

# The Role of Sambucus nigra Extracts in Animal Models of High Blood Pressure

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**Abstract** - Natural polyphenols are well-known to have the chemical and physical qualities that help protect vital biomolecules including lipids, proteins, and nucleic acids against oxidation. Specific enzymatic measurements and non-specific indicators were used to assess the level of oxidative stress in experimentally produced arterial hypertension by the administration of L-NAME. Results demonstrated the antioxidant and protective effect of Sambucus nigra extract on biochemical markers and histological changes in experimental arterial hypertension. Glutathione-peroxidase and superoxide-dismutase activities are markedly reduced in the hypertension group compared to the polyphenol-protected group. The polyphenolic extract of Sambucus nigra may be useful as a nutritional supplement in chronic cardiovascular and metabolic illnesses if its effects on the functionality of endothelial cells, such as membrane sensitivity and intracellular signalling, are understood.

**Keywords** - Sambucus nigra, arterial hypertension, oxidative stress.

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## INTRODUCTION

Among the many phytochemicals found in foods including vegetables, fruits, olive oil, and wine, polyphenols (flavonoids, lignans, stilbenes, etc.) are the most varied and have been shown to play protective roles against disease (Liu 2003; George et al. 2009).

Flavonoids are a key component of the polyphenol superfamily. As soon as they enter the human body, bioflavonoids trigger a favourable biochemical response (Mennen et al. 2004). Because of its ability to reduce capillary fragility and permeability, bioflavonoids are often prescribed as a preventative measure and treatment for a variety of deficiencies (Yao et al. 2004).

Regular consumption of polyphenol-rich foods and beverages is associated with a reduced risk of a variety of pathological conditions, including arterial hypertension (AHT), coronary heart disease, stroke, diabetes mellitus, and cancer, according to several epidemiological studies (Dauchet et al. 2005; Bayard et al. 2007). Proteins and many vitamins (such as vitamins C, folic acid, and pantothenic acid) are among the co-active substances found in fresh berries of the

European elder, Sambucus nigra L. (Caprifoliaceae) (Elderberry) (Sidor & Gramza-Michaowska, 2015). Flavonoids (kaempferol, astragaloside, quercetin, rutin, isoquercetin, hyperoside) (up to 3.0%), triterpenes (about 1%), sterols (about 1%), phenolic acids (about 3%) and essential oil (up to 0.15%) are just some of the secondary metabolites found in this fruit (Ghosh & Scheepens 2009; Cunha et al. 2016).

Both blood pressure and fluid homeostasis are controlled by the renin-angiotensin-aldosterone system (RAAS). Renin inhibitors (Aliskiren) may be a viable option to angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) for the treatment of AHT, with the added benefit of providing multi-organ protection (heart, kidney, brain) (Gradman et al. 2005). When used with an ACEI or ARB, Aliskiren can be helpful since it decreases plasma renin activity, which increases when ACEIs and ARBs are used alone (Allikmets 2007).

The study aimed to highlight the effects of the combination of the renin inhibitor and the S. nigra extract on biochemical markers as well as heart rate, systolic blood pressure, and diastolic blood pressure.

**MATERIAL AND METHODS**

It was decided to wash and shade-dry some elderberries (*Sambucus nigra* L., Caprifoliaceae). We used a magnetic stirrer to extract 50 grammes of dried, powdered fruit with two 250-milliliter volumes of acidulated methanol (0.5% HCl). Singleton and Rossi's approach was used to calculate the total phenolic content of elder fruit extract. Total phenolic content was calculated as the number of gallic acid equivalents (GAE) per 100 grammes of extract. All solution absorbencies were measured with a V-550 Able Jasco UV-VIS spectrophotometer. The mean of the standard deviations of three measurements is presented.

