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Positive Stimulatory Potentials of Coconut (*Cocos nucifera L.*) Juice Extract on *in vivo* Antioxidants, Renal Function and Lipid Profile of Male Wistar Rats

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Authors' contributions

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

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ABSTRACT

Coconut juice is a natural drink from coconut fruit. This study was aimed at evaluating its positive potential on biochemical indices. Fresh coconut fruits were de-dshelled and washed. The cotyledon was broken to extract the water which was used in blending the fruits. The extract was filtered and the filtrate was collected in a vial. Twenty healthy male Wistar rats weighing 160 -180 g, were grouped into two groups of ten rats each and were treated as follows for four weeks. Group A: control rats received oral dose of 2 mL/kg body weight of distilled water once daily for 28 days, and group B: received oral dose of 2 mL/kg body weight of coconut juice extract once daily for 28 days, both groups were, however, allowed free access to feed and water *ad-libitum*. The animals were weighed before and on completion of the experimental protocol. Blood was also collected via

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cardiac puncture and used for renal function and lipid profile assay, kidneys were excised and weighed, homogenized and the supernatant was used for antioxidant enzyme evaluation. Findings showed that there was no significant change ($p>0.05$) in the kidney-to-body weight ratio and renal function indices. Significant reduction ($p<0.05$) was seen in cholesterol, triglycerides, LDL but with an increase ($p<0.05$) in HDL. Antioxidant enzymes were significantly increased ($p<0.05$). The study concludes that coconut juice extract has positive stimulatory potentials on antioxidants, renal functions and lipid parameters of wistar rats.

Keywords: Coconut juice extract; antioxidants; lipid profile; renal function.

1. INTRODUCTION

Foods rich in natural antioxidants can be used as a subterfuge to reduce morbidity and mortality primarily due to oxidative stress [1] and the prevention of degenerative diseases [2] such as diabetes, cancer, rheumatoid arthritis, Parkinson's, Alzheimer's, and osteoporosis. “Antioxidants are also potent chemical agents in mitigating the ageing process. Reactive oxygen species (ROS) and other free radicals generated during cellular metabolism are very unstable and react rapidly with other cellular metabolites in the body, leading to cell cellular injury and increased apoptosis” [3,4]. “Epidemiological evidence has implicated excessive free radicals and associated oxidative stress arising from an imbalance between prooxidants and antioxidants as the primary factor in nephrotic diseases and kidney damage” [5,6]. “In the food industry, oxidation is a major cause of deterioration in food, these deteriorations often affect the nutritional value, and organoleptic properties of the food, leading to undesirable off-flavours and potentially toxic reaction products” [7]. Thus, antioxidants play a vital role in both food systems and in the human body to reduce oxidative stress. Renal function is vital for homeostasis, as the kidneys play important pleiotropic roles including removal of metabolic waste products and maintenance of water-electrolyte balance and blood pressure. Yan et al. [4] posited that “synthetic antioxidants has been implicated to threaten human health, antioxidants from natural sources have attracted more attention”. Coconut fruit, botanically called *Cocos nucifera, L* is a member of the Arecaceae family, it provides several health benefits outside its nutritional content. Coconut fruit juice is a natural and nutritious drink from the coconut fruit harvested from the coconut palm tree widely grown and cultivated in tropical countries like Nigeria, Indonesia, India, and the Philippines. Coconut fruit and fruit juice are rich in essential vitamins, amino acids, minerals, enzymes and growth hormones [8-10]. These documented food values make Coconut fruit and juice therapeutic in nature as it help maintain osmotic pressure inside and outside the cell [11,12], and Prevent oxidative stress via its antioxidant potential [4,13], positive inhibitory ability in lipid peroxidation [14], improved lipid profile levels [15], improved blood pressure [16], cardioprotective potentials [17,18], anti-inflammatory [19], antidiabetic [1], haemoglobin boasting potentials and as diarrhoea therapy [20]. With the plethora of scientific evidence validating the potential health benefits of coconut fruits and juice, this present study is therefore aimed at investigating the positive stimulatory potentials of coconut juice extract on *invivo* antioxidants and renal function and lipid profile of male Wistar rats.

2. MATERIALS AND METHODS

2.1 Sample Preparation

Samples of fresh *Cocos nucifera L* fruits were purchased from a local fruit market in Amasoma, Bayelsa State, Nigeria. The fruit was identified and authenticated at the Department of Plant Science and Biotechnology, Niger Delta University, Amasoma. The shell of the coconut fruit was removed and washed properly to remove debris and avoid contamination. The cotyledon was broken to extract the water which was later used in blending the fruits. The extract was filtered with Whatman No. 1 filter paper and the resulting filtrate was collected in labelled vials and kept in a refrigerator at $-4℃$ until use.

