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Comparison of Potential Antihypertensive and Antioxidant Between Aqueous Extract of Purple Sweet Potato Tuber and Captopril in Hypertensive Patients

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Abstract
Hypertension is a cardiovascular disease that accompanied by oxidative stress. Treatment of hypertension with conventional drugs such as captopril could be expected to cope oxidative stress, but often cause side effects such as cough. It is necessary to find an alternative medicine instead of captopril, which has antihypertensive and antioxidant activities. Purple sweet potato tubers has been studied as an antioxidant *in vivo*, and has shown to decrease blood pressure in hypertensive rats. The purpose of this study was to compare the aqueous extract of purple sweet potato and captopril in relation with theire effects on blood pressure and oxidative stress in hypertensive patients. This research was limited clinical trials with randomized pre - test and post- test control group design, with a population of hypertensive patients. A total of 30 hypertensive patients were included in this study and they were divided into three groups of 10 patients each. The control group was given captopril only, treatment-1 group was given a purple sweet potato aqueous extract only, and treatment-2 were given a combination of captopril and purple sweet potato extract. This treatment was carried out for four weeks. The results showed that all treatments significantly ($p<0.05$) decreased the blood pressure and blood MDA levels. However a significant ($p<0.05$) increase in SOD was resulted from the group given aqueous extract of purple sweet potato tuber, while in the group given captopril, an increase in SOD was not significant ($p > 0.05$). The conclusion from this study is that the aqueous extract of purple sweet potato obviously decreased the blood pressure and blood MDA levels that comparable to captopril, and a better ability to increase blood SOD levels in hypertensive patients.
Keywords: Purple sweet potato, captopril, antioxidant, hypertensive patients

1. Introduction

Chronic hypertension will cause oxidative stress that can lead to disruption of endothelial function that will aggravate hypertension and cause complications. Antihypertensive drugs like captopril can decrease blood pressure and cope the oxidative stress due to captopril function as antioxidants through inhibition of NAD (P) H oxidase (Bolterman *et al*., 2005; Miller *et al*., 2007). The weakness of captopril is often cause side effects such as cough that causing treatment failure. So that necessary to find affordable alternative drugs that has antihypertensive and antioxidant properties so can replace captopril. In today's society life there is an increasing utilization of herbal medicines as an affordable alternative medicine.

Epidemiological studies proved that eating fruits and vegetables that contain flavonoids regularly can reduce cardiovascular diseases, through antioxidant effects (Knekt, 2002). Flavonoids from various plants can improve vascular endothelial function (Engler, 2004), through an increase the bioavailability of nitric oxide (NO), so it can decrease blood pressure (Erdman, 2007; Han, 2007; Morris, 2007). Anthocyanin pigments is one of flavonoids and has been shown to decrease blood pressure (Middleton, 2000; Lila, 2004; Shindo, 2007). Purple sweet potato tubers contain anthocyanins that are proven to cope 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).

Purple sweet potato aqueous extract that found in Bali was contain high enough of anthocyanins (Suprapta, 2004) and have been studied to reduce blood pressure in hypertensive rats (Jawi *et al*., 2012), and in the elderly hypertensive patients (Jawi *et al*., 2014). This study wants to prove whether the antihypertensive and antioxidant effect of aqueous extract of purple sweet potato comparable to captopril in patients with mild to moderate hypertension.

2. Materials and Methods

This study was a limited clinical trials by randomized control group pre-test and post-test design, with moderate hipertensive patients that come to one of private practice of medical doctor at Singapadu and one in Denpasar, Bali. Samples that meet the inclusion criteria (age 40-50 years, moderate hypertensive, similar socio-

economic class, do not suffer from certain diseases and are willing to be sampled for the study) were selected as samples of this study. The total samples were 30 patients. All of those patients were divided into three groups of treatments. Group one as a control group, were given captopril with the dose of 25 mg, two time a day for 4 weeks. Group two as treatment one, were given aqueous extract of purple sweet potato tuber at the dose of 3 x 60 ml every day for 4 weeks. Group three as treatment two, were given combination of aqueous extract of purple sweet potato tuber at the dose of 3 x 60 ml every day and captopril at the dose of 25 mg two time a day for 4 weeks.

