PRINT ISSN 1119-8362
Electronic ISSN 2659-1502

Full-text Available Online at
https://www.ajol.info/index.php/jasem
http://www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage.
Vol. 27 (1) 51-55 January 2023

Evaluation of Protective Potential of Aqueous Seed extract of Ripe Fruits of *Carica papaya* on Cyanide Induced Kidney Damage in Male Wister Rats

***OTTUH, P; KADIRI, HE**

Department of Biochemistry, Delta State University, Abraka, Delta State, Nigeria

**Corresponding Author Email: peter.progress97@gmail.com; Tel: +2349068831770*
Co-Authors Email: hekad@yahoo.com

ABSTRACT: This study aimed to evaluate the protective potential of aqueous seed extract of ripe *Carica papaya* fruits on cyanide induced kidney damage in male Wister rats using 24 male rats divided into five groups. The animals were sacrificed at the end of the experimental period and serum and kidney were harvested for biochemical and histological analysis following standard procedures. Estimation of kidney function markers such as creatinine and urea and assessment of electrolytes of toxicological relevance; sodium ion, potassium ion, bicarbonate ion and chloride ion were carried out. The study revealed that cyanide stimulated alterations in kidney function makers: urea, creatinine and serum electrolytes. The result indicated that aqueous seed extract of *Carica papaya* fruits significantly increase Urea, creatinine, Cl^-, HCO^{3-}, K^+ and Na^+ activities in the rats induced with cyanide when compared with the positive control. However, the concentrations were significantly decreased in the treated groups when compared with the groups induced with cyanide. Histological analysis showed cyanide induced structural distortions of the kidney tissues. Treatment with *Carica papaya* seed extract was able to mitigate these damages. This study indicates that aqueous seed extract of ripe fruits of *Carica papaya* possesses nephro-protective properties and can be used as an antidote for cyanide poisoning.

DOI: **https://dx.doi.org/10.4314/jasem.v27i1.8**

Cite this paper as: OTTUH, P; KADIRI, H. E. (2023). Evaluation of Protective Potential of Aqueous Seed extract of Ripe Fruits of *Carica papaya* on Cyanide Induced Kidney Damage in Male Wister Rats. *J. Appl. Sci. Environ. Manage.* 27 (1) 51-55

Dates: Received: 29 November 2022; Revised: 22 December 2022; Accepted: 11 January 2023; Published: 31st January 2023

Keywords: Cyanide, *Carica papaya*, kidney

It has long been recognized that some plant materials possess antioxidant properties. Medicinal plants continue to emphasize the global need for effective ways of using plant parts (such as seeds, leaves, stems, roots, etc.) to treat many diseases affecting humans. (Asagba *et al.*, 2017). Cyanide (CN) has been recognized as a common environmental pollutant associated with several adverse health consequences such as carcinogenesis, hepatotoxicity, renal impairment as well as disruption of normal endocrine and reproductive functions. (Kadiri and Asagba, 2015; Tara *et al.*, 2019). Cyanide appears naturally as glycosides in over 2000 plants. Ingesting such plants has been reported to cause acute cyanide toxicity and mortality in live stocks and man (Kadiri, 2018). As a result of the increasing use of cassava in animal feeds there is greater exposure to dietary toxins from cyanogenic glycosides (Kadiri and Asagba, 2015). Cyanide can be found in some insecticides, rodenticides, metal polishes and fumigant. Certain bacteria and fungi synthesize cyanide as component of cyanogenic glycosides to provide a source of nitrogen and for self-defense. Some foods eaten by humans which contain cyanide include yams, sorghum and maize. Cyanide is also present in apple and almond seeds. Eating such foods without proper preparation may lead to cyanide intoxication. The toxicity of cyanide is as a result of its high potency as a