2.2 Experimental Animals

Twenty (20) healthy adult male Wistar albino rats weighing 160-180g were used for this study. They were obtained from the animal house unit of the Department of Pharmacology, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria, and were maintained under standard housing conditions (photoperiod: 12h natural light and 12h dark). The animals were acclimatized for

two weeks and were fed pelletized growers' feed and were exposed to clean tap water throughout the period of the study.

2.3 Experimental Design

The animals were grouped into two groups of ten (10) rats each in a standard plastic rat cage and were treated as follows according to their body weights for four (4) weeks. Group A: control rats received 2 mL/kg body weight of distilled water once daily, and group B: the treatment group received 2 mL/kg body weight of the coconut juice extract once daily.

2.4 Sample Collection

At the end of the experimental period, and 12 hours after the last oral drug administration, the animals were re-weighed after which they were anaesthetized in a chloroform chamber and blood samples collected via cardiac puncture into plain sample bottles. The blood samples were allowed to stand for 20 minutes for coagulation to take place, afterwards, the blood samples were centrifuged at 2000 rpm for 10 minutes and the supernatant (serum) was collected and stored in the refrigerator before biochemical assay. Furthermore the kidneys were quickly excised and weighed, after which they were homogenized with TRIS buffer and centrifuged at 3000 rpm for 20 minutes, the supernatant was collected and stored in the refrigerator until analysis.

2.5 Changes in Body Weight

Rats in all groups were weighed on the first day and at the end of experimental period. The percentage change in body weight was calculated using the expression below:

$$\%\ change\ in\ body\ weight\ = \frac{final\ body\ weight - initial\ body\ weight}{initial\ body\ weight} \times 100\%$$

2.6 Kidney as Ratio of Body Weight

Kidneys were removed and weighed immediately. The kidney ratio was calculated as a percentage using the expression below:

$$\frac{weight\ of\ kidney\ (g)}{body\ weight\ (g)} \times 100\%$$

2.7 Assay Kits/Reagents

Assay kits for cholesterol, triglyceride, low density lipoprotein cholesterol, high density lipoprotein cholesterol, superoxide dismutase, glutathione s-transferase and catalase are product of Biosystem, Biosystems S.A., Costa Brava, Barcelona, Spain. Assay kits for blood urea nitrogen, creatinine and uric acid are products of Fortress Diagnostic Ltd, United Kingdom. All other reagents were of analytical grade and standard suppliers.

2.8 Biochemical Estimations of Lipid Profile

The biochemical estimation of total cholesterol and triglyceride were determined by Colorimetric method as described by Ochei and Kolhatkar [21], low-density lipoprotein cholesterol and high-density lipoprotein cholesterol were quantitatively determined spectrochemically by adopting the method described by Grove [22] and Burstein et al. [23] respectively, the ratio of LDL to HDL was determined from the expression stated below Kpomah and Arhoghro [24].

$$The\ ratio\ of\ LDL\ to\ HDL\ (Atherogenic\ index) = \frac{Level\ of\ LDL}{Level\ of\ HDL}$$

2.9 Biochemical Estimation of Antioxidant Enzymes and Renal Function Parameters

SOD was assayed by the method described by Misra & Fridovich [25]. GST activity was assayed by the method of Habig et al. [26]. CAT activity was quantitatively determined by the method of Cohen et al. [27]. BUN was evaluated by the modified Berthelot method according to Tobacco et al. [28]. CRT was assayed by the Colorimetric kinetic method of Bartels et al. [29]. UA was assessed using the enzymatic Colorimetric method of Duncan et al. [30].

2.10 Statistical Analysis

Data were expressed as Mean ± Standard Deviation for ten (10) replicate determinations. Mean differences between the treated group and the control group were compared using student's t-test. Data were analyzed using SPSS version 16 for windows (IBM Corp, USA). $p<0.05$ was set as the level of significance. The charts were plotted using Graphpad Prism 8.

3. RESULTS

3.1 The Effect of Coconut Juice Extract on Changes in Body Weight

The results of the effect of coconut juice extract on changes in body weight is depicted in Fig. 1.

The oral administration of the coconut juice extract caused significant changes ($p < 0.05$) on the final body weight (FBW) and percentage changes in body weight (CBW), however, non-significant changes ($p > 0.05$) was not observed with respect to kidney weight (KW) and relative kidney weight (RKW).