Wistar white rats weighing an average of 250-280 g each were used in the study, and they were randomly assigned to one of four groups of 12: - Group M - the control group; - Group HTA - the animals given L-NAME 40 mg/kg body/day, i.p., every 2 days, for 8 weeks; - Group P - the animals given polyphenols in the form of solution, from the extract obtained from the *Sambucus nigra* fruit

The Minami method (Minami and Yoshokawa, 1979), which employs the pyrogallol as an O<sub>2</sub> anion generator, was utilised to quantify superoxide dismutase (SOD). The Gross and Beutler method (Beutler et al., 1990) was used to quantify glutathione peroxidase (H<sub>2</sub>O<sub>2</sub>: GSH oxidoreductase) (GSH-Px), with results given as M oxidised GSH per minute per gramme of haemoglobin or per milligramme of protein. Ohkawa's method with tiobarbituric acid (TBARS) was used to calculate the malondialdehyde (MDA) concentration, which is an index of lipid peroxidation (Ohkawa et al., 1979). On an EOS BRAVO automatic analyzer, uric acid concentrations were calculated using a colorimetric approach based on Siedel's original work.

Analysis of statistical information. The information is presented in the form of mean SEM (SEM). The paired or unpaired t-test was used for statistical analysis. For a certain significance level, the following differences were taken into account in the interpretation of the statistical data: p>0.05, not statistically significant; p<0.05, significant; p<0.01, strong statistical significance; p<0.001, very strong statistical significance.

**DISCUSSION AND RESULTS**

Serum glutathione peroxidase (GSH-Px) activity is considerably lower in the rats in group HTA compared to rats in group M after oxidative stress is heightened (Table I). Serum GSH-Px activity was found to be

higher in the HTA+P group rats than in the HTA group rats, suggesting that the polyphenolic protection provided by the HTA+P group rats was responsible for this finding. Group HTA animals have considerably lower values for SOD serum activity compared to both the M and HTA+P groups of rats. The serum SOD activity of the HTA+P rats is higher than that of the unprotected HTA rats (Table II).

Malondialdehyde (MDA) levels show statistically significant differences across groups (p<0.01) for group P compared with group M, for group HTA +P compared with group HTA, and for group HTA compared with group M.

Uric acid levels are statistically elevated in both the HTA and HTA+P groups compared to the control group (Table III).

The antioxidant and pro-oxidant effects of phenolic antioxidants like *Sambucus nigra* extract are determined by the ratio of their reduced to their oxidised (phenoxyl radicals or quinone/quinone methide intermediates) forms (Ursini et al., 1999). The quantity of polyphenols has been linked to both their antioxidant and pro-oxidant properties, with low quantities provoking antioxidant defence metabolism and high concentrations leading to reactive oxygen species (ROS) generation (Masella et al., 2005).

**Table 1: Serum GSH –Px activity in white Wistar rats**

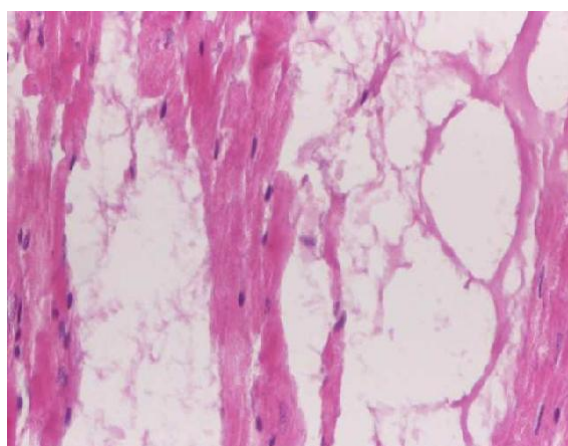
	M	P	HTA+P	HTA
GSH-Px (µmoliGSSG/min/mL)				
Mean value ± standard deviation	2.64±0.22	2.52±0.66	1.63±0.16	1.29±0.22
Variation coefficient, %	7.58	32.0	6.69	8.46
Statistical significance				
	P / M	HTA +P / M	HTA / M	HTA +P / HTA
	p>0.05	p<0.001	p<0.001	p=0.01

