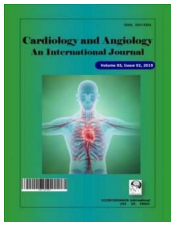

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Assessment of the effect of Watermelon and Aloe Vera on Cadmium Induced Heart Damage in Adult Wistar Rats (*Rattus novergicus*)

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Authors' contributions

This work was carried out in collaboration between all authors. Authors ODO, SAA and HBA designed the study, wrote the protocol and wrote the first draft of the manuscript. Author SAA managed the literature searches and analyses of the study performed the spectroscopy analysis. Authors O. O. Adeleye and O. O. Adeyinka managed the experimental process. Author UAY identified the species of plant. All authors read and approved the final manuscript.

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ABSTRACT

The aim of the study was to investigate the antioxidant property of watermelon and aloe vera against cadmium damaging effect on the heart and the packed cell volume of the blood. Thirty five Wistar rats were obtained and acclimatized for two weeks. They were randomly divided into 7 groups, five rats each. Animal in individual groups were induced intraperitoneally with 3.0 mg/kg of

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cadmium sulphate and were treated with aloe vera and water melon at 40 mg/kg, animals in control group received 3.0 mg/kg of PBS as shown in Table 1. The research lasted for 4 weeks. The enzymes analysis on antioxidant activity and packed cell volume was considered statistically significant at ($p<0.05$) based on Mean±SEM. The packed cell volume significantly increased for watermelon group 5 and aloe vera group 6 when compared to normal control group 1. Group 3, 6 and 7 were statistically significant when compared to the mean value of the normal control while group 4 and 5 were not statistically significant for Malondialdehyde (MDA), Catalase (CAT) and Glutathione peroxidase (GPx). None was statistically significant for Superoxide Dismutase (SOD). Group 2, 3, 4, 6 and 7 were statistically significant for acetylcholinesterase (AChE). The results from this experiment demonstrate the high degree of potency in aloe vera over watermelon in preventing oxidative damage due to cadmium interaction with the animal system. Watermelon only was not able to provide significant benefit against cadmium damaging activities. However, in combination with aloe vera, watermelon can be effective against cadmium activity and they are dose dependent, which justified the antioxidant properties of both plants extract to ameliorate cadmium toxicity in the heart tissue.

Keywords: Cadmium sulphate; watermelon; aloe vera; antioxidants; pack cell volume.

1. INTRODUCTION

Cadmium (Cd) is a highly toxic element and is naturally present in all parts of the environment, which includes; food, water, and soil [1] and by the World HealthOrganization is a major concern for public health [2]. It is a non-essential element and has a half-life which is extremely persistent in the environment [3,4]. By means of long-range atmospheric transport, cadmium releases can be carried to and deposited on areas remote from its sources of emission [5]. Cadmium is sourced naturally from volcanic activities, forest fires and generation of sea-salt aerosols, thus increasing cadmium levels in the environment [6].Through non-ferrous mining and refining processes, manufacturing and application of phosphate fertilizers, fossil fuel combustion, production and use of nickel-cadmium batteries, cadmium can enter the environment [7,8]. Humans are at risk to cadmium exposure through the food chain because cadmium is not degraded in the environment [9]. Exposure to the toxicity of cadmium is through inhalation of its particle or fumes during industrial operation [10]. Cadmium accumulates in the organ it enters, affecting the cell physiology and growth [11,12], induces disorders in the humoral and cellular immune responses [13,14], cause alteration of total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein and very low density lipoprotein concentration in the blood [15]. Cadmium and its associated metals lead, copper, zinc, mercury, arsenate and vanadium, have been found out to have the ability to produce reactive oxygen species (ROS), which results in lipid peroxidation and antioxidant enzymes alterations, leading to oxidative stress [16].