3.2 The Effects of Coconut Juice Extract on the Lipid Profile of Male Wistar Rats

The results of the effect of coconut juice extract on lipid profile is shown in Fig. 2. The result indicated significant reduction ($p < 0.05$) in the concentrations of total cholesterol (T.Chol), triglycerides (TG), low density lipoprotein cholesterol (LDL) and the ratio of LDL/HDL. The coconut juice extract also brought about significant increase ($p < 0.05$) on the value of high density lipoprotein cholesterol (HDL).

3.3 The Effect of Coconut Juice Extract on Renal Function of Male Wistar Rats

The effect of coconut juice extract on renal function of male Wistar rats in mg/dL after 28 days treatment regimen is presented in Fig. 3. The results obtained indicated a non-significant change ($p > 0.05$) on the concentrations of blood urea nitrogen (BUN), creatinine (CRT) and uric acid (UA).

3.4 The Effect of Coconut Juice Extract on Antioxidant Enzymes of Male Wistar Rats

The effect of coconut juice extract on antioxidant enzymes of male Wistar rats in unit/mg tissue is presented in Fig. 4. Findings from the result indicated a significant increase ($p < 0.05$) in concentrations of antioxidant parameters of superoxide dismutase (SOD), Glutathione-S-transferases (GST) and catalase (CAT)

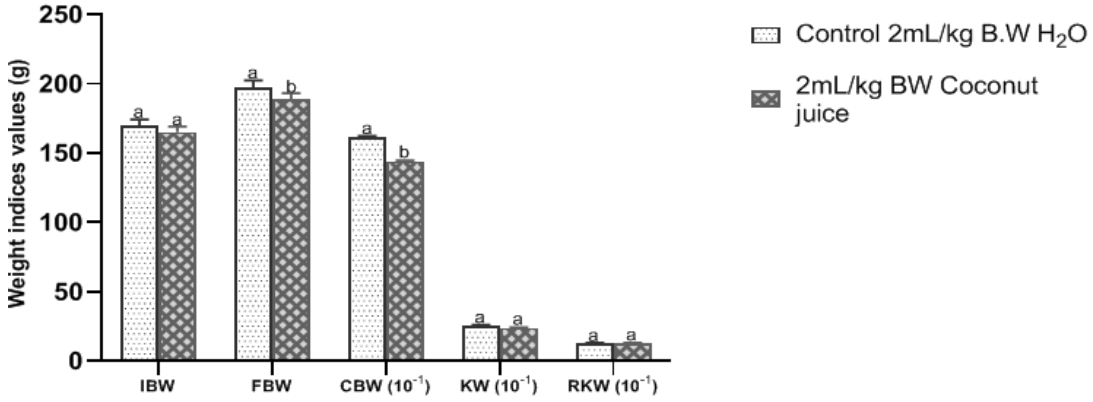

Fig. 1. Effect coconut juice on body weight indices (IBW- Intial Body Weight, FBW- Final Body Weight, %CBW- %Change in Body Weight, KW- Kidney Weight, RKW- Relative Kidney Weight)
Column of bars of same parameter having same letter identification are not significantly different (p>0.05) while those with different letters are significantly different (p>0.05)

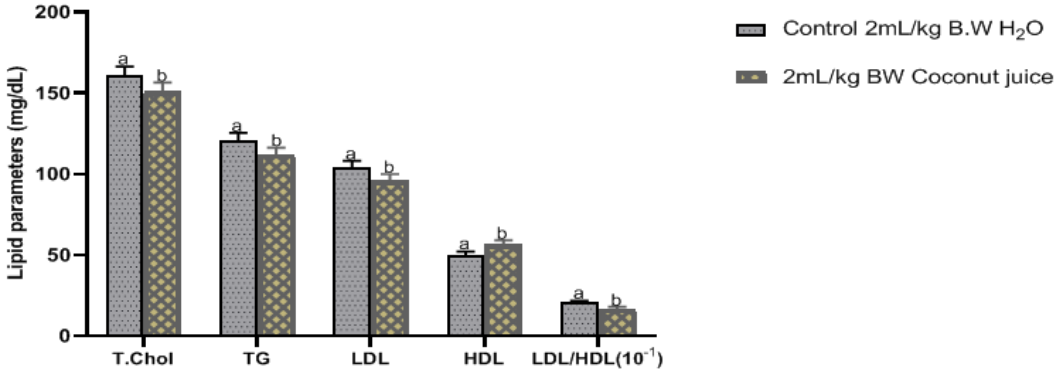

Fig. 2. Effect of coconut juice extract on lipid profile of male wister rats
Column of bars of same parameter having different letters notation are significantly different (p>0.05)