All of these patients in all group were diagnosed, treated and followed-up in the outpatient clinic of a private doctor. Criteria for exclusion from these patient included a history of severe renal or liver dysfunction, malignancy, diabetes, smoking and the use of antioxidant or multivitamins supplements. The study was approved by the ethics committee of the Medical Research Institute of Medical Faculty, Udayana University with the number of 1131/UN.14.2/litbang/2014, and informed written consent was obtained from each patient, before enrollment. The blood pressure of all patients were evaluated every week during the study.

Biochemical Assays

Blood samples from all patients were taken at the beginning and one month after treatment to measure lipid peroxidation (MDA). Quantification was done based on thiobarbituric acid reactive substances (TBARS) method and calculated as malondialdehyde (MDA) as a biomarker of oxidative stress. To conform the oxidative stress, the level of superoxide dismutase (SOD) in the blood was also examined by commercially available kit (Cayman, Ann Arbor, MI, USA).

Statistical Analysis

All data were presented as mean $\pm$ SD. Paired t-test was used to assess the effect of therapies used at baseline and one months after treatment. Differences were considered significant at $p<0.05$. ANOVAs was used to assess the differences between group of study. All statistical analyses were performed using SPSS statistical software (version 10).

3. Results

Blood Pressure

The results showed significant ($p<0.05$) decline in systolic and diastolic blood pressure in patients treated with captopril group (control) and in aqueous extract of purple sweet tuber group. The group treated with a combination of captopril and aqueous extract of purple sweet potato tubers showed significant ($p<0.05$) decline in systolic blood pressure. In the captopril group the average of initial systolic blood pressure was 160 ± 13.33 mmHg, decreased to 140 ± 7.81 mmHg. While the initial diastolic blood pressure was 94 ± 5.16 and decreased to 82 ± 3.49 mmHg. In the group of extract of purple sweet potato tuber, the average initial systolic blood pressure 158 ± 11.35 mmHg, decreased to 137 ± 12.74 mmHg. While the initial diastolic blood pressure was 93 ± 9.54 and decreased to 83 ± 7.88 mmHg.

The decrease of blood pressure in the captopril group and the group of aqueous extract of purple sweet potato tuber were not statistically different ($p> 0.05$), for one month of treatment. Decrease in systolic blood pressure at captopril group and aqueous extract of purple sweet potato tuber was almost the same *i.e.* 23 mmHg and 20 mmHg. The decline in diastolic blood pressure in both groups also almost the same, namely 10.8 mmHg in the aqueous extract of purple sweet potato group and 10.0 mmHg in the captopril group. While the group of combined treatment only decreased the systolic blood pressure. Comparison of the average systolic and diastolic blood pressure during the first month is presented in Figure 1.

