RESVERAVINE®
Antioxidante e protetor cardíaco extraído do cacho de uva e equivalente ao vinho
http://aformulabr.com.br/qrcode/resveravineatv01.pdf
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Antioxidante e protetor cardíaco extraído do cacho de uva e equivalente ao vinho

**DESCRIÇÃO**
Resveravine® é um extrato de *Vitis vinifera L.*, cultivado no sul da França e padronizado em 20% de polifenóis da classe dos estilbenos, no mínimo 12% de ε-Viniferin e 6% de Trans-Resveratrol.

**MECANISMO DE AÇÃO**
Resveravine® atua aumentando as enzimas antioxidantes, conferindo a resistência ao estresse oxidativo, estimulando a reparação das lesões nas células endoteliais, diminuindo a geração de espécies reativas de oxigênio (ROS), culminando numa atividade antioxidante. Resveravine® modula os mecanismos fundamentais, como ativação da SIRT-1, nas doenças neurodegenerativas e relacionadas ao envelhecimento, promovendo longevidade celular. Resveravine® atua também como um potente inibidor da enzima conversora da angiotensina (ECA) e elevando a taxa de produção de óxido nítrico, que promovem efeito significativo na redução da pressão arterial.

**INDICAÇÕES**
- Hipertensão;
- Antioxidante;
- Modulação de mecanismos em doenças neurodegenerativas.

**DOSE USUAL**
Recomendação oral de 5 a 30mg ao dia.

**SUGESTÕES DE FÓRMULAS**

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<th>Resveravine®</th>
<th>Tocotrimax®</th>
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<td>15mg</td>
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**Modo de uso:** 1 dose, 1 vez ao dia. **Indicação:** antioxidante e anti-inflamatório.

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<th>Resveravine®</th>
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<td>15-30mg</td>
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**Modo de uso:** 1 dose, 1 vez ao dia. **Indicação:** adjuvante na terapia de doenças cardiovasculares.

**PRINCIPAIS REFERÊNCIAS**

Greater effectiveness of ε-viniferin in red wine than its monomer resveratrol for inhibiting vascular smooth muscle cell proliferation and migration.

Resveratrol is a strong candidate for explaining an irreversible correlation between red wine consumption and coronary heart disease. The present study examined the effect of ε-viniferin, a dehydrodimer of resveratrol, on vascular smooth muscle cells (VSMCs), because ε-viniferin functions are poorly understood in spite of its comparable content to resveratrol in red wines and grapes. Both ε-viniferin and resveratrol inhibited platelet-derived growth factor-induced cell proliferation, migration, and reactive oxygen species (ROS) production, in addition to inducing nitric oxide generation. ε-Viniferin was more effective than resveratrol in these effects, except for inhibiting ROS production. The compounds also increased the expression of the antioxidant enzyme, hemeoxygenase-1, via transcription factor Nrf2. The phosphatidylinositol 3-kinase-Akt pathway was implicated in resveratrol-dependent nuclear Nrf2 accumulation, whereas extracellular signal-regulated kinase and p38 were involved in ε-viniferin-induced Nrf2 accumulation. These data suggest that ε-viniferin may function more effectively than resveratrol in different mechanisms and cooperatively with resveratrol in preventing atherosclerosis.

ε-Viniferin is more effective than its monomer resveratrol in improving the functions of vascular endothelial cells and the heart.

The present study compared the effects of resveratrol and its dimer ε-viniferin on vascular endothelial cells (VECs) functions, and on the blood pressure and cardiac mass of spontaneously hypertensive rats (SHRs). Treatment of VECs with these compounds enhanced cell proliferation via nitric oxide generation and protected the cells from oxidative stress by suppressing increases in intracellular oxygen species. ε-Viniferin was more potent than resveratrol in most of these effects. ε-Viniferin, but not resveratrol inhibited angiotensin-converting enzyme activity in vitro. Three weeks of ε-viniferin treatment (5 mg/kg) reduced the systolic blood pressure and improved the whole cardiac mass and left ventricle mass indexes in SHRs. In contrast, resveratrol administration (2.5 mg/kg) failed to lower the blood pressure and significantly improve these mass indexes. These data suggest that ε-viniferin as well as resveratrol may be involved in protecting the functions of VECs and the heart.

Effects of resveratrol on cerebral blood flow variables and cognitive performance in humans: a double-blind, placebo-controlled, crossover investigation.

