.

Soft Gel Technologies is the exclusive manufacturer of Sytrinol in soft gelatin capsules and offers Sytrinol in three convenient forms:

- As a stand-alone ingredient (150mg per softgel)
- Combined with plant sterols, for a two-pronged approach
- In turnkey custom formulations, to meet your company’s specific needs
Scientific Substantiation

Open-Label Pilot Trials

**Design:** Two open-label pilot trials were conducted on Sytrinol, both enrolling subjects between the ages of 19 and 65. The first group was comprised of 12 adults and the second of 10. The subjects were not taking any cholesterol-lowering medication. During the trial, study participants took 300mg Sytrinol per day for four weeks. Each group served as its own control. Fasting blood lipids were measured at baseline and at the end of the study period.

**Results:** After analyzing the data, it was clear that Sytrinol achieved such promising results for the maintenance of healthy levels of total cholesterol, LDL-C, and triglyceride levels that the researchers initiated a larger controlled study.1

Double-Blind, Placebo-Controlled Trial

**Design:** The following trial was a 12-week, double-blind, placebo-controlled, randomized study — the gold standard of scientific research. A total of 120 subjects took 300mg Sytrinol daily or placebo. Blood lipids were measured at baseline and at four, eight, and 12 weeks.

**Results:** Analyzing the data, researchers found that compared to subjects in the placebo group, those taking Sytrinol had more effectively maintained healthy levels of total cholesterol, LDL-cholesterol, and triglycerides.2 It is also important to note that cardio-protective HDL-cholesterol levels and LDL-C to HDL-C ratios were also maintained within normal levels.3

Serum Bioavailability Trial

**Design:** When it comes to bioavailability, delivery systems matter. This was made clear by a randomized, crossover bioavailability study in which 10 subjects between the ages of 18 and 75 took an identical single large dose (1,053mg Sytrinol) in softgels, hard shell capsules, or hard shell capsules with lecithin. Using LC/MD/MS analysis, researchers tracked levels of nobiletin and tangeretin in subjects' blood for 48 hours after administration.

**Results:** Sytrinol in softgel capsules was significantly more bioavailable than either Sytrinol in hard shell capsules or hard shells with lecithin. The difference was remarkable. Subjects taking softgels had nearly seven times the level of nobiletin in their blood as those taking hard shell capsules and nearly fourteen times the level of tangeretin.4

Safety Studies

Sytrinol was granted self-affirmed GRAS status and its safety has been confirmed in two animal studies. In an acute oral toxicity test, 10 rats were administered a single dose of 300mg Sytrinol/kg body weight. They were observed for 14 days following the dose and no symptoms of toxicity were noted, either gross or microscopic. The LD50 was established to be 1,000mg/kg body weight.

In a second, larger, sub-chronic toxicity test, 80 rats were repeatedly administered several different doses of Sytrinol. No adverse effects were observed at a dosage of 500mg/kg body weight, which is equivalent to over 100 times the recommended dose for humans. (See Charts 1 and 2)

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**Sytrinol was well-tolerated in all clinical studies, and there were no adverse events reported.**

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**Chart 1: AUC – Nobiletin and Tangeretin**

AUC (area under the curve) is the total number of micrograms detected in the serum x min/L over a 48-hour period. The higher the result, the greater the bioavailability.

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<tr>
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<th>Tangeretin</th>
<th>Nobiletin</th>
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<td>A (AUC0-48h)</td>
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<td>B (AUC0-48h)</td>
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<td>C (AUC0-48h)</td>
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Mean ± SEM

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**Chart 2: Cmax – Nobiletin and Tangeretin**

Cmax is the maximum concentration of X found in the serum. The higher the value, the greater the bioavailability.

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<thead>
<tr>
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<th>Nobiletin</th>
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<td>A (Cmax)</td>
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<td>C (Cmax)</td>
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Mean ± SEM

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1. Sytrinol in softgels
2. Sytrinol in hard shell capsule
3. Sytrinol in hard shells with lecithin
4. See Charts 1 and 2
Mechanism of Action

Two-thirds of cholesterol is manufactured by the body. Thus, for consumers looking for a solution for maintaining healthy cholesterol levels, targeting cholesterol synthesis is a more promising strategy than blocking absorption from dietary sources. However, ingredients that block absorption of dietary cholesterol (such as plant sterols) can also be used in combination with Sytrinol in order to target cholesterol at both its sources.

Sytrinol works in three ways:

1. **Inhibits cholesterol synthesis***
   The tocotrienols in Sytrinol inhibit the action of HMG CoA, an enzyme involved in LDL-cholesterol synthesis, without inhibiting the production of CoQ10. Additionally, the citrus PMFs (tangeretin and nobiletin) decrease apolipoprotein B (apoB), a structural protein needed for LDL-cholesterol synthesis.*5,6,7

2. **Inhibits triglyceride synthesis***
   Tangeretin decreases DGAT, the final enzyme in the pathway for triglyceride synthesis.*8

3. **Supports cytokine balance***
   Citrus PMFs tip the balance away from excitatory cytokines (particularly TNF-α), which are undesirable, to inhibitory ones, which support heart health.*9,10

Why Choose Sytrinol?

- 100% Natural. Sytrinol is made from citrus PMFs from immature citrus fruit and peels and tocotrienols (isomers of vitamin E) derived from sustainably sourced virgin red Malaysian palm oil.
- Clinically effective. Sytrinol has been shown to be effective at maintaining cholesterol and triglyceride levels already within a normal range in three clinical trials.*
- Not diet-specific. Sytrinol works on cholesterol production within cells, not on dietary cholesterol.
- Bioavailable. A bioavailability study found that the citrus PMFs in Sytrinol are significantly more bioavailable when taken in softgels versus hard shell capsules.
- Patent-protected. Sytrinol is protected by the following patents. US Patent Nos: 6,239,114; 6,251,400; 6,987,125; 7,683,095 and 6,184,246.
- Safe and well-tolerated. Sytrinol has been tested for safety and has been granted self-affirmed GRAS status.
- Easy and convenient. Sytrinol softgels are easy to swallow and the effective dose is just 300mg/day, making dosing convenient.
- Kosher-certified. Sytrinol has been certified Kosher by KOF-K.
- Allergen-free. Sytrinol does not contain any of the eight major allergens.
- Pure. Sytrinol is non-GMO, non-irradiated, and non-ETO-treated.
- Turnkey solution. Sytrinol is available from Soft Gel Technologies as a green, oval finished-dosage softgel, providing 150mg Sytrinol per softgel.

References


*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.