What do healthful berries, red wine, and an Ayurvedic medicinal preparation for cardiovascular wellness, Drakshasava, have in common?
Company History
Sabinsa Corporation, founded in 1988, is a manufacturer and supplier of herbal extracts, cosmeceuticals, minerals and specialty fine chemicals. Sabinsa’s mission is to provide alternative and complementary natural products for human nutrition and well-being. Over the past two decades, Sabinsa has brought to market more than 100 standardized botanical extracts and privately funded several clinical studies in conjunction with prestigious institutions in support of these products. Its present operations have grown to employ 1,000 people worldwide in ten manufacturing, R&D and/or distribution facilities. Additionally, botanical cultivation efforts undertaken by the organization now total nearly 40,000 acres to ensure sustainable supplies on its key products. All products intended for human consumption are certified Kosher with many even Halal certified.

Science and Technical Merit
Emphasis on developing and bringing to market products with scientific and clinical substantiation is Sabinsa’s core business philosophy and is in large part responsible for fueling the company’s ongoing commercial success. With more than 100 scientists working full time conducting ongoing research both in India and the United States, Sabinsa continues to develop and patent beneficial nutrients for the world market.

Proprietary/Intellectual Property
Presently Sabinsa currently owns over 65 USA & International patents, and has over two dozen pending patent applications worldwide. The company has many well recognized trademarked ingredients such as Bacopin®, BioPerine®, Boswellin®, Citrin®, Cosmoperine®, Curcumin C3 Complex®, DigeZyme®, Fabenol®, FenuFibers®, Fenusterols®, ForsLean®, Gugulipid®, Gymnema Sylvestre GS4®, LactoSpore®, LeanGard®, Momordicin®, Picroliv®, Saberry®, Salaretin®, Selenium SeLECT®, Silbinol®, and Venocin®.

With global sales and marketing offices in 6 countries, we are here to support you.
INTRODUCTION

What do healthful berries, red wine, and an Ayurvedic medicinal preparation for cardiovascular wellness, Draksha-sava, have in common? A high content of stilbenes (phenylpropanoid compounds), notably resveratrol and its analogue pterostilbene, that are known to have diverse pharmacological activities (Roupe, et al., 2006). Several phenylpropanoids are antimicrobial compounds, secondary metabolites synthesized by plant cells in response to attack by grazing animals or pathogen infestation, and are classified as phytoalexins (Langcake, et al. 1977). Pterostilbene is one such compound, identified in Vitis vinifera leaves (Langcake et al., 1979).

Additional biological roles have been described for stress-induced phenylpropanoids. These include signaling of defense responses, protection against UV light damage, and increase in bioavailability of poorly absorbed nutrients (Dixon et al., 1995, Schmidlin, et al, 2008). Sabinsa offers Silbinol® and pTeroWhite®, proprietary natural pterostilbene ingredients, for nutritional and cosmetic applications respectively, extracted from the dried heartwood of Pterocarpus marsupium.

Silbinol® and pTeroWhite® are registered trademarks of Sabinsa Corporation.
Stilbenes have been isolated from diverse plant families, including grape (Vitaceae), pine (Pinaceae), peanut (Fabaceae) and sorghum (Poaceae). Over the last 15 years, research and commercial interest in plant stilbenes has escalated, in the light of their biological activities and possible pharmacological applications (Chong, et al; 2009). Resveratrol (Figure 1(a)) which was postulated to be involved in the health benefits associated with a moderate consumption of red wine (Pendurthi, et al; 1999) (the “French paradox”) is the subject of extensive research (Lekli, et al; 2009). Several published reports on the health benefits of resveratrol exist, describing its potential to slow the progression of a wide variety of chronic conditions, (including various forms of cancer, and cardiovascular diseases), as well as to extend the life spans of various organisms. A major breakthrough in anti-aging research was the identification of genetic pathways that are regulatory master keys in the aging process, a prominent one being the Silent information regulator (SIRT) pathway. Resveratrol was found to increase SIRT1 (the type found in humans) activity 13-fold, with potentially beneficial effects in healthy aging and life-span (Howitz, et al., 2003). Resveratrol “mimics” the effects of caloric restriction, which is known to increase lifespan. Caloric restriction is associated with increased SIRT1.