BACKGROUND: The many putative beneficial effects of the polyphenol resveratrol include an ability to bolster endogenous antioxidant defenses, modulate nitric oxide synthesis, and promote vasodilation, which thereby improves blood flow. Resveratrol may therefore modulate aspects of brain function in humans. OBJECTIVE: The current study assessed the effects of oral resveratrol on cognitive performance and localized cerebral blood flow variables in healthy human adults. DESIGN: In this randomized, double-blind, placebo-controlled, crossover study, 22 healthy adults received placebo and 2 doses (250 and 500 mg) of trans-resveratrol in counterbalanced order on separate days. After a 45-min resting absorption period, the participants performed a selection of cognitive tasks that activate the frontal cortex for an additional 36 min. Cerebral blood flow and hemodynamics, as indexed by concentration changes in oxygenated and deoxygenated hemoglobin, were assessed in the frontal cortex throughout the posttreatment period with the use of near-infrared spectroscopy. The presence of resveratrol and its conjugates in plasma was confirmed by HPLC after the same doses in a separate cohort (n = 9).
RESULTS: Resveratrol administration resulted in dose-dependent increases in cerebral blood flow during task performance, as indexed by total concentrations of hemoglobin. There was also an increase in deoxyhemoglobin after both doses of resveratrol, which suggested enhanced oxygen extraction, that became apparent toward the end of the 45-min absorption phase and was sustained throughout task performance. Cognitive function was not affected. Resveratrol metabolites were present in plasma throughout the cognitive task period. CONCLUSION: These results showed that single doses of orally administered resveratrol can modulate cerebral blood flow variables.

Antihypertensive, vasodilator and antioxidant effects of a vinifera grape skin extract.

Cumulative evidence suggests that moderate wine consumption exerts a cardioprotective effect. We investigated the occurrence of an antihypertensive effect of an alcohol-free hydroalcoholic grape skin extract (GSE) obtained from skins of a vinifera grape (Vitis labrusca) in experimental rodent hypertension models. The vasodilator effect of GSE (polyphenols concentration 55.5 mg g(−1)) was also assessed in the isolated mesenteric vascular bed of Wistar rats and the antioxidant effect was studied on lipid peroxidation of hepatic microsomes. Oral administration of GSE significantly reduced systolic, mean and diastolic arterial pressure in Wistar rats with desoxycorticosterone acetate-salt and NG-nitro-L-arginine methyl ester (L-NAME) induced experimental hypertension. In the rat isolated mesenteric vascular bed pre-contracted with norepinephrine, bolus injections of GSE induced endothelium-dependent vasodilatation that was substantially inhibited by L-NAME, but not by indometacin, tetraethylammonium or glibenclamide. Lipid peroxidation of hepatic microsomes estimated as malondialdehyde production was concentration-dependently inhibited by GSE. In conclusion, the antihypertensive effect of GSE might be owing to a combination of vasodilator and antioxidant actions of GSE. These findings also suggest that the beneficial effect of moderate red wine consumption could be owing to an antihypertensive action induced by compounds occurring in the skin of vinifera grapes.

Protective action of a hydroalcoholic extract of a vinifera grape skin on experimental preeclampsia in rats.

OBJECTIVE: This study was designed to determine the protective effects of a vinifera grape skins extract (GSE, 200 mg/kg/day) on the deleterious effect observed in experimental preeclampsia, a condition where reduced nitric oxide production and increase in oxidative stress are present. METHODS: A condition similar to preeclampsia was induced by chronic inhibition of nitric oxide synthesis by L-NAME (60 mg/kg/day, orally) in pregnant rats. Blood pressure (systolic, mean and diastolic) was measured with the tail cuff method on day 20 of pregnant control rats; pregnant rats treated with L-NAME, L-NAME plus GSE or GSE from day 13 to day 20 of pregnancy. Glucose was infused in anesthetized pregnant rats at day 20 and blood glucose and insulin were estimated at time zero, 15, 30, 45 and 60 minutes after beginning of glucose infusion. The number of fetus alive was also estimated at day 20 of pregnancy. In parallel, blood pressure was measured in non-pregnant and in non-pregnant rats treated with L-NAME during 7 days. RESULTS: Increase in arterial pressure, reduction of alive fetus at the end of pregnancy and increase in insulin resistance was observed in pregnant L-NAME rats but not in pregnant L-NAME plus GSE rats or in pregnant GSE rats. Increase in arterial pressure was also observed in non-pregnant L-NAME rats. CONCLUSION: The present study demonstrated a protective effect of GSE in experimental preeclampsia since the deleterious effect induced by L-NAME that is, increased in stillbirth, hypertension and insulin resistance were significantly reduced by oral treatment with the extract. Probably an endothelium-dependent vasodilator effect and an antioxidant action play an important role on the effects of GSE in experimental preeclampsia.
Grape skin extract protects against programmed changes in the adult rat offspring caused by maternal high-fat diet during lactation.

