
ORIGINAL ARTICLE**Antioxidant and Cardioprotective Effect of Coconut Water against Doxorubicin Induced Cardiomyopathy**

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Abstract:

Background: Cardiomyopathy is a chronic disorder affecting the muscle of the heart. It may result in to heart failure. *Aim:* To investigate the effects of coconut water on antioxidant and cardiac markers on doxorubicin induced cardiomyopathy in wistar rats. *Material and Methods:* 21 wistar rats were divided into 3 groups of 7 rats per group. Group I served as Control while Group II and Group III were administered 2.5mg/Kg doxorubicin. Group III in addition was administered with 3ml of coconut water for 28 days. *Results:* The results obtained showed that the level of Lactate Dehydrogenase (LDH), Aspartate Aminotransferase (AST) and Alanine Aminotransferase were significantly increased in Group II when compared with the Control Group ($P < 0.05$). On the other hand, the level of antioxidant vitamins C and E were significantly decreased in Group II when compared with the Control Group. However, on the treatment with coconut water, the cardiac enzymes were decreased while antioxidant vitamins improved. *Conclusion:* This could probably imply that coconut water possess beneficial antioxidant and cardioprotective potentials.

Key Words: Antioxidants, Cardioprotective, Coconut Water, Doxorubicin.

Introduction:

Coconut water is the liquid that one finds inside a young green coconut [1]. It is the natural nutritious wholesome beverage that possesses a series of nutritional and therapeutic positional [2]. In the tropics it is not only regarded as a refreshing beverage but also a health tonic. Coconut water is an important liquid that satisfies thirst and as well invigorates the body and brings about a sense of well being and renewed health [3]. Research has shown that coconut water contains a variety of nutrients like minerals, vitamins, antioxidants, amino acids, enzymes and growth factors. Coconut is a good source of the major minerals like calcium, magnesium, and potassium. It also contains some trace elements like zinc, selenium, iodine, manganese, boron, and molybdenum [4]. Really, coconut is a refreshing drink with electrolyte content similar to human plasma. It is a popular natural support drink for oral rehydration and has a unique nutritional profile which provides much nutritional potential [5]. Coconut water has therapeutic effect on the urinary and reproductive systems. It is reported that coconut water clears bladder infections, remove kidney stones and improve sexual vitality [6]. On the other hand, doxorubicin is a cytotoxic

antibiotic. It is mainly given intravenously for the treatment of lymphomas, leukaemias and cancer [7]. It has been reported that high dose of doxorubicin has severe adverse effect on the heart. Hence, higher cumulative doses may lead to cardiomyopathy [8]. This actually leads to the disorder of the heart muscle. There is growing evidence that reactive oxygen species generated during doxorubicin overdose contributes to cardiomyopathy. The role of these reactive oxygen species in cardiomyopathy and the potential antioxidant protective effect of natural compounds on affected tissues are topics of current interest [8]. However, free radicals are regularly being produced in the body as a result of normal metabolic activities [9]. A prolonged intake of doxorubicin increases the rate of free radical generation causing weakening of cell function and cytolysis. This is a major negative effect of doxorubicin administration. Oftentimes, excessive free radical generation occurs in the body and the oxidant system cannot cope with such phenomenon. The use of antioxidants as a protective mechanism against cardiac related problems is attracting unflinching interest in this area. Therefore, this study tends to investigate the cardioprotective and antioxidant effects of coconut water in doxorubicin induced cardiomyopathy in wistar rats.

Material and Methods:

Coconut water:

Coconut 7 to 8 months of age was harvested from the coconut trees grown at Ndibinama Duruewuru Amucha, Njaba LGA of Imo State Nigeria. The coconuts were dehusked, broken carefully and the liquid endosperm (coconut water) was collected and was used in the experiment.

Experimental Animals:

The wistar rats weighing between 180 – 210g were used for the study. The wistar rats were kept in a laboratory animal unit with a 12hour light/dark cycle. Throughout the experiment, the room temperature was maintained. Also, the rats were maintained on a standard chow diet and water *ad libitum*. After acclimatization, the experimental rats were randomly grouped into 3 groups of 7 rats each. The first group of animals which served as normal control was given distilled water. Group II was given 2.5mg/kg of doxorubicin only. Group III was given 2.5mg/kg of doxorubicin and 3ml of coconut water. The duration of experimental period was 28 days. In all groups, the administration of doxorubicin, coconut water was through oral route. This treatment was by oral compulsion. All animals were allowed free access to food and water throughout the experiment.

Ethics:

All experiments were conducted in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals [10].

