

# Protective Effects of Anthocyanin Extract from Purple Sweet Potato (*Ipomoea batatas* L.) on Blood MDA Levels, Liver and Renal Activity, and Blood Pressure of Hyperglycemic Rats

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**ABSTRACT:** There has been a dynamic progression in the study of purple sweet potatoes, particularly in regard to their antioxidant compounds, such as anthocyanins. Antioxidants can reduce oxidative stress due to hyperglycemia, therefore research into the protective effects of hyperglycemia is essential. This study was conducted to investigate the protective effects of anthocyanin extracts from purple sweet potatoes on blood malondialdehyde (MDA) levels, liver and renal activity, and blood pressure in hyperglycemic rats. Anthocyanin from purple sweet potato (APSP) was extracted with ethanol-citric acid 3% solvent. Twenty-four rats were split into four experimental groups: (i) healthy rats; (ii) hyperglycemic rats without anthocyanin treatment; (iii) hyperglycemic rats treated with APSP extract at a dose of 50 mg/kg; and (iv) hyperglycemic rats treated with APSP extract at a dose of 100 mg/kg. Rats received treatment for 35 days. The results showed that consumption of APSP significantly reduced levels of MDA in the blood, and liver and renal systems. APSP could reduce the urea and creatinine levels, which are indicative of improved renal function. In addition, APSP could decrease serum glutamate oxalacetate transaminase and serum glutamate pyruvate transaminase levels, indicative of protective activity of the extract on liver, and decrease systolic blood pressure. Accordingly, it was concluded that APSP could be developed as a functional food for treatment of diabetes.

**Keywords:** anthocyanin extract, antioxidant activity, hyperglycemic, MDA, purple sweet potato

## INTRODUCTION

Sweet potato is a healthy food recommended by the Food and Agriculture Organization of the United Nations, due to the presence of beneficial metabolites such as  $\beta$ -carotene, anthocyanins, vitamins (B1, B2, C, and E), and minerals (Ca, Mg, K, and Zn) (Kim et al., 2012). Purple sweet potato (PSP) is a variety of sweet potato rich in anthocyanins. The anthocyanins in PSP are mostly 3,5-diglucosidederivatives of cyanidin or peonidin, and caffeoyl, feruloyl, and *p*-hydroxybenzoyl (Liu et al., 2017). Anthocyanins have attracted lots of attention because of their potential biological and pharmacological benefits. For example, anthocyanin from PSP has many antioxidant activity (Zhang et al., 2009; Wu et al., 2012; Hu et al., 2016), anti-cancer (Lim et al., 2013), antidiabetic (Matsui et al., 2002; Jang et al., 2012; Zhao et al., 2013; Jang et al., 2019), anti-inflammatory (Wang et al., 2010), and hepatoprotective activities (Sun et al., 2014; Wang et al.,

2014a; Wang et al., 2014b).

Many varieties of sweet potato are grown in Indonesia, including PSP. PSP (*Ipomoea batatas* L.) contains the antioxidant anthocyanin, which can decrease blood glucose levels in hyperglycemic rats (Herawati and Santoso, 2013). However, the protective effects of anthocyanin extracts from PSP in rats (e.g., on liver and renal system) has not been reported. The protective effects of anthocyanin extracts on the liver can be investigated by analysis of serum marker enzymes [serum glutamate oxalacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT)], and the protective effects on the renal system can be investigated by analysis of urea and creatinine levels. Therefore, the purpose of this study was to investigate the protective effects of anthocyanin extracts from PSP on blood malondialdehyde (MDA) levels, liver and renal function, and blood pressure in hyperglycemic rats.

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## MATERIALS AND METHODS

### Materials and extract preparation

Local PSPs were obtained from Srigading, Sanden, Bantul, Yogyakarta, Indonesia. PSPs were processed into flour following the method by Herawati and Santoso (2013). PSP tubers were peeled, washed with clean water, sliced into small pieces, and dried using a cabinet dryer at 50~60°C for 12 h. The dried slices were milled using a hammer mill and sieved using a 1 mm sieve. The flour was then packed inside bags and stored at room temperature.