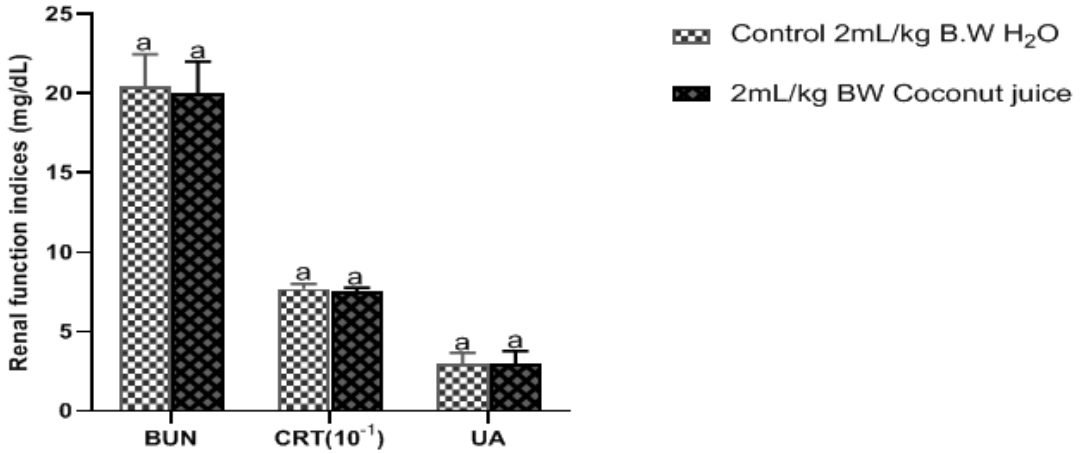

Fig. 3. The Effect of coconut juice extract on kidney function parameters of male wistar rats (BUN-Blood Urea Nitrogen, CRT-Creatinine, UA-Uric Acid)

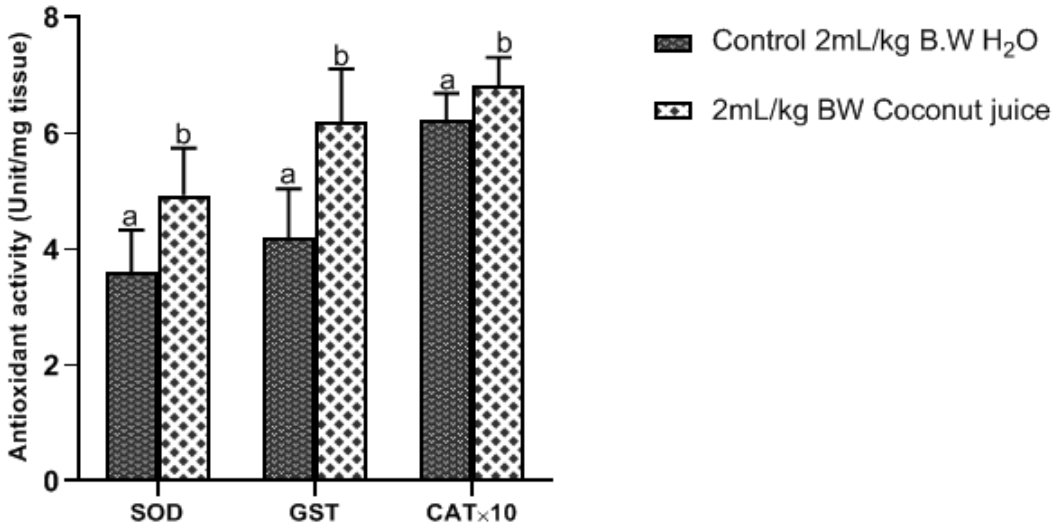

Fig. 4. Effect of coconut juice extract on antioxidant enzymes of kidney of male wistar rats

4. DISCUSSION

"Change in body weight is a subtle index of the general health status and well-being of animals" [31,32]. The results obtained showed that all rats in the respective groups experienced an increase in body weight after the treatment regimen. These increases in body weight were more pronounced in the control group with a 16.12 % increase and 14.4 % for the coconut water extract treated group. Coconut water although low in calories [33] is rich in bioactive enzymes like acid phosphatase, dehydrogenase, diastase, peroxidase and RNA polymerases [1], these enzymes can boost metabolic activities like digestion, the increased metabolism is directly proportional to the rate at which fat and fat-associated nutrients burn [34], hence the difference between the percentage increase between among the control group and the coconut extract treated groups but could be seen to cause an enhanced and optimal serum lipid profile of the Wistar rats when compared to the control group. "Levels of lipid parameters, such as total cholesterol, triglyceride, low density lipoprotein cholesterol, and high density lipoprotein cholesterol are key indices of cardiovascular health" [35]. "The oral route administration of the coconut juice extract caused a significant decrease ($p<0.05$) in total cholesterol, triglyceride, LDL and LDL/HDL with a concomitant significant increase ($p<0.05$) in HDL levels. This positive stimulation potential of lipid parameter induced by the coconut juice extract has been linked with reduced cardiovascular risk" [36]. "Weight gain is a function of excessive adipogenesis, which is often regulated by the sterol regulatory element-binding proteins