Antioxidants are reducing agents that are capable of decreasing oxidation reactions by interacting with intermediates of the reaction, or by reacting with the oxidizing agent and preventing the reaction directly [17]. Aloe vera and watermelon have been said to contain antioxidant effect [18,19]. Watermelon fruit has deep green or yellow coloured smooth thick exterior rind with gray or light green vertical stripes. Generally, watermelon flesh is the main consumable portion; however, outer rind is also used in some parts of the world [20-22]. Watermelon contributes nutritional agents as antioxidants (e.g. lycopene, beta-carotene) and some specific amino acids (e.g. arginine, citrulline). 100 g of watermelon consumed provides 30 Kcal to the body as it contains almost 92% water and 7.55% of carbohydrates, out of which 6.20% are sugars and 0.40% dietary fiber [23,24]. Vitamins like thiamine, riboflavin, niacin and folate are also present [25]. Additionally, it is a good source of potassium and also contains magnesium, calcium, phosphorus and iron [26]. Aloe vera one of about 400 species in the genus Aloe and is commonly known [27]. All aloes have spined or smooth fleshy leaves [27,28]. Aloe vera (*Aloe barbadensis* Miller) is a cactus-like plant that grows readily in hot, dry climates and currently, because of demand, is cultivated in large quantities [29]. *Aloe barbadensis* Miller (Ab), one of the aloe vera types, is the most commonly used form for commercial and also therapeutic purposes in North America, Europe, and Asia [30]. Aloes contains amino acids, an thraquin one derivatives and their glycosides which have cathartic and detoxifying effect on body organs as well contain others bioactive substances such

as auxins, gibberellins, minerals, vitamins, aspirin like compound, magnesium lactate and various enzymes like superoxide dismutase (SOD) and catalase [29]. The thick fleshy leaves of aloe plants contain cell wall carbohydrates such as cellulose and hemicellulose and storage carbohydrates such as acetylated mannans [31]. The aim of the study is to investigate the antioxidant property of watermelon and aloe vera against cadmium damaging effect on the heart and the packed cell volume.

2. MATERIALS AND METHODS

2.1 Plant Material

Three watermelon fruitsand aloe vera plants were obtainedand authenticated and assigned with voucher number (No. FHI. 110256) in the Department of Botany, Bingham University, Nigeria.

2.2 Preparation of Cadmium solution

Cadmium salt of Sigma product was obtained at a Scientific Laboratory Store, Yanyan, Nigeria. 0.008 g (8 mg) of Cadmium ($3CdSO_4.8H_2O$) was weighed using a sensitive weighing balance and then dissolved in 5 ml of phosphate buffer at PH 7.4.

2.3 Preparation of Plant Extracts

2.3.1 Aqueous watermelon extract

The watermelon fruits were washed and weighed. They were peeled and cut into slices. The seeds were removed. The slices were blended and then filtered using a sieve. The aqueous extract was placed in a water bath and allowed to evaporate to paste form. The paste was weighed and diluted with phosphate buffer (1:2) [32].

2.3.2 Aqueous aloe vera extract

Aloe vera plant was washed and cut open to remove the gel. The gel was homogenized using an electric blender and turned into a container and refrigerated. The residue and the gel obtained were weighed. The extract was diluted with water (1:2) and then placed in the water bath for 15 minutes. It was allowed to cool and then filtered. The aqueous extract was turned into a container and stored in a cool place [33].

2.3.3 Phytochemical analysis of plant extracts

Phytochemical analysis of the watermelon and aloe vera plant extract for the following phytochemicals: alkaloids, saponins, tannins, flavonoids, carbohydrates, steroids, anthraquinones, cardiac glycosides were carried out in Pharmacognosy laboratory, Pharmacology Department, Jos University Teaching Hospital, Nigeria as described by method of [34].

3. Experimental Animal

Thirty five Wistar rats (50 g-176 g) were obtained from National Veterinary Research Institute, Vom, Jos, Nigeria. They were housed in the Bingham University animal house in 12 hour of light and 12 hour of dark. The rats were allowed to acclimatize for 2 weeks. They were provided with feed and water (Vital Feed Growers (Pelletised) produced by Grand Cereals Ltd, Nigeria) *ad libitum*. All experimental investigations were done in compliance with humane animal as stated in the “Guide to the care and use of Laboratory Animals Resources”. National Research Council, DHHS, Pub. No NIH 86 – 23 [35] and in accordance with ethical approval of the Anatomy Department, Bingham University, Karu, Nigeria.

3.1 Experimental Design

The experiment lasted for 4 weeks. The rats were divided into seven groups, 5 rats in each group.

At the termination of the experiment, the rats in Table 1 were fasted overnight and then sacrificed by cervical dislocation. The hearts were collected for enzyme analysis and the blood from the heart was obtained for the measurement of the packed cell volume.