PSP powder was extracted following on the method developed by Matsui et al. (2001). The flour were extracted using a solvent (4:1 ratio of ethanol to citric acid 3%) for 2 h at 40°C on a hot plate. Then, the extract was filtered by Whatman paper and evaporated using a rotary vacuum evaporator for 12 h at 50°C.

### Animals

Eight-week-old male Sprague-Dawley rats (200~250 g) were obtained from Gadjah Mada University, Yogyakarta, Indonesia. Rats were housed in cages under standard conditions of 26°C, a relative humidity of 60% and with a 12-h light/dark cycle. Rats were fed a standard pellet diet with water available *ad libitum*.

The experimental design was approved by the Medical and Health Research Ethics Committee (MHREC), Faculty of Medicine, Gadjah Mada University, Ministry of National Education (Reference number: KE/FK/361/EC). The animals were used after 9 days acclimatization to the laboratory environment, and were fasted overnight before experiments.

### Experimental design

A total of 24 male rats were randomly divided into four experimental groups of six rats: (i) healthy rats; (ii) hyperglycemic rats without anthocyanin treatment; (iii) hyperglycemic rats treated with anthocyanin extract at a dose of 50 mg/kg; and (iv) hyperglycemic rats treated with anthocyanin extract at a dose of 100 mg/kg. The grouping of rats was based on simple random sampling of taking any rat into a group. First, rats were acclimatized for 9 days with a standard pellet diet (AIN-93 M) and *ad libitum* water. Hyperglycemic was then induced in rats by single intraperitoneal injection of alloxan 120 mg/kg body weight (Farsani et al., 2016; Mostafavinia et al., 2016; Rahimi-Madiseh et al., 2017; Abdullah et al., 2018). Five days after administration of alloxan, fasting blood glucose levels were examined. Anthocyanin extracts were given to two experimental groups of hyperglycemic rats for 35 days. No samples were lost during the study. After 35 days of treatment, all rats were sacrificed using ether anesthesia. We then performed *in vivo* analysis of (i) MDA, a product of lipid oxidation, in the blood, and

liver and renal systems, (ii) SGOT and SGPT levels, (iii) urea and creatinine levels, and (iv) systolic blood pressure (SBP).

### Chemical analyses

Serum sample were obtained by sinus orbitalis. For MDA analysis, thiobarbituric acid reactive concentrations were determined by spectrophotometric analysis (Ohkawa et al., 1979). The reaction between thiobarbiturate and MDA forms a pink chromogen, the absorbance of which can be measured at a wavelength of 532 nm (Jovanović et al., 2013). Enzymatic kits were used to determine urea and creatinine levels, and SBP was measured with a tail-cuff plethysmography sphygmomanometer.

### Statistical analysis

Data were expressed as means±standard error (SE). All statistical analyses were performed using the SPSS version 16 (SPSS Inc., Chicago, IL, USA). The results were analyzed using an one way analysis of variance (ANOVA), followed by Duncan's multiple range post-hoc test to determine significant differences between groups (*P*-values <0.05).

## RESULTS AND DISCUSSION

This section is organized as follows: (i) analysis of MDA levels; analysis of serum marker enzymes (SGOT and SGPT), indicative of protective effects on the liver; (iii) analysis of urea and creatinine levels, indicative of protective effects on the renal system; and (iv) analysis of SBP.

### MDA levels

Our results showed that PSP powder has a water content of 5.28% and anthocyanin content of 91.86 mg/100 g of flour or 96.98 mg/100 g dry weight. In contrast, the extract contains 8.31 mg/g anthocyanin and exhibits antioxidant activity (i.e., capturing free radical activity) of 79.61%, as determined by DPPH assays (Herawati and Santoso, 2013). Two experimental groups received anthocyanin. The levels of MDA in the blood, liver, and renal system after 35 days are shown in Table 1.