(SREBP) which are a family of transcription factors that mediate lipid homeostasis through its action in the expression of successive enzymes needed for the endogenous synthesis of cholesterol, fatty acids, triacylglycerol and phospholipids. SREBP expression results in an accumulation of lipid droplets, cholesterol homoeostasis, and an increase in high levels of the serum lipid profile" [37]. Lazic et al., [38] posited that "changes in organ weight of animals are a positive indicator of chemically induced organ damage. The effect of the coconut water extract from the study had no significant change ($p > 0.05$) in the relative weight of the kidneys when compared to the control group, an indication of proportional growth with no adverse or toxicity effect".

"The kidneys play a vital role in the everyday metabolism of the cell via its role in the excretion of waste products and toxins like urea, uric acid and creatinine, metabolic regulation of extracellular fluid volume, serum osmolality and electrolyte balance, coupled with the production of hormones like erythropoietin and 1,25 dihydroxy vitamin D and renin" [39,40]. "Evaluation of renal function activity is key in the diagnosis, management and treatment of patients with kidney disease and pathologies affecting renal function. Urea, the principal nitrogenous waste formed during protein metabolism and whose concentration in blood is dependent upon the relationship between its production and excretion, increased value above the normal range may indicate kidney disease, shock, dehydration, diabetes, acute myocardial infarction while a decreased value below normal may portend liver failure, impaired absorption and overhydrating" [41]. Creatinine is a breakdown product of creatine phosphate, which occur primarily as a result of muscle metabolic activities and is then excreted by glomerular filtration during normal regular renal function. Higher values of creatinine above 1.5 mg/dL is an indication of impairment in liver function. Uric acid is a breakdown metabolite from purine metabolism, abnormally high levels of uric acid is associated with a condition called gout. The non-significant changes (p≥0.05) in values of urea, creatinine and uric acid, when compared to the control, is a positive indication that the coconut water extract had no adverse effect on the renal function indices of the rats.

Cells of organisms are fortified with antioxidant defense systems that mitigate the effect of relative oxidative stress induced by exposure to toxicants. Adwas et al. [6], posited that "oxidative stress occurs when the balance between reactive oxygen species (ROS) formation and detoxification favours an increase in ROS levels leading to disturbed cellular function. ROS causes injury to cellular macromolecules leading to lipid peroxidation, nucleic acid, and protein alterations". "The formation of lipid peroxidation and the subsequent alteration of nucleic acid and protein are primary etiological factors in the initiation and progression of various metabolic and neurodegenerative diseases" [42]. "Oxidative stress is associated with disrupted redox regulation mechanism and cellular signalling pathways that can lead to the formation of numerous types of cancer cells and oncogenic initiation and propagation" [43,44]. Antioxidants in cells include catalases, superoxide dismutases (SOD), and glutathione peroxidases (GPX), their induction is usually in response to specific toxicants and pollutants that can induce oxidative stress [45] (Azab et al., 2019). SOD scavenges superoxide radicals converting them to H_2O_2 [32]. GPx brings about the reduction in levels of hydrogen peroxide, lipid hydroperoxides and other organic hydroperoxides (Azab et al., 2019). "Glutathione-S-transferases (GST) a representative of the major class of detoxifying enzymes [46], which form a family of multifunctional proteins implicated in the cellular detoxification of cytotoxic and genotoxic xenobiotic compounds and the protection of tissues against oxidative damage" [47,48]. Catalase is an enzyme present in virtually all aerobic cells, it shields such cells from oxidative stress by catalyzing the speedy decomposition of hydrogen peroxide in two forms of reactions depending on its peroxidative and catalytic activities [49]. The oral administration of coconut juice extract, however, had a significant increase in the level of antioxidant enzymes studied, as evidenced by the increased value of SOD, GST and CAT activity. These increases may be attributed to the antioxidant boasting capacity of phytochemicals and nutritional ingredients present in coconut juice extract [2,17]. These nutrients include the amino acid L-arginine which from literature can significantly reduce the rate of generation of free radicals, increase glutathione peroxidase (GPx) activity and with potent antioxidant activity [1,18], the sulphur containing amino acid methionine, is a key player in the biosynthesis of glutathione. Coconut juice extract is also rich in ascorbic acid, which decreases lipid peroxidation in rats [18]. Other active components in coconut juice extract include cytokines, selenium, zinc, manganese and

copper [1]. Cytokines is a potent antioxidant against free radical-induced cell damage [19]. Selenium is one of the micronutrients that form the enzyme GPx [50-53].

