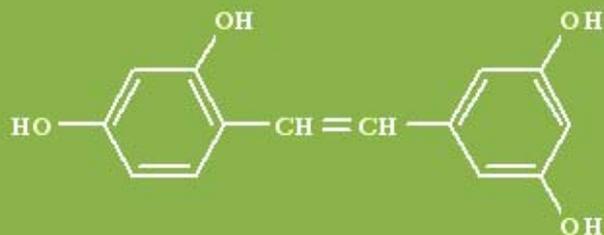


OxyResvenox™



OxyResvenox™



SABINSA CORPORATION

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OxyResvenox™

Product Write-up

Introduction

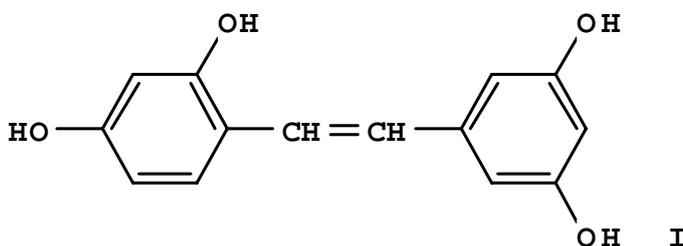
Resveratrol is well known as an ingredient of red wine and has been extensively studied to show several biological activities of¹:

- Free radical scavenging,
- Alteration of eicosanoid metabolism,
- Inhibition of platelet aggregation,
- Anti-inflammatory activity,
- Anticancer activity, and
- Estrogenic activity.

OxyResvenox™

OxyResvenox™ is the registered trade mark of Oxyresveratrol from Sabinsa. Oxyresveratrol is an analog of Resveratrol and is of synthetic origin. US Patent 7,253,324, granted to Sabinsa specifically protects the process for the synthesis of biologically active polyphenolic compounds like Pterostilbene, Resveratrol and Oxyresveratrol by novel dealkylation.

Oxyresveratrol contains an additional hydroxy group at position 2' of the stilbene moiety. Oxyresveratrol (2', 3, 4', 5-tetrahydroxystilbene) is a stilbenol, a derivative of stilbene, and is produced in plants with the help of the enzyme stilbene synthase. Stilbenes are polyphenolic compounds that act as cancer chemopreventive agents².



Structure of Oxyresveratrol

The hydroxystilbene compounds including oxyresveratrol and resveratrol showed potent inhibitory effect on tyrosinase activity¹. Oxyresveratrol is also naturally present in *Morus alba L.*, *Morus bombycis*.

Product Information:

IUPAC Name:	4-[(E)-2-(3,5-dihydroxyphenyl)ethenyl]benzene-1,3-diol
Synonyms:	<i>trans</i> -2,3',4,5'-tetrahydroxystilbene
Molecular Formula:	C ₁₄ H ₁₂ O ₄
Molecular Weight:	244.24268 g/mol.
Mass:	244.0736

Potential applications of Oxyresveratrol:

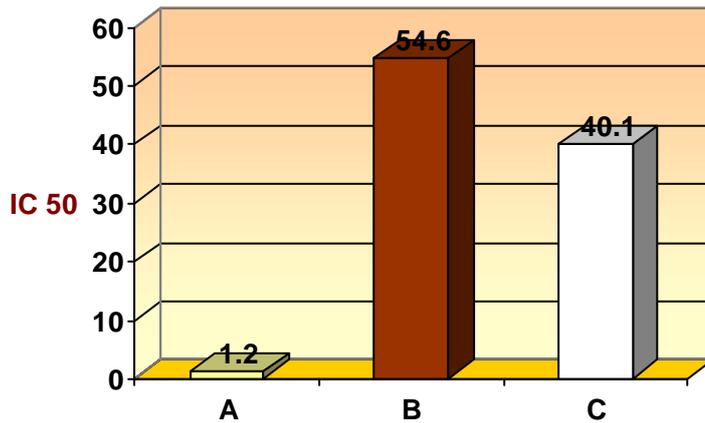
1. A potent tyrosinase inhibitor:

Oxyresveratrol exhibits a potent inhibitory effect on dopa oxidase activity of tyrosinase which catalyzes rate-limiting steps of melanin biosynthesis.³

Oxyresveratrol with 0.3 to 5 μM exhibited potent and dose-dependent inhibitions (25 to 84%) on the enzyme activity, where 50% of inhibition was shown at the concentration of about 1 μM.