3.2 Packed Cell Volume

The blood obtained from the rats in Table 1 was placed in an EDTA bottle. A heparinized capillary tube was used to collect blood from the bottle and then plasticin was used to seal up the end of the tube placed in the blood. The heparinized capillary tube was then placed in the haematocrit centrifuge and then centrifuged for 10 minutes at 11000 rpm. The centrifuged blood in the capillary tube was then placed in the haematocrit reader to obtain results of the packed cell volume of the blood.

3.3 Enzyme Analysis

The hearts of animals in Table 1 were placed in 5% sucrose solution, were homogenized and centrifuged at 4000 rpm for 10 minutes and the

Table 1. Animal treatment groups

S/N	Groups	Administration
1	Control group	Phosphate buffer (3 mg/kg) intra-peritoneally
2	Induced group	$3CdSO_4.8H_2O$ intra-peritoneally (3 mg/kg)
3	Therapeutic group	Vitamin C (100 mg/kg/) and vitamin E (300 mg/kg) orally, once daily
4	Therapeutic and induced group	Vitamin C (100 mg/kg) and vitamin E (300 mg/kg/bw) orally, once daily + $3CdSO_4.8H_2O$ intra-peritoneally (3 mg/kg)
5	Treatment group	$3CdSO_4.8H_2O$ intra-peritoneally (3 mg/kg) + Watermelon extract (80 mg/kg) orally, twice daily
6	Treatment group	$3CdSO_4.8H_2O$ intra-peritoneally (3 mg/kg) + Aloe vera extract (80 mg/kg) orally, twice daily
7	Treatment group	$3CdSO_4.8H_2O$ intra-peritoneally (3 mg/kg) + Watermelon (40 mg/kg) and Aloe vera extract (40 mg/kg) orally, twice daily

supernatant collected. The supernatants obtained were used to carry out the following enzyme activities adopting first principle methods as described; acetylcholinesterase (AChE) [36], superoxide dismutase (SOD) [37], Glutathione (GPx) [38], Catalase (CAT) [36] and Malondialdehyde (MDA) [38].

3.4 Statistical Analysis

The data obtained from the enzyme analysis and packed cell volume of the animal were analyzed by one-way ANOVA statistical analysis using MedCalc version 13- © 1993-2014 Med calc software bvba and represented in mean ± standard error of mean.$p<0.05$ was considered statistically significant in comparison with the control.

4. RESULTS

Tables below shows results of Assessment of the effect of Watermelon and Aloe Vera on Cadmium Induced Heart Damage in *Rattus novergicus.*

Table 2. Average weight of the rats at different periods of the experiment represented in Mean ± SEM

Group	Average weight before induction	Average weight 2 days after induction	Average weight on the 23rd day	Average weight before sacrifice
Control	90.20±19.492	92.40±19.619	141.60±13.956[a]	147.80±13.343
Induced	144.00±10.025	144.80±9.769	174.80±5.704[a]	177.80±6.269
VIT C+VIT E	139.40±11.070	141.00±11.167	153.80±8.218	145.00±9.232
VIT C+ VIT E+ induced	126.40±12.217	128.20±11.196	155.00±9.618[a]	146.80±9.728
Watermelon	126.40±2.542	118.80±1.985[a]	162.20±6.240[a]	166.40±6.470
Aloe vera	123.80±9.970	125.40±10.856	145.60±11.647	149.60±10.875
Watermelon + aloe vera	140.00±14.071	137.60±13.545	148.40±6.904	151.60±9.304

$p<0.05$ was measured as statistically significant. [a] represents that the present weight is statistically significant when compared to the weight before induction

Table 3. Phytochemical screening of watermelon and aloe vera extract

Bioactive constituents	Watermelon extract	Aloe vera extract
Alkaloids	+ + +	+ + +
Saponins	+	-
Tannins	-	-
Flavonoids	+	+
Carbohydrates	+ +	+ + +
Steroids	+ +	+ +
Anthraquinins	-	-
Cardiac glycosides	+	+ +

Key - Negative, + Present + + More Present, + + + Highly Present

Table 4. Packed cell volume of rats represented in Mean ± SEM

Group	Packed cell volume (%)	P-value
Control	32.9±1.2083	
Induced	31.3±0.7176	P=0.09
VIT C+ VIT E	33.4±0.7969	P=0.5644
VIT C+ VIT E+ induced	29.0±3.7417	P=0.3561
Watermelon	38.5±0.7071*	P=0.0014
Aloe vera	37.5±0.7071*	P=0.0029
Watermelon + aloe vera	36.1±1.6310	P=0.1213

