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Purple Sweet Potato Aqueous Extract Lowers Blood Pressure and Prevents Oxidative Stress in Hypertensive Elderly Patients at Nyuhkuning Village, Mas, Ubud, Bali

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Abstract
Purple sweet potato tubers found in Bali are rich in anthocyanins and has been studied as an antioxidant in experimental animals. Aqueous extract of purple sweet potato tubers has been shown to lower blood pressure through increased expression of endothelial nitric oxide synthase (eNOS) in hypertensive rats. Research on the antihypertensive and antioxidative effects of aqueous extract of purple sweet potato tubers in hypertensive patients has not been done. The purpose of this study was to prove that the aqueous extract of purple sweet potato tubers could lower blood pressure and prevent oxidative stress in hypertensive patients especially in the elderly ones. This study was a limited clinical trial with one group pre- and post-test design, involving the elderly population in Nyuhkuning Village, Mas, Ubud, Bali as subjects of study. Seventeen subjects were included in this study with baseline characteristics such as 60-69 years of age, blood pressure above 140/95 mmHg, and does not suffer from certain diseases. After being given aqueous extract of purple sweet potato for one month, they showed a decrease in systolic and diastolic blood pressure significantly ($p < 0.05$), a decrease in MDA level accompanied by an increase in blood superoxide dismutase (SOD) level significantly ($p < 0.05$). From these results, it can be concluded that the aqueous extract of purple sweet potato tuber can lower blood pressure and prevent oxidative stress in hypertensive elderly patient.
Keywords: aqueous extract of purple sweet potato tuber, elderly patients, hypertension, oxidative stress

1. Introduction

Cardiovascular disease is the main cause of disability that strikes the elderly in Indonesia. Hypertension is one of the important cardiovascular diseases because it requires life-long treatment, due to its easiness to cause various complications in the elderly. Hypertension is usually accompanied by oxidative stress that will aggravate endothelial dysfunction and facilitate the occurrence of complications of hypertension (Touyz, 2004; Edwards *et al*., 2007; Cavanagh *et al*., 2010). Giving antioxidants could be expected to prevent endothelial dysfunction in patients with hypertension (Cavanagh *et al*., 2010).

Animal studies proved that flavonoids from various plants could alleviate oxidative stress. Epidemiological data also proved that eating fruits and vegetables containing flavonoids regularly can reduce cardiovascular disease, through their antioxidative effects (Knekt, 2002). Flavonoids from various plants can improve the function of vascular endothelium (Engler , 2004), through increased bioavailability of nitric oxide (NO), which can lower blood pressure (Erdman, 2007; Han, 2007; Cavanagh *et al*., 2010). Anthocyanin pigments is one of many types of flavonoid, and have been shown to lower blood pressure (Middleton, 2000; Lila, 2004; Shindo, 2007).

Purple sweet potato tubers in Bali contain high amount of anthocyanins (Suprapta, 2004), and has been shown to overcome oxidative stress *in vitro* (Padda, 2006; Lachman *et al*., 2009; Jiao *et al*., 2012) and *in vivo* (Kano *et al*., 2005; Jawi *et al*., 2008; Garcia-Alonso *et al*., 2009). Aqueous extract of purple sweet potato tuber could lower blood pressure in hypertensive rats (Jawi *et al*., 2012). The study examining the effects of antioxidants from purple sweet potato in humans, especially in hypertensive patients, has not been done. This study was a limited clinical trial to prove the blood pressure-lowering effect of aqueous extract of purple sweet potato in elderly who suffer from mild to moderate hypertension.

2.Materials and Methods

Treatment with extract

This study was a limited clinical trials with one group pre- and post-test design, involving the elderly population of 88 individuals in Nyuhkuning village, Mas, Ubud, Bali, Indonesia. Subjects that meet the inclusion criteria (60-75 years old, moderate hypertension, similar socio-economic class, does not suffer from certain diseases, and are willing to be involved in the study) were 17 individuals. All of them were given aqueous extract of purple sweet potato tuber at the daily dose of 3 x 60 mL for 4 weeks.