Maternal overnutrition during suckling period is associated with increased risk of metabolic disorders in the offspring. We aimed to assess the effect of Vitis vinifera L. grape skin extract (ACH09) on cardiovascular and metabolic disorders in adult male offspring of rats fed a high-fat (HF) diet during lactation. Four groups of female rats were fed: control diet (7% fat), ACH09 (7% fat plus 200 mg kg(−1) d(−1) ACH09 orally), HF (24% fat), and HF+ACH09 (24% fat plus 200 mg kg(−1) d(−1) ACH09 orally) during lactation. After weaning, all male offspring were fed a control diet and sacrificed at 90 or 180 days old. Systolic blood pressure was increased in adult offspring of HF-fed dams and ACH09 prevented the hypertension. Increased adiposity, plasma triglyceride, glucose levels and insulin resistance were observed in offspring from both ages, and those changes were reversed by ACH09. Expression of insulin cascade proteins IRS-1, AKT and GLUT4 in the soleus muscle was reduced in the HF group of both ages and increased by ACH09. The plasma oxidative damage assessed by malondialdehyde levels was increased, and nitrite levels decreased in the HF group of both ages, which were reversed by ACH09. In addition, ACH09 restored the decreased plasma and mesenteric arteries antioxidant activities of superoxide dismutase, catalase and glutathione peroxidase in the HF group. In conclusion, the treatment of HF-fed dams during lactation with ACH09 provides protection from later-life hypertension, body weight gain, insulin resistance and oxidative stress. The protective effect ACH09 may involve NO synthesis, antioxidant action and activation of insulin-signaling pathways.

Effects of trans-resveratrol on hypertension-induced cardiac hypertrophy using the partially nephrectomized rat model.

Trans-Resveratrol (resveratrol) has been shown to have beneficial effects on the cardiovascular system in a number of studies. It is, however, unclear whether this naturally occurring compound can protect against cardiac hypertrophy. The aim of the present study was to investigate the effects of resveratrol on cardiac hypertrophy in vivo and the potential underlying mechanisms involving endothelin (ET), angiotensin (Ang) II and nitric oxide (NO) in partially nephrectomized rats. Animal models bearing cardiac hypertrophy were replicated in male Sprague-Dawley rats following partial nephrectomy (PNX). Resveratrol (10 or 50 mg/kg) was administered to rats by gavage for 4 weeks. Simultaneous PNX and sham operation controls were simultaneously established in the present study. The systolic blood pressure (SBP) of rats was measured at baseline and, along with heart weight, after 4 weeks treatment. Serum ET-1, AngII and NO concentrations were determined. In the present study, it was shown that, compared with rats in the sham-operated group, rats in the PNX group had significantly higher SBP (154.1 +/- 22.7 mmHg), heart weight (1.69 +/- 0.24 g) and serum ET-1 (125.70 +/- 26.27 pg/mL) and AngII serum concentrations (743.63 +/- 86.50 pg/mL), whereas serum NO concentrations were lower (21.1 +/- 6.9 micromol/L; all P < 0.05). These values in the sham control group were 114 +/- 10 mmHg, 1.28 +/- 0.13 g, 52.44 +/- 21.85 pg/mL, 528.7 +/- 158.5 pg/mL and 53.21 +/- 23.87 micromol/L, respectively. After 4 weeks treatment with 50 mg/kg resveratrol, SBP, heart weight and ET-1 and AngII concentrations had decreased to 135.4 +/- 15.8 mmHg, 1.39 +/- 0.15 g, 97.11 +/- 26.74 pg/mL and 629.64 +/- 116.18 pg/mL, respectively. However, the serum NO concentration had increased to 40.1 +/- 14.6 micromol/L. These values were significantly different from those obtained for the PNX group. In conclusion, trans-resveratrol appears to be able to protect against the increase in SBP and subsequent cardiac hypertrophy in vivo and the mechanisms responsible may involve, at least in part, modulation of NO, AngII and ET-1 production.
SIRT1 protects against microglia-dependent amyloid-beta toxicity through inhibiting NF-kappaB signaling.

Accumulating evidence suggests that neurodegeneration induced by pathogenic proteins depends on contributions from surrounding glia. Here we demonstrate that NF-kappaB signaling in microglia is critically involved in neuronal death induced by amyloid-beta (Abeta) peptides, which are widely presumed to cause Alzheimer disease. Constitutive inhibition of NF-kappaB signaling in microglia by expression of the nondegradable I kappaBalpha superrepressor blocked neurotoxicity, indicating a pivotal role for microglial NF-kappaB signaling in mediating Abeta toxicity. Stimulation of microglia with Abeta increased acetylation of RelA/p65 at lysine 310, which regulates the NF-kappaB pathway. Overexpression of SIRT1 deacetylase and the addition of the SIRT1 agonist resveratrol markedly reduced NF-kappaB signaling stimulated by Abeta and had strong neuroprotective effects. Our results support a glial loop hypothesis by demonstrating a critical role for microglial NF-kappaB signaling in Abeta-dependent neurodegeneration. They also implicate SIRT1 in this pathway and highlight the therapeutic potential of resveratrol and other sirtuin-activating compounds in Alzheimer disease.

REFERÊNCIAS


