



Review Article

Potential of Flavonoid in Mahkota Dewa to Reduce Systolic and Diastolic Blood Pressure in Patient with HypertensionS. O. Abed^{1,*}

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ABSTRACT

Treating hypertension by using antihypertensive drugs and diuretics has many harmful side effects. Mahkota Dewa fruit can be used as alternative treatment with minimal side effects. As generally known that blood pressure increases slowly with age, which makes hypertension a critical disease to the elderly. This disease could be treated using flavonoid compounds that is contained in Mahkota Dewa fruit because it is effective in reducing blood pressure.

Introduction

Hypertension is generally known as one of the degenerative disease, as it often occurs on elderly. It is an increase in systolic blood pressure of more than 140 mmHg and a diastolic blood pressure of more than 90 mmHg on two measurements with the interval of five minutes in a adequate state. Based on JNC (Join National Commit) 7, hypertension is divided into four types: normal, pre-hypertensive, hypertension 1 and hypertension 2. ^[1,2]

According to the data taken from World Health Organization (WHO), around 972 million people or 26.4% of the population worldwide are afflicted with hypertension. This percentage is predicted to increase until around 29.2% in 2025. Approximately 333 million of the 932 million people are in developed countries and the remaining 639 million are in developing countries including Indonesia.

Common causes of hypertension include atherosclerosis (thickening of the arterial wall which decreases blood vessel elasticity), genetic factors, obesity and stress. ^[1,2]

Hypertension is a dangerous disease if not handled and prevented properly. Complications of hypertension are a cause of increased mortality in the world. It is estimated that hypertension causes 45% of deaths due to heart disease and 51% of deaths due to stroke. Deaths caused by cardiovascular disease, especially coronary heart disease and stroke are estimated to continue to reach 23.3 million deaths in 2030. ^[2,3,4]

Treatment of hypertension is growing in this millennium era and in general the treatment of hypertension is divided into two, namely non-

pharmacology and pharmacology. Non-pharmacological treatment consists of controlling hypertension with a healthy lifestyle, while pharmacologically treated with antihypertensive drugs and diuretic drugs.^[1,3]

The use of antihypertensive drugs has many side effects that can be detrimental to the body. Such an increase in urinary excretion by thiazide diuretics results in hypokalemia, hyponatremia and hypomagnesiemia. Blockade of receptor-2 in the bronchi by beta blockers can cause bronchospasm.^[1,2] Hyperkalemia due to ACE inhibitors due to decreased aldosterone production. Other side effects caused by ACE inhibitors such as bradycardia, myocardial contractile disorders and cold hands due to beta-2 receptor blockade in peripheral vascular smooth muscle. Therefore, alternative treatments are needed to reduce blood pressure with minimal side effects.^[2,3]

Research continues to grow and leads to the use of herbal medicines in reducing blood pressure, one of which is the potential of the god's crown in lowering blood pressure. Mahkota dewa (*Phaleria macrocarpa*) is a plant that tastes from Papua which can be used as an alternative treatment for lowering blood pressure. The flavonoid content in the god's crown has benefits in reducing blood pressure.^[1,3,4]

Discussion

Hypertension is a condition where the systolic blood pressure is more than 140 mmHg and the diastolic blood pressure is more than 90 mmHg on two measurements with an interval of five minutes in a state of adequate rest / calm. Hypertension is also often referred to as the silent killer because it is a deadly disease. Hypertension is also a degenerative disease; generally blood pressure slowly increases with age.^[2,3,4]

According to WHO data, around 972 million people around 26.4% suffer from hypertension and are predicted to increase to 29.2% in 2025. Of the 972 million people with hypertension, 333 million are in developed countries and 639 million are in developing country. Based on Basic Health Research (RISKESDAS) in 2013, the highest disease in the elderly was hypertension with a prevalence of 45.9% at the age of 55-64 years, 57.6% at the age of 65 years and 74% at the age of > 75 years.^[3,4]

Risk factors for hypertension are age, gender, genetic factors, smoking habits, excessive salt consumption, consumption of saturated fats, consumption habits of alcoholic beverages, obesity, lack of physical activity, stress and use of estrogen. Some studies show that a person who is overweight or obese is more than 20% and hypercholesterol has a greater risk of hypertension.^{2,3,5}

During this time the community paid less attention to the dangers of hypertension. Even though the prevalence of hypertension is quite high, hypertension can cause quite serious complications. Hypertension can cause complications such as heart swelling, coronary heart disease and brain blood vessel rupture which will cause paralysis or death.^[3,6,7]

How to prevent hypertension from causing complications requires proper and efficient handling. There are two ways to deal with hypertension, namely non-pharmacology and pharmacology. Non-pharmacological therapy can be done by modifying lifestyles such as regular exercise, quitting smoking, not consuming alcohol and reducing salt intake.^[6,7,8]