These patients were diagnosed, treated, and followed-up in a private outpatient clinic owned by a general physician at Nyuhkuning. Criteria for exclusion were a history of severe renal or liver dysfunction, malignancy,

diabetes, smoking, and the use of antioxidant or multivitamin supplements. This study was approved by the ethics committee of the Medical Research Institute of Medical Faculty, Udayana University, with the approval number of 141/U.N.14.2/litbang/2014. Written informed consent was obtained from each participant, before enrollment in this study. The blood pressure of all patients were evaluated every week during the study.

Biochemical Assays

At the beginning and after one month of the study, blood samples of all of the patients were taken for the examination of lipid peroxidation, that was measured using thiobarbituric acid reactive substances (TBARS) method and calculated as malondialdehyde (MDA) level as a biomarker of oxidative stress. The level of superoxide dismutase (SOD) in the blood was examined using commercially available kit (Cayman, Ann Arbor, MI, USA).

Statistical Analysis

All data have been presented as mean ± SD. Paired t-test was used to assess the effect of therapies used at the beginning of the study and one month after treatment. Differences were considered significant at $p < 0.05$. All statistical analysis were performed using SPSS statistical software version 10.

3.Results

Blood pressure

All of the patients were given aqueous extract of purple sweet potato tuber at a dose of 3 x 60 ml everyday for 4 weeks. The results showed a decrease in systolic (from 165 ± 19.2 mmHg to 140 ± 13.9 mmHg) and diastolic (from 92 ± 10.4 to 80 ± 6.34 mmHg) blood pressure. The decrease was significant as tested using t-test ($p < 0.05$). The comparison of mean systolic and diastolic blood pressure for one month of study is presented in Figure 1.

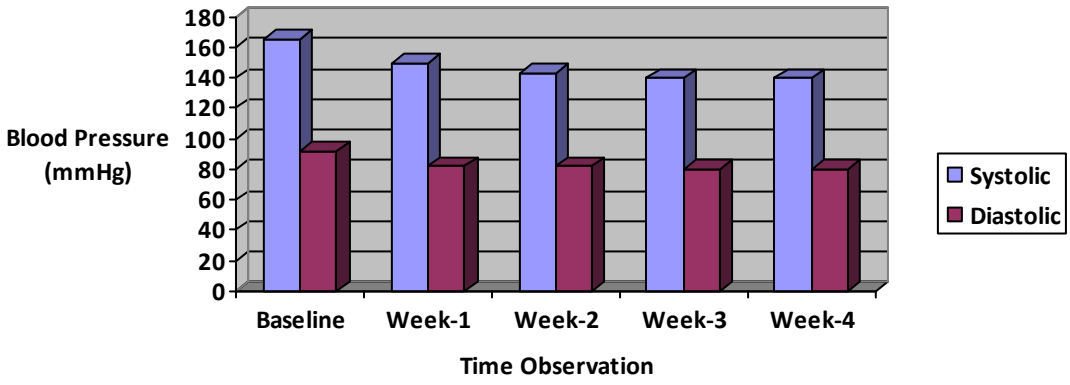

Figure 1
Comparison of means of systolic and diastolic blood pressure for a month of study

Blood levels of SOD and MDA

Results of blood level of MDA and SOD for hypertensive patients conducted prior to and after the administration of aqueous extract of purple sweet potato tuber for 4 weeks are presented in Table 1 and Figure 2. There were significant increase of blood SOD levels and decrease of blood MDA levels after one month of treament with aqueous extract of purple sweet potato tuber at the daily dose of 3 x 60 mL orally.

Table 1 . Level of SOD and MDA in the vlood of hypertensive patients treated with aqueous extract of purple sweet potato

Examine	SOD±SD (U/gHb)	MDA±SD (mmol/l)
Baseline **	435.34 ±59.57[a*]	5.58 ±1.46[a*]
After 4 weeks***	540.72 ± 58.18[b]	4.38 ± 1.39[b]

*Means followed by different letters (superscript letters) in the same column was significantly different ($p<0.05$).