MDA levels are indicative of lipid oxidation. Our results showed that MDA levels in the blood, liver, and renal system were significantly enhanced in hyperglycemic rats. Indeed, hyperglycemic induced oxidative stress and increased levels of lipid peroxide and MDA. This damages the structure and fluidity of membrane, thereby impairing membrane functions. However, MDA was significantly decreased in the blood, liver and renal system of hyperglycemic rat that received anthocyanin extracts. Anthocyanin in PSP tubers has antioxidant activity, which prevents oxidative stress in blood and organs, and decreases

**Table 1.** Malondialdehyde (MDA) levels in rats after 35 days of treatment

Treatment group	Blood MDA (mmol/L)	Liver MDA (nmol/g)	Renal MDA (nmol/g)
Healthy	2.32±0.14 <sup>a</sup>	3.55±0.23 <sup>a</sup>	2.97±0.12 <sup>a</sup>
Hyperglycemic	8.38±0.22 <sup>d</sup>	9.61±0.18 <sup>d</sup>	8.75±0.13 <sup>d</sup>
Hyperglycemic + low dose APSP extract	3.52±0.11 <sup>c</sup>	5.85±0.19 <sup>c</sup>	4.17±0.17 <sup>c</sup>
Hyperglycemic + high dose APSP extract	2.78±0.13 <sup>b</sup>	4.36±0.12 <sup>b</sup>	3.78±0.20 <sup>b</sup>

Data are mean±standard deviation.

The same letter (a-d) in the same column, indicates samples are not significantly different at a significance level of 95%. In this table, each group has different letters under same column indicator, and are therefore significantly different. The same letters in different column are not connected.

APSP: anthocyanin from purple sweet potato.

levels of MDA. Administration of PSP aqueous extracts, which contain anthocyanin, can therefore decrease levels of MDA (Jawi et al., 2008; Satriyasa, 2016).

Anthocyanins may attenuate diabetic renal injury via suppression of reactive oxygen species, and protect mitochondrial function (Wei et al., 2018). Administration of anthocyanins enhances antioxidant function and decreases oxidative stress, thus decreases levels of MDA. Anthocyanins are phenolic compounds that have the ability to inhibit the formation of free radicals and catalytic metal for chelating redox reactions, thereby increasing total antioxidant capacity (Roussel et al., 2009). Anthocyanins (e.g., cyanidin and peonidin) can inhibit oxidation of low density lipoproteins in a concentration-dependent manner (Yi et al., 2010). Our results showed that MDA levels in the blood, liver, and renal system decreased by a greater extent in rats that received a high dose of APSP compared with a low dose of APSP. Similarly, in mice fed a high-fat diet, administration of anthocyanin from PSP reduced the level of oxidative stress-associated advanced glycation endproducts receptors and thioredoxin interacting proteins (Shan et al., 2014).

A limitation of this study is that it only investigates the effect of one polyphenol (anthocyanin) in PSP. Other components, such as copigments, may also have roles in reducing hyperglycemic by inhibiting  $\alpha$ -glucosidase enzymes and by exhibiting antioxidant activity (Esatbeyoglu et al., 2017). Although copigments are present at a lower quantity than anthocyanin, we recommend it is investigated in future studies.

### Protective effect of anthocyanin

The protective effect of anthocyanin extracts on the liver can be analyzed using serum marker enzymes. Both SGOT and SGPT are clinical indicators of liver damage. Hyperglycemic damages hepatocytes, causing GTP and GOT enzyme to enter the blood circulation and, consequently, elevating blood SGPT and SGOT levels. In this study, administration of APSP significantly decreased SGOT and SGPT levels in hyperglycemic rats (Table 2). At the higher experimental dose (100 mg/kg) APSP extracts significantly decrease SGOT and SGPT levels to a

**Table 2.** Serum marker enzymes in rats after 35 days of treatment (unit: U/L)

Treatment group	SGOT	SGPT
Healthy	18.69±0.23 <sup>a</sup>	22.19±0.43 <sup>a</sup>
Hyperglycemic	38.56±0.31 <sup>d</sup>	45.30±0.47 <sup>d</sup>
Hyperglycemic + low dose APSP	24.28±0.32 <sup>c</sup>	27.95±0.37 <sup>c</sup>
Hyperglycemic + high dose APSP	20.61±0.32 <sup>b</sup>	25.57±0.32 <sup>b</sup>

Data are mean±standard deviation.

The same letter (a-d) in the same column, indicates samples are not significantly different at a significance level of 95%. In this table, each group has different letters under same column indicator, and are therefore significantly different. The same letters in different column are not connected.

APSP: anthocyanin from purple sweet potato.

SGOT, serum glutamate oxalacetate transaminase; SGPT, serum glutamate pyruvate transaminase.

greater extent than the lower dose (50 mg/kg), indicating greater protective activity on the liver. Anthocyanin compounds can improve hepatocyte function, thereby decreasing levels of SGPT and SGOT.