Oxyresveratrol exhibited about a 150-fold more potent inhibitory effect than resveratrol (3,4',5-trihydroxystilbene). The results indicate that both the number and positions of hydroxy groups in oxyresveratrol seem to play a critical role in exerting the inhibitory effect on dopa oxidase activity of mushroom tyrosinase³

Kojic acid, a well known depigmenting agent, exhibited a 32- fold weaker inhibitory effect on the enzyme activity than did oxyresveratrol in view of the IC₅₀ value. The inhibitory potencies were in order of oxyresveratrol > kojic acid = resveratrol > rhapontigenin = 3,5-dihydroxy-4_-methoxystilbene in view of the IC₅₀ values.



A – Oxyresveratrol B - Resveratrol C – Kojic Acid

Fig.1. Dose-dependent inhibitory effects on mushroom tyrosinase

2. Anti - Melanogenesis ⁴:

Anti-melanogenesis activity and tyrosinase inhibition by *Morus bombycis* heartwood extract (MBHE) was higher than that of other extracts (bark, rootbark and leaf) of *Morus bombycis*.

The oxyresveratrol content was found to be higher in the *Morus bombycis* heartwood extract (MBHE) than that of other extracts (bark, rootbark and leaf) of *Morus bombycis*.

These results suggest that oxyresveratrol plays a key role in the inhibitory effect of MBHE on melanin synthesis.

3. Anti - browning agent ⁵:

It was found that oxyresveratrol could effectively inhibit browning in cloudy apple juices at a concentration as low as 0.01% and that mulberry twig extract also showed remarkable anti-browning effects on cloudy apple juices.

4. Antioxidant effect ⁶:

Chemical investigation of the Ethanol extract of *Morus alba* L. (Moraceae), revealed the presence of Oxyresveratrol.

Oxyresveratrol showed superoxide scavenging effects with the IC₅₀ values $3.81 \pm 0.5 \mu\text{M}$, Oxyresveratrol exhibited a DPPH free radical scavenging effect (IC₅₀ = $23.4 \pm 1.5 \mu\text{M}$). Oxyresveratrol also showed hepatoprotective effects with EC₅₀ values $32.3 \pm 2.62 \mu\text{M}$, on tacrine-induced cytotoxicity in human liver-derived Hep G2 cells.

5. Anti-inflammatory effect ⁷:

The anti-inflammatory effects of mulberroside A and oxyresveratrol using the carrageenin-induced model of inflammation were investigated in rats. Mulberroside A and oxyresveratrol significantly reduced paw edema. The mechanism of the anti-inflammatory action of Oxyresveratrol was suggested to be mainly due to the inhibition of iNOS expression rather than iNOS enzyme activity.

Oxyresveratrol significantly inhibited LPS-evoked nuclear translocation of NF-kappaB and cyclooxygenase-2 (COX-2) activity in RAW 264.7 cells.

The results suggest that the anti-inflammatory properties of oxyresveratrol might be correlated with inhibition of the iNOS expression through down-regulation of NF-kappaB binding activity and significant inhibition of COX-2 activity.

6. Neuroprotective Effect ⁸:

Oxidative stress is one of the major pathological factors in the cascade that leads to cell death in cerebral ischemia. Investigations show the neuroprotective effect of a naturally occurring antioxidant, oxyresveratrol, to reduce brain injury after cerebral stroke.

Oxyresveratrol revealed a dose-dependent neuroprotective effect in an in vivo stroke model. This may prove to be beneficial for a therapeutic strategy to limit brain injury in acute brain ischemia.

Summary:

OxyResvenox™, an important analog of Resveratrol exhibited a potent inhibitory effect on dopa oxidase activity of tyrosinase which catalyzes rate-limiting steps of melanin biosynthesis.