** The result of hypertensive blood tests before being given a aqueous extract of purple sweet potato tuber.

*** After 4 Weeks is the result hypertensive patients blood test after administration of aqueous extract of purple sweet potato tuber 3 x 60 mL, everyday for 4 weeks.

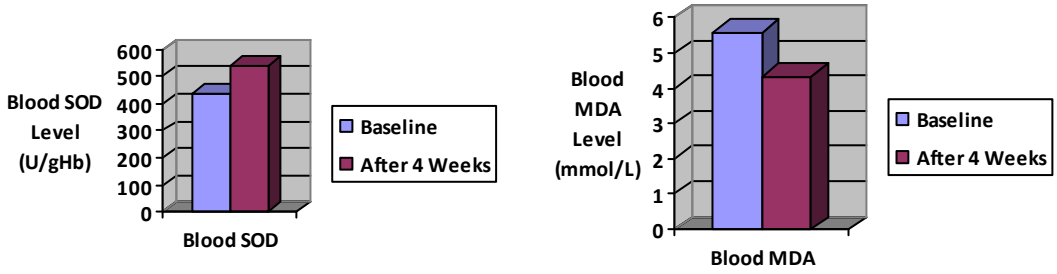

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Figure 2

Comparison of blood SOD (left) and MDA (right) level of hypertensive patients prior to and after treated with purple sweet potato aqueous extract for a month.

4. Discussion

Blood pressure

This study showed significant decrease in systolic and diastolic blood pressure ($p < 0.05$) of hypertensive patients given aqueous extract of purple sweet potato tuber with the daily dose of 3 x 60 mL for one month. The high anthocyanins, a group of antioxidants, content of aqueous extract of purple sweet potato tubers (Suprapta, 2004), can reduce oxidative stress. Oxidative stress will cause a decrease in NO as a powerful vasodilator, subsequently causing vasoconstriction which will cause an increase in blood pressure. Anthocyanins found in plants can also regulate various signaling in blood vessels, thus preventing various cardiovascular disorders, including hypertension (Wallace, 2011).

Increased blood pressure is a pathological condition that would cause an increase in free radical formation in the blood vessels. Research has shown that in hypertensive patients increased formation of superoxide ions and hydrogen peroxide, accompanied by a decrease in the synthesis of nitric oxide (NO) as well as a decrease in antioxidant bioavailability, resulting in impaired function of various cells that will lead to multiple organ complications of hypertension (Touyz, 2004). Sources of free radical in hypertensive patients are endothelial cells, adventitial, and smooth muscle cells of blood vessels, as these cells contain NADPH oxidase, an important enzyme that catalyzes superoxide ions synthesis (Touyz, 2004; Madamanchi, 2004). In the hypertensive state there is an increase in the activity of NADPH oxidase, resulting in increased superoxide ions and a decrease in NO bioavailability which in turn will aggravate hypertension, accompanied by increased oxidative stress (Touyz, 2004).