Blood collection:

Twenty four hours after the last dose of doxorubicin and coconut water was administered, the animals were anaesthetized with chloroform vapour, quickly brought out of the jar and sacrificed. Whole blood was collected by cardiac puncture from each animal into clean dry test tubes. The blood was allowed to stand for about 15minutes to clot and further spun in a westerfuge centrifuge (model 1384) at 10,000g for 5 minutes. Serum was separated from the clot with Pasteur pipette into sterile sample tubes for the measurement of the biochemical

parameters.

Biochemical Analysis:

Serum LDH was determined using Randox Kit, while serum AST and ALT were assayed by the method of Reitman and Frankel [11]. Serum vitamin C was assayed by the 2, 4 – dinitrophenylhydrazine method described by Tietz [12]. The vitamin E was assayed by the method of Tietz [13] in which vitamin E caused the reduction of ferric to ferrous ion which then forms a red complex with α,α -dipyridyl.

Statistical Analysis:

The values were expressed as mean \pm standard deviation. The student t-test was used to calculate the significant differences at $P < 0.05$.

Results:

The levels of serum vitamins C and E (Table I)

Table 1: The Effects of Coconut Water on Antioxidant Vitamins of Control and Experiment Groups

| Groups | Vitamin C (mg/dl) | Vitamin E (mg/dl) |
|--------|-------------------|-------------------|
| I | 1.64 \pm 0.10 | 1.96 \pm 0.28 |
| II | 0.91 \pm 0.12* | 1.21 \pm 0.61* |
| III | 1.31 \pm 0.12* | 1.41 \pm 0.46* |

*Significantly different from control ($P < 0.05$)

Table 2: The Effects of Coconut Water on Cardiac Markers on Control and Experiment Groups

| Groups | LDH (ii/L) | AST(ii/L) | ALT/(ii/L) |
|--------|-------------------|-----------------|------------------|
| I | 146.9 \pm 5.1 | 11.8. \pm 4.4 | 10.1 \pm 2.7 |
| II | 198.7 \pm 12.1* | 23.1 \pm 8.3* | 19.9. \pm 7.3* |
| III | 181.2 \pm 10.8* | 16.9 \pm 4.7* | 15.8 \pm 4.9* |

*Significantly different from control ($P < 0.05$)

were significantly decreased in Group II when compared with Control Group ($P < 0.05$) but was slightly increased in Group III when compared with Group II. On the other hand, the levels of LDH, AST and ALT (Table 2) were significantly increased in Group II when compared with Group I ($P < 0.05$) but was significantly decreased in Group III when compared with Group II ($P < 0.05$).

Discussion:

Coconut water is a heart tonic and is used to strengthen the heart as well as improve circulation [1]. In this present study, the level of LDH, AST and ALT were significantly increased in wistar rats doxorubicin induced cardiomyopathy in Group II when compared with Group I (Control). The heart tissue damage induced by doxorubicin in rats was indicated by the increased level of serum cardiac makers. Doxorubicin induced myocardiopathy like other disease condition is mainly believed to involve the production of free radicals. This is consistent with the work of Ragavendran et al [14]. The principle is that doxorubicin is bound with ferric iron to induce the generation of free radicals. Hence, impairment of cell functioning is induced. Oxidative stress as a result of toxic effects of doxorubicin on the tissue plays an important role in the pathogenesis of cardiomyopathy. The reactive oxygen species (ROS) generated tend to cause cell damage [15], resulting in heart tissue injury, hence, elevation in cardiac markers. However, the treatment of Group III with coconut water significantly decreased the level of LDH, AST and ALT. This is in line with the work of Bhagya et al [2]. This could be attributed by the possession of interesting components like cytokinins by the co-

conut water. Cytokinins are group of hormones that regulate growth, development and aging [16, 17]. They are also known as anti-aging hormones. Cytokines regulate cell division and influence the rate at which plants age.

Coconut water is the richest natural dietary cytokinins. It has been reported that consumption of a rich source of cytokinins such as coconut water may produce beneficial effects, and reduce the risk of cardiovascular diseases. Furthermore, the antioxidant vitamins C and E were significantly decreased in doxorubicin induced cardiomyopathy when compared with control. This may be associated with the elevation in the generation of reactive oxygen species [18, 19]. The level of vitamin E was depleted in Group II when compared with Group I. Doxorubicin induced cardiomyopathy is linked to oxidative stress. Some evidence suggests that oxidative cellular injury caused by free radicals contribute to the development of cardiomyopathy. This damage may be associated with reactive oxygen species that promotes lipid peroxidation [20, 21].

However, on treatment with coconut water in Group III tends to increase antioxidant vitamins. Vitamin C and E are important non-enzymatic antioxidants involved in cushioning the effect of free radicals produced during doxorubicin induced cardiomyopathy.