Pterostilbene, a structural analog of resveratrol, is more stable in vivo than resveratrol. Pterostilbene (3,5-dimethoxy-4′-hydroxy-trans-stilbene) (Figure 1(b)) was originally isolated from the heartwood of red sandalwood (*Pterocarpus santalinus*) (Spath and Schlager, 1940). Its presence in grape vines and blueberries was also reported later (Adrian et al., 2000; Langcake, 1977; Langcake et al., 1979; Rimando et al., 2004).

Interestingly, Pterostilbene was identified as the major phenolic compound in *drakshasava*, a traditional Ayurvedic medicinal preparation used to treat cardiovascular and related problems (Paul, B. et al., 1999), and in wood of *Pterocarpus marsupium*, (Indian kino) used by Ayurvedic practitioners in the treatment of diabetes (Manickam et al., 1997, www.silbinol.com).
PHYTOCHEMISTRY

Stilbenes are characterized by a 1,2-diphenylethylene backbone. Most plant stilbenes are derivatives of the basic unit trans-resveratrol (3,5,4-trihydroxy-trans-stilbene) (Fig 1(a)):

![Resveratrol Structure](image1.png)

**FIGURE 1(a): RESVERATROL**

![Pterostilbene Structure](image2.png)

**FIGURE 1(b): PTEROSTILBENE**

BIOLOGICAL ACTIVITY OF PTEROSTILBENE

Pterostilbene (Fig 1(b)) shares many chemical, physiological and pharmacological similarities with resveratrol and several activities are validated in published studies. Analgesia (Remsberg et al., 2008), anti-ageing (Joseph et al., 2008), anti-diabetic (Satheesh and Pari, 2008; Manickam et al., 1997; Pari and Satheesh, 2006), anti-inflammatory (Hougee et al., 2005; Pan et al., 2008) (Remsberg et al., 2008), anti-obesity (Rimando et al., 2005), antioxidant (Satheesh and Pari, 2006; Kim et al., 2009; Perecko et al., 2008; Remsberg et al., 2008; Rimando et al., 2002), neuroprotection (Joseph et al., 2008; Meng et al., 2008; Pan et al., 2008) and hypolipidemic activity (Rimando, et al., 2005; Satheesh and Pari, 2008) have also been reported.
SALIENT FEATURES

- Pterostilbene is better absorbed, and more biologically active than resveratrol.
- Pterostilbene antifungal properties are 5-10 times more powerful than resveratrol.
- Pterostilbene is more effective than resveratrol as an inhibitor of DNA synthesis in the human adenocarcinoma HT-29 cell line.
- Pterostilbene demonstrated the highest induction of PPARα, a nuclear receptor protein significant in lipid metabolism, in a comparative study with resveratrol and other stilbenes.
- Pterostilbene was found to be more effective than resveratrol in inhibiting cell membranes against lipid peroxidation.
- Pterostilbene was found to be solely responsible for the anti-inflammatory effects of *Pterocarpus marsupium* extract, notably its selective COX-2 inhibitory action.
- Pterostilbene is metabolically more stable than resveratrol and confers intended benefits without undergoing extensive metabolism as resveratrol.
- Pterostilbene has been shown to be ameliorating dyslipidemia (in diabetic rats) thus contributing to cardiovascular health benefits.
- pTeroWhite® is potentially more effective than resveratrol in inhibiting pro-inflammatory enzymes *in vitro*.
- pTeroWhite® is more effective than resveratrol in inhibiting melanogenesis and supports skin tone lightening and dyschromia management.
- pTeroWhite® effectively protects the skin from damage by ultraviolet radiation. Its *in vitro* efficacy is comparable to resveratrol.

ANTIOXIDANT SUPPORT

The antioxidant activities of trans-resveratrol, pterostilbene and quercetin, and the effect of their combination were investigated in human erythrocytes *in vitro*. Peroxide ion induced lipid peroxidation was assessed by measuring the amount of thiobarbituric acid reactive species.