Antioxidants or antihypertensive drugs that have beneficial antioxidative properties may be expected to prevent complications in patients with hypertension (Edwards *et al.*,, 2007; Cavanagh *et al*., 2010). Aqueous extract of purple sweet potato tuber has been shown to contain relatively high amount of anthocyanins (Suprapta , 2004), and as an antioxidant in experimental animals (Jawi *et al*., 2008; Jawi and Budiasa, 2011) to cope with oxidative stress. The results of this study are consistent with other studies on hypertensive rats in which the administration of aqueous extract of purple sweet potato tuber lowers blood pressure and improves eNOS expression in hypertensive rats induced by NaCl (Jawi *et al*., 2012). This study is also consistent with studies which show that intake of foods rich in flavonoids/anthocyanins for 14 years can prevent the occurrence of hypertension up to 8 % in both men and women (Cassidy, 2012). Other studies have also proved that flavonoids can lower blood pressure as much as 5.88 mmHg and 3.50 mmHg, for systolic and diastolic blood pressure level respectively (Hooper *et al*., 2008). This result is also parallel with another study showing that red wine polyphenolic compounds (RWPCs), a flavonoid, is able to induce relaxation of blood vessels through increased NO, as a result of an increase in eNOS activity by various mechanisms. RWPCs can also increase the release of prostacyclin, and inhibit synthesis and decrease the effect of endothelin-1, resulting in relaxation of blood vessels (Han, 2007). Various types of anthocyanins from plants have been shown to lower blood pressure by various mechanisms. Cyanidin-3-glucoside, a typical anthocyanin pigment, increase the expression of eNOS in arterial endothelial cells *in vitro* (Xu, 2004). Provision of anthocyanin-rich foods such as purple corn, can lower blood pressure and pulse rate compared with controls, therefore anthocyanin can lower blood pressure in experimental animals (Shindo, 2007). Blood pressure-lowering effects due to administration of anthocyanin or foods with a high content of anthocyanin is established through antioxidative properties of anthocyanins, because ROS plays an important role in causing impaired endothelial function. Anthocyanins from chokeberry, bilberry, and

eldeberry had been shown to maintain endothelial function properly after being exposed to ROS *in vitro* (Bell, 2006). Research on the role of NO on blood vessels relaxation resulting in decreased blood pressure due to NO has been widely studied. Oxidative stress can reduce vascular relaxation response due to decreased NO bioavailability. Giving antioxidants is very useful in this regard, especially antioxidants derived from plants such as anthocyanin (Mann , 2007). Thus the use of purple sweet potato tubers in the future is promising for the prevention or treatment of hypertension through its antioxidative properties.

Blood levels of SOD and MDA

The results prove that the aqueous extract of purple sweet potato tuber can lower blood MDA and increase blood SOD level significantly in hypertensive patients ($p < 0.05$). Thus, the aqueous extract of purple sweet potato tuber can prevent oxidative stress in hypertensive patients. Oxidative stress in patients with hypertension is caused by increased activity of the enzyme NAD(P)H oxidase, resulting in increased production of superoxide ions. Increased superoxide ions will decrease NO bioavailability that subsequently aggravate oxidative stress on hypertension (Touyz, 2004).

The content of anthocyanins in aqueous extract of purple sweet potato is quite high, and can be attributed to its effect in reducing oxidative stress, indicated by lower blood MDA level in hypertensive patients. Mechanisms and site of actions of flavonoids are highly variable. Antioxidative effect of quercetin, a flavonoid, has been shown in *in vitro* studies. It prevents oxidative stress through increased Nrf2 transcription factor, thereby increasing the expression of HO-1 protein (Maher and Hanneken, 2005). The role of flavonoid in increasing endogenous antioxidant depends on the type of flavonoid *per se*. Some flavonoids or anthocyanins are able to turn extracellular signal-regulated protein kinase (ERK), c-jun N-terminal kinase (JNK) or p38, which in turn will increase the Nrf2 taken into the nucleus and binds to the antioxidant response element (ARE), resulting in increased antioxidant gene expression, including genes resulting in increased SOD level (Han, 2007).

Particularly in vascular endothelium, high amount of ROS will disrupt the function of NO in regulating the function of blood vessel relaxation (Xu, 2004; Mann, 2007). The provision of flavonoids-containing food, such as aqueous extract of purple sweet potato tuber, may decrease oxidative stress. The flavonoids contained in purple sweet potato tuber are able to retain NO as a potent vasodilator, prevent the increase in blood pressure, and decrease blood MDA level.

5. Conclusion

From the results of the study, it can be concluded that aqueous extract of purple sweet potato tubers can lower blood pressure in elderly hypertensive patient by increasing the SOD level as endogenous antioxidant, thus decreasing MDA level in the blood.

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