OxyResvenox™, finds potential applications as an Anti-tyrosinase, Anti-oxidant and Anti-inflammatory ingredient. Oxyresveratrol showed potent inhibitory effect with an IC₅₀ value of 1.2 μM on mushroom tyrosinase activity which was 32 fold stronger inhibition than kojic acid, a de-pigmenting agent used as the cosmetic material with skin whitening effect

In view of skin lightening, de-pigmentation and anti-inflammatory potential it can also used in cosmetic formulations as an anti-aging ingredient.

References:

1. Yeon Mi Kim, Jieun Yun, Chong-Kil Lee, Hwanghee Lee, Kyung Rak Min. **Oxyresveratrol and Hydroxystilbene Compounds: Inhibitory Effect on Tyrosinase and Mechanism of Action.** *The Journal of Biological Chemistry*. 2002 May 3, 277(18): 16340-16344.
2. Fresco P, Borges F, Diniz C, Marques MP. **New insights on the anticancer properties of dietary polyphenols.** *Med Res Rev*. 2006 Nov;26(6):747-66.
3. Nam-Ho Shin ^a, Shi Yong Ryu ^b, Eun Ju Choi ^b, Seh-Hoon Kang ^c, IL-Moo Chang ^d, Kyung Rak Min ^a and Youngsoo Kim ^{a,1}
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Oxyresveratrol as the Potent Inhibitor on Dopa Oxidase Activity of Mushroom Tyrosinase Received 2 January 1998. Available online 12 April 2002.
4. **In vitro and in vivo Evaluation of Morus bombycis Heartwood Extract (MBHE) on Melanogenesis Inhibition.** Ji Young Moon, Young Min Ham, Jae Woo Kim, Ju Ho Kim, Sun Young Moon, Young Kyoung Seo, Hee Kyung Lee, Ji Hwoon Beak, Jae Sook Koh, Byoung-Sam Yoo. Cosmetic R&D Center, OSMAX Inc. Hwa Sung, Gyeonggi 445-746, South Korea.
5. Haitao Li, Ka-Wing Cheng, Chi-Hin Cho, Zhendan He, and Mingfu Wang. **Oxyresveratrol as an Antibrowning Agent for Cloudy Apple Juices and Fresh-Cut Apples.** *Agric. Food Chem.*, 55 (7), 2604-2610, 2007.
6. **Hepatoprotective and free radical scavenging activities of prenylflavonoids, coumarin, and stilbene from Morus alba.** Oh, Hyuncheol; Ko, Eun-Kyung; Jun, Jung-Yang; Oh, Myung-Hoon; Park, Sung-Uk; Kang, Ki-Hong; Lee, Ho-Sub; Kim, Youn-Chul. Professional Graduate School of Oriental Medicine, Wonkwang University, Iksan, S. Korea. *Planta Medica* (2002), 68(10), 932-934.
7. Chung KO, Kim BY, Lee MH, Kim YR, Chung HY, Park JH, Moon JO. **In-vitro and in-vivo anti-inflammatory effect of oxyresveratrol from Morus alba L.** *J Pharm Pharmacol*. 2003 Dec;55(12):1695-700.
8. Andrabi, S. A., Spina, M. G., Lorenz, P., Ebmeyer, U., Wolf, G., Horn, T. F. W. **Oxyresveratrol (trans-2,3',4,5'-tetrahydroxystilbene) is neuroprotective and inhibits the apoptotic cell death in transient cerebral ischemia.** Institute for Medical Neurobiology, Otto-von-Guericke University Magdeburg, Leipziger Strasse-44, Haus 36, D-39120, Magdeburg, Germany. *Brain Research*, 2004 (Vol. 1017) (No. 1/2) 98-107.

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"The vision of a research scientist takes on social and commercial expressions." This in short explains the genesis and growth of the Sabinsa – Sami Labs Group of Companies.

Company Profile:

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 ten years, Sabinsa has brought to market more than 50 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 1000 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.

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