**indicates a statistically significant mean difference atp< 0.05 when values are compared to control*

Table 5. Showing acetylcholinesterase activity (10^{-8}mols/min/g) activity represented in Mean ± SEM and P- value of control and treated group

Group	Mean±SEM	P-value
Control	6.2056±1.270	
Induced	2.5260±0.5622*	P=0.0028
VIT. C+ VIT. E	3.2148±0.8434*	P=0.0239
VIT. C+ VIT. E+ INDUCED	5.2812±0.2810*	P=0.0302
Watermelon	5.5108±0.8434	P=0.4563
Aloe vera	3.2148±0.8434*	P=0.0239
Watermelon+aloe vera	1.8364±0.2814**	P<0.0001

**indicates a statistically significant mean difference at p<0.05 and ** at p<0.001 when values are compared to control*

Table 6. Showing the enzyme activities of Malondialdehyde (MDA), Catalase (CAT), Superoxide Dismutase (SOD) and Glutathione Peroxidase (GPx) in mean ± standard error of mean of control and treated group

Group	MDA (10^{-8} units/mg)	CAT (µmols/mg)	SOD (unit/min)	GPx (µmols/mg)
Control	4.6940±0.4820	3.1900±0.3511	1.9920±0.0150	1.1482±0.1073
Induced	4.5060±0.4005	2.7780±0.3846	1.6080±0.2405	1.0262±0.1597
VIT C+ VIT E	3.8040±0.0186**	2.9860±0.0264*	2.2080±0.4852	0.9570±0.0080**
VIT C+ VIT E+ Induced	5.6240±1.0118	3.2000±0.6328	1.9920±0.0150	1.1698±0. 2310
Watermelon	3.9800±0.4671	3.3480±0.3725	2.8080±0.7301	1.1928±0.1063
Aloe vera	5.4000±0.1089*	4.4300±0.0274**	2.8080±0.7301	1.4684±0.0141**
Watermelon+ aloe vera	6.3120±0.0471**	4.0240±0.0175**	2.6080±0.2405	1.0214±0.0205*

**indicates a statistically significant mean difference at p< 0.05 and ** at p<0.0001 when value is compared to control*

5. DISCUSSION

The present study examined the ability of cadmium (Cd) to cause damage to the heart tissue and to determine the ameliorativeeffect of watermelon and aloe vera against Cd damage to the heart. Cd action is dependent on the species, type of Cd compound, dose size and frequency, age and interaction with various dietary components [39]. Watermelon and aloe vera plant have been identified with antioxidant properties capable of scavenging reactive oxygen species [40,41].

The average weight of rats in each group was compared to the previous average weight of the rat in the same group. Cd induced group showed no statistical significant change in weight when the average weight of the rats before induction was compared to the average weight of rats two days after induction. A study carried out on the effect of Cd on weight showed no significant difference in weight after Cd induction [42]. There was no statistical significant change in average weight in group 3, vitamin C and E. In group 4, vitamin C, E and induced, there was no significant difference when the average weight of the rats before induction at day 23 was compared to the average weight of rats after induction, before sacrifice. In the watermelon group 5, there was statistical significant decrease in average weight after induction when compared to the average weight before induction. This does not support Lu [42] where Cd did not cause

significant weight difference. There was also significant increase when the average weight of the rats was compared to the average weight after induction. This suggests the possibility of watermelon to cause increase in weight as a protective effect against Cd. This can be due to its antioxidant property [19,43]. There was no statistical significant change in average weight of the aloe vera group 6 and aloe vera and watermelon group 7.

Normal packed cell volume in rats, ranges from 37.6-50.6% [44]. Cd did not significantly decrease the PCV of the induced group 2 as compared to the normal control group 1. However, studies have shown that Cd has the capability of reducing PCV in different animals [45-48]. Cd causes the destruction of erythrocytes [49] thereby reducing PCV. Watermelon treatment in group 5 and aloe vera treatment in group 6, increased the packed cell volume in adult Wistar rats induced with Cd to 38.5% and 37.5% respectively which falls within the normal range for rats [44]. Increase in packed cell volume in group 7 which was treated with watermelon and aloe Vera was not statistically significant.

