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Effect of *Arachis Hypogaea* Seed Oil on the Antioxidant and Cardiac Function Biomarkers of Isoprenaline Induced Oxidative Stress Mediated Cardaic Injury in Albino Rats.

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EXECUTIVE SUMMARY

The oxidant and antioxidant imbalance in the cardiomyocytes that favors the accumulation of oxidants, leading to cellular damage, constitutes oxidative stress. Generally, cells will initiate an adaptive system to protect them against the dangerous effects of oxidative stress, but when the oxidant concentration often exceeds the cell's adaptive capacity, the cell will experience exacerbated oxidative stress. This present study is designed to check the antioxidant and cardioprotective effect of the oil against isoprenaline induced oxidative stress/myocardial infarction in rats. Thirty albino rats were randomly divided into five (5) groups of six rats per group. Group 1 served as the normal control, group 2 was the negative control (administered 85mg/kg of isoprenaline only), group 3 through 5 were pretreated with 5ml/kg, 10ml/kg and 20ml/kg body weight of the *Arachis Hypogaea* seed oil respectively for 21 days. Myocardial infarction was induced in the rats using subcutaneous injection of 85mg/kg Isoprenaline (ISO) for two consecutive days (19^{th} and 20^{th}) at 24hours interval. The result showed that isoprenaline significantly ($p<0.05$) produced myocardial infarction because there was significant ($p<0.05$) increase in CK-MB activity, Troponin I level, LDH activity and MDA concentration of the negative control group compared to the normal control and *Arachis Hypogaea* seed oil pretreated groups. The *Arachis Hypogaea* seed oil significantly ($p<0.05$) decrease CK-MB activity, Troponin I level, LDH activity, and MDA concentration compared to the negative control. There was significant ($p<0.05$) increase in the SOD and Catalase oil pretreated groups compared to the negative control. The study is suggested that the *Arachis Hypogaea* seed oil could serve as an agent for the prevention of oxidative stress mediated cardiac injury.

Keywords: Myocardial Infarction, antioxidant, *Arachis Hypogaea* seed oil, oxidative stress Isoprenaline

Introduction

Generation of free radicals or reactive oxygen species (ROS) during metabolism and other activities beyond the antioxidant capacity of a biological system gives rise to oxidative stress. Oxidative stress plays a role in heart diseases, neurodegenerative diseases, and cancer and in the aging process. This concept is supported by increasing evidence that oxidative damage plays a role in the development of chronic, age-related degenerative diseases, and that dietary antioxidants oppose this and lowers risk of disease. Myocardial infarction (MI) is a common occurrence of heart disease ischemia (IHD). Despite rapid advances in the treatment of coronary artery diseases (CAD), MI remains the leading cause of death in the developed world and a major pathological problem worldwide (Khalil *et al*., 2015; Zhi *et al*., 2020). Myocardial ischemic damage has a complex pathogenic mechanism that is still unknown. According to many reports, oxidative stress, inflammatory reaction, calcium overload, and apoptosis are all involved in its pathogenesis (Yaseen *et al*., 2017). The development of oxidative stress is generally associated with cardiac failure and myocardial myocardial level of reactive oxygen species (ROS). In general, oxidative stress occurs as a result of changes in the body's endogenous antioxidant content and the generated ROS involved in oxidative stress (Seshadri, 2021).

Antioxidants are very important and useful likewise as the delay or slow down the process of oxidation among cells which often leads to heart failure. Antioxidant when present in low concentrations compared to those of an oxidisable substrate significantly delays or prevents oxidation of that substance. It is reported that the antioxidant constituents of plant materials provide protection from coronary heart disease and cancer and protect the body from damage caused by free radical induced oxidative stress.