Quercetin and pterostilbene protected erythrocyte membranes against lipid peroxidation (*IC₅₀* values 64 ± 8.7 microM and 44.5 ± 7.8 microM, respectively). *Resveratrol was significantly less effective*. Combinations consisting of two compounds (molar ratio 1:1) influenced lipid peroxidation in a concentration-dependent manner. At lower concentrations, resveratrol with quercetin or
pterostilbene synergistically inhibited the oxidative injury of membrane lipids. At higher concentrations, an additive effect was observed. The authors concluded that these protective effects may partially explain the health benefits of these bioactive micro-components when together in the diet (Mikstacka, et al, 2010).

The antioxidant effect of pterostilbene in rats with induced diabetes has been assessed. Diabetes decreases the activity of superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase and reduced glutathione significantly in liver and kidney tissues. There were significant improvements in activities of these enzymes, after the rats were treated with pterostilbene at a dose of 40 mg/kg for six weeks. The increased levels of lipid peroxidation measured as thiobarbituric acid reactive substances (TBARS) in liver and kidney of diabetic rats were also normalized by treatment with pterostilbene. Chronic treatment of pterostilbene remarkably reduced the pathological changes observed in liver and kidney of diabetic rats. These results substantiate the in vivo antioxidant efficacy of pterostilbene (Satheesh and Pari, 2006).

**CANCER CHEMOPREVENTIVE SUPPORT**

CYP1A1 and CYP1B1 are the inducible forms of cytochrome P450 expressed in extrahepatic tissues, which are responsible for the biotransformation of polycyclic aromatic hydrocarbons, heterocyclic amines and estradiol, to the carcinogenic intermediates. Pinostilbene (3,4’-dihydroxy-5-methoxystilbene), desoxyrhapontigenin (3,5-dihydroxy-4’-methoxystilbene), and pterostilbene (3,5-dimethoxy-4’-hydroxystilbene) were found to be very potent inhibitors of CYP1A1 catalytic activity with Ki values of 0.13, 0.16 and 0.57 microM, respectively (Mikstacka, et al., 2007).

Cancer chemo-preventive effects were observed in rodent models (Cichocki et al., 2008; Suh et al., 2007). As an intervention, pterostilbene significantly induced growth arrest and/or apoptosis in various transformed cells (Billack et al., 2008; Ferrer et al., 2005; Pan et al., 2007; Priego et al., 2008; Remsberg et al., 2008; Rimando et al, 2008; Tolomeo et al., 2005). Pterostilbene induced apoptosis in human gastric cancer cells (Pan, et al, 2007), breast cancer cells (Alosi, et al., 2010, Chakraborty, et al., 2010), prostate cancer cells (Chakraborty, et al., 2010; Wang, et al, 2010), bladder cancer cells (Chen, et al., 2010), liver cancer cells (Hasiah, et al., 2010, Pan, et al, 2009b), lung cancer cells (Schneider, et al, 2010) and melanoma cell lines (Schneider, et al, 2009). Pterostilbene inhibits Matrix metalloproteinase 9 (MMP9) and alpha-methylacyl-CoA recemase (AMACR), two very well
known metastasis inducers (Chakraborty, et al, 2010; Pan, et al., 2008b, Pan, et al., 2009). Pan, et al. used Silbinol® 90%+ in these studies.

Anti-metastatic efficacy was demonstrated in a mouse model with highly malignant B16 F10 melanoma cells (Ferrer et al., 2005). The mechanism was attributed to Direct NO-induced cytotoxicity, ceramide-induced mitochondrial permeability transition, and apoptosis activation (Ferrer, et al., 2007).

Treatment of pancreatic cancer cells in vitro with Pterostilbene was found to inhibit cell proliferation and/or cause cell death, cell cycle arrest, mitochondrial membrane depolarization, and activation of effector caspases (cysteine-aspartic proteases that play essential roles in apoptosis, tumor necrosis and inflammation). Pterostilbene may therefore have benefits in supporting the management of pancreatic cancer (Mannal, et al, 2010).

