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Cardio Protective Effects of Natural Honey on Animal Model of Hypertension

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Abstract

Hypertension, also known as high blood pressure, is a leading cause of cardiovascular disease and premature death worldwide. Fresh honey is consumed worldwide and is claimed to be highly medicinal and has therapeutic effects against a wide range of medical conditions. We investigated the cardio protective effect of natural honey in in animal model of hypertension. Forty (40) male albino rats, with average weight (120 ±10 g) were administered with high salt diet, HSD (80 g NaCl + 1 kg of diet and 1% NaCl in drinking water (10 g of NaCl + 1 L distilled water) for 10 weeks to induce hypertension in the rats. Following confirmation, hypertensive male rats were randomly selected for the experiment. Twenty (20) albino rats (15 hypertensive rats and 5 normotensive rats) were divided into 4 groups, Groups A-D. Group A: (Normotensive Control) no administration was given; Groups B-D (hypertensive rats) received the following treatments. Group B was treated with natural honey (15 ml/kg), Group C treated with hydrochlorothiazide (0.15 mg/kg), daily for 21 days; while Group D received no treatment, until the end of the 21 days administrations. Three consecutive blood pressure readings were taken in the end, and cardiac alterations were assessed via biochemical and histopathological analyses. Results showed that salt-induced hypertension caused a marked elevation of the cardiac biochemical parameters. The histopathological results agree with the biochemical findings. However, and interestingly, natural honey (15 ml/kg oral) showed significant efficacy in the recovery and protection on the heart as the standard anti-hypertensive drug, hydrochlorothiazide ($p < 0.05$ or $p < 0.01$). Natural honey has a cardi protective effects and may manage high blood pressure.

Keywords: Hypertension, Salt, Natural Honey, Hydrochlorothiazide, Cardiovascular Disease

1. Introduction

Hypertension is the major cause of death from non-communicable diseases, such as cardiovascular disease, around the world [1, 2]. The majority of people with high blood pressure have no known reason and are classed as having primary hypertension. However, 5-10 % of these patients may develop secondary hypertension, indicating that there is an underlying and potentially treatable reason. Secondary hypertension affects people of all ages; however, it is more common in teenagers and young adults[3]. Hypertension is a chronic high rise in blood pressure caused by blood in circulation pushing on the walls of the

arteries, the body's primary blood vessels [4]. More than 90% of hypertensive patients have no known cause. It is the product of a complicated relationship between genetics, environment, and lifestyle. Consumption of natural honey, which is claimed to be high in anti-oxidative polyphenolic compounds; which have been demonstrated to help manage blood pressure in several studies.

Honey is a natural sweetener obtained from the plant nectar, pollen and resin [5]. It has been known to be effective in traditional medicine for decades. Since pre-historical times, honey is well known for its nutritional and therapeutic values. Honey is mainly made up of carbohydrates (most especially fructose and glucose). The sweet taste of honey is as a result of supersaturated solution of monosaccharides like fructose (about 38%) and glucose (about 31%). Honey also contains a number of minor constituents, most of them are naturally occurring antioxidant. They are phenolic acids, flavonoids, certain enzymes (glucose oxidase and catalase), ascorbic acid, carotenoid-like substances, organic acids, Maillard reaction products, amino acids and proteins [6].

Based on the studied relationship between oxidative stress and high blood pressure, using an agent that can have both antioxidant and antihypertensive properties can go a long way in the prevention, management and treatment of hypertension. In addition to the fact that natural honey can be easily gotten from our local markets around the country, honey is rich in phenolic acids, amino acids (such as arginine and glutamate), flavonoids and ascorbic acid, these are widely known for their antioxidant properties which have been seen to have antihypertensive effects [7].

The effect of natural honey on hypertension is quite objectionable, but due to its anti-oxidant properties, study on its hypertensive effect is becoming relevant. Only few studies have shown that hypertension could be affected by the intake of natural honey, and most of these research were done in America. There is also a rise in the incidence of hypertension, due to the unhealthy lifestyle of individuals and in addition the little to no progress seen in the use of treatment drugs, coupled with the side effects of these drugs. Therefore, we hypothesize that honey and its antioxidant properties could improve the treatment and management of hypertension. The aim of this study is to assess the cardioprotective effects of natural honey on salt-induced hypertension in rats.

2. Materials and Methods

2.1 Laboratory Animal

Twenty (20) albino adult rats, weighing (110 ± 10 g), were procured from the University of Nigeria's College of Veterinary Medicine's animal home. The rats were housed in a metallic cage with a regular temperature of 22 ± 3 ºC and a 12-hour light-dark cycle. The animals were monitored for 14 days earlier than the experiment date, in order to allow them to acclimatize to the environment. The experimental design and management complied with institutional regulations detailing the use of rats and the guidelines for the care and use of vertebrates in study published by the American Physiological Society [8].