5. CONCLUSION

Findings from this study established that the oral administration of 2 mL/kg body weight of coconut juice extract administered for twenty-eight days had positive stimulatory potential on cell antioxidants (SOD, GST and CAT). Boast in antioxidants has been shown in literature to prevent oxidative stress, the primary cause of most metabolic and neurodegenerative diseases. Findings from this study also indicated that the coconut juice extract had a positive health-promoting effect on lipid profile with no attendant adverse effect on renal function as indicated by no significant change ($p<0.05$) in values of urea, uric acid and creatinine.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All animal experimental protocols were approved by the Committee of Scientific Ethics at Niger Delta University, Wilberforce Island, and were carried out by its guidelines for animal use.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Zulaikhah ST. Health benefits of Tender Coconut Water (TCW). International Journal of Pharmaceutical Sciences and Research. 2019;10(2):1-9.
2. Muhammad NE. Coconut water vinegar ameliorates recovery of acetaminophen-induced liver damage in mice. BMC Complementary and Alternative Medicine. 2018;18:195
3. Shahidi F, Zhong Y. Novel antioxidants in food quality preservation and health promotion. European Journal of Lipid Science Technology. 2010;112:930–940.
4. Yan Y, He F, Li Z, Xu R, Li T, Su J, Liu X, Zhao M, Wu W. The important role of apolipoprotein A-II in ezetimibe driven reduction of high cholesterol diet-induced atherosclerosis. Atherosclerosis. 2018; 280:99-108.
5. Arhoghro EM, Kpomah DE, Uwakwe AA. Curative potential of aqueous extract of lemon grass (*Cymbopogon Citratus*) on cisplatin induced hepatotoxicity in albino wistar rats. Journal of Physiology and Pharmacology Advances. 2012;2(2):282-294.
6. Adwas AA, Elsayed ASI, Azab AE. Oxidative stress and antioxidant mechanisms in the human body. Journal of Applied Biotechnology Bioengineering. 2019;6(1):43–47.
7. Dong SY, Zeng MY, Wang DF, Liu ZY, Zhao YH, Yang HC. Antioxidant and biochemical properties of protein hydrolysates prepared from Silver carp (*Hypophthalmichthys molitrix*). Food Chemistry. 2008;107:1483–1493.
8. Johnkennedy N, Joy DN, Ndubueze EH, Melvina N, Richard E, Vitus O. Antioxidant and cardioprotective effect of coconut water against doxorubicin induced cardiomyopathy. Journal of Krishna Institute of Medical Sciences University. 2013;2:37-41.
9. Lukose RM. The chemical composition of tender coconut (*Cocos Nucifera L.*) water and coconut meat and their biological effect in human body. International Journal of Green and Herbal Chemistry. 2013;2(3):723-9.
10. Oluwarotimi EA, Odubanjo VO, Adesanmi JI, Alo OJ, Aminu RS, Faturoti IE. Antioxidant capacity and effect of coconut water on $AlCl_3$ amnesic-induced drosophila melanogaster. Journal of Analytical Techniques and Research. 2021;3:1-13.
11. Fife B. Coconut water for health and healing. USA: Piccadily Books, Ltd; 2008.
12. Geetha V, Bhavana KP, Chetana R, Gopala Krishna AG, Suresh Kumar G. Studies on the composition and in-vitro antioxidant activities of concentrates from coconut testa and tender coconut water. Journal of Food Processing & Technology. 2016;7(5):1-5.
13. Sunil L, Prakruth A, Prasanth Kumar PK, Gopala Krishna AG. Coconut Water - A Nature's miracle health drink: Chemistry, health benefits, packaging, storage, and technologies: A review; 2020.