AChE activity is inhibited by Cd, lead and copper [50]. AChE activity varies in different species [51]. The normal control group 1 therefore has normal AChE activity. Cd significantly decreased AChE activity in group 2 when compared to the normal control group 1. This suggests the capability of Cd in decreasing AChE activity as studies in other species have explained [52,53]. Group 6 treated with only aloe vera showed improvement in AChE activity than the induced group 2 and was significant when compared to the normal control group 1. This improvement is possibly due to its antioxidant property [40,54]. Watermelon treatment in group 5 showed no statistical significance in improving AChE. Group 7 treated with aloe vera and watermelon was significant when compared to the normal control group 1 but there was no increase in AChE activity.

Malondialdehyde activity is used to determine the level of lipid peroxidation in cells [55]. Cd did not significantly induce lipid peroxidation in group 2 as compared to the normal control group 1. This could be because the dose of Cd administered was not sufficient enough to cause lipid peroxidation [39]. Group 6 treated with only aloe vera and group 7 treated with aloe vera and watermelon when compared to the normal control group 1 were significant. MDA activity in these groups, 6 and 7 was higher than that of the normal control group 1 which could be due to the initial increase in lipid peroxidation when Cd was administered. Decrease in MDA activity did not occur in these groups. Watermelon treatment group 5 did not show significance.

Catalase (CAT) one of the most important antioxidant enzymes is present in the peroxisomes of nearly all aerobic cells, preserves and protects the cell from the toxic effects of hydrogen peroxidase (H_2O_2) catalyzing $H_2O_2$and decomposition it into molecular oxygen and water without producing free radicals [55]. CAT activity in the induced group 2 was decreased by Cd compared to the normal control group 1 but was not significant. Studies involving the capability of Cd reduction of CAT activity have been established [55] but this dependent on dosage and frequency of the Cd administered to the induced group, 2 [39,55]. Group 6, treated with only aloe vera administered and group 7, treated with aloe vera and watermelon showed significant increase in CAT activity when compared to the normal control suggesting the potency of aloe vera in inhibiting the activity of Cd against CAT when administered only or combined with watermelon. Watermelon group 5 did not show significant increase in CAT activity. Studies have shown the presence of CAT in watermelon and aloe vera plant [29]. Watermelon might not have been significant because of the decreased level of its antioxidant property duringits preparation or possibly due to long term storage [56,57].

Superoxide dismutase catalyzes the disproportionation of superoxide radicals (O_2^-), generated in to H_2O_2 and O_2 [58]. SOD activity in the Cd induced group 2, and group 4 induced with Cd after pre-treatment with vitamin C and E, showed decrease and similarity respectively when compared to the SOD activity in the normal control group 1, but this decrease was not significant. Groups receiving vitamin C and E only, watermelon only, aloe vera only and aloe vera and watermelon combined (3, 5, 6 and 7) had increase in SOD activity but it was not significant. Antioxidants scavenge free radicals [17]. Aloes have been said to contain superoxide dismutase amongst its chemical composition [29].

Glutathione peroxidase assists reduced glutathione in scavenging dangerous oxidative metabolites in the cell by converting hydrogen peroxide to water [59]. Glutathione peroxidase

activity in Cd induced group 2 did not significantly decrease when compared to the normal control group 1. Cd is capable of decreasing antioxidant activity but this is dependent on factors like dosage, age, frequency and specie [39]. Group 6, treated with aloe vera demonstrated significant increase in GPx activity when compared to the normal control group 1. This suggests the presence of GPx in aloe vera as an antioxidant capable of scavenging Cd deleterious effect on glutathione [60]. There was slight increase in GPx activity for watermelon group 5, but it was not significant. Watermelon have antioxidant enzyme that can be decreased due to long storage and temperature [56,57]. Although the group 7, treated with both aloe vera and watermelon was significant, there was no increase in the GPx activity when compared to the controlcontrary to the presence of the antioxidant present in these plants [56,60].

6. CONCLUSION

The results from this experiment demonstrate high degree of potency in aloe vera over watermelon in preventing oxidative damage due to cadmium interaction. Watermelon treated rats only was not able to provide significant benefit against cadmium damaging activities. However, in combination with aloe vera, watermelon was observed to be effective against cadmium activity and they are dose dependent.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All the authors hereby declare that all the Experiments have been examined and approved By the appropriate ethics committee and have Therefore been performed in line with the ethical Procedure laid down in 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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