2.2 Experimental Design

A total of forty (40) male albino rats, with average weight (120 ±10 g) were administered with high salt diet, HSD (80 g NaCl + 1 kg of diet and 1% NaCl in drinking water (10 g of NaCl + 1 L distilled water) for 10 weeks to induce hypertension in the rats. We confirmed hypertensive rats after three consecutive readings using a digital tail cuff using a Non-invasive blood pressure monitor (NIBP). Hypertensive male rats were randomly selected for the experiment. Twenty (20) albino rat (15 hypertensive rats and 5 normotensive rats) were divided into 4 groups, Groups A-D. Group A: (Normotensive Control) no administration was given; Groups B-D (hypertensive rata) received the following treatments. Group B hypertensive rats treated with natural honey (15 ml/kg), Group C hypertensive rats treated with hydrochlorothiazide (0.15 mg/kg), daily for 21 days; while Group D hypertensive rats received no treatment, until the end of the 21 days administrations. Three consecutive blood pressure readings were taken in the end, and cardiorenal injuries and alterations were assessed via various biochemical analyses.

2.3 Animals Sacrifice and Sample Collection

Under chloroform anesthesia, blood samples for biochemical analysis were taken from the left ventricle of the heart. The heart and kidneys were excised for histopathological analyses.

2.4 Biochemical Analyses

2.4.1 Measurement of Cardiac Biomarkers

Creatine kinase myocardial band (CK-MB) level was determined using kinetic colorimetric technique [9]. Randox Lactate dehydrogenase (LDH) kit was used to measure LDH. Reitman and Frankel's colorimetric approach was used to determine Aspartate transaminase (AST) [10].

2.5 Histopathological Analysis

The paraffin wax embedding method was employed to prepare the removed heart and kidney tissues. Sections of each organ were made at a thickness of 5 microns, and Hematoxylin and Eosin staining technique was used for better general examination of the tissues [11]. An Olympus™ light microscope was used to examine the tissue sections.

2.6 Statistical Analysis

Version 7.0 of Graph Pad Prism (San Diego, CA, USA) was used to analyze the data. The results of the biochemical experiments were presented as mean ± SEM (standard error of mean). One-way analysis of variance (ANOVA) was used to determine the degree of significance. Probability levels below 0.05 ($p<0.05$) were taken as being significant.

3. Results

3.1 Biochemical Results

The functionality of the heart was established by estimating the serum level of CK-MB (U/L), LDH (U/L) and AST (U/L). A statistically significant ($P<0.05$) elevated levels of CK-MB (U/L), LDH (U/L) and AST (U/L), were seen in salt-treated group D (negative control) when compared with group A (normal control) and group C (positive control). The co-administration of salt and natural honey or hydrochlorothiazide separately, restored the level of these parameters to near normal when compared with salt-treated group (negative control). Furthermore, we observed that natural honey showed better cardioprotection than hydrochlorothiazide (positive control) against high dose of salt (Table 1).

3.2 Histopathological Results

In Fig 1, Myocardial fibres appear normal. The cardiac fibres showed a well conserved morphology. The heart section salt-treated group (negative control) showed normal myocardial fibres but abnormal changes were observed. There was moderate cellular infiltration and evidence of oedema seen as increased spaces between the fibres (Fig 4). However, the cardiac fibres of test group rats (natural honey) appear normal (Fig 2). Also, the majority of the myocardial fibres of positive control group rats appear normal while some appear wavy (Fig 3). The histopathological findings were in tandem with the biochemical results as we observed that natural honey showed better cardioprotection than hydrochlorothiazide (positive control) against high dose of salt.

Table 1: Statistical Comparison of cardiac biomarkers of treated groups with negative controls Groups

Group	CK-MB (U/L)	LDH (U/L)	AST (U/L)
A: Normal Control	189.98 ± 12.01**	185.57 ± 16.24**	19.75 ±2.91*
B: Salt + Honey (15ml/kg)	198.83 ± 16.47*	196.82 ± 13.17**	20.87 ± 4.27*
C: Salt + HCTZ (0.15mg/kg)	200.79± 13.72*	198.75 ±14.45**	22.09 ± 3.74*
D: Salt Alone	249.06 ± 19.79	242.91 ± 14.02	42.13 ± 8.97

Values given as Mean ± SEM. **p<0.01 or *p<0.05 is significant when salt alone (negative control) is compared with all other groups.