Pterostilbene is also potentially beneficial in the chemoprevention of colon cancer and liver cancer. Pterostilbene (Silbinol® 90%+) was found to inhibit colorectal aberrant crypt foci (ACF) and colon carcinogenesis via suppression of multiple signal transduction pathways as determined in azoxymethane-treated mice (Chiou, et al., 2010). In a rat liver cell line, pterostilbene from Vitis coignetiae was found to offer protection against H₂O₂-induced inhibition of gap junctional intercellular communication (Kim, et al., 2009).

**ANTI-INFLAMMATORY ACTIVITY**

Pterostilbene (Silbinol® 90%+) shows potent anti-inflammatory activity, mediated through inhibition of pro-inflammatory enzymes and cytokines. The effects of pterostilbene on the activation of upstream signaling pathways and transcription factors involved were investigated, in colon cancer cells. The p38 MAPK was identified as a key mediator for the inhibitory effect of pterostilbene on the formation of iNOS (inducible nitric oxide synthase) and COX-2. Pterostilbene down-regulates inflammatory iNOS and COX-2 gene expression in macrophages by inhibiting the activation of NFkB (nuclear transcription factor significant in inflammation) (Pan et al, 2008b).

Pterostilbene was also found to be more potent than resveratrol as an inhibitor of the proliferation of cultured HT-29 colon cancer cells, and inflammatory mediators (Paul, S. et al., 2009).
HT-29 cells were incubated with different concentrations of pterostilbene or resveratrol for 1, 2, and 3 days, and cell proliferation was estimated by measuring [3H]thymidine incorporated into DNA. The 3-day incubation gave the strongest growth inhibition, and there was a dose-dependent effect. Pterostilbene was a more potent inhibitor of proliferation (IC\textsubscript{50}, 22.4 microMol/L) when compared with resveratrol treatment (IC\textsubscript{50}, 43.8 microM/L) under the same conditions. A triple combination of TNF-α, IFN-γ, and LPS resulted in a marked induction of iNOS and COX-2, and pterostilbene reduced the induction of iNOS and COX-2 in a dose-dependent manner. Quantitative RT-PCR data showed that the regulation of iNOS and COX-2 occurred at the transcriptional level with pterostilbene effectively down-regulating the cytokine induction of iNOS and COX-2 mRNA. Treatment with a mixture of cytokines induced mRNA synthesis for proinflammatory cytokines, such as IL-1β, and this was significantly inhibited by pterostilbene.

\textit{Pterocarpus marsupium} extract containing pterostilbene was found to selectively inhibit COX-2, an enzyme in the inflammatory cascade. Furthermore, the selective COX-2 inhibitory activity of \textit{Pterocarpus marsupium} extract was attributed to its content of pterostilbene. In a comparative study, \textit{Pterocarpus marsupium} extract, pterostilbene and resveratrol inhibited PGE\textsubscript{2} (prostaglandin E\textsubscript{2}) production from LPS-stimulated human peripheral blood mononuclear cells (PBMC) with IC\textsubscript{50} values of 3.2 ± 1.3 microg/mL, 1.0 ± 0.6 microM and 3.2 ± 1.4 microM, respectively. Based on the calculated pterostilbene content of \textit{Pterocarpus marsupium} extract, \textit{PGE}_2 inhibition by \textit{Pterocarpus marsupium} extract was attributed solely to its content of pterostilbene. Furthermore, in a COX-1 whole blood assay (WBA) \textit{Pterocarpus marsupium} extract was not effective while in a COX-2 WBA, \textit{Pterocarpus marsupium} extract decreased PGE\textsubscript{2} production indicating COX-2 specific inhibition. In humans, 450mg \textit{Pterocarpus marsupium} extract resulted in elevated pterostilbene levels in serum, which were below the active concentration observed \textit{in vitro}. Supplementation in humans with 450mg \textit{Pterocarpus marsupium} extract is considered safe, based on a long history of use, the absence of abnormal blood cell counts and blood chemistry values and the absence of extract-related adverse events (Hougee, et al, 2005).