respiratory poison in all aerobic forms of Life (Patrick *et al.,* 2016) .In addition to acute cyanide intoxication, chronic toxicity has been suggested that the most widespread problems arising from cyanide are from chronic dietary, industrial and environmental sources (Coentrao and Moura, 2011). Cyanide has also been proven to induce oxidative stress and damage in a number of biological systems (Coentrao and Moura 2011; Desharnais *et al*, 2012). Two antidotes (sodium nitrite and sodium thiosulfate) are usually utilized to reduce or stop the effects of cyanide poisoning. However, researches are ongoing to find more effective and cost effective ways to manage this poisoning. In recent times, plants and plants-based materials are being tested as possible antidotes for cyanides toxicity in animals. One important plant commonly grown in the tropical regions of the world with nutritional and health promising benefits is carica papaya. *Carica papaya* Linn.(Family.caricaceae) is a perennial, herbaceous plant with copious milky latex reaching to 6-10 meters tall. It's erect stem is about 30cm thick and roughened with leaf scars.The unripe fruit is used traditionally among the various tribes in Nigeria for the treatment of various human and veterinary diseases including malaria, hypertension, diabetes mellitus, hyper cholesterolaemia, jaundice, intestinal heiminthiasis and for the management of socks cell anemia. The *Carica papaya L*, is also one of the major fruit crops cultivated in tropical and sub-tropical zones of the world. The largest production is in Central and South American mainly in Brazil, Asia and in Africa. World production of papaya in 2009 was over 10 million tons, which was almost 1.5 times higher than that in 1999 (Joachim and Siri, 2021). Studies have been carried out on *papaya* seeds and it has been proven to have various phytochemicals that are beneficial (Joachim and Siri, 2021). To the best of our knowledge, there has been no scientific report to show the protective effect of aqueous extract of seeds of ripe *Carica papaya* fruits against cyanide induced kidney injury and its possible antidote effect. Therefore, the objective of this study was to evaluate the protective potential of aqueous extract of ripe fruits of *Carica papaya* seeds on cyanide induced kidney damage in male wister rats

MATERIALS AND METHODS

Collection of plant material and identification: Ripe fruits of *Carica papaya* was plucked from delta state university, Delta state, Nigeria. It was identified by a taxonomist Mr. M.E Ozioma from botany department of Delta state university and given a voucher number (DELSUH127). The fruits were washed thoroughly under a running water to remove any contaminant. It was peeled and the seeds was removed and rinsed under slow running water. After rinsing, it was air dried for weeks at an open space within the laboratory confinement of the Department of Biochemistry, Delta State University, Abraka, Nigeria, at room temperature. After air drying, the seeds were ground into a powder with an electric blender (Binatone, BLG 500, and Japan). One hundred gram of the powdered seeds was soaked for 48 hours in 500ml of distilled water and deionized water respectively. The extract was filtered and concentrated using rotary evaporator.

Experimental design: Male Wister rats were used for this study and randomly divided into six groups (n=6).Group 1 which served as the normal control received neither cyanide nor *C. papaya* seed extract, Group 2 served as the positive control and was given cyanide only. Group 3(standard control) received cyanide and sodium thiosulphate (500 mg / Kg body weight) a standard cyanide antidote, Group 4, 5 and 6 received cyanide and 100, 200 and 400 mg of *C. papaya* seed extract respectively. Groups 2-5 were administered cyanide orally by gavage in form of KCN at a concentration of 4 mg/kg body weight. (A sub-lethal dose) (Satpute *et al.,* 2010). The dose of the plant extract administered to Groups4, 5 and 6 was in the range of the safe dose as reported by Kanadi *et al.,* (2019). All the rats were sacrificed after 8weeks.

Biochemical analysis: The serum and kidney was collected and urea, creatinine and electrolytes levels were analyzed. Creatinine activity was determined using the method of Bartels and Bohmer (1972). Urea activity was determined using the method of Weatherburn (1967). Sodium ion $Na^{+,}$ Potassium ion $K^{+,}$ Bicarbonate ion CO_3^- and Chloride Cl^- were determined calorimetrically according to standard procedures using commercially available diagnostic kits (teco diagnostic kits).

Histological analysis: kidney histology was done following the method of Zhang *et al* (2017).

RESULTS AND DISCUSSION

The effect of *C. papaya seed* extraction the urea and creatinine concentrations in the serum of rats induced with cyanide toxicity is indicated in Table- 1.

Table 1: Effect of aqueous extract of *C. papaya* seeds on serum urea and creatinine of rats exposed to cyanide intoxication

	Creatinine (mmol/L)	Urea (mmol/L)
A	1.233±0.18 [a]	15.71±3.3 [a]
B	3.300±0.15 [b]	29.40±1.4[b]
C	1.367±0.18 [a]	16.24±1.1[a]
D	1.533±0.53 [a]	13.83±0.5 [a]
E	1.733±0.06 [a]	19.13±1.7[a]
F	1.333±0.17 [a]	17.12±1.5 [a]

Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at p< 0.05.

