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Dose-dependent Effect of Avocado Peel Hydroethanolic Extract on Antioxidant Status of Heart and Kidney Tissue Homogenates in Wistar Rats

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

This study evaluated the dose-dependent effect of avocado (*Persea americana*) peel hydroethanolic extract on antioxidant status of heart and kidney tissue homogenates in wistar rats. A total of 60 wistar rats were used and the study period lasted for 42 days. The animals were randomly sampled into six (6) groups; Group *i* -normal untreated wistar rats, *ii -P. americana* peel extract (50 mg/kg), *iii-* lead acetate (100 mg/kg), *iv- P. americana* peel extract (50 mg/kg) + lead acetate (100 mg/kg), *v-P. americana* peel extract (100 mg/kg) + lead acetate (100 mg/kg) and *vi- P. americana* peel extract (150 mg/kg) + lead acetate (100 mg/kg). Biomarkers assayed for include antioxidant enzymes superoxide dismutase, catalase and glutathione peroxidase; non-enzyme antioxidant reduced glutathione; isoprostanes and malondialdehyde. The extract caused a dose-dependent increase in antioxidant enzymes and non-enzyme markers when administered alone and when combined with

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lead acetate most especially at doses 100 mg/kg and 150 mg/kg. The extract also caused a significant dose-dependent decrease in isoprostanes and malondialdehyde. From the outcome of this study, avocado peel extract has an effect on antioxidant status of both the heart and kidney, but this effect is dose-dependent.

Keywords: Heart; kidney; homogenates; P. americana; antioxidant.

1. INTRODUCTION

In our world today, medicinal plants have continued to attract attention. The search for effective methods of treatment has been the main reason behind most scientific research. Various parts of plants like the seeds, peels, roots, stems, leaves and bark have been investigated to determine the medicinal value in management of several diseases that threaten the existence of mankind. Many essential and orphan drugs used in biomedicine today are direct or indirect products from plants due to its bioactive constituents or phytochemicals such as; flavonoids, alkaloids, anthocyanin, steroids and tannins. Phytochemicals are bioactive agents derived from plant materials [1]. In recent years, phytochemicals have been extensively investigated as important constituents of medicinal agents. Thus it is highly anticipated that phytochemicals will be used for treatment of several diseases especially those affecting vital organs. Avocado or *Persea americana* (luraceae) is one of over 150 different species. The *P. americana* is cultivated in both tropical and subtropical regions of the world [2]. The peel of *P. americana* has very rare applications in ethno–medicine, although it has been reported to contain antioxidants [3]. The oil from avocado peel has several health benefits like its application in management of obesity. *P. americana* peel has been reported to possess analgesic and anti-inflammatory activities [4]. The antioxidant activity of *P. americana* seed alone was found to be greater than 70% [5]. The fruit is fatty and subtly flavored, and of smooth, almost creamy texture. *P. americana* in many countries such as Brazil, Mexico, South Africa and India are frequently used for preparation of milkshakes and ice-cream [6]. Lead acetate is an agent used to induce toxicity in various experimental designs, which includes neurotoxicity, cardiotoxicity and hepatotoxicity. The heart and kidney are both vital organs. The heart as a muscular pump and the kidney as an excretory as well as endocrine organ are necessary for normal functioning of the body. Death due to heart and kidney diseases is a major challenge in our world today. The high cost of medical procedures needed to manage these diseases can be a serious burden especially to low income earners. Because a considerable percentage of world's population are low income earners [7], it is therefore of utmost importance that alternative source of medicines are discovered to help reduce the difficulty faced by most people with respect to heart and kidney diseases. This study will determine the protective effect of avocado peel on antioxidant status of heart and kidney tissue homogenates in wistar rats.

2. MATERIALS AND METHODS

2.1 Ethical Approval

This study was approved by the research ethics committee of Madonna University, Nigeria. This experiment was carried out according to the guidelines of animal experimentation in the university.

2.2 Plant Collection

Fresh avocado pears were purchased from Fruit Garden market in Port Harcourt, Rivers State, in November, 2018. The fruits were authenticated at Department of Plant Science and Biotechnology, University of Port Harcourt, Rivers State, Nigeria. The fruits were washed carefully with distilled water and NaCl. The peel was carefully separated from the edible portion and was taken to the laboratory for extract preparation.