These results suggest that \textit{Pterocarpus marsupium} extract and more specifically pterostilbene can potentially support the management of inflammation, and since inflammation is considered to be the root cause of chronic diseases, which further supports general health and wellness. Benefits in supporting a healthy body weight and composition, normal blood sugar and blood lipid levels, and the management of symptoms of inflammation such as pain and swelling in the joints, are anticipated, and are supported by laboratory studies.
With reference to potential skin care applications, topically applied resveratrol significantly inhibited COX-2 expression and activation of nuclear factor-κB (NF-κB) induced by tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA) in mouse epidermis. In an effort to determine its mechanism of action, researchers compared the effects of resveratrol and pterostilbene on various cytokines and inflammatory mediators. Resveratrol and pterostilbene significantly reduced activator protein 1 (AP-1) and NF-κB activation. Reduced activation of transcription factors decreased the expression and activity of COX-2 and inducible nitric oxide synthase (iNOS). In most assays, pterostilbene was either equally or significantly more potent than resveratrol (Cichocke, et al., 2008).

PTEROSTILBENE SUPPORTS INSULIN SENSITIVITY, NORMAL BLOOD SUGAR LEVELS AND NORMAL BLOOD LIPID LEVELS

The peroxisome proliferator-activated receptors (PPARs) are a group of nuclear receptor proteins that function as transcription factors regulating the expression of genes and thereby affect cellular differentiation and development, as well as carbohydrate, protein and lipid metabolism.

Researchers evaluated four stilbenes (resveratrol, resveratrol trimethyl ether, pterostilbene and piceatannol) at levels of 1, 10, 100, and 300 μM using ciprofibrate (a hypolipidemic drug that works through the induction of PPARα - the receptor pertaining to lipid metabolism), as positive control. The *in vitro* model used was activation of endogenous PPARα in H4IIEC3 cells. *Pterostilbene demonstrated the highest induction of PPARα showing 8 and 14-fold increases in luciferase activity at 100 and 300 μM, respectively, relative to the control* (Rimando, et al.; 2005).

Pterostilbene significantly lowered the blood glucose level of hyperglycemic rats, and the effect was comparable to that of 1,1-dimethylbiguanide (metformin) (Manickam, et al., 1997). An aqueous extract of heartwood of *Pterocarpus marsupium* has been tested clinically and found to be effective

Hypercholesterolemic hamsters fed with pterostilbene at 25 ppm of the diet showed 29% lower plasma low density lipoprotein (LDL) cholesterol, 7% higher plasma high density lipoprotein (HDL) cholesterol, and 14% lower plasma glucose as compared to the control group. The LDL/HDL ratio was also statistically significantly lower for pterostilbene, as compared to results for the control animals, at this diet concentration. *Results revealed that pterostilbene acts as a PPARα agonist and may be a more effective PPARα agonist and hypolipidemic agent than resveratrol* (Rimando, et al., 2005).

The streptozotocin-nicotinamide type 2 model shares a number of features with human Type 2 diabetes, and is characterized by a moderate stable hyperglycaemia, glucose intolerance, and an altered but significant glucose-stimulated insulin secretion. Diabetic rats were orally administered pterostilbene (10, 20, 40mg/kg) for 2, 4 and 6 weeks; pterostilbene at 40mg/kg was found to significantly decrease plasma glucose. A significant decrease in glucose and significant increase in plasma insulin levels were observed in normal and diabetic rats treated with pterostilbene at 40mg/kg, along with a significant reduction of glycosylated hemoglobin and an increase in total hemoglobin level. The activities of the hepatic enzymes such as hexokinase was significantly increased, whereas glucose-6-phosphatase, fructose-1,6-bisphosphatase were significantly decreased by the administration of pterostilbene in diabetic rats. A comparison was made between the action of pterostilbene and the antidiabetic drug – metformin (Pari and Satheesh, 2006). The researchers postulated that *pterostilbene induces release of insulin from the existing β-cells of the pancreas*.