Available:https://www.researchgate.net/profile/SunilL/publication/346773633.
Assess on 11/06/22

14. Zulaikhah ST, Anies Ari S, Santosa E. Effects of tender coconut water on antioxidant enzymatic superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and lipid peroxidation in mercury exposure workers. International Journal of Science and Research. 2015;4(12):517-524.
15. Radenahmad N, Sawangjarn K, Mitranun W, Sayoh. Beneficial effects of young coconut juice feeding on the lipid, renal and liver profiles, in ovariectomized rats: Preliminary novel findings. Songklanakarin Journal of Science and Technology. 2016;38(1):57-65.
16. Farapti SS, Parlindungan S. Effect of tender coconut water on systolic and diastolic blood pressure in prehypertensive women. Health Science Indones. 2013; 4(2):64-68.
17. Agbafor SO, Elom ME, Ogbanshi AO, Oko AJ, Uraku VUO, Nwankwo BA, Ale Obiudu KI. Antioxidant property and cardiovascular effects of coconut (*Cocos nucifera*) water. International Journal of Biochemistry Research & Review. 2015;5(4):259-263.
18. Lima E, Sausa C, Meneses L, Ximenes N, Junior MA, Vasconcelos G, Lima N, Patrocinio M, Macedo D, Vasconcelos S. *Cocos nucifera* (L.) (Arecaceae): A phytochemical and pharmacological review. Brazilian Journal of Medical and Biological Research. 2015;48(11):953-964.
19. Ajeigbe KO, Ndaman ZA, Amegor OF, Onifade AA, Asuk AA, Ibironke GF, Olaleye SB. Anti-nociceptive and anti-inflammatory potential of coconut water (*Cocos Nucifera L.*) in rats and mice. Australian Journal of Basic and Applied Sciences. 2011;5(9):1116-1122.
20. Mulyanti ED, Kis D, Noor W. Effectiveness of tender coconut water (*Cocos nucifera*) against parasitemia index and haemoglobin levels in malaria infection. International Journal of Pharmaceutical Sciences and Research. 2016;7(9):3873-3876.
21. Ochei J, Kolhartkar A. Enzymology. In: Medical laboratory science: Theory and practice. Tata McGraw-Hill Publishing Company Limited. New Delhi. 2008:163-175.
22. Grove TH. Effect of reagent pH on determination of high density lipoprotein cholesterol by precipitation with sodium phosphotungstate-magnesium. Clinical Chemistry. 1979;25(4):560-564.
23. Burstein M, Schoinick HR, Mortin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. Journal of Lipid Research. 1970;11(6):583-595.
24. Kpomah ED, Arhoghro EM. Effects of doses of *Bryophylum pinnatum* and glibenclamide on serum glucose and lipid profile in alloxan-induced diabetic rats. Indian Journal of Drugs and Diseases. 2012;1(5):124-128.
25. Misra HP, Fridovich I. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. Journal of Biological Chemistry. 1972;247(10):3170-3175.
26. Habig WH, Pabst MJ, Jakoby WB. Glutathione S-transferases. The first enzymatic step in mercapturic acid formation. Journal Biological Chemistry. 1974;249(22):7130-139.
27. Cohen GD, Dembiec C, Marcus J. Measurement of catalase activity in tissue extracts. Analytical Biochemistry. 1970;34:30-38.
28. Tobacco A, Meiattini F, Moda E, Tarli P. Simplified enzymic/colorimetric serum urea nitrogen determination. Clinical Chemistry. 1979;25:336–337.
29. Bartels H, Bohmer M, Heuerli C. Micro-determination of creatinine. International Journal of Clinical Chemistry. 1971;32:81-85.
30. Duncan P, et al. A candidate reference method for uric acid in serum. II. Inter laboratory testing. Clinical Chemistry. 1982;28:291.
31. Arthur FKN, Woode E, Terlabi EO, Larbie C. Evaluation of acute and subchronic toxicity of *Annona muricata* (Linn.) aqueous extract in animals. European Journal of Experimental Biology. 2011;1(4):115-124.
32. Arhoghro EM, Kpomah ED. Alanine aminotransferase and aspartate aminotransaminase activities in wistar rats fed with *Musa paradisiaca* (plantain) stem pulp in aluminium chloride induced hepatic oxidative stress. Journal Applied Sciences and Environmental Management. 2022;26(6):1057-1062.
33. Mohamad NE, Yeap SK, Ky H, Ho WY, Boo SY, Chua J, Beh B, Sharifuddin SA,

Long K, Alitheena NB. Dietary coconut water vinegar for improvement of obesity-associated inflammation in high-fat-diet-treated mice. Food & Nutrition Research. 2017;61:1368322.
Available:https://doi.org/10.1080/16546628.2017.1368322

