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Effects of Ethanolic Seed Extract of *Dacryodes Edulis* on the of Paraquat Induced on Testicular Toxicity in Male Adult Wistar Rats

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ABSTRACT

Dacryodes edulis, a multipurpose plant contains high concentrations of antioxidants, antiinflammatory agents that protect against tissue damage. The study was aimed at determining the ethanolic seed extract of dacryodes edulis on the of paraquat induced on testicular toxicity in male adult wister rat. Fifty-four adult male albino wister rat weighing between 150-180g were used for the study. LD 50 was determined for both dacryodesedulis and paraquat. The rats used for this experiment were distributed into eight groups. Group A (control group) while B C D E F G H were the treated group. (group B paraquat 0.1ml only for4 weeks, group C paraquat only for 2 weeks, group D paraquat + 500mg/kg of dacryodes edulis, group E paraquat only for 2 weeks and discontinued, Group F paraquat +1000mg/kg of dacryodes edulis for 4 weeks' group G and H received 500mg/kg and 1000mg/kg of dacryodes edulis for 4 weeks. At the end of the experiment animals were anesthetized and samples were collected for assessment. The result from this study shows that paraquat produces destructive effects on testes evaluations, There was significant increase in LH, FSH testosterone level, was high in group C E F. There was also a significant decrease in the body weight and relative organ weight throughout the period of administration. Histopathological finding reveals distortion of the testicular tissues with mild toxicity in group B. The treated group showed sign of recovery and reversal effect of paraquat. In conclusion the ethanolic seed extract of dacryodes edulis possess ability to improve sperm morphology in paraquat toxicity.

KEYWORDS: Testes, Toxicity, Dacryodes Edulis, Ethanol.

INTRODUCTION

Dacryodes edulis (African pear tree) is a tropical oleiferous fruit tree that possesses enormous potential in Africa (Kengué, 1990). It is commonly known as Ube by the Igbos, Mzembe by the Tivs of Nigeria(Burkill, 1985). Various parts of the plantare used in traditional medicine to treat several diseases in different areas (Okafor, 1983; Duru *et al*, 2012). The fruits are edible, and the bark, leaves, stem, and roots are employed for a variety of purposes (Neuwinger 2000; Jirovetz *et al.*, 2003,and Waruhiu *et al.*, 2004). The bark resin is used in Nigeria to treat parasitic skin disease and jiggers (Hutchinson, 1963). Seeds of *Dacryodes edulis* are chewed by the Tiv people of Nigeria as a remedy for stomach

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problems like diarrhoea, dysentery etc (Ajibesin, 2008), the wood serves for firewood and carpentry (Ndoye *et al.*, 1997), while the entire tree is used in agroforestry systems for soil conservation, fertility, shade and apiculture (Ndangang, 1989). *Dacryodes edulis* fruit or safou is popular in the diets of many Africans. It can be eaten raw, roasted or boiled in hot water, and is eaten alone or used in garnishing cooked or roasted maize. It could also be used as spread to eat bread (Duru *et al.*, 2012). *Dacryodes edulis* has a potential to improve nutrition andfood security (Ayuku *et al.*, 2000). Paraquat (1, 1'-dimethyl-4, 4'-bipyridilium dichloride - PQ), is one of the most widely used herbicides and holds a large share of the global herbicide market till today, it is a non-

selective quaternary nitrogen herbicide, commonly used as a desiccant and defoliant in a variety of crops all around the world (Dasta, 1978; Bismuth et al., 1982, Bismuth et al., 1990; Raghu et al., 2013).Paraquat is also known as methyl viologen because of its dark blue-green colour (Dinis-Oliveira et al., 2008). It has been considered as a toxic compound over the past 60 years, which is why it is classified as a moderately hazardous herbicide and placed in class II poison for acute toxicity (WHO, 2009). Paraquat was found to be highly toxic towards animals and humans with fatalities being reported by Kelly et al., 1978 and Florkowski et al., 1992. The main risks are due to deliberate dose dependent ingestion resulting in multiple organ failure and death (Florkowski et al., 1992). Other routes of toxic exposure are inhalation, ocular and skin contacts (Bataller et al., 2000; Baharuddin et al., 2011). Toxicity resulting from skin exposure is more common in concentrated forms and causes irritation while prolonged contact leads to severe systemic toxicity or even death (Bataller et al., 2000; Marrs and Adjei, 2003).