The result shows that urea and creatinine concentrations were significantly increased in the serum of group 2 rats (rats given Cyanide only) when compared with the normal control. At the end of the 8th weeks, treatment of cyanide intoxicated rats with 100, 200 and 400 mg/kg of aqueous extract of *C. papaya* (Groups 4, 5 and 6) significantly reduced the level of creatinine and urea in the serum of the treated rats when compared with the negative control not treated.

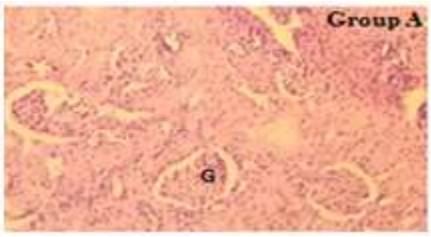
Effect of *C. papaya* seed extract on the electrolytes concentrations in the kidney of rats induced with cyanide toxicity is indicated in Table 2. The result shows that in chloride, bicarbonate and potassium electrolytes tested there was significantly increased group 2 rats (rats given Cyanide only) at the end 8thweek when compared with the normal control. At the end of the 8th weeks, treatment of cyanide intoxicated rats with 100, 200 and 400 mg/kg of aqueous extract of *C. papaya* (Groups 4, 5 and 6) significantly reduced the level of chloride, bicarbonate and potassium electrolytes in the treated rats when compared with the negative control not treated.

Table 2: Effect of aqueous extract of *C. papaya* seed on kidney electrolytes of rats exposed to cyanide intoxication

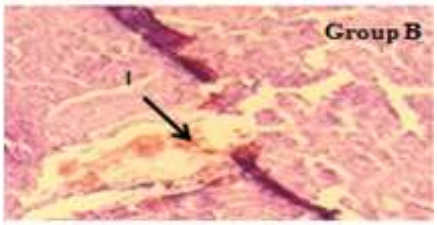
	Bicarbonate	Chloride	Sodium	Potassium
A	19.33±2.5[a]	47.75± 3.9 [a]	105.7±3.2 [a]	3.8±0.3 [a]
B	54.67 ± 4.1[b]	121.29 ± 5.1 [b]	100.3 ± 4.0[a]	10.0 ± 0.25[b]
C	25.67 ± 1.5[a]	58.44 ± 4.9 [a]	119.0± 5.0[a]	3.8 ± 1.4[a]
D	26.67± 2.0[a]	56.4±49.0 [a]	119.7 ± 4.0[a]	4.8 ±0.3[a]
E	24.33 ± 3.2[a]	54.7± 5.0 [a]	125.7 4.0[a]	4.4 ±0.15[a]
F	24.67 ± 2.5[a]	59.72 ±3.7 [a]	113.7 ±5.0 [a]	3.9±1.4[a]

Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at p< 0.05.

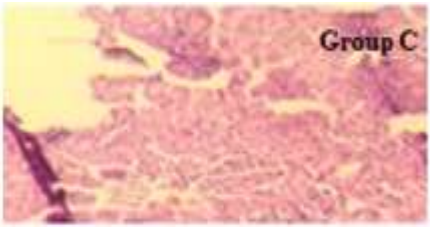
Histological findings: The histological findings from the study of the effect of aqueous extract of *Carica papaya* seeds on the kidney of cyanide intoxicated rats are represented in Plate 1 for Groups A to F..



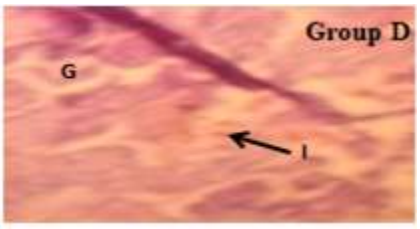
Group A: Rat kidney histology of normal control: showing normal proximal tubular cells (PT) with glomerulus (G) attached to bowman's capsule (BC) (H&E stain x400).



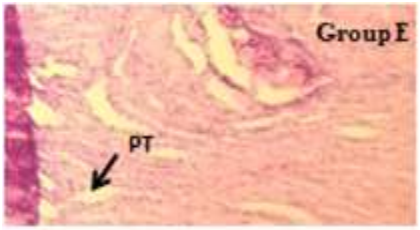
Group B: CN control, showing severe inflammation of glomerulus (G) (H&E stain x 400).