Pharmacological therapy uses antihypertensive drugs and diuretics, such as thiazide diuretics (bendoflumetiazid), beta-blockers (propranolol,

atenolol), Angiotensin Converting Enzymes (ACE) inhibitors (eg captopril, enalapril), angiotensin II antagonists (eg candesartan, losartan), calcium channel blockers (eg amlodipine, nifedipine) and alpha blocker (for example doksasozin). The use of antihypertensive drugs and diuretics has long been used in the medical world. But the use of this drug has side effects that can be detrimental to the body. [2,3,4,5,6]

The use of thiazide diuretics increases urinary excretion and results in hypokalemia, hyponatremia and hypomagnesiemia. Interference with uric acid excretion can lead to hyperuricemia, so caution must be exercised on thiazide diuretics in gout sufferers. Blockade of beta-2 receptors by beta blockers in the bronchi can result in bronchospasm. Other side effects caused by beta blockers are bradycardia, myocardial contractile disorders, elevated triglyceride levels and cold foot hands due to beta-2 receptor blockade in vascular smooth muscle [4,5,6]. The use of ACE inhibitors can also cause hyperkalemia because it reduces aldosterone production, so potassium supplementation and the use of potassium-sparing diuretics should be avoided in patients receiving ACE inhibitor therapy. Redness of the face, dizziness, swelling of the ankles are often found due to the effects of vasodilation of Channel Calcium Blockers. [2,6,7,8,9,10]

The many side effects caused by antihypertensive drugs and diuretics make alternative treatments an option in reducing blood pressure in hypertensive patients. Research leads to the treatment of herbs. One of them is the use of the crown of god (*Phaleria macrocarpa*). [5,6,7,11]

Mahkota dewa is an herbal plant originating from Papua. Research on the efficacy of the crown of gods has been started since the beginning of the millennium in 2000. The compounds contained

therein such as antihistamines, alkaloids, flavonoids, phenols, saponins, lignans, essential oils and sterols in fruit flesh work as hepatoprotectors, help treat leukemia, control sugar blood and lower blood pressure with minimal side effects. [7,8,10,11,12]

Flavonoid compounds contained in the crown of god have an effect in lowering blood pressure. Flavonoids are compounds consisting of 15 carbon atoms, where two benzene rings (C6) are bound to a propane chain (C3) to form a C6-C3-C6 arrangement. Flavonoids are a phenolic compound that is found in nature. These compounds are red, purple and blue as well as yellow substances found in plants. [5,6,8,12,13]

In plants of high size, flavonoids are found both in the vegetative part and inside the flower. These compounds play a role in determining the color, taste, smell, and nutritional quality of food. Plants generally only produce certain flavonoids. Flavonoids play a role in the survival of plants from pests, diseases, competition, interactions with microbes, seed dormancy, protection against UV rays, signaling molecules in various transduction pathways and signal molecules in pollination and male fertility. [8,9,10,14,15]

The mechanism of flavonoids in reducing blood pressure is associated with ACE and acts as a diuretic. Flavonoids have the ability to inhibit ACE. ACE is known to play an important role in the process of hypertension, namely forming angiotensin II from angiotensin I. Angiotensin II causes blood vessels to narrow, which can raise blood pressure. In this case, flavonoids act as ACE inhibitors which cause blood vessels to dilate so much blood flow to the heart and decreases blood pressure. [1,2,6,7,16]

The content of flavonoids, polyphenols, can also increase the activity of Nitric Oxide Synthase (NOS) in vascular endothelial cells. Flavonoids can also synthesize Nitrogen monoxide (NO) in endothelial cells. This active substance is able to diffuse directly and synthesize NO in the endothelium and smooth muscle which in turn stimulates guanylate cyclase to form Cyclic Guanosine Monophosphate cGMP resulting in vasodilation ^[9,12,13]. Flavonoids can also activate the Endothelium Derived Relaxing Factor (EDRF), causing vasodilation of blood vessels and can reduce blood pressure. ^[5,6,13,15,16]

Flavonoids also work as a diuretic, flavonoids work to increase urine production and electrolyte output, which functions like potassium, which absorbs liquid electrolyte ions such as sodium in the intracellular to extracellular entry into the kidney tubules. Flavonoids also work by increasing the Glomerular Filtration Rate (GFR) so as to cause the kidneys to be able to release waste products quickly. In addition, flavonoids also have a protective effect on endothelium and inhibit platelet aggregation by reducing levels of prostacyclin (a substance produced by vascular endothelial cells) and leukotirene levels, thereby reducing the risk of coronary heart disease. ^[4,5,7,8,15]

Conclusion

Hypertension is often called the silent killer because it is a deadly disease. Hypertension is also a degenerative disease, generally blood pressure increases slowly with age. Pharmacological therapy using antihypertensive drugs and diuretics has side effects that are very detrimental to the body. Alternative medicine using the crown of god (*Phaleria macrocarpa*) has the effect of lowering blood pressure with minimal side effects. Flavonoids in the crown of god have a mechanism to reduce blood pressure associated with ACE and act as a diuretic. Thus it is expected that the

mortality rate due to hypertension can decrease in the future by using the crown of gods with minimal side effects.

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