Extract preparation: Extraction was done using hydro-ethanol (1:4 *v/v*), following standard procedures [3].

Experiment design: Sixty (60) wistar rats weighing between 160-220 g were collected from experimental animals unit and allowed to acclimatize at the animal house of Department of Human Physiology, Madonna University, Rivers State, Nigeria at 25 ± 2°C and 45-55 relative humidity through normal day/night cycle. The animals were fed with pelletized commercial rat feed (Pfizer livestock co. Ltd, Aba, Nigeria) and distilled water *ad libitum*. The rats were assigned into six (6) groups of ten (10) rats each as given below:

Groups	Treatments
i	Normal untreated wistar rats (Normal control)
ii	*P. americana* peel extract (50 mg/kg)
iii	Lead acetate (100 mg/kg)
iv	*P. americana* peel extract (50 mg/kg) + Lead acetate (100 mg/kg)
v	*P. americana* peel extract (100 mg/kg) + Lead acetate (100 mg/kg)
vi	*P. americana* peel extract (150 mg/kg) + Lead acetate (100 mg/kg)

The study period was 42 days (6 weeks).

2.3 Sacrifice and Homogenate Preparation

Few hours after treatment on day 42, the animals were anaesthetized with diethyl-ether and sacrificed in other to collect the heart and kidney from the thoracic and abdominal regions respectively. Heart and kidney tissue homogenate was prepared following already described procedures [7].

2.4 Biochemical Analysis

Using standard procedures [7], the oxidative stress biomarkers assayed for include the antioxidant enzymes-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) and non-antioxidant enzyme glutathione reductase (GSH). Other oxidative stress biomarkers that serve as secondary products of lipid metabolism which include malondialdehyde (MDA) and isoprostanes (F_2isoP) were also assayed for. SOD was assayed for using iodophenol nitrophenol phenyl tetrazolium (INT), CAT was assayed for using hydrogen peroxide. GPx analysis was done by measuring the rate of NADPH oxidation. MDA was assayed for using thiobarbituric acid, F_2isoP was assayed for using ELISA [7].

2.5 Statistical Analysis

The data collected was statistically analyzed using IBM®SPSS version 20.0. All values were statistically significant at a confidence interval less than or equal to 95%.

3. RESULTS

The extract caused a dose dependent increase in antioxidant enzymes SOD, CAT and GPx. As the dose of extract administered was increased there was also a gradual increase in the level of these antioxidants as well as the non-enzyme antioxidant GSH. This increase was most significant in group *vi* administered the highest dose of the extract.

There was a dose-dependent decrease in lipid peroxidative products MDA and F_2isoP of heart tissue homogenate. Lead acetate treatment alone caused a significant increase in MDA and F_2isoP but this effect was dose-dependently suppressed by the extract. This suppression or antagonism was well noticed in group *vi* for both biomarkers.

The extract dose-dependently increased the antioxidants SOD, CAT, GPx and GSH. This antioxidant-enhancing effect it has on the kidney is similar to the effect it has on the heart.

MDA and F_2isoP were gradually decreased as the dose of the extract was increased from 50 to 150 mg/kg. The extract caused a dose-dependent decrease in both biomarkers in kidney tissue homogenate.

Table 1. Dose-dependent effect of *P. americana* (avocado) peel on antioxidant enzyme and non-enzyme status of heart tissue homogenate

Groups	SOD (u/ml)	%c→i	CAT (u/g)	%c→i	GPx (µg/ml)	%c→i	GSH (µg/ml)	%c→i
i	231.0±1.4	0	201.4±0.2	0	90.2±0.1	0	40.1±0.1	0
ii	343.1±2.1*	48.5	272.3±1.3*	35.2	143.4±2.2*	59.0	67.4±0.2*	68.1
iii	141.2±3.0*	-38.9	80.4±1.0*	-60.0	43.2±1.2*	-52.1	23.2±0.3*	-42.1
iv	230.3±0.2	-0.3	194.1±0.3*	-3.6	83.2±1.4*	-7.8	40.3±1.0	0.5
v	301.2±1.3*	30.4	220.3±0.2*	9.4	122.0±0.3*	35.3	47.1±0.3*	17.5
vi	344.4±1.2*	49.0	250.4±0.2*	24.3	142.0±1.4*	57.4	63.1±0.3*	57.4

