NanoRESVERATROL contains the antioxidant, anti-aging, polyphenol resveratrol in our proprietary in our proprietary lipid phospholipid NanoSphere “Intraoral Delivery System”. Resveratrol is prevalent in such foods as red wine, green tea, apples, berries, pomegranates, and dark chocolate. Yet despite wide acclaim for its properties, when taken orally resveratrol has very low bioavailability, and even the small portion that enters the bloodstream is rapidly metabolized.

The NanoRESVERATROL solid lipid nanosphere delivery system enters the bloodstream through the oral via transmucosal absorption. This prevents presystemic metabolism of resveratrol and provides up to 5-7 times greater bioavailability and bioactivity than an orally ingested Resveratrol supplement. NanoRESVERATROL is designed to help sustain blood levels, achieve higher potency responses, increase circulatory half-life, and enhance site-specific actions. Plus, NanoRESVERATROL can cross the blood-brain barrier.

An Antioxidant and Cellular Protective with Delivery Problems

Resveratrol is a polyphenolic phytoalexin. It is a stilbenoid, a derivate of stilbene, and is produced in plants with the help of the enzyme stilbene synthase. It exists as two structural isomers: cis- (Z) and trans- (E), with the trans-isomer shown in the image. Trans-resveratrol can undergo isomerisation to the cis form when heated or exposed to UV irradiation.

Scientists believe have found resveratrol to be an extraordinarily effective antioxidant and cellular protective based on laboratory and animal studies. But resveratrol poses an extraordinary problem: although it’s well absorbed (at least 70%) by the gut, its bioavailability is almost zero, owing to its rapid and extensive metabolism to two types of chemical derivatives: sulfates and glucuronides.

It appears that most of the conversion of resveratrol to these metabolites occurs in the gut (the metabolites are readily absorbed into the bloodstream, however), and the process is completed by the liver within about half an hour. The result is that unmetabolized resveratrol is virtually undetectable in the blood.

Some researchers have suggested that the large body of laboratory research on which the therapeutic reputation of resveratrol largely rests may be irrelevant, because the agent used may have been the wrong agent, namely, resveratrol rather than its metabolites. Another possibility is that Resveratrol may depend for its bioavailability on the presence of the myriad other compounds (including many other polyphenolics) with which it coexists in nature, i.e., in the grapes and in red wine, because these compounds may inhibit its metabolism to sulfates and glucuronides in our bodies.

Because resveratrol is so extensively metabolized in the gut before it even has a chance to reach the bloodstream it’s essential to improve its bioavailability by bypassing the digestive tract in favor of a more direct route to the blood. Indeed, such a route is available through the mucosa of the oral cavity by an intraoral delivery system that encapsulates resveratrol into “Solid lipid NanoSpheres”.

The Underpinnings of the NEURVANA NanoSphere Delivery System

The NanoRESVERATROL delivery system is based on the pharmaceutical industry models. The nano-sized lipid particle spheres are less than 75 nm in diameter and formed from bioactive phospholipids and simple lipids. These natural lipids are bioidentical to the enriched phosphatidylcholine phospholipid fraction sold in Europe.
Solid lipid nanospheres are dynamic structured, particles created from natural lipids that possess an outer phospholipid membrane layer and an inner lipid MCT core phase. The essential phospholipid mono outer layer stabilizes the inner core and protects the encapsulated contents from degradation. The lipophilic interior of the outer membrane and inner core can incorporate high levels (up to 90%) of nutraceutical substances.

**The Benefits of Intraoral Delivered Resveratrol**

**NanoRESVERATROL**’s intraoral delivery system can improve the bioavailability of resveratrol by bypassing the digestive tract from intraoral administration through the mucous membranes of the mouth. Intraoral administration delivers free, unmetabolized resveratrol via the jugular vein into the systemic circulation and carries the resveratrol from the systemic circulation across cell membranes to target intracellular structures. **NanoRESVERATROL** can produce higher blood levels of Resveratrol. Based on comparative pharmaceutical nanoparticle delivery system research, **NanoRESVERATROL** provides 5-7 times greater bioavailability and intra-cellular bio-activity than any orally ingested resveratrol supplement, including micronized resveratrol.

**The Advantages of NanoRESVERATROL’s NanoSphere Intraoral Delivery System:**

- Shields Resveratrol from metabolism in the liver to inactive metabolites to maintain high blood levels
- Helps sustain higher blood levels, achieve higher potency responses, increase circulatory half-life, and enhance site-specific actions
- Delivers Resveratrol from the systemic circulation to intracellular structures
- Readily crosses the blood-brain barrier
- 5-7 times greater bioavailability and intra-cellular bioactivity than orally ingested Resveratrol

**Heart Protecting Antioxidant**

Resveratrol is a powerful antioxidant with heart-protective effects. Resveratrol inhibits platelet aggregation (the process by which blood clots are formed) and lipid peroxidation, which is an important factor in the development of atherosclerosis. The lipids in question are those that are carried in the bloodstream by LDL (low-density lipoprotein, or “bad cholesterol”), and their degradation by oxidizing agents such as free radicals facilitates their incorporation into artery-clogging plaque.

**Neuroprotective and Cognitive Enhancer**

Recent studies have revealed resveratrol’s neuroprotective effects and its value for the central nervous system (CNS), including its ability to boost memory and cognition. Studies demonstrate that resveratrol can lessen amyloid-β peptide-induced (plaque) toxicity, protect against cerebral ischemic injury, and shield neurons from induced excitotoxicity. One study found grape polyphenols (of which resveratrol is believed to be the most active) were highly effective in inhibiting alcohol induced oxidative stress in the brain.