Paraquat mainly affects the lungs, where it accumulates at up to 6–10 times the plasma concentration, sequestered in pulmonary type I, type II and Clara cells (Krieger and Krieger, 2001; Cope *et al.*, 2004; Shuler *et al.*, 2004; Dinis-Oliveira *et al.*, 2008,). Oxygen-free radicals are formed resulting in acute alveolitis 1–3 days' post-exposure. Tachypnoea, dyspnoea and cyanosis begin from 2 to 7 days' post-exposure. If the affected animal or human survives, diffuse alveolar septal fibrosis and compensatory type II pneumocyte hyperplasia develop followed by pulmonary fibrosis (chronic phase). Refractory hypoxaemia and eventual death occur from 5 days to several weeks later (Gfeller and Messonnier, 1998; Cope *et al.*, 2004; Dinis-Oliveira *et al.*, 2008; Gawarammana and Buckley, 2011).

MATERIALS AND METHOD

This study was conducted in the Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Anambra State. The animals were acclimatized for two weeks and the actual experimental protocol lasted for 4 weeks. Fifty-Four (54) Male Albino Wistar Rats weighing between 130-180g (22 for LD_{50} determination and 32 for the experiment proper), were purchased from Animal House, University of Nigeria, Nsukka, and housed in Nnamdi Azikiwe University Animal Farm, Nnewi, Nnewi North Local Government Area, Anambra state.

Paraquat in the form of Paraquat dichloride was be purchased from Agro-allied division of new market Owerri, Imo State

2kg of *Dacryodes edulis* seed was purchased from Nkwo market at Nnewi, Nnewi North L.G.A of Anambra State. Identification of this seed was carried out in the Department of Pharmacognosy of the Faculty of Pharmacy, Nanmdi Azikwe University (NAU).

Twenty-four hours after the last administration, the animals were anesthetizied with diethyl ether in a close jar, blood samples were collected through ocular puncture using heparinized capillary tube and put into plain serum bottle, and then serum were separated by centrifugation and was stored in a refrigerator of temperature -18°c for biochemical analysis. Thereafter, the animals were anesthetized using diethyl ether. Each animal was placed on the dissecting board, pinned to the board and dissecting set (sharp scalpel on scalpel holder for making incision; scissors for cutting and dissecting forceps for harvesting) were used to harvest the testes which was immediately weighed before transferring into 10% formal saline for proper fixing for histological sectioning.

Small slices of testes tissue were taken and passed through several stages of tissue processing before embedding in paraffin. Five-micron thick sections were stained with hematoxylin and eosin (H & E) as described by Carleton, (1976); Bancroft and Gamble, 2002 for demonstrating histoarchitecture of the liver, kidney and testes tissues.

Data were analysed using SPSS version 25. Data were subjected to inferential statistics, and values were presented as Mean \pm Standard error of Mean (SEM) using tables. hormonal test, semen quality and relative organ weight was analysed using one way Anova followed by post hoc LSD multiple comparism. Body weight was analysed using t-test. Data was considered significant at p <0.05.