Key; All values statistically significant (*) at P≤0.05. %c→i=percentage change relative to control

Table 2. Dose-dependent effect of *P. americana* (avocado) peel on secondary products of lipid peroxidation of heart tissue homogenate

Groups	MDA (µg/ml)	%c→i	F_2isoP (µg/ml)	%c→i
i	40.2±2.1	0	71.4±0.2	0
ii	17.2±0.3*	-57.2	43.2±0.1*	-39.5
iii	67.1±0.4*	67.0	112.0±0.4*	-56.7
iv	24.3±0.1*	-40.0	75.7±0.1*	6.02
v	37.2±0.1*	-7.46	71.0±0.2*	-0.6
vi	20.1±0.3*	-50	32.3±0.4*	-54.8

Key; All values were statistically significant (*) at P≤0.05. %c→i=percentage change relative to control

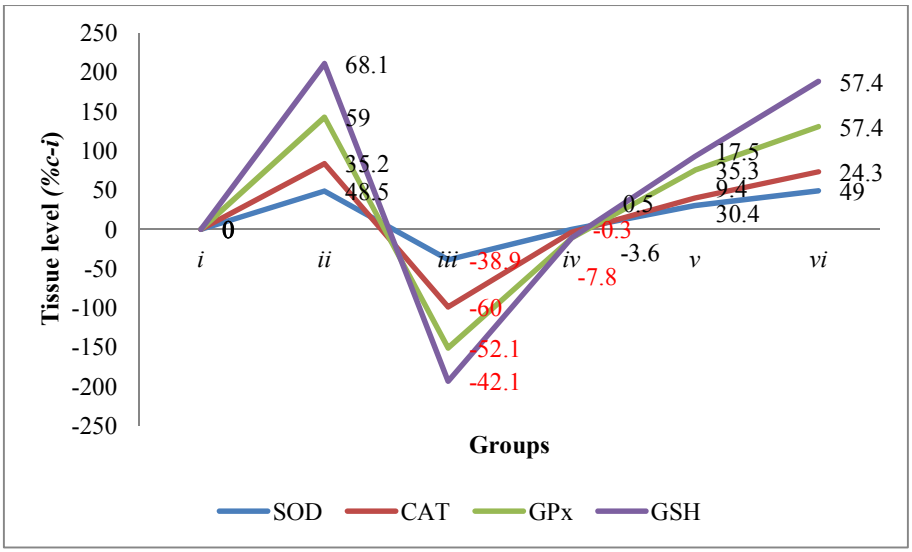

Fig. 1. Dose-dependent effect of *P. americana* (avocado) peel on antioxidant enzyme and non-enzyme status of heart tissue homogenate using percentage change relative to control

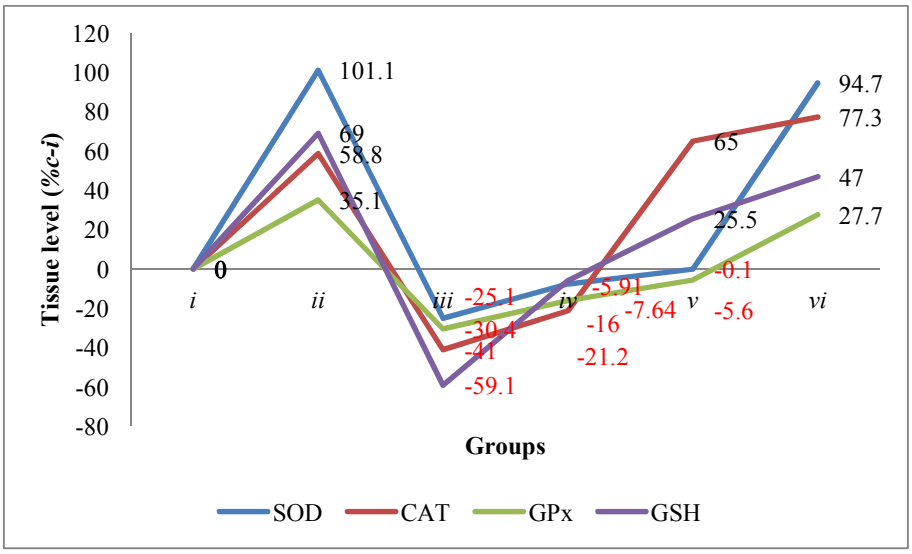

Fig. 2. Dose-dependent effect of *P. americana* (avocado) peel on antioxidant enzyme and non-enzyme status of kidney tissue homogenate using percentage change relative to control

