

# Antihypertensive role of antioxidants

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## Introduction

Hypertension is the most common risk factor for cardiovascular disease, which is the leading cause of mortality and morbidity worldwide. It is predicted that by 2025, as many as 29% of the population will suffer from hypertension (Kearney et al., 2005). Risk factors that lead to hypertension are gender, age, smoking, total cholesterol and HDL, diabetes, obesity, family history, early onset of menopause, and psychological and socio-economic factors, but in recent times, oxidative stress is often mentioned as one of the risk factors involved in raising blood pressure (Montezano et al., 2012). In any biological system, the formation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) is one of the most important balances (Arcambal et al., 2019). ROS is known for rapidly inactivating endothelial nitric oxide (NO), the most important endogenous vasodilator, thereby promoting vasoconstriction and raising blood pressure. Some preclinical and clinical studies have concluded that antioxidant therapy is important in the treatment of hypertension, i.e the use of antioxidant compounds such as alpha-tocopherol (vitamin E), ascorbic acid (vitamin C), plants containing polyphenols, and some antihypertensive drugs such as the new Beta-blockers (carvedilol, metoprolol) which have antioxidant pleiotropic effects. (Rajeh et al., 2017). The aim of this paper is to conclude whether antioxidants as supplements can significantly reduce blood pressure.

## Materials and methods

For the preparation of this scientific work were used data obtained by searching the relevant medical scientific literature that covers the given topic.

A systematic search of the literature was performed through the free PubMed research engine which has access primarily to the MEDLINE databases with references and abstracts from the biomedical sciences.

## Results and discussion

### Vitamin E

Vitamin E is a powerful cleanser of peroxy radicals, an antioxidant that breaks the chain of damage to biological membranes by free radicals. The mechanism of action is: (1) up-regulation of eNOS, (2) down-regulation of NADPH oxidase, (3) regulation of mitochondrial synthesis of ROS, (4) (Baradaran et al., 2014) purification of ROS. However, when it comes to hypertension, vitamin E may have an antihypertensive effect but that effect is very small and only in limited patients who have vitamin E deficiency. On the other hand, high doses of vitamin E may increase the risk of high blood pressure, especially in patients with type 2 diabetes mellitus. In a study by Ward et al. (2007) prescribed appropriate antihypertensive therapy. Patients were given 400 mg (600 IU) of mixed tocopherols of which 60% gamma-tocopherol, 25% delta tocopherol and 15% alpha tocopherol. Patients showed an increase in blood pressure of 6.8 mmHg systolic and 3.6 mmHg diastolic. (Ward et al., 2007)

### N-acetylcysteine (NAC)

NAC is an antioxidant that is a donor of the sulfhydryl group (SH) and plays an important role in controlling oxidative stress (González, 2014). The main mechanisms of action are (1) protection against oxidation of Tetrahydrobiopterin (BH4) and (2) clearance of free ROS. In the study by Arsalat K. et al, patients with resistant hypertension were studied where one group of subjects (A)

received NAC in combination with ACEi, while the other group of subjects (B) received only ACEi. The results showed that in group A systolic blood pressure decreased by 18mmHg and diastolic by 13mmHg, while in group B systolic blood pressure decreased by 7mmHg and diastolic by 3.1mmHg (Khaledifar et al., 2015). However, there are no human studies showing the efficacy of NAC used alone without combination with antihypertensive drugs.

### Melatonin

A growing number of studies have shown that melatonin is a powerful direct scavenger of free radicals. Unlike most other known radical scavengers, melatonin is a multifunctional and universal antioxidant. The high lipophilicity and hydrophilicity of melatonin enable its rapid transfer to other organs and fluids, and melatonin can easily pass through cell membranes. Some effects of melatonin are mediated by specific membrane receptors, but many seem to rely on its potential as a direct scavenger of free radicals, a process that does not require a receptor. The safety of exogenous melatonin for humans has been demonstrated in many studies. In the study by Grossman E. all, the power of methons was examined to reduce blood pressure levels with nocturnal hypertension, which is associated with a higher risk of death and mortality. Weekly results showed that administrator melatones at a dose of 2 mg at bedtime by 4 reduced diastolic systolic pressure from  $136 \pm 9$  mmHg to  $130 \pm 10$  mmHg, while slightly reducing diastolic pressure from  $72 \pm 11$  mmHg to  $69 \pm 9$  mmHg (Grossman et al., 2006). In a study by Frank et al., male patients with uncomplicated, untreated essential hypertension were studied. Melatonin 3 doses were administered 1 hour before bedtime in a dose of 2.5 mg. The results showed that nocturnal systolic blood pressure decreased by 6 mmHg while nocturnal diastolic blood pressure decreased by 4 mmHg. This can be considered a significant reduction in blood pressure as a reduction in systolic blood pressure of 2 to 3 mmHg is of clinical importance (Scheer et al., 2004). According to the current system review, the extent to which the antioxidant effects of melatonin contribute to its anti-hypertensive benefits requires further investigation.

### Conclusion

From the reviewed literature we could conclude that oxidative stress is one of the risk factors for hypertension, and the safest approach to prevent it is a change in lifestyle and the acquisition of healthy habits including foods rich in antioxidants.

Of the antioxidants reviewed in this review, the best results with a significant reduction in blood pressure showed melatonin which can reduce nocturnal systolic blood pressure to 6 mmHg.

The use of antihypertensive drugs in combination with antioxidants seems to be the most effective treatment in the management of hypertension because in combination they will reduce blood pressure by influencing the molecular mechanisms involved in the regulation of both vascular function and oxidative status.

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