Medicinal plants contain a variety of antioxidant compounds that defend against a variety of diseases, making them viable therapeutic options. Herbal medicines have a long history of use; they are now of great medical and public interest around the world as possible sources of new drug lead molecules (Seshadri, 2021). Peanuts (*Arachis Hypogaea* L.) belong to the legume family and have spread to other parts of the world, from South America (Hammons et al., 2016). It is grown mainly in Georgia, China, India, the United States of America, Nigeria, Indonesia, Argentina, and in low amounts in

Turkey (Freitas et al., 2007). In 2019, while worldwide peanut production was approximately 48 million tons, it was 169 thousand tons in Turkey. About 8.4 grams of 12.9 grams and 4.9 g of 11.1 grams of oilseeds consumed per day in the United States and European Union countries are due to consumption of peanuts. Moreover, peanut butter is a famous stable food and constitutes 50% of peanut consumption in the United States (Jenkins et al., 2008). Frequent nut consumption, including that of peanut, is associated with a reduced risk of developing diabetes and cardiovascular disease. The exact mechanisms are not known but may relate to beneficial changes in blood lipids and reduction in oxidative damage and inflammatory biomarkers. This present study investigated the effect of *Arachis Hypogaea* seed oil on cardiac marker indices, lipid peroxides, and the antioxidant enzyme defense system in oxidative stress-induced cardiac injury.

MATERIALS AND METHODS

Chemicals

Methanol was product of Sigma Aldrich Chemical Company Sule and Arhoghro 164 Ltd, Poole, England. Rat feed were purchased from Pfizer Nigeria Plc. Biochemical kits were products of Randox Diagnostics, Crumlin, UK.

2, 2'-diphenyl-1-picrylhydrazyl hydrate (DPPH) was obtained from the Sigma chemical company, St. Louis, USA. Carvedilol, Capoten and Isoprenaline were purchased from Selleck chemicals, Germany.

Collection amd preparation of Plant sample

Arachis hypogea seeds were purchased from Relief market. The seed samples were washed with distilled water and sun dried for about two days and fried.

The dried and fried sample was pulverized and preserved in cellophane bags until when required for use.

Extraction of oil

Extraction of *Arachis hypogaea* seed oil was done according to a method described by Fatiqa *et al.* (2015).

Experimental animals

Thirty Albino rats (200 ± 40g) were procured from animal house farm Veterinary Medicine, Michael Okpara University of Agriculture Umudike. They were housed in standard transparent cages with wheat husk bedding, renewed every 24h. They were kept under controlled room temperature and humidity (18 to 29 °C; 30 to 70%) in a 12h light-dark cycle. Animals were acclimatized for two weeks to laboratory conditions before starting the studies. The rats were given standard laboratory diet and water *ad libitum*. Care of experimental animals were taken as per the guidelines given by Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA), Ministry of Environment and Forests (Animal Welfare Division), Umuahia Abia State, Nigeria.

Experimental Design

Total 30 albino rats were allocated randomly into 5 groups (6 animals per group). Myocardial infarction was induced in rats by giving Isoprenaline (ISO) (85 mg/kg) subcutaneously (s.c.) for two subsequent days at the interval of 24h. Distribution of study groups was as follow:

Group 1 (Normal control), Rats were given distilled water orally for 21 days and normal saline s.c. on the day 19 and 20

Group II (Negative control). Isoprenaline (85mg/Kg b.wt.) was administered subcutaneously to the rats for two consecutive days to induce oxidative stress/myocardial infarction. This group were treated with the oil.

Group III: Rats of this group were pretreated with *Arachis hypogaea* seed oil 5ml/kg b.wt once daily for three weeks and then two consecutive doses of Isoprenaline (85mg/Kg b.wt.) sc. on day 19 and 20

Group IV: Rats of this group were pretreated with *Arachis hypogaea* seed oil 10ml/kg b.wt once daily for three weeks and then two consecutive doses of Isoprenaline (85mg/Kg b.wt.) sc. on day 19 and 20

Group V (Preventive Group). Rats of this group were pretreated with *Arachis hypogaea* seed oil 20ml/kg b.wt once daily for three weeks and then two consecutive doses of Isoprenaline (85mg/Kg b.wt.) sc. on day 19 and 20

After the treatments, the rats were sacrificed through cervical dislocation and blood samples were collected via cardiac puncture into a plain sample bottles for biochemical analysis.

Biochemical parameters estimation

Creatinine kinase-MB (CK-MB), Troponin and lactate dehydrogenase (LDH) were determined according to methods described by Abubaker *et al*. (2012).

Antioxidant estimation

Estimation of superoxide dismutase (SOD) was done using the method of Misra and Fridovich (1972). Catalase was done by the method of Hugo e. Aebi (1984). Marker of lipid peroxidation malondialdehyde (MDA) was done by the method of Slater and Sawyer (1971).

