

Abstracts Pterostilbene and PPARs:

1. Neurobiol Aging. 2012 Sep;33(9):2062-71. doi: 10.1016/j.neurobiolaging.2011.08.015. Epub 2011 Oct 7.

Low-dose pterostilbene, but not resveratrol, is a potent neuromodulator in aging and Alzheimer's disease.

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Recent studies have implicated resveratrol and pterostilbene, a resveratrol derivative, in the protection against age-related diseases including Alzheimer's disease (AD). However, the mechanism for the favorable effects of resveratrol in the brain remains unclear and information about direct cross-comparisons between these analogs is rare. As such, the purpose of this study was to compare the effectiveness of diet-achievable supplementation of resveratrol to that of pterostilbene at improving functional deficits and AD pathology in the SAMP8 mouse, a model of accelerated aging that is increasingly being validated as a model of sporadic and age-related AD. Furthermore we sought to determine the mechanism of action responsible for functional improvements observed by studying cellular stress, inflammation, and pathology markers known to be altered in AD. Two months of pterostilbene diet but not resveratrol significantly improved radial arm water maze function in SAMP8 compared with control-fed animals. Neither resveratrol nor pterostilbene increased sirtuin 1 (SIRT1) expression or downstream markers of sirtuin 1 activation. Importantly, markers of cellular stress, inflammation, and AD pathology were positively modulated by pterostilbene but not resveratrol and were associated with upregulation of peroxisome proliferator-activated receptor (PPAR) alpha expression. Taken together our findings indicate that at equivalent and diet-achievable doses pterostilbene is a more potent modulator of cognition and cellular stress than resveratrol, likely driven by increased peroxisome proliferator-activated receptor alpha expression and increased lipophilicity due to substitution of hydroxy with methoxy group in pterostilbene.

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2. Bioorg Med Chem. 2008 Apr 1;16(7):3800-8. doi: 10.1016/j.bmc.2008.01.051. Epub 2008 Jan 31.

Design, synthesis, biological evaluation and docking studies of pterostilbene analogs inside PPARalpha.

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Pterostilbene, a naturally occurring analog of resveratrol, has previously shown PPARalpha activation in H4IIEC3 cells and was found to decrease cholesterol levels in animals. In this study, analogs of pterostilbene were synthesized and their ability to activate PPARalpha was investigated. Among analogs that was synthesized (E)-4-(3,5-dimethoxystyryl)phenyl dihydrogen phosphate showed activity higher than pterostilbene and control drug ciprofibrate. Docking of the stilbenes inside PPARalpha showed the presence of important hydrogen bond interactions for PPARalpha activation.

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3. J Agric Food Chem. 2005 May 4;53(9):3403-7.

Pterostilbene, a new agonist for the peroxisome proliferator-activated receptor alpha-isoform, lowers plasma lipoproteins and cholesterol in hypercholesterolemic hamsters.

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Resveratrol, a stilbenoid antioxidant found in grapes, wine, peanuts and other berries, has been reported to have hypolipidemic properties. We investigated whether resveratrol and its three analogues (pterostilbene, piceatannol, and resveratrol trimethyl ether) would activate the peroxisome proliferator-activated receptor alpha (PPARalpha) isoform. This nuclear receptor is proposed to mediate the activity of lipid-lowering drugs such as the fibrates. The four stilbenes were evaluated at 1, 10, 100, and 300 microM along with ciprofibrate (positive control), for the activation of endogenous PPARalpha in H4IIEC3 cells. Cells were transfected with a peroxisome proliferator response element-AB (rat fatty acyl CoA beta-oxidase response element)-luciferase gene reporter construct. Pterostilbene demonstrated the highest induction of PPARalpha showing 8- and 14-fold increases in luciferase activity at 100 and 300 microM, respectively, relative to the control. The maximal luciferase activity responses to pterostilbene were higher than those obtained with the hypolipidemic drug,

ciprofibrate (33910 and 19460 relative luciferase units, respectively), at 100 microM. 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 from in vitro studies showed that pterostilbene acts as a PPARalpha agonist and may be a more effective PPARalpha agonist and hypolipidemic agent than resveratrol. In vivo studies demonstrate that pterostilbene possesses lipid and glucose lowering effects.

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