34. Vaishnavi S. Can I have tender coconut water daily? Acta Scientific Nutritional Health. 2019;3(10):89-90
35. Chu P, Pandya A, Salomon JA, Goldie SJ, Hunink MGM. Comparative effectiveness of personalized lifestyle management strategies for cardiovascular disease risk reduction. Journal American Heart Association. 2016;5:e002737.
36. Hedayatnia M, Asadi Z, Zare-Feyzabadi R, Yaghooti-Khorasani M, Ghazizadeh H, Ghaffarian-Zirak, R, Nosrati-Tirkani A, Mohammadi Bajgiran M, Rohban M, Sadabadi F, Rahimi HR. Dyslipidemia and cardiovascular disease risk among the MASHAD study population. Lipids Health Disease. 2020;19(1):1-1.
37. Ahn TG, Yang G, Lee HM. Molecular mechanisms underlying the anti-obesity potential of prunetin, an O-methylated isoflavone. Biochemical Pharmacology. 2013;85(10):1525–1533.
38. Lazic SE, Semenova E, Williams DP. Determining organ weight toxicity with Bayesian causal models: Improving on the analysis of relative organ weights. Scientific Reports. 2020;10:6625.
Available:https://doi.org/10.1038/s41598-020-63465-y
39. Nwankpa P, Ekweogu CN, Egwurugwu JN, Chukwuemeka OG, Etteh CC, Ugwuezumba PC, Emengagha FC. Assessment of kidney function indices in male albino wistar rats administered ethanol stem extract of *Dennettia tripetala* (pepper fruit). Biochemical Pharmacology. 2018;7:242.
DOI: 10.4172/2167-0501.1000242
40. Tejchman K, Kotfis K, Sienko J. Biomarkers and mechanisms of oxidative stress-last 20 years of research with an emphasis on kidney damage and renal transplantation. International Journal of Molecular Sciences. 2021;22(15):8010.
Available:http://dx.doi.org/10.3390/ijms22158010
41. Zulaikhah ST, Sampurna S. Tender coconut water to prevent oxidative stress due to mercury exposure. IOSR Journal Environmental Science Toxicology and Food Technology. 2016;10:35–38.
42. Azab AE, Albasha MO, Elsayed ASI. Prevention of nephropathy by some natural sources of antioxidants. Yangtze Medicine. 2017;1:235-266.
43. Gill CI, Boyd A, McDermott E, McCann M, Servili M, Selvaggini R, Taticchi A, Esposto S, Montedoro G, McGlynn H, Rowland I. Potential anti-cancer effects of virgin olive oil phenols on colorectal carcinogenesis models *in vitro*. International Journal of Cancer. 2005;117(1):1-7.
44. Miranda-Vilela AL, Portilho FA, de Araujo VG, Estevanato LL, Mezzomo BP, Santos F, Lacava ZG. The protective effects of nutritional antioxidant therapy on ehrlich solid tumour-bearing mice depend on the type of antioxidant therapy chosen: Histology, genotoxicity and haematology evaluations. Journal of Nutritional Biochemistry. 2011;(11):1091-8.
45. Cheung CC, Zheng GJ, Li AM, Richardson BJ, Lam PK. Relationships between tissue concentrations of polycyclic aromatic hydrocarbons and antioxidative responses of marine mussels, *Perna viridis*. Aquatic Toxicology. 2001;52(3-4):189-203.
46. Hayes JD, Pulford DJ. The glutathione S-transferase supergene family: Regulation of GST and the contribution of the isoenzymes to cancer chemoprotection and drug resistance. Critical Reviews in Biochemistry and Molecular Biology. 1995;30(6):445-600.
47. Pickett CB, Lu AY. Glutathione S-transferases: gene structure, regulation, and biological function. Annual Reviews Biochemistry. 1989;58:743-64.
48. Christophe M, Perfusion A, Pascal B. Analgesic, non-ulcerogenic and antioxidant activities of the aqueous stem bark extract of *Morinda lucida* (rubiaceae) in mice. Journal of Applied Life Sciences International. 2017;11(3):1–10.
49. Al-Abrash AS, Al-Quobaili FA, Al-Akhras GN. Catalase evaluation in different human diseases associated with oxidative stress. Saudi Medical Journal. 2000;21(9):826-30.
PMID: 11376358
50. Bhagya D, Prema L, Rajamohan T. Therapeutic effects of tender coconut water on oxidative stress in fructosa fed insulin resistant hypertensive rats. Asian Pacific Journal of Tropical Medicine. 2012:270-276.

51. Chronic Kidney Disease among Adults: A Population-Based Study. Nutrients, 11: 2949-2960
52. Mohamed A, Nadia I, Zakhary LA, Simona GB, Raghvendra AB, Nikhat JS. Ageing, metabolic, and degenerative disorders: Biomedical value of antioxidants. Hindawi Oxidative Medicine and Cellular Longevity. 2018:2. Article ID 2098123 Available:https://doi.org/10.1155/2018/2098123
53. Shi Z, Taylor AW, Riley M, Byles J, Liu J, Noakes M. Association between dietary patterns, cadmium intake and chronic kidney disease among adults. Clinical Nutrition. 2018;37:276–284.

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