Statistical Analysis

Values were represented as Mean ± SD. Data obtained was subjected to one-way Analysis of Variance (ANOVA) and group means were compared using Duncan's new multiple range tests. Differences were considered to be significant at ($p \leq 0.05$).

Results and Discussion

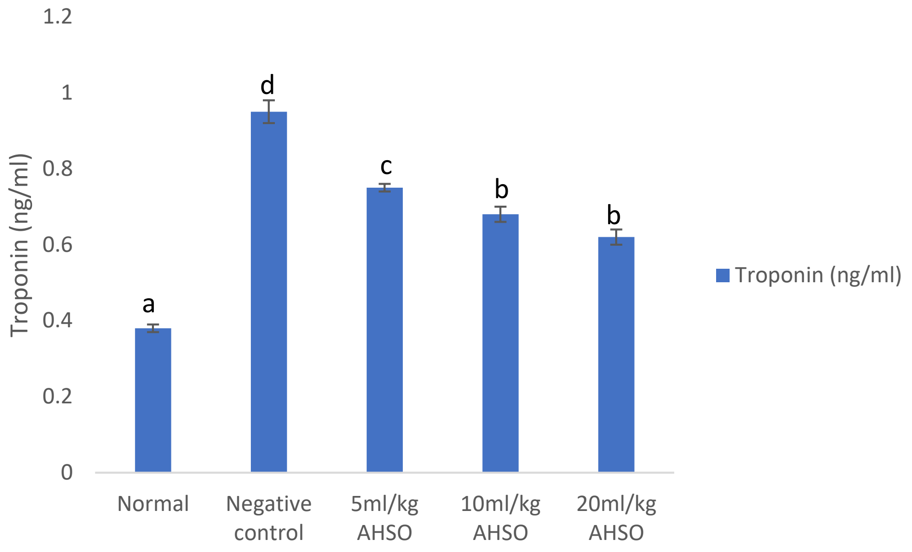

Figure 1: Effect of *Arachis hypogaea* seed oil on Troponin level of isoprenaline induced myocardial infarction in rats

The result of the effect of the extracted oil on the troponin level was shown in figure 1. There was significant ($p<0.05$) decrease in the Troponin level of groups administered orally *Arachis hypogaea* seed oil when compared with the negative control group.

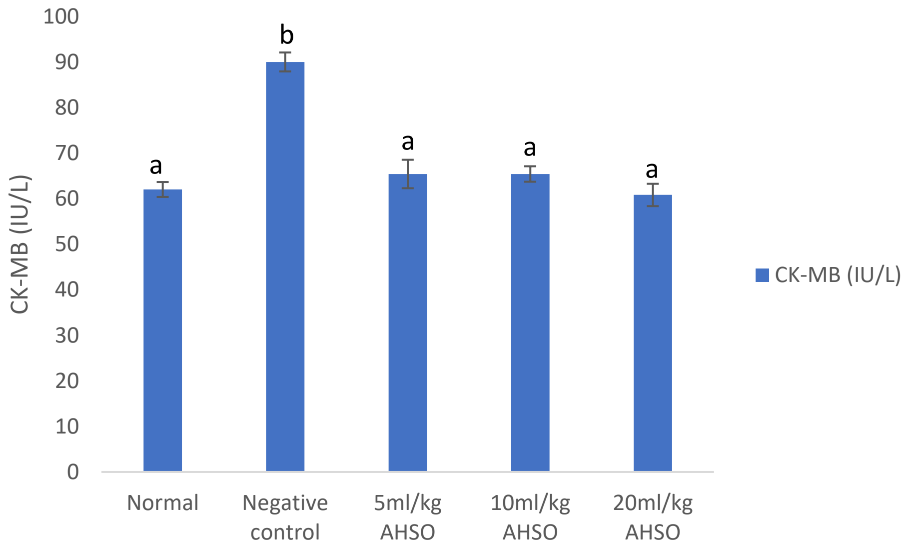

Figure 2: Effect of *Arachis hypogaea* seed oil on CK-MB level of isoprenaline induced myocardial infarction in rats

Figure 2 showed result of the effect of *Arachis hypogaea* seed oil on CK-MB level. There was significant ($p<0.05$) decrease in the CK-MB activity of groups administered orally *Arachis hypogaea* seed oil when compared with the negative control group. There was also non-significant ($p>0.05$) increase in CK-MB level of the groups administered extracted oil when compared with the normal control.