RESULTS AND DISCUSSION

Initial Weight	Final Weighty	Difference in	Percentage of Weight	Р-	T-Value
(g)	(g)	Weight (g)	Difference (%)	Value	
$150. \pm 4.08$	230 ± 12.90	80.00	53.33	0.02	-5.06
213.33 ± 14.52	163.33 ± 3.33	-50.00	-23.43	0.10	2.88
175. <u>±</u> 8.66	167.50 ± 2.50	-7.50	-4.29	0.49	-0.79
167.50 ± 4.78	195.00 ± 19.07	27.50	16.42	0.12	-2.20
167.50 ± 4.78	217.50 ± 14.36	50.00	29.85	0.01	-4.62
170 ± 5.77	233.33 ± 17.63	63.33	37.25	0.04	-4.35
152.50 ± 8.53	187.50 ± 8.53	35.00	22.95	0.03	-3.65
150.00 ± 4.08	180.00 ± 4.08	30.00	20	0.02	-4.24
	Initial Weight(g) $150. \pm 4.08$ 213.33 ± 14.52 $175. \pm 8.66$ 167.50 ± 4.78 167.50 ± 4.78 170 ± 5.77 152.50 ± 8.53 150.00 ± 4.08	Initial WeightFinal Weighty(g)(g) $150. \pm 4.08$ 230 ± 12.90 213.33 ± 14.52 163.33 ± 3.33 $175. \pm 8.66$ 167.50 ± 2.50 167.50 ± 4.78 195.00 ± 19.07 167.50 ± 4.78 217.50 ± 14.36 170 ± 5.77 233.33 ± 17.63 152.50 ± 8.53 187.50 ± 8.53 150.00 ± 4.08 180.00 ± 4.08	Initial WeightFinal WeightyDifference in(g)(g)Weight (g) $150. \pm 4.08$ 230 ± 12.90 80.00 213.33 ± 14.52 163.33 ± 3.33 -50.00 $175. \pm 8.66$ 167.50 ± 2.50 -7.50 167.50 ± 4.78 195.00 ± 19.07 27.50 167.50 ± 4.78 217.50 ± 14.36 50.00 170 ± 5.77 233.33 ± 17.63 63.33 152.50 ± 8.53 187.50 ± 8.53 35.00 150.00 ± 4.08 180.00 ± 4.08 30.00	Initial WeightFinal WeightyDifference inPercentage of Weight(g)(g)Weight (g)Difference (%)150. ± 4.08230 ± 12.9080.0053.33213.33 ± 14.52163.33 ± 3.33-50.00-23.43175. ± 8.66167.50 ± 2.50-7.50-4.29167.50 ± 4.78195.00 ± 19.0727.5016.42167.50 ± 4.78217.50 ± 14.3650.0029.85170 ± 5.77233.33 ± 17.6363.3337.25152.50 ± 8.53187.50 ± 8.5335.0022.95150.00 ± 4.0830.0020	Initial WeightFinal WeightyDifference inPercentage of WeightP-(g)(g)Weight (g)Difference (%)Value150. ± 4.08230 ± 12.9080.0053.330.02213.33 ± 14.52163.33 ± 3.33-50.00-23.430.10175. ± 8.66167.50 ± 2.50-7.50-4.290.49167.50 ± 4.78195.00 ± 19.0727.5016.420.12167.50 ± 4.78217.50 ± 14.3650.0029.850.01170 ± 5.77233.33 ± 17.6363.3337.250.04152.50 ± 8.53187.50 ± 8.5335.0022.950.03150.00 ± 4.0830.00200.02

Data was analyzed using t-test and values were considered significant at P < 0.05. WD= weight difference.

Result from table 4.1 below showed that there was a significant (p<0.05) increase in the body weight in group A, as the final weight was 53.33% greater than the initial weight. Group B showed a decrease in weight that was not significant (p>0.05) when the initial weight was compared to the final weight to the tone of 23.43%. Group C showed a decrease in weight that was not significant (p>0.05) when the initial weight to the tone of 4.29%. Group D showed an increase in weight that was not significant (p>0.05) as the final weight was 16.42% greater

than the initial weight. Group E showed a significant increase (p<0.05) in the weight when the initial weight was compared to the final weight to the tone of 29.85%. Group F showed a significant increase (p<0.05) in the weight when the initial weight was compared to the final weight to the tone of 37.25%. Group G showed a significant increase (p<0.05) in the weight when the initial weight was compared to the final weight to the tone of a significant increase (p<0.05) in the weight was compared to the final weight to the tone of 22.95%. Group H showed a significant increase (p<0.05) in the weight when the initial weight was compared to the final weight to the tone of 20%.