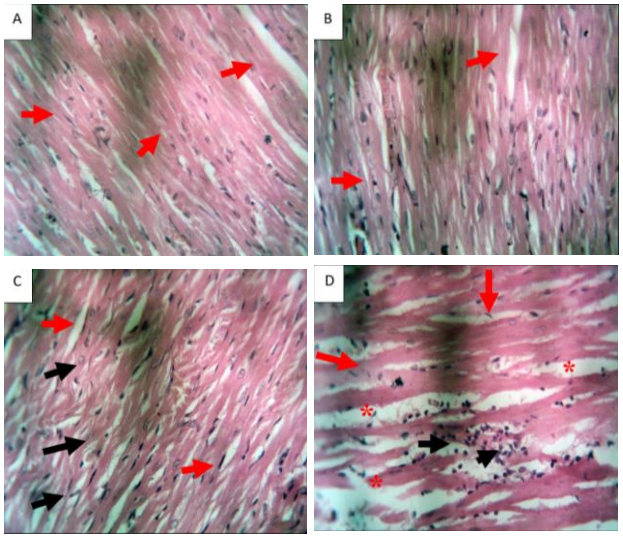

Fig 1: Plate A) Representative micrograph of the heart of animals in group A. Myocardial fibres (arrows) appear normal. Plate B): Representative micrograph of the heart of animals in group B. Myocardial fibres (arrows) appear normal. Plate C): Representative micrograph of the heart of animals in group C. Majority of the myocardial fibres (red arrows) appear normal while some appear wavy (black arrow). Plate D): Representative micrograph of the heart of animals in group D. Myocardial fibres (red arrows) appear normal. There is moderate cellular infiltration (black arrows) and evidence of oedema (*) seen as increased spaces between the fibres. **Stain**: Haematoxylin and Eosin. **Magnification**: X400.

4. Discussion

Numerous investigations have shown the well-established link between high blood pressure and dietary salt intake. In addition to lowering blood pressure and the prevalence of hypertension, dietary sodium reduction is also linked to a decline in cardiovascular disease morbidity and mortality [12]. For all types of hypertension, non-pharmacological therapies are advised, such as limiting alcohol intake, reducing sodium intake, adopting a heart-healthy diet, quitting smoking, increasing physical activity, and managing weight [13]. Eating plant foods with a high antioxidant chemical content is advantageous since it will reduce the prevalence of several chronic diseases, such as diabetes, cancer, and cardiovascular diseases, by managing oxidative stress [14]. An example is honey. Honey is a naturally occurring chemical that has a wide range of medical benefits, including antibacterial, hepatoprotective, hypoglycemic, reproductive, antihypertensive, and antioxidant characteristics [15]. The aim of this study was to evaluate the effects of honey on cardiac biochemical parameters, on salt-induced hypertension in rats.

The cardiac biochemical parameters, which include Creatine Kinase Myocardial Band (CK-MB), Lactate Dehydrogenase (LDH), Aspartate Aminotransferase (AST), were more elevated in the group administered with salt alone (affected group), in this study. From the results, it was shown that the CK-MB, LDH and AST levels were significantly increased compared to the normal control group. It has been demonstrated that excessive sodium intake, which the World Health Organization defines as greater than 5g sodium per day, causes a significant rise in blood pressure and is associated to the development of hypertension and its cardiovascular consequences [12]. Several studies have also shown that CK-MB, LDH and AST values are influenced by gender, age, race, and amount of muscle mass. These factors were put into consideration will procuring the experiment rats, as such the rats were of the same age, gender, weight range (100-140g) and all had restricted movement [16, 17]. Therefore, the observed increases in CK-MB, LDH, and AST were due to myocardial injury which happened as a result of salt-induced hypertension.

The CK-MB, LDH, and AST levels were seen to be significantly decreased in group that was administered with salt and the standard antihypertensive drug; hydrochlorothiazide (positive control group), when compared to that of the affected group (salt alone). The first line of treatment for essential hypertension is still frequently thiazide diuretics since they are more effective at preventing one or more of the major forms of the condition from cardiovascular disease [14]. Thiazide use rapidly increases fluid loss to urine by reducing sodium reabsorption, which causes a decrease in extracellular fluid (ECF) and plasma volume. A decrease in venous return, an increase in renin release, a decrease in cardiac output, and a drop in blood pressure are all caused by this volume loss. Certain thiazide diuretics appear to have antioxidant effects that may help in the treatment of hypertension.

The mechanism of action of the anti-oxidative properties of honey has been established in several studies, this can be compared to the anti-oxidative effect exhibited by the hydochlorothiazide drug. Based on the result, it was also observed that the group that received salt diet and subsequently oral administration of honey have a significant reduction in their CK-MB, LDH, and AST levels, when compared to the group that received salt diet alone. This result shows a cardio-protective effect of honey, which correlates with a study carried out by Bt Hj Idrus *et al.* [18], where it was stated that honey exerts cardio-protective effect by limiting the increase in cardiac damage indicators (CK-

MB, AST, and ALT), amidst other cardio-protective mechanism of honey. These results also correlates with a study carried out by Erejuwa *et al*. [19]. Where it was observed that the systolic blood pressure was significantly lower in the honey-treated spontaneously hypertensive rats than in the spontaneously hypertensive rats control.

5. Conclusion

The present study showed salt induced hypertension, as shown by an increase in cardiac biomarkers. However, the administration of natural honey subdued the adverse effects. Thus, this study suggests that natural honey is of health benefits to patients suffering from salt-induced hypertension. Further suggestion would advised a reduced dietary sodium intake.

6. Compliance with Ethical Standards

Acknowledgments

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Disclosure of Conflict of Interest

The author(s) declared no potential conflicts of interest.

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