Having established that the level of antioxidant vitamins were lowest in Group II and higher in Group III, it is indicative that the consumption of coconut water can protect the tissue from a high risk of oxidative damage which may be associated with doxorubicin induced cardiomyopathy.

Conclusion:

This study indicates that consumption of coconut water possesses a cardioprotective potential.

References:

1. Macalalag EV and Macalalag AL. Bukolysis: Young coconut water renoeclysis for urinary stone dissolution. *IntSurg* 1987; 72:247.
2. Bhagya D, Prema L, Rajamohan T. Tender coconut water maintains the level of electrolytes and renin in fructose-fed hypertensive rats. *Int J Biol Med Res* 2010; 1(3): 44-48.
3. Alleyne T, Roache S, Thomas C, Shirley A. The control of hypertension by use of coconut water and mauby: two tropical food drinks. *West Indian Med J* 2005; 54(1):3-8.
4. Bhagya D, Prema L, Rajamohan T. Beneficial effect of tender coconut water on blood pressure and lipid levels in experimental hypertension. *Journal of Cell and Tissue Research* 2010; 10(1): 2139-2144.
5. Sandhya VG, Rajamohan T. Beneficial effects of coconut water feeding on lipid metabolism in cholesterol fed rats. *J Med Food* 2006 Fall; 9(3):400-407.
6. Anurag P and Rajamohan T. Cardioprotective effect of tender coconut water in experimental myocardial infarction. *Plant foods for Human Nutrition* 2003; 58(3):1-12.
7. Nnodim, JK and Udujih, HI. Cardioprotective effect of Gnetumbucholzianum leaf extract against doxorubicin cardiomyopathy in wistar rats.

- Novel Science International Journal of Medical Science* 2012; 1(3): 61-64.
8. Hawthorn J. Oxford dictionary of Medicine. Oxford University press 1999: 173-174.
 9. Nnodim JK, Nwanjo HU, Okolie NJ, Opara AU, Nwosu DC, OKoroiwu I, Dike J, Okorie H, Nwadike CN, Uduji HI. Effects of *XylopiAethiopica* Fruits on reproductive hormonal level in rats. *Global Journal of Medicinal Plant Research* 2013; 1(1): 29-31.
 10. Ochei J and Kolhatkar A. Care and use of experimental animals. In Medical Laboratory Science Theory and practice, Tata McGraw-Hill India; 2007: p1213-1232
 11. Reitman S and Frankel S. A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases, *Am J ClinPathol* 1957; 28(1):56-63.
 12. Tietz W. Clinical guide to laboratory tests. W.B Saunders Company Philadelphia; 1976a: 220-226.
 13. Tietz W. Ascorbic acid: In fundamentals of clinical chemistry. W.B Saunders Company Britain; 1976b:p419-429.
 14. Ragavendran P, Sophia D, Arulraj C, Gopalakrishnan VK. Cardioprotective effect of aqueous, ethanol and aqueous, ethanol extract of *AervaLanata* (Linn) against doxorubicin induced cardiomyopathy in rats. *Asian Pacific Journal of Tropical Biomedicine* 2012; 2(1):S212-S218.
 15. Melchiorre K, Sutherland GR, Liberati M, Thilaganathan B. Preeclampsia is associated with persistent postpartum cardiovascular impairment. *Hypertension* 2011; 58(4):708-715.
 16. Shukitthale B, Carey A, Simon I, Mark DA, Joseph IA, Effects of Concord grape juice on cognitive and motor deficits in aging. *Nutrition* 2006; 22(3):295-30.
 17. Barja G. Free radicals and aging. *Trends Neurosci* 2004; 27(10):595-600.
 18. Mechiore K and Basky T. Maternal cardiac function in Preeclampsia. *Current opinion in obstetric and Gynaecology* 2011; 23(6):440-447.
 19. Avci A, Atli T, Erguder B, Varli M, Devrim E, Demir O, Duraku I, Turgay M. Effects of grape consumption on plasma and erythrocyte antioxidant parameters in elderly subjects. *Turk J Med Sci* 2010; 40(4):525-529.
 20. Rho KA, Kim MK. Effects of different grape formulations on antioxidative capacity, lipid peroxidation and oxidative DNA damage in aged rats. *J NutrSci Vitaminol (Tokyo)* 2006; 52(1):33-46.
 21. Rogers EJ, Milhalik S, Orthiz D, Shea TB. Apple juice prevents oxidative stress and impaired cognitive performance caused by genetic and dietary deficiencies in mice. *J Nutr Health Aging* 2004; 8(2):92-7.

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