Groups	Relative Testicular Weight	P-Value
	(g) Mean \pm SEM	
А	0.80 ± 0.01	0.01
В	0.57 ± 0.10	0.00
С	0.68 ± 0.01	0.21
D	0.75 ± 0.11	0.52
Е	0.64 ± 0,06	0.47
F	0.63 ± 0.01	0.54
G	0.71 ± 0.02	0.14
Н	0.72 ± 0.04	0.11
F-Value	1.45	

Table 4.2 shows the effect of ethanoic seed extract Dacryodes edulis on paraquat-induced toxicity on relative organ weight

Data was analyzed using ANOVA, followed by Post Hoc LSD multiple comparism, and data was considered significant at (p < 0.05).

Result from table 4.2 Results of the relative testicular weight showed an increase in organ weight that was not significant (p>0.05) in groups C, D, E, F, G and H, while a significant

increase in organ weight (p<0.05)in group A when compared to group B.

Table 4.6 shows the effect of ethanoic seed extract *Dacryodes edulis* on paraquat-induced toxicity on LH, FSH, & Testosterone

Groups	Luteinizing Hormone	Р-	FSH	P-Value	Testosterone	P- Value
	(m/u/ml)	Value	(m/u/ml)		(ng/ml)	
А	2.37 ± 0.13	0.000	0.32 ± 0.03	0.201	4.20 ± 0.03	0.986
В	1.14 ± 0.12		0.12 ± 0.14		4.10 ± 0.03	
С	2.14 ± 0.12	0.000	0.46 ± 0.17	0.392	4.24 ± 0.16	0.683
D	1.80 ± 0.01	0.000	0.94 ± 0.03	0.001	7.51 ± 0.10	0.000
Е	2.68 ± 0.09	0.000	0.41 ± 0.0	0.578	8.04 ± 0.07	0.000
F	3.85 ± 0.08	0.000	0.32 ± 0.14	1.000	11.36 ± 0.28	0.000
G	3.28 ± 0.06	0.000	1.23 ± 0.08	0.000	7.33 ± 0.08	0.000
Н	3.46 ± 0.18	0.000	1.66 ± 0.12	0.000	9.00 ± 0.05	0.000
F-Value	75.36		25.05		687.65	

Data was analyzed using ANOVA, followed by Post Hoc LSD multiple comparism, and data was considered significant at (p < 0.05).

Result from table 4.6 below showed a significant increase (p<0.05) in luteinizing hormone level in groups A, C, D, E, F, G, and H when compared to group B. Result of Follicular Stimulating hormone showed a significant (p<0.05) increase in group D, G, and H, while an increase that was not

significant (p>0.05) in groups A, C, and E when compared to group B. Testosterone result showed a significant (p<0.05) increase in groups D, E, F, G, and H, and increase that was not significant (p>0.05) in groups A and Cwhen compared to group B.

Table 4.7 shows the effect of ethanoic seed extract *Dacryodes edulis* on paraquat-induced toxicity on Active motility, Sluggish motility, and Non-motile Semen

Groups	Active Motility (%)	P- Value	Sluggish Motility (%)	P-Value	Non-Motile (%)	P- Value
А	85.00 ± 2.88	0.001	6.66 ± 1.66	0.669	8.33 ± 1.66	0.000
В	20.00 ± 11.45		11.66 ± 1.66		68.33 ± 13.01	
С	65.00 ± 2.88	0.009	10.00 ± 0.00	0.886	25.00 ± 2.88	0.000
D	74.66 ± 0.33	0.023	17.66 ± 1.45	0.608	7.66 ± 1.45	0.000
Е	56.66 ± 23.33	6.029	31.66 ± 21.66	0.100	10.00 ± 0.00	0.000
F	72.23 ± 4.33	0.003	12.66 ± 1.45	0.932	15.006 ± 2.88	0.000
G	70.00 ± 5.77	0.005	17.66 ± 1.45	0.608	12.33 ± 4.33	0.000
Н	61.66 ± 13.64	0.015	21.66 ± 6.66	0.396	16.66 ± 7.26	0.000
F-Value	3.24		0.94		12.37	

Data was analyzed using ANOVA, followed by Post Hoc LSD multiple comparism, and data was considered significant at (p<0.05).