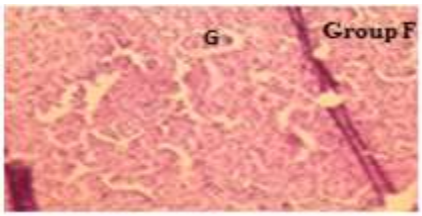
Group C: CN + thiosulphate, showing normal proximal tubular cells (PT) and glomerulus (G) (H&E stain x 400).



Group D: CN+ 100 mg/kg pawpaw, showing mild inflammation of glomerulus (G) (H&E stain x 400).



Group E: CN+200 mg/kg pawpaw, showing mild inflammation of glomerulus (G) and proximal tubular cell (H&E stain x 400).



Group F: CN + 400 mg/kg pawpaw showing proximal tubule (PT). No damage (H&E stain x 400).

Plate 1: Effect of aqueous extract of *Carica papaya* seeds on the kidney of cyanide intoxicated rats are represented in Plate 1 for Groups A to F.

Medicinal plants make up an important natural wealth of the country by playing a key role in primary health of mankind.(Okochi *et al*., 1999)*Carica papaya* is a known medicinal plant reported to possess health benefits against many diseases (Shaban *et al.,* 2021). This health benefits are attributed to the presence of many bioactive phytochemicals in various parts of the plant including the seeds. *C. papaya* seed is used as a natural medicine, it is recognized for its antioxidant and hypolipidemic activity (Kumar and Devi, 2017). Cyanide is a very poisonous chemical and previous studies (Kadiri *et al.* 2020; Akinmoladun *et al.,* 2021) have indicated that sub chronic and chronic administration can lead to toxicity.

Assessment of the levels of excretory metabolites such as urea, and creatinine are generally used methods in the assessment of renal function (Kadiri, 2018). Cyanide has been confirmed to cause kidney damage in various organisms. The result from this current study is in line with these findings as renal toxicity was indicated by the observed increase in creatinine and urea concentrations in the serum. However treatment of cyanide intoxicated rats with *C. papaya* restored the concentration of creatinine to near normal level. The reduction in creatinine and urea concentrations is an indication that the *C. papaya* must have had a protective effect due to its antioxidant properties which has been investigated in earlier studies carried out on *C. papaya* (Madinah *et al.*, 2015). Measurement of electrolytes (Na^+, K^+, CO_3^- and Cl^-) are used as potential biomarkers of chemical exposure and effects (Kanadi *et al.,* 2019). The maintenance and balance of electrolytes is important for normal cellular function. Electrolyte imbalance can occurif there is an abnormal increased or decreased in electrolyte levels in toxin-exposed animals (Nwankpa *et al.,* 2018). The imbalance might obstruct proper nerve conduction and lead to death (Kanadi *et al.,* 2019). In this study, the increased levels of serum Na^+, K^+, $HCO_3^-$and Cl^- corroborated the observed increases in the serum levels of urea and creatinine. The kidney is responsible for the regulation of various electrolytes and maintenance of homeostasis, for example Na^+ and K^+ are major components of extracellular and intracellular fluids respectively and these physiological state are regulated by the kidney, therefore the elevated levels of these electrolytes could indicate renal dysfunction particularly at glomerular and tubular levels. Also, HCO_3^- and Cl^- are reabsorbed in the proximal tubule and therefore the high level of these electrolytes could imply renal damage at the tubular level. However the serum levels of all the electrolytes studied were restored towards normal with administration of aqeous extract of *Carica papaya* seed. This findings is in accordance with the study carried out by Kanadi *et al.,* 2019 where *Carica papaya* seeds extract was able to reverse high levels of kidney electrolytes.

In conclusion the present study has demonstrated that administration of aqueous seed extract of ripe *Carica papaya* fruits to rat may effectively prevent cyanide-induced nephro-toxicity.

REFERENCE

Akinmoladun, AC; Adelabu, AA; Saliu, IO; Adetuyi, AR; Olaleye, MT. (2021). Protective properties of *Spondias mombin Linn* leaves on redox status, cholinergic dysfunction and electrolyte disturbance in cyanide-intoxicated rats. *Sci. Adv.*104 (2): 1-17

Asagba, SO; Ezedom T; Kadiri HE, (2015). Influence of Farmyard manure and some morphological and biochemical parameters of cowpea (*Vignaunguiculata*) seedling grown in cadmium-treated soil. *Env. Sci.Poll.Res*. 24(30):23735-23743

Bartels,H; Bohmer, M. (1972). In vitro determination of creatinine and urea. *Clin. Chem.* 2(37): 193 - 197

Coentrao, L; Mourad, D; (2011). Acute cyanide poisoning among jewelry and textile industry workers.*Am. J. Emerg. Med.* 29(1):78-81

Desharnais, B; Huppé, G; Lamarche, M; Mireault, P; Skinner, CD; (2012). Cyanide quantification in post-mortem biological matrices by headspace GC–MS. *Forensic Sci. Int.* 222(1-3): 346–351.