Table 3. Dose-dependent effect of *P. americana* (avocado) peel on antioxidant enzyme and non-enzyme status of kidney tissue homogenate

Groups	SOD (u/ml)	%c→i	CAT (u/g)	%c→i	GPx (µg/ml)	%c→i	GSH (µg/ml)	%c→i
i	120.4±1.2	0	80.1±0.2	0	76.4±2.1	0	32.1±0.1	0
ii	242.1±0.3*	101.1	127.2±1.4*	58.8	103.2±0.4*	35.1	54.2±2.0*	69.0
iii	90.2±0.1*	-25.1	47.3±1.3*	-41.0	53.2±0.3*	-30.4	13.1±0.1*	-59.1
iv	111.2±0.4*	-7.64	63.1±0.4*	-21.2	64.2±1.0*	-16.0	30.2±4.1*	-5.91
v	120.3±1.3*	-0.1	132.2±0.3*	65.0	72.1±0.2*	-5.6	40.3±0.1*	25.5
vi	234.4±0.3*	94.7	142.0±2.1*	77.3	97.6±0.4*	27.7	47.2±1.3*	47.0

Key; All values were statistically significant (*) at P≤0.05. %c→i=percentage change relative to control

Table 4. Dose-dependent effect of *P. americana* (avocado) peel on secondary products of lipid peroxidation of kidney tissue homogenate

Groups	MDA (µg/ml)	%c→i	F_2isoP (µg/ml)	%c→i
i	47.2±0.4	0	34.2±0.3	0
ii	21.4±0.2*	-54.7	13.1±1.3*	-61.7
iii	76.2±1.2*	61.4	56.7±1.2*	65.8
iv	54.6±1.1*	15.7	44.2±0.3*	29.2
v	43.2±0.2*	-9.3	32.1±1.3*	-6.1
vi	24.1±0.3*	-48.9	21.0±0.1*	-38.6

Key; All values were statistically significant (*) at P≤0.05. %c→i=percentage change relative to control.

4. DISCUSSION

Although scientific evidence on therapeutic application of avocado peel is rare, avocado fruit has been reported to be an abundant source of bioactive constituents capable of preventing or ameliorating several symptoms related to heart and kidney diseases [8]. Phytochemicals are important chemicals found virtually in plants and their different parts and at different concentrations [9,10]. From previous reports, phytochemicals present in avocado peel includes flavonoids, alkaloids, steroids, saponins and tannins [3]. Flavonoids are potent water-soluble [11,12], antioxidants [13] and free radical scavengers. They prevent oxidative cell damage [14], have strong anticancer activity and protect against all stages of carcinogenesis. Flavonoids have been reported to lower the risk of heart and kidney diseases, inflammation and represent the most common and widely distributed groups of plant phenolic compounds [13]. In this study, the concentration of flavonoids in avocado peel may be just enough to increase or boost the level of antioxidants and prevent the generation of free radical species and subsequent oxidative stress in heart and kidney tissues. Alkaloids are also therapeutically important plant secondary metabolites. Isolated pure form of alkaloids and their synthetic derivatives are used as basic medicinal agents in management of several diseases but most especially heart diseases. Phenols, another important phytochemical in avocado peel, have been extensively researched as disease-preventing agents. Phenols may also be responsible for their ability to act as anti-oxidants. Avocado peel at 50 mg/kg treatment may increase antioxidant status and prevent oxidative stress but this effect is even more pronounced when the dose administered is further increased up to 150 mg/kg. Lead acetate caused toxic effect, and is in agreement with early reports [15]. From this study, the ability for avocado peel extract to affect the level of antioxidants in heart and kidney tissues depends on the treatment dose. There is a directly proportional relationship between the dose of the extract administered and the level of both enzyme and non-enzyme antioxidants in heart and kidney tissues, but an inversely proportional relationship between the dose of treatment and the level of oxidative stress products of lipid peroxidation like malondialdehyde and isoprostanes.

5. CONCLUSION

From the outcome of this study, avocado peel extract has an effect on antioxidant status of both the heart and kidney, but this effect is dose-dependent.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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