Result from table 4.7 showed that active motility revealed a significant increase (p<0.05) in-groups A, C, D, E, F, G, and H when compared to group B.

increase (p<0.05) in groups D, E, F, G, and H when compared to group B.

Non-motile sperms showed a significant decrease (p<0.05) in groups A, C, D, E, F, G, and H when compared to group .

Sluggish motility, result revealed a decrease that was not significant (p>0.05) in groups A and C, while a significant

Table 4.8 shows the effect of ethanoic seed extract Dacryodes edulis on paraquat-induced toxicity on Normal and Abnorma
Sperm cells

Groups	Normal Sperm Cells (%)	P- Value	Abnormal Sperm cells (%)	P-Value
А	85.00 ± 5.00	0.00	15.00 ± 5.00	0.00
В	36.66 ± 3.33		63.33 ± 3.33	
С	70.00 ± 5.77	0.00	30.00 ± 5.77	0.00
D	80.00 ± 0.00	0.00	20.00 ± 0.00	0.00
Е	75.00 ± 2.88	0.00	25.00 ± 5.00	0.00
F	65.00 ± 2.88	0.00	35.00 ± 2.88	0.00
G	75.00 ± 2.88	0.00	25.00 ± 2.88	0.00
Н	78.33 ± 3.33	0.00	21.66 ± 3.33	0.00
F-Value	17.09		17.09	

Data was analyzed using ANOVA, followed by Post Hoc LSD multiple comparism, and data was considered significant at (p<0.05).

Result from table 4.8 showed a significant increase (p<0.05) in Normal sperm cells in group A, C, D, E, F,G, and H when compared to group B. Abnormal sperm cell result showed a

significant decrease (*p*<0.05) in group A, C, D, E, F,G, and H when compared to group B.

Table 4.9 shows the effect of ethanoic seed extract Dacryodes edulis on paraquat-induced toxicity on Total Sperm Count

				Sperm cour	nt	P-value	F-value
Total	Sperm	count	Group A	6.49	±1.17	0.00*	
(x10^6/r	nl)		Group B	1.18	±0.24		
			Group C	3.02	±0.04	0.113	
			Group D	5.39	±0.74	0.00*	9.24
			Group E	4.08	±1.49	0.02*	
			Group	8.59	±0.13	0.00*	
			Group G	2.61	±0.62	0.21	
			Group H	3.90	±0.36	0.03*	

Data was analyzed using ANOVA, followed by Post Hoc LSD multiple comparism, and data was considered significant at (p < 0.05).

Result from table 4.9 below showed a significant increase (p<0.05) in the mean total sperm count in-group A, D, E, F,

and H, and an increase that was not significant (p>0.05) in groupss C and G when compared to group B.

Histopathological Findings



PLATE 1 (Group A) Testes: Photomicrographs of testes tissue show normal histology. Seminiferous tubules are intact with active spermatocytes (white short arrow) and spermatogonium (white long arrow) (H&E x 400 x100).



Plate 2 (Group B: Paraquat Only) Testes: Photomicrographs of testes tissue show mild spermatogenic arrest (white arrow). Seminiferous tubules are intact with deactivated spermatocytes and spermatogonium (Arrow head) (H&E x 100 x400).



Plate 3 (Group C: administered with paraquat for two weeks only). Photomicrographs of testes tissue show normal histology. Seminiferous tubules are intact with mild active spermatocytes and spermatogonium. There is no injury (H&E x 100 x400).



Plate 4 (Group D: administered with paraquat for 2weeks and treated with H.D of *edulis*). Photomicrographs of testes tissue show normal histology. Seminiferous tubules are intact with active spermatocytes and spermatogonium (Arrow head). There is no injury (H&E x 400 x100).



Plate 5 (Group E: Paraquat 2-weeks and discontinued). Photomicrographs of testes tissue show normal histology. Seminiferous tubules are intact with active spermatocytes and spermatogonium. There is no injury (H&E x 100 x400).