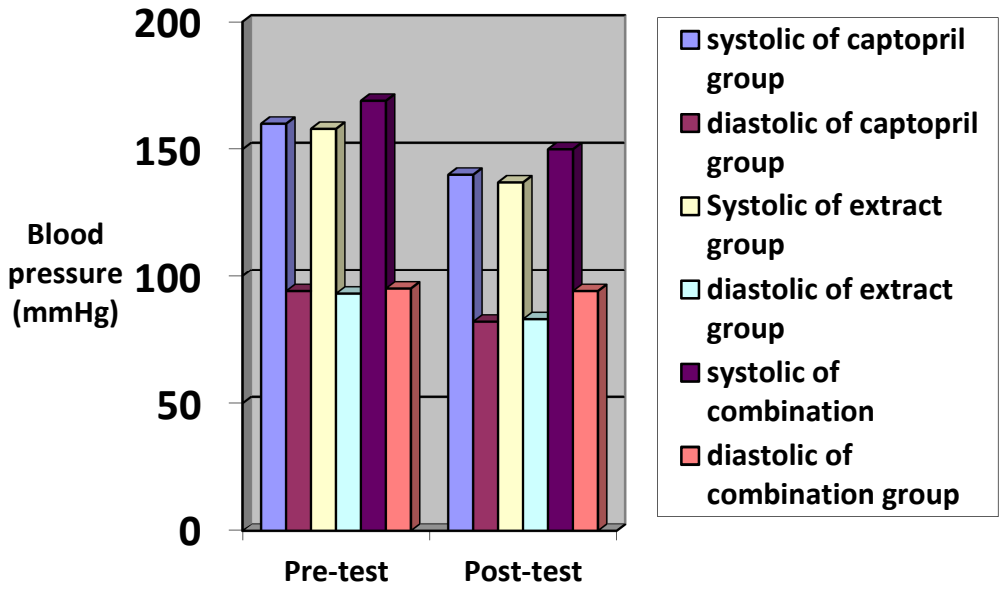

Figure 1
The comparison of systolic and diastolic blood pressure between groups

MDA and SOD in Blood

The blood MDA and SOD levels of hypertensive patients significantly ($p<0.05$) changed in all three groups of patients. The levels of the decrease in MDA and the increase in SOD at either control or treatment group. Statistically significant decrease in MDA occurred in all groups ($p <0.05$), but the increase in SOD in a group treated with captopril was not significant ($p> 0.05$). In the control group (treated with captopril) average blood MDA levels at the beginning of treatment was 6.84 ± 0.68 nmol / ml, decreased to 5.80 ± 0.79 nmol / ml ($p<0,05$). While the blood SOD levels at the beginning of treatment was 456.52 ± 32.94 U / gHb increased to 515.96 ± 82.75 U / gHb, at the end or after one month of treatment. Statistically, the number of SOD was not significant ($p>0,05$).

In the treatment group 1 (a group treated with aqueous extract of purple sweet potato tuber) average blood MDA levels at the beginning of treatment was 6.95 ± 1.13 nmol / l, decreased to 5.38. ± 0.99 nmol / ml ($p<0,05$). While the blood SOD levels at the beginning of treatment was 396.13 ± 36.81 U / gHb increased to 530.78 ± 83.32 U / gHb, at the end or after one month of treatment ($p<0,05$). In the treatment group 2 (treated with captopril in combination with aqueous extract of purple sweet potato tubers) average blood MDA levels at the beginning of treatment was 7.09 ± 0.68 nmolm / l, decreased to 5.82 ± 0.60 nmol / l ($p<0,05$). While the blood SOD levels at the beginning of treatment was 445.40 ± 21.79 U / gHb be 566.40 ± 80.00 U / gHb, at the end or after one month of treatment ($p<0,05$). Comparison of the average blood levels of MDA and SOD at the beginning of treatment and at the end of treatment is presented in Figure 2 and Figure 3.

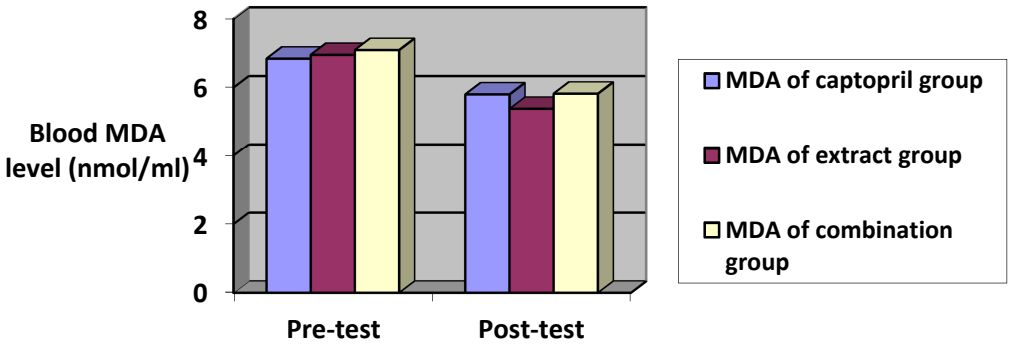

Figure 2
Blood MDA level of patients at begining (pre-test) and after one month (post-test)

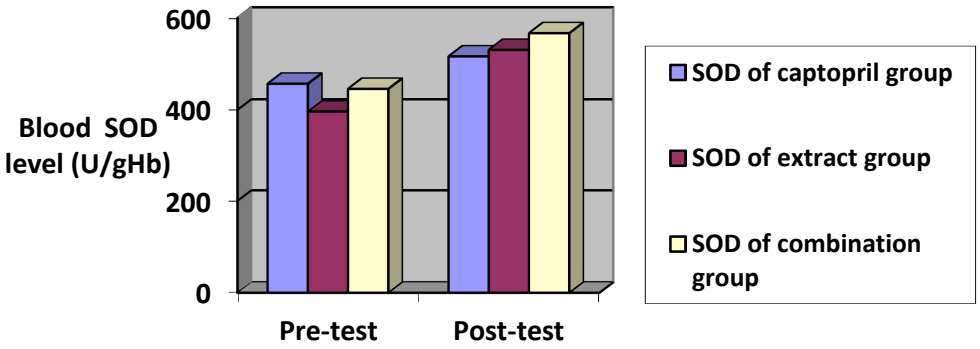

Figure 2
Blood SOD level of patients at begining (pre-test) and after one month of treatment (post-test)