Joachim, MD; Siri, AA. (2021). Nutraceutical value of *Carica papaya*: A review, *Sci. Afr*. 13(1): 56-62

Kadiri, HE; Okoro, I; Ichipi-Ifukor, P. (2020). *Tetrapleuratetraptera* Fruit Protects Against

Cyanide Induced Toxicity in Rats. *Iraqi J. Sci.* 61(10): 2504-2514

Kanadi, MA; Wudil, AM; Alhassan, AJ; Ngwen, AL; Yaradua, AI; Nasir, A. (2019) Acute toxicity studies and Phytochemical constituents of different solvents extracts of *Carica papaya seeds*. *Asian J. Plant Sci.* 2(3):1-9.

Kumar, NS; and Devi, S. (2017). The surprising health benefits of *papaya* seeds: A review. *Int. J. Res. phytochem. Pharmacol*. 6(1):424–429

Kadiri, HE; and Asagba, SO. (2015). The biochemical effects of cyanide on the activity of the transaminases and Alkaline phosphatase in broilers (*Gallus domesticus*). *American J.Biochem. 5* (2):23-29.

Kadiri, HE. (2018). The ameliorating effects of honey on some biochemical parameters on rats exposed to cyanide.*Biokemistri*, 30(1): 13-20

Madinah, N; Nozmo, M; and Ezekiel, I. (2015). The protective effects of aqueous extract of *Carica papaya* seeds in paracetamol induced nephrotoxicity in male wistar rats. *Afr. Health Sci*. 15(2): 25-31

Nwankpa, P; Etteh, CC; Ekweogu, CN; Chikezie, PC; Chukwuemeka, OG; Egwurugwu, JN. (2018).Effect of ethanol root and leave extracts of *Sida acuta* on some kidney function Indices and electrolytes in Albino Wistar rats. *Int. J. Curr. Microbiol. Appl. Sci*,7 (2): 2759-2766

Okochi, VI; Gbenle, GO; Kazeem, A; Fagbenro-Beyloku, AF; Igbodudu; Arukwe, U (1999). Effect of water extract of *Tetrapeura tetraptera* (Aidon) on Hematological and Biochemical parameters in Rats infected with *Trypanosomabrucei. Nig. Quart. J. Hosp. Med*. 9(1):66-70.

Patrick, JS; Christina, LK; Seth, TG; Peter, H; Claire, MM; Kristen, MP; Carol, LS; Edgar, JW. (2016). Characterization of a Mouse Model of Oral Potassium Cyanide Intoxication: *Int. J. Toxicol.* 35(5**)**:584-603.

Satpute, R; Hariharakrishnan, J; Bhattacharya R. (2010). Effect of alpha-ketoglutarate and N-acetyl cysteine on cyanide-induced oxidative stress mediated cell death in PC12 cells. *Toxicol. Ind Health*, 26(1):297-308.

Shaban, NZ; El-Kot, SM; Awad, OM; Hafez, AM; Fouad, MG. (2021). The antioxidant and anti-inflammatory effects of *Carica papaya Linn*. Seeds extract on CCl4-induced liver injury in male rats.*BMC Complement Altern. Med*. 21 (1): 1-15

Tara, BH; Patrick, CN; Alyssa, EW; Sari, BM; Mathew, B; Gerry, RB; Vikhhyat, SB; (2019). A review on ingested cyanide: Risks, chemical presentation, diagnostics and treatment challenges: *J Med Toxicol*, 15(2): 128-133.

Weatherburn, MW. (1967) Urease-Berthelot Colorimetric Method for in Vitro Determination of Urea. *Anal. Chem*. 39(1): 971-974.

Zhang, Y; Gan, R; Li, S; Zhou, Y; Li, A; Xu, D; and Li, H. (2015). Anti-oxidant phytochemicals for the protection and treatment of chronic diseases. *Molecules*, 20(12): 21138-21156.