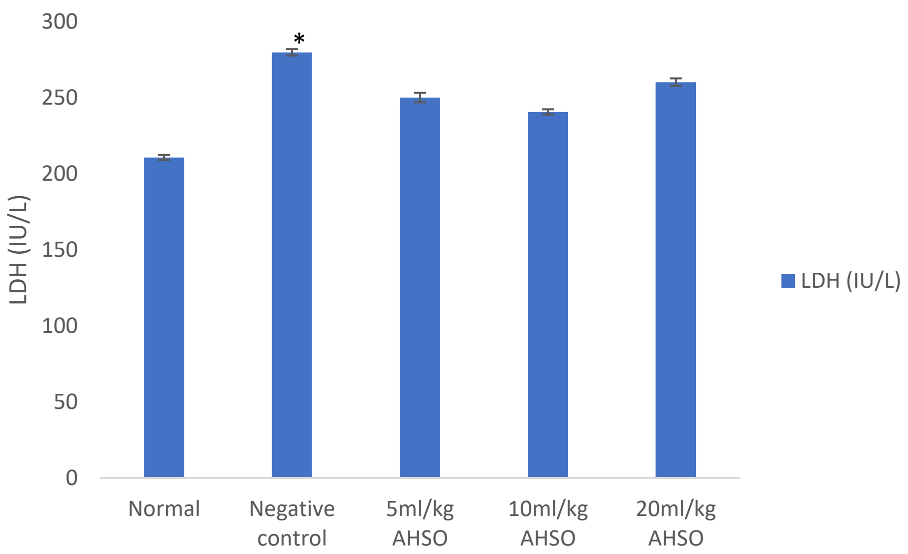

Figure 3: Effect of *Arachis hypogaea* seed oil on LDH level of isoprenaline induced myocardial infarction in rats

The result in figure 3 shows the effect of *Arachis hypogaea* seed oil on LDL level. There was significant ($p<0.05$) decrease in the Lactate dehydrogenase (LDH) activity of groups administered orally *Arachis hypogaea* seed oil when compared with the negative control group.

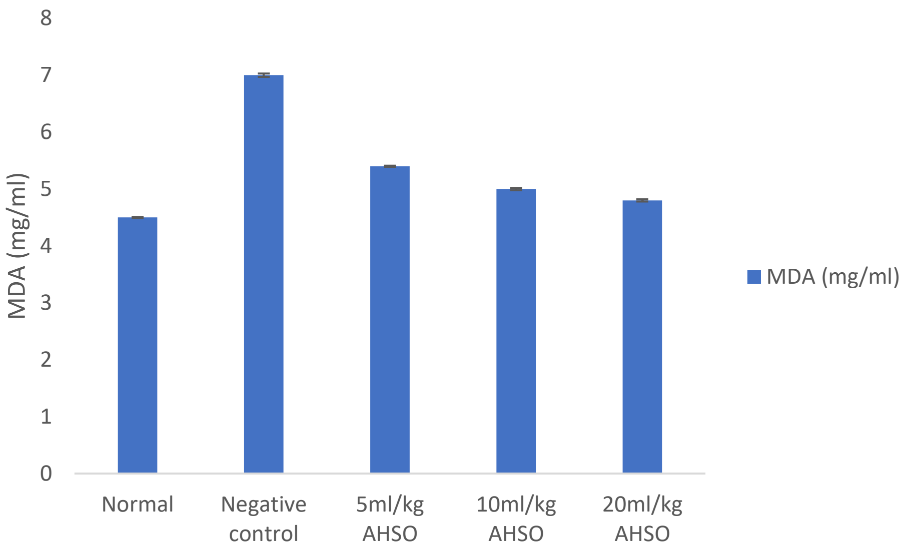

Figure 4: Effect of *Arachis hypogaea* seed oil on MDA level of isoprenaline induced myocardial infarction in rats

The result in figure 4 shows the effect of *Arachis hypogaea* seed oil on MDA level. There was significant ($p<0.05$) decrease in the Malondialdehyde (MDA) level of groups administered orally *Arachis hypogaea* seed oil when compared with the negative control group. There was also non-significant ($p>0.05$) increase in MDA level of the groups administered *Arachis hypogaea* seed oil when compared with the normal control