4. Discussion

In this study, the blood pressure decreased significantly after administration of captopril, purple sweet potato tuber aqueous extract or a combination of captopril with aqueous extract of purple sweet potato tubers, except for diastolic blood pressure in the group treated with combination of captopril and purple sweet potato aqueous extracts. Decrease in systolic and diastolic blood pressure in the captopril group and group of purple sweet potato tuber aqueous extracts were not statistically different. These results proved that the aqueous extract of purple sweet potato tubers can decrease blood pressure in patients with mild to moderate hypertension, with similar potential with captopril. Antihypertensive potential (especially on systolic blood pressure) combination of captopril with aqueous extract of purple sweet potato tubers was similar to a single drug, so it does not need to be combined. The decrease in blood pressure due to the provision of aqueous extract of purple sweet potato tubers caused by high content of anthocyanin which is a flavonoid (Suprapta *et al*., 2004).

The results are consistent with research by Cassidy *et al*. (2011) who proved that eating foods containing flavonoids regularly for 14 years, especially anthocyanins, flavan-3 flavone and-ol can prevent the occurrence of hypertension up to 8%, which allegedly caused by vasodilatation effects of flavonoids.

Besides the vasodilator effects of anthocyanins, it is also expected to decrease blood pressure through an antioxidant effect and through various signaling mechanisms that are protective against cardiovascular system

(Wallace 2011). Anthocyanins are also shown to increase the expression of eNOS, such as anthocyanin cyanidin-3-glucoside can boost the expression of eNOS in the endothelium *in vitro*, which allegedly eNOS plays a role in maintaining blood pressure and maintain the integrity of the blood vessels, so as to protect the body from cardiovascular disorders (Xu *et al*., 2014)), because anthocyanins have cardio protective effects (Zafra-Stone *et al.*, 2007).

The results of MDA and SOD levels in the blood also showed significant changes between pre-test and post-test examination. These results proved that the aqueous extract of purple sweet potato can decrease blood MDA level and increase SOD level in hypertensive patients significantly ($p < 0.05$). Thus the aqueous extract of purple sweet potato tubers can prevent oxidative stress in patients with hypertension. Oxidative stress in patients with hypertension caused by the increase of activity of the enzyme NAD (P) H oxidase, resulting in the increase of the production of superoxide ions. The increase superoxide ions will decrease the bioavailability of NO that would aggravate oxidative stress in hypertension (Touyz, 2004).

High anthocyanin content in the aqueous extract of purple sweet potato tubers can reduce oxidative stress that can decrease blood MDA in hypertensive patients. The mechanism of anthocyanin or flavonoids to cope with oxidative stress is vary. Flavonoids (quercetin) has been shown can prevent oxidative stress through the increase of transcription factor Nrf2, thereby increasing the expression of indigenous antioxidant (Maher and Hanneken, 2005). The role of flavonoids to increase endogenous antioxidant depending on the type of flavonoid. Some flavonoids or anthocyanins can stimulate extracellular signal-regulated protein kinase (ERK), c-jun N-terminal kinase (JNK) and p38, which in turn will increase the Nrf2 into the nucleus and binds to the antioxidant response element (ARE) resulting in the increase of antioxidant gene expression including SOD gene resulting in the increase of SOD (Han, 2007).

In blood vessels, especially in endothelial, the high level of reactive oxygen species (ROS) will cause disruption of the function of NO in regulating the relaxation of blood vessel (Xu, 2004; Mann, 2007). The decrease of oxidative stress due to the provision of flavonoids, can maintain the NO that is a potent vasodilator, which can prevent the increase in blood pressure.

As a conclusion, the aqueous extract of purple sweet potato tubers can decrease blood pressure and prevent the oxidative stress by decreasing MDA and increasing SOD level in the blood of patients with hypertension. The effectiveness of this treatment was comparable with captopril. Effect of captopril in combination with purple sweet potato tuber extract on blood pressure and levels of MDA and SOD in patients with hypertension was equal to a single drug.

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