In a subsequent study, evidence for the hypolipidemic effect of pterostilbene in experimental Type 2 diabetes, was established. Oral administration of pterostilbene¹ (40mg/kg bodyweight) to streptozotocin-nicotinamide induced diabetic rats for 6 weeks significantly reduced the elevated serum very low density lipoprotein (VLDL) and low density lipoprotein (LDL)-cholesterol levels and *significantly increased the serum high-density lipoprotein (HDL)-cholesterol level*. In addition, pterostilbene also significantly lowered the levels of triglycerides, phospholipids, free fatty acids and total cholesterol in the serum, liver and kidney of diabetic rats. The results are summarized in Figure 2 and Figure 3 (Satheesh and Pari, 2008).

¹ Silbinol® 90%+ was used in this study
FIGURE 2:
EFFECT OF PTEROSTILBENE ON CHANGES IN LEVELS OF LIPOPROTEINS AND CHOLESTEROL IN RATS
Mean values from 6 rats in each group

FIGURE 3:
EFFECT OF PTEROSTILBENE ON CHANGES IN PLASMA LEVELS OF GLUCOSE IN RATS
Mean values from 6 rats in each group
These results point towards the potential utility of pterostilbene in supporting the management of metabolic syndrome and in supporting a healthy body weight and composition.

Another study that explored the healthful roles of traditionally used plant extracts in an animal model of fructose induced increased serum glucose, insulin and triglyceride levels, found that feeding *Pterocarpus marsupium* extract at 1g/kg/day for 30 days, significantly reduced hypertriglyceridaemia and hyperinsulinaemia (Grover, et al., 2005).

**CARDIOVASCULAR HEALTH BENEFITS**

Vascular smooth muscle cells are the main cellular component in the arterial wall, and abnormal proliferation of these cells plays a pivotal role in the pathogenesis of atherosclerosis and restenosis after angioplasty, and possibly in the development of hypertension. In a recent study, Pterostilbene significantly inhibited the DNA synthesis and proliferation of platelet-derived growth factor (PDGF)-BB-induced stimulated vascular smooth muscle cells in a concentration-dependent manner, and down regulated cell cycle related proteins. These effects suggest the potentially beneficial role of pterostilbene in supporting cardiovascular health and wellness (Park, et al, 2010).

**PTEROSTILBENE IN HEALTHY AGING, MEMORY AND COGNITION**

Recent research suggests that Pterostilbene is potentially more effective that resveratrol in supporting memory and cognitive functions during aging. Researchers compared the effects of resveratrol and its analogues for efficacy in reversing the deleterious effects of aging in 19 month old Fischer 344 rats. Two sets of experiments were performed. Experiment I utilizing resveratrol and six resveratrol analogues, examined their efficacies in preventing dopamine-induced decrements in calcium clearance following oxotremorine-induced depolarization in COS-7 cells transfected with M1 muscarinic receptors (MACHR) that are sensitive to oxidative stressors.

Experiment II utilized the most efficacious analogue (pterostilbene) from experiment I and fed aged rats a diet with a low (0.004%) or a high (0.016%) concentration of pterostilbene. Results indicated that pterostilbene was effective in reversing cognitive behavioral deficits, as well as dopamine release, and working memory was correlated with pterostilbene levels in the hippocampus (Joseph, et al., 2008).
ANTIFUNGAL ACTIVITY

Although trans-pterostilbene identified in Vitis vinifera leaves was found to be just a minor component of the phytoalexin response of plant, its antifungal activity is reported to be relatively high in comparison to resveratrol and viniferins, the other known stress metabolites in grape (Langcake, et al., 1977, 1979). More recent reports indicate that pterostilbene is 5 to 10 times more effective than resveratrol in inhibiting the germination of conidia Botrytis cinerea and sporangia of Plasmopara viticola (Jeandet et al., 2002).

COSMECEUTICAL BENEFITS

At a suggested level of 0.1-0.5% w/w in cosmetic formulations, pTeroWhite® offers antioxidant and anti-inflammatory (anti-aging) support, lightens skin tone; supports dyschromia management, and is a valuable adjunct to sun-care and after sun-care compositions. Laboratory studies revealed its healthful role in offering protection against damaging ultraviolet radiation. The DPPH (2,2-Diphenyl-1-Picrylhydrazyl) radical scavenging test is a standard method to determine antioxidant activity. Figure 4 depicts the comparative efficacy of pterostilbene, resveratrol and a commonly used skin lightening agent, kojic acid, in quenching free radicals.