**Table 2: Serum SOD activity in white Wistar rats**

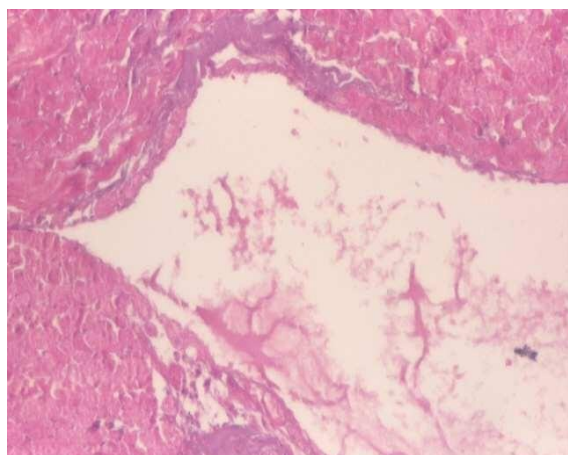
	M	P	HTA+P	HTA
SOD (U/mL)				
Mean value ± standard deviation	3.59±0.37	5.09±0.85	3.28±0.30	3.01±0.26
Variation coefficient, %	10.3	16.69	8.09	9.48
Statistical significance				
	P / M	HTA +P / M	HTA / M	HTA +P / HTA
	P=0.001	p>0.05	p<0.01	p<0.01

The observed results demonstrate a substantial decrease in the MDA serum concentration, leading to a large decrease in the serum lipid peroxide in the HTA+P rats as compared to the P group.

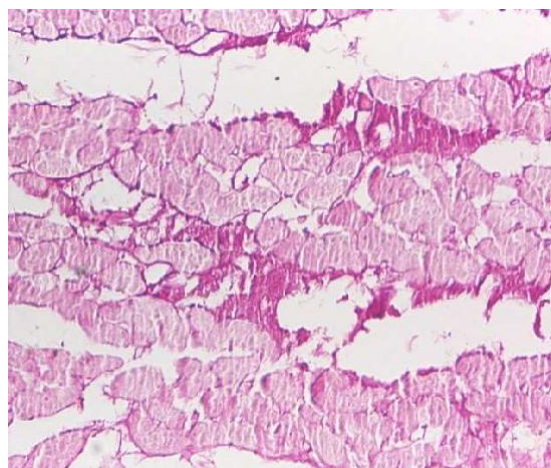
Uric acid is produced when the enzymes xanthine oxidase and xanthine dehydrogenase oxidise the amino acids hypoxanthine and xanthine, respectively. However, we also decided to look into the uric acid level because this factor affects the total antioxidant capacity. The signal was found to be indicative of oxidative stress in general. However, a high uric acid level may also supply the body with useful antioxidant protection.



**Figure 1: Longitudinal section through the myocardial fiber, HTA group (HE, X20)**



**Figure 2: Cross Section through the myocardial fiber, HTA group (HE, X10)**



**Figure 3: Cross section through the myocardial fiber, HTA group (PAS, X20)**

*Sambucus nigra* extract has the potential to be useful in the treatment of disease caused by oxidative stress due to its antioxidant properties, namely its capacity to reduce LDL-oxidation and scavenge free radicals. To build functional foods or new foods with health related claims, it will be useful to selectively activate those metabolic pathways leading to the synthesis of more stable or bioactive end products of polyphenols.

### CONCLUSIONS

Hypertensive rats given polyphenolic protection showed significantly reduced cardiac changes. *Sambucus nigra* polyphenolic extract may be useful as a nutritional supplement in chronic cardiovascular and metabolic illnesses due to its cardio-protective properties.

Reduced endothelial dysfunction and enhanced myocardial perfusion following treatment with *Sambucus nigra* extract antioxidants in early hypertension.

Additional research is needed to determine whether or not variations in the *Sambucus nigra* extract metabolism products are associated with the degree to which dietary polyphenols reduce the risk of cardiovascular disease.

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