Plate 6 (Group G: L.D of *Dacryodes edulis*). Photomicrographs of testes tissue show normal histology. Seminiferous tubules are intact with active spermatocytes and spermatogonium. There is no injury (H&E x 100 x400).



Plate 7 (Group H: H.D of *Dacryodes edulis*). Photomicrographs of testes tissue show normal histology. Seminiferous tubules are intact with active spermatocytes and spermatogonium. There is no injury (H&E x 100 x400).

Findings from table 3 revealed a significant increase (p<0.05) in LH in groups (A, C, D, E, F, G, & H), FSH (group D, G, & H) and testosterone level ingroups D, E, F, G, & H) when compared to paraquat control (group B). The mechanism of action in the significant increase in the hormonal level in the treated groups following administration of *Dacryodes edulis*, which contains flavonoids and polyphenols compounds present, thus attenuating oxidative damages caused by free radicals. However, there was a significant decrease (p<0.05) in paraquat control when compared to normal control (group A). This is attributed to the generation of reactive oxygen species resulting from oxidative stress by PQ intoxication.

The findings of this study as shown in table 4 showed a significant increase (p<0.05) in active motility in group C, D, E, F, G, & H when compared to paraquat control (group B). Non-motile sperm showed a significant decrease (p<0.05) in group C, D, E, F, G, & H when compared to group B. The precise mechanism of action is due to the presence of flavonoids and polyphenolic compounds present in Dacryodes edulis attenuating oxidative damages caused by PQ intoxication. Although, in group E, PQ intoxication showed a reverse effects of sperm motility changes. However, paraquat control group when compared to normal control showed a significant decrease (p<0.05) in active motility and significant increase (p<0.05) in non-motile sperm. This is attributed to generation of ROS production by PQ intoxication. This study confirms the results of Chen et al., (2017) who reported a significant decrease in sperm motility following paraquat administration. This study further supports the findings of Eduardo et al., (2018) findings agrees with report of this present study on motility of sperm cells following administration of paraquat.

The findings of this study as shown in table 5 showed a significant increase (p < 0.05) in normal sperm cells in group C, D, E, F, G, & H when compared to paraquat control (group B). Abnormal sperm cell showed a significant decrease (p<0.05) in group C, D, E, F, G, & H when compared to group B. The precise mechanism of action is due to the presence of flavonoids and polyphenolic compounds present in Dacryodes Edulis attenuating oxidative damages caused by PQ intoxication. Although, in-group E, PQ intoxication showed a reverse effects of semen motility changes. However, paraquat control group when compared to normal control showed a significant decrease (p<0.05) in normal sperm cell and significant increase (p<0.05) in abnormal sperm. This is attributed to generation of ROS production by PQ intoxication. This study agrees with Chen et al., (2017) who reported a significant decrease in sperm viability following paraquat administration. Eduardo et al., (2018) findings agrees with report of this present study on viability of normal sperm cell.

Findings from table 6 showed a significant increase (p<0.05) total sperm count in groups D, E, F, & H when compared to paraquat control (group B). This is attributed to polyphenols and flavonoids present in*Dacryodes edulis*. However, when paraquat control was compared to normal control, there was a significant decrease (p<0.05) in total sperm count. This is present of ROS generation by PQ intoxication. This study agrees with Chen *et al.*, (2017) who reported a significant decrease in sperm count following paraquat administration. Eduardo *et al.*, (2018) findings agrees with report of this present study on sperm count, which showed a significant decrease following paraquat administration

Testicular histology showed a mild spermatogenic arrest, with the seminiferous tubules intact with deactivated spermatocytes and spermatogonium as observed in-group B. This study is in line with Shanker *et al.*, (2011); Atashpour *et al.*, (2017); while there was an increase in spermatogenesis in the treated groups.

CONCLUSION

This study showed that the ethanolic seed extract of *Dacryodesedulis* improved sperm morphology issues following paraquat intoxication in adult male witsar rats. The ethanolic seed extract of *Dacryodesedulis* was able to protect the Testes histoarchitecture, and reduce enzymes activities caused by PQ intoxication.

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