Inhibition of melanin formation in in vitro cell culture and inhibition of the enzyme tyrosinase (that catalyzes the rate limiting step in the synthesis of melanin) are standard tests used to determine skin tone lightening potential of active compounds. Figure 5(a) shows the comparative effects of kojic acid, pTeroWhite® and resveratrol on melanogenesis in cell culture, and Figure 5(b) shows melanin formation in cells cultured with and without pTeroWhite®. pTeroWhite® perceptibly inhibits melanin formation.

Figure 6 shows their comparative efficacy of pTeroWhite® and resveratrol in protecting cells against the effects of ultraviolet radiation, as measured in in vitro cell culture experiments.
pTeroWhite® (natural pterostilbene 90%) is carefully extracted from the heartwood of Pterocarpus marsupium, conveniently blends with your cosmetic formulations, to offer antioxidant coverage and protection against ultraviolet light, effectively lighten skin tone, and reduce the appearance of wrinkles and sun damage. At 0.1-0.5% w/w in cosmetic compositions, pTeroWhite® is more efficacious than resveratrol, in supporting skin texture and tone, on account of its improved stability.
**DPPH INHIBITION**

![Bar chart showing DPPH inhibition](image)

Lower the IC$_{50}$, greater is the activity

**FIGURE 4: ANTIOXIDANT ACTIVITY – DPPH INHIBITION**

**MELANIN INHIBITION**

![Bar chart showing melanin inhibition](image)

Lower the IC$_{50}$, greater is the activity

**FIGURE 5(a): COMPARATIVE MELANIN INHIBITION**
MELANOGENESIS INHIBITION BY pTeroWhite® 90%

**FIGURE 5(b): MELANOGENESIS INHIBITION IN CELL CULTURE**

![Untreated cells vs. pTeroWhite® 90% treated cells](image)

IC$_{50}$ of pTeroWhite® 90% for melanin inhibition -0.55µg/ml

UV PROTECTION POTENTIAL OF pTeroWhite® 90%

**FIGURE 6: UV PROTECTION**

![Graph showing UV protection potential](image)

Lower the IC$_{50}$, greater is the activity

pTeroWhite® vs. Resveratrol

IC$_{50}$µg/ml
PHARMACOKINETICS & METABOLISM

The higher biological activity of pterostilbene may be linked to its relatively higher bioavailability as compared to resveratrol. Structurally, the methoxy substitution improves lipophilicity and cellular transit, and increases the metabolic stability of the molecule. Pterostilbene is therefore less rapidly glucuronidated and sulfated as compared to resveratrol, (which carries the hydroxyl group). Recent research, wherein pterostilbene was intravenously administered at a level of 20mg/kg in rats, (Remsberg, et al., 2008) revealed a glucuronidated pterostilbene metabolite in serum and urine. Another pharmacokinetic study in rats showed improved pharmacokinetic characteristics over resveratrol. The terminal elimination half-life and clearance of pterostilbene were 96.6 ±23.7 minutes and 37.0 ±2.5mL/min/kg, respectively, while its absolute oral bioavailability was 12.5 ±4.7 percent (Lin, et al., 2009).

A MORE RECENT STUDY IDENTIFIED NINE NOVEL URINARY METABOLITES IN PTEROSTILBENE (Silbinol®90%+) FED MICE.

- pterostilbene glucuronide
- pterostilbene sulfate
- mono-demethylated pterostilbene glucuronide
- mono-demethylated pterostilbene sulfate
- mono-hydroxylated pterostilbene
- mono-hydroxylated pterostilbene glucuronide
- mono-hydroxylated pterostilbene sulfate
- mono-hydroxylated pterostilbene glucuronide sulfate

These were all identified using liquid chromatography / atmospheric pressure chemical ionization and electrospray ionization tandem mass spectrometry. The structures of these metabolites were confirmed by analyzing the MS^n (n = 1-3) spectra (Shao, et al., 2010).