Other studies using just resveratrol, found evidence of its neuroprotective effects against cell death mediated by or caused by oxidative stress. In addition, they described evidence for anti-inflammatory effects and for anti-cell mutation effects. A new study has found that resveratrol can improve memory in diabetics by decreasing the activity of acetylcholinesterase (AChE), thereby boosting cholinergic memory function while enhancing cognition.
Longevity Promoter

Current research is focusing on the longevity properties of Resveratrol by acting as a mimetic of “Caloric Restriction”. Caloric restriction has been shown repeatedly to be one of the most effective means of slowing the rate of aging, preventing or delaying degenerative conditions and extending healthy lifespan. Experiments demonstrate similar gains in maximum lifespan in virtually every organism in which caloric restriction has been tested.

Scientists recently identified a class of regulatory longevity genes that are shared by almost all living organisms that appear partially responsible for the effect of caloric restriction. These genes have been designated as sirtuins. Once triggered the longevity genes “switch on” and induce defensive changes at the cellular level, such as slowing metabolism and enhancing cellular respiration to help the body adapt.

The human sirtuin, SIRT-1, has been shown to suppress the p53 enzyme system that helps to inhibit tumor growth and trigger apoptosis programmed cell death. By suppressing p53 activity, SIRT-1 prevents premature aging and apoptosis that is induced when cellular DNA is damaged or stressed. This gives cells an opportunity to repair the damage. A second sirtuin, SIR2, has been shown to become activated when placed under stress that increases DNA stability, speeds cellular repair and increases total cell lifespan.

A research team from Harvard University began to search for other methods of modulating sirtuin activity without resorting to starvation. The researchers discovered that several plant metabolites acted as sirtuin-activating compounds (STACs), and that the most potent activator of sirtuins was resveratrol.

Diabetic Protection

Daily supplements of resveratrol may improve how the human body responds to insulin, the hormone responsible for sugar and fat metabolism. Hungarian researchers reported that a daily dosage of resveratrol reduces insulin resistance in people with type-2 diabetes.

The capacity of resveratrol to stimulate sirtuins and lead to the control of diabetes adds another dimension to the benefits of resveratrol. Researchers studied effects of resveratrol on diabetic mice. It was seen that sirtuins, which are proteins expressed in those parts of the brain that regulate glucose metabolism, were activated by resveratrol. By using resveratrol over a period of time the researchers found that both hyperglycemia or high blood sugar and hyperinsulinemia or the excess levels of insulin in the blood were normalized for the animals.

Polyphenolic compounds such as resveratrol have been shown to protect neurons against a variety of neurodegenerative conditions, including cognitive deficits associated with diabetes. In a Brazilian study, giving resveratrol to diabetic rats was able to prevent learning and memory impairment induced by diabetes.

Fatty Liver Prevention

Extensive research in animals has revealed that resveratrol significantly decreases the occurrence nonalcoholic fatty liver disease. The prevalence of nonalcoholic fatty liver disease (NAFLD) is high. NAFLD is linked to obesity, diabetes mellitus, and hypertriglyceridemia. Approximately 20% of patients with NAFLD will eventually develop cirrhosis.
Other researchers found that resveratrol prevent alcoholic fatty liver disease. Alcohol-fed mice given resveratrol had less fat in their livers and the fat broke down more quickly than alcohol-fed mice not give resveratrol. In other words, resveratrol helps prevent fat buildup in the liver that goes hand-in-hand with chronic alcohol use.

**Inflammation Fighter**

Resveratrol is proven to reduce inflammation in humans that could lead to heart disease, stroke, and type-2 diabetes. People taking resveratrol also showed suppression of the inflammatory protein tumor necrosis factor, or TNF, and other compounds that increase blood vessel inflammation and interfere with insulin action, causing insulin resistance and the risk of developing diabetes.

**Cancer Inhibition**

Resveratrol may help prevent the occurrence of cancer. Resveratrol has been shown to interfere with all three stages of carcinogenesis - initiation, promotion and progression through multiple mechanisms. These mechanisms include inhibition of the transcription factor NF-kB, cytochrome P450 isoenzyme CYP1A1, androgenic actions and the expression of the genes that code for the cyclooxygenases (COX-1 and COX-2), which are implicated in many cancers, as well as the expression of the gene for another cancer-related enzyme called ornithine decarboxylase. Plus resveratrol has been shown to induce Fas/ Fas ligand mediated apoptosis, p53 and cyclins A, B1 and cyclin-dependent kinases cdk 1 and 2. Furthermore, resveratrol possesses antioxidant and anti-angiogenic properties.

**DOSAGE AND ADMINISTRATION**

SHAKE WELL BEFORE EACH USE. Put 1 dropper (1 ml) between cheek and gum 1-2 times daily. For maximal absorption, hold in mouth 60 seconds before swallowing.

**SUPPLEMENT FACTS**

<table>
<thead>
<tr>
<th>Serving size: 0.8 ml</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Servings per container: 60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patent-pending NanoBioSpheres™ complex (phospholipids, safflower oil, ethanol, medium-chain triglycerides, glycerin, glyceryl stearate, ascorbyl palmitate)</td>
<td>775 mg</td>
<td>*</td>
</tr>
<tr>
<td>Resveratrol (99%)</td>
<td>100 mg</td>
<td>*</td>
</tr>
</tbody>
</table>

* Daily Value not Established

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.