Consistent with our results, previous studies have reported that anthocyanin decreases SGOT and SGPT in diabetic mice (Alli et al., 2017; Ranjan et al., 2017). For example, anthocyanin in the form of cyanidin 3-caffeoyl-*p*-hydroxybenzoylsophoroside-5-glucoside inhibited hepatic glucose secretion in hyperglycemic mice. Furthermore, anthocyanin extracts reduced cardiac cell inflammation and hypertrophy, and attenuated cardiac fibrosis to protect cardiac function (Liu et al., 2015; Chen et al., 2016).

### Urea and creatinine level

High levels of urea and creatinine in hyperglycemic rats is indicative of impaired renal function. Indeed, diabetic people often have high amounts of nitrogen compounds (urea and creatinine) in plasma and urine, resulting from decreased protein synthesis and increased muscle proteolysis (Gray and Cooper, 2011). In a previous study, consumption of PSP (i.e., anthocyanin) reduced body weight and the ratio of urine albumin to creatinine in high fat diet mice (Esatbeyoglu et al., 2017). In the current study, urea and creatinine levels significantly de-

**Table 3.** Urea and creatinine level in rats after 35 days of treatment (unit: mg/dL)

Treatment group	Urea	Creatinine
Healthy	14.60±0.45 <sup>a</sup>	0.46±0.01 <sup>a</sup>
Hyperglycemic	73.58±1.79 <sup>d</sup>	3.81±0.07 <sup>d</sup>
Hyperglycemic + low dose APSP	37.53±2.45 <sup>c</sup>	0.94±0.01 <sup>c</sup>
Hyperglycemic + high dose APSP	26.85±0.81 <sup>b</sup>	0.74±0.03 <sup>b</sup>

Data are mean±standard deviation.

The same letter (a-d) in the same column, indicates samples are not significantly different at a significance level of 95%. In this table, each group has different letters under same column indicator, and are therefore significantly different. The same letters in different column are not connected.

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creased after administration of APSP compared with hyperglycemic rats (Table 3). These results are indicative of improved renal activity, possibly induced by bioactive compounds present in APSP extracts. Bioactive compounds have positive effects on reducing kidney failure and extracellular dehydration (Alejandro et al., 2013; Amaya-Cruz et al., 2015). Previously, Pérez-Beltrán et al. (2017) reported fruit rich anthocyanin puree decreased levels of plasma glucose, urea, and creatinine in hyperglycemic rats.

### Blood pressure

Consumption of APSP extracts decreased the SBP of hyperglycemic rats (Table 4). These results are consistent with those from other studies investigating the antihypertensive activity of anthocyanin. Anthocyanin exhibits a vasoprotective effect by relaxing the isolated rings of the aorta, an effect compatible with the relaxing vascular effect induced by several antihypertensive compounds (Guzmán-Gerónimo et al., 2017). Phenolic compounds such as flavonoids and anthocyanins may decrease blood pressure through antagonizing Ca, inhibiting angiotensin converting enzymes and activating endothelial nitric oxide synthase (Mohtashami et al., 2019).

In conclusion, consumption of APSP significantly decreased the levels MDA in the blood, liver and renal system in hyperglycemic rats. Furthermore, APSP reduced urea and creatinine levels, which are indicative of improved renal activity. In addition, ASAP decreased SGOT and SGPT levels, indicative of protection of the liver protective, and lowered SBP. Therefore, APSP may be developed as a functional food for treatment of diabetes with additional health benefits.

### AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

**Table 4.** Systolic blood pressure in rats after 35 days of treatment (unit: mmHg)

Treatment group	Systolic blood pressure
Healthy	99.8±1.72 <sup>a</sup>
Hyperglycemic	139.17±2.04 <sup>d</sup>
Hyperglycemic+low dose APSP	116.67±2.80 <sup>c</sup>
Hyperglycemic+high dose APSP	106.50±1.87 <sup>b</sup>

Data are mean±standard deviation.

The same letter (a-d) in the same column, indicates samples are not significantly different at a significance level of 95%. In this table, each group has different letters under same column indicator, and are therefore significantly different. The same letters in different column are not connected.

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