SAFETY

Silbinol® and pTeroWhite® are safe for use in nutraceutical and cosmeceutical compositions. The acute oral toxicity (LD₅₀) of pterostilbene in rats was found to be 1750mg/kg body weight, signifying a high margin of safety in the suggested level of use of up to 450mg of Silbinol®, for nutraceutical benefits. The primary skin irritation potential was found to be zero, validating the safety of pTeroWhite® for topical use.

Dietary administration of high doses of pterostilbene did not induce any adverse effects in mice. Mice were fed for 28 days at doses of 30, 300, and 3000mg/kg body weight/day of pterostilbene, quercetin, or a mixture of both, which are equivalent to 5, 50, and 500 times, respectively, the
estimated mean human intake of these polyphenols being 25mg/day. Daily oral administration of either polyphenol, or a mixture of both did not cause mortality during the experimental period. No significant body weight gain or difference in feed consumption was observed in the male or female animals. Red blood cell number and the hematocrit increased after polyphenols administration, as compared to control groups. Biochemical parameters were not affected. Histopathological examination revealed no alterations in clinical signs or organ weight at any dose (Ruiz, et al., 2009).

CONCLUSIONS

Silbinol® can be used singly or in combination with resveratrol in nutraceutical compositions to support wellness and healthy aging. pTeroWhite® is an effective natural ingredient in cosmetic compositions that support skin texture and even tone, and in sun-care and after-sun care formulations. Contact Sabinsa for further information, samples and formulation guidelines.
REFERENCES


Natural Pterostilbene: Bioactive Phytonutrient

**Authors:**

® Sabinsa, Venocin®, Sylvestre GS4®, LactoSpore®, LeanGard®, Momordicin®, ingredients such as Bacopin®, BioPerine®, Boswellin®, Citrin®, patents, and has over two dozen pending patent applications. Presently Sabinsa currently owns over 65 USA & International patents beneficial nutrients for the world market.

**Science and Technical Merit**

products. All products intended for human consumption are total nearly 40,000 acres to ensure sustainable supplies on its key manufacturing, R&D and/or distribution facilities. Additionally, operations have grown to employ 1,000 people worldwide in ten.

brought to market more than 100 standardized botanical extracts alternative and complementary natural products for human specialty fine chemicals. Sabinsa's mission is to provide supplier of herbal extracts, cosmeceuticals, minerals and with global sales and marketing offices in 6 countries, we are here to support you.

³ Complex®, DigeZyme®, Fabenol®, [Image -791x1469 to -751x1553]

texture and tone, on account of its improved stability. antioxidant coverage and protection against ultraviolet light, effectively lighten skin tone, Pterocarpus marsupium pTeroWhite® (natural pterostilbene 90%) is carefully extracted from the heartwood of cardiogenic and related cardiovascular and related diseases), as well as to extend the life spans of various organisms. A major breakthrough in a wide variety of chronic conditions, (including various forms of cancer, and cardiovascular disease and in wood of)

Phenylpropanoids are antimicrobial compounds, secondary such compound, identified in . Complexes, phytoalexins, (Manickam et al., 1997, treatment of diabetes and in wood of)
Pterostilbene, a structural analog of resveratrol, is more stable in vivo than resveratrol. increased SIRT1. caloric restriction, which is known to increase lifespan. Caloric restriction is associated with aging process, a prominent one being the Silent information regulator (SIRT) pathway. Resveratrol anti-aging research was the identification of genetic pathways that are regulatory master keys in the (Figure 1(a): RESVERATROL) and (Figure 1(b): PTEROSTILBENE) in plant stilbenes has escalated, in the light of their biological activities and possible pharmacological roles for. (Remsberg et al., 2008), (Joseph et al., 2008; Meng et al., 2008; Pan et al., 2008) and (Satheesh and Pari, 2006), (Satheesh, 2006), (Manickam et al., 1997; Pari and Satheesh, 2006), (Kim et al., 2009; Perecko et al., 2008; Remsberg et al., 2002), (Satheesh and Pari, 2008) have also been reported.

**MELANIN INHIBITION**

**DPPH INHIBITION**

**MELANOGENESIS INHIBITION BY pTeroWhite® 90%**

**Fact: Sabinsa cultivates, harvests and manufactures Coleus forskohlii and turmeric.**