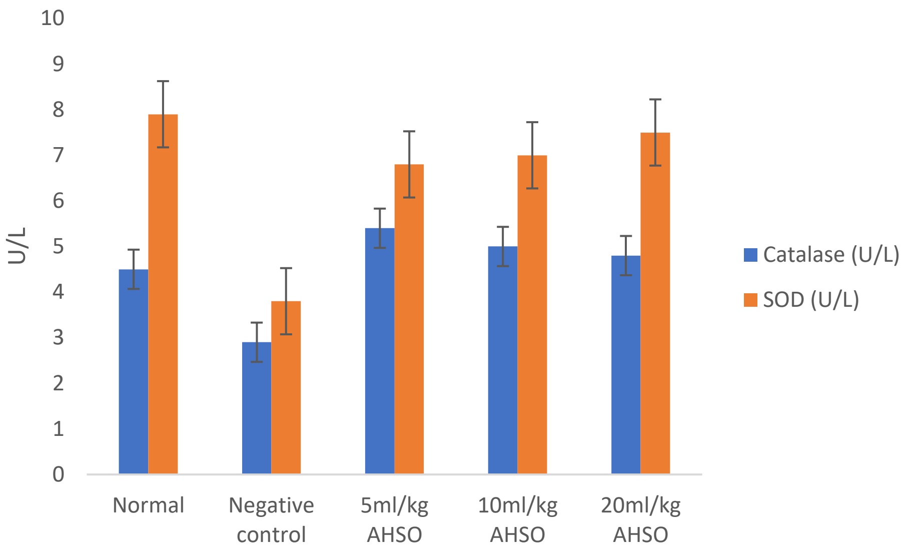

Figure 5: Effect of *Arachis hypogaea* seed oil on Catalase and SOD levels of isoprenaline induced myocardial infarction in rats

There was significant ($p<0.05$) increase in the endogenous antioxidant enzymes (catalase, Superoxide dismutase - SOD) activities of groups administered *Arachis hypogaea* seed oil when compared with the negative control group (figure 5).

DISCUSSION

Isoprenaline is an auto-oxidation catecholamine that leads to free radicals generation which cause sodium and potassium channel failure dependent on ATP, overload calcium, attack of cell protein, attacks on carbon links between the multiple insaturated fatty acids. Cell death occurs as a result of a free radical attack, resulting in cardiac tissue necrosis. Cardiotoxicity is thought to be caused by isoprenaline's development of free radicals (Krishna and Sundararajan, 2018). Thus, the determination of CK-MB isoenzyme, LDH and Troponin is a useful parameter for assessing myocardial damage. Pretreatment with the *Arachis hypogaea* seed oil prevented depletion of CK-MB isoenzyme, Troponin, LDH from cardiomyocytes as compared to isoprenaline group (Negative control). This could be as a result of the polyunsaturated fatty acid that has been reported to be found in the *Arachis hypogaea* seed oil. This study revealed that the level of lipid peroxides, as measured by MDA, was significantly higher in the isoprenaline-treated group (negative control). Superoxide dismutase (SOD) which is a reactive oxygen species (ROS) protective enzyme, is found in the mitochondrial matrix and protects cells from the harmful effects of super oxide anion generated by the peroxidative process in tissues. The increase in SOD activity as seen in figure 5 may be attributed to the *Arachis hypogaea* seed oil's ability to scavenge free radicals. However, all the administered doses of the oil resulted in substantial increases in the levels of this enzyme, indicating the good antioxidant activity of the oil. Catalase is a peroxisomal enzyme found in the heart's mitochondria. It is one of the antioxidant protective enzymes that is needed for the conversion of hydrogen peroxide to oxygen and water (Krishna and Sundararajan, 2018). Isoprenaline induced oxidative stress in the rat which was evident in the reduced catalase activity but the *Arachis hypogaea* seed oil showed a good radical protective potential.

Conclusion

The administration of the *Arachis hypogaea* seed oil protected the animal from cardiac damage and antioxidant depletion. The overall cardioprotective effect of this *Arachis hypogaea* seed oil is most likely due to its antioxidant property and ability to counteract free radicals.

Conflict of interest

The authors declare that no conflict of interest exists with respect to this work

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