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Research Article

Datura stramonium extract modulates some glycolytic enzymes in the cardio-renal compartments of male albino rats

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ABSTRACT

Datura Stramonium (DS) is a plant with both pharmacological and toxicological effects, it is also a well documented drug of abuse. Physicians have reported a surge in energy in those intoxicated by DS. This study was conducted to ascertain the effects of DS on some glycolytic enzymes in the heart and kidney of male albino rats. Twenty-five male Wistar rats weighing between 180g and 200g were randomly distributed into five groups (I, II, III, IV, and V). Group I (control group) received distilled water while groups II, III, IV, and V received graded doses (50mg/kg, 100mg/kg, 200mg/kg, and 400mg/kg body weight) of aqueous extract of DS respectively for twenty-eight days. Animals were sacrificed at the end of exposure, hearts and kidneys were removed. Activities of some glycolytic enzymes (hexokinase, aldolase, pyruvate kinase, and lactate dehydrogenase) were determined spectrophotometrically. One-Way ANOVA followed by Tukey's test was used to analyze the data obtained, $p < 0.05$ was considered significant. An increase in the activities of hexokinase, aldolase, pyruvate kinase, and lactate dehydrogenase were observed in both compartments when compared to the control. Increases observed in most cases appeared to be dose-dependent. The increases observed in these enzymes involved in energy generation pathway might be the reasons behind surges in the energy level of patients with DS intoxication as observed by the physicians.

Keywords: *Datura stramonium*, graded doses, glycolytic enzymes, dose-dependent.

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INTRODUCTION

Medicinal plants have been in use since man's existence, and virtually all known plants have one or more medicinal purposes. The therapeutic use of plants is still

widely practiced in some nations, particularly developing nations, despite breakthroughs in pharmacology (Birjees *et al.*, 2021). According to estimates from the World Health Organization (WHO),

primary healthcare for some portions of the population in African and Asian nations is currently provided via herbal medicine (Chintamunnee and Mahomoodally 2012). This is due to the high expenses of modern treatments and the inaccessibility of healthcare facilities (Marshall N. T, 1998). Researchers all over the world are exploring the vast array of plants to isolate, purify, and characterize the active ingredients in these medicinal plants for drug synthesis and other useful purposes. Although it is widely accepted that the medicinal prowess of these plants is due to the existence of phytochemicals (Ullah *et al.*, 2014). Efforts are also in full gear to understand the mechanism of action of the active ingredients found in medicinal herbs.

Datura stramonium (DS) belongs to the family Solanaceae and originated in America but has been introduced to many parts of the world. It has been called different names like the devil's apple, thorn apple, jimson weed, and some others. DS is found throughout Nigeria, especially in dumpsites, bushy environments, and abandoned or dilapidated buildings. It is called gegemu in Yoruba, haukata yaro in Hausa and myaramuo in Igbo. DS is a medicinal plant, it has anti-inflammatory properties, stimulates the neurological system, clears respiratory congestion, treats dental and skin infections, and relieves toothaches (Soni *et al.*, 2012). The anti-diabetic properties of *Datura stramonium* have been well-documented (Bamlaku and Gedefaw, 2020, Oladipo *et al.*, 2019). Despite the medicinal uses of DS, multiple organ toxicity of different parts of the plants has been reported (Ogunmoyole *et al.*, 2019). Its hallucinogenic effects are also well-documented (Forrester, 2006). Owolabi *et al* 2023 also reported significant changes in sperm analysis and testicular histomorphology following the administration of *Datura stramonium* extract. Teenagers intentionally consume the plant in search of its euphoric and psychedelic effects, especially those who have a history of abusing other substances (Tranca *et al.*, 2017). Young people are prone to DS intake because, unlike other illicit drugs, they are readily available at no cost of purchase (Luigi *et al.*, 2010). Despite the fact that several research works has been done on the medicinal and toxicological effects of *Datura stramonium*, no work has been done on the effects of this popular plant on the glycolytic enzymes hence the need for this research work.

MATERIALS AND METHODS

Chemicals and reagents

Tris-HCl, magnesium chloride, hydrazine sulfate, magnesium sulfate, glucose-6-phosphate dehydrogenase, and adenosine diphosphate were obtained from Sigma Aldrich, Missouri, USA.), reduced

adenine dinucleotide (NADH), glucose, fructose-1,6-bisphosphate, phosphoenol pyruvate, and lactate dehydrogenase were obtained from Carl Roth, Germany. The kit used for the determination of lactate dehydrogenase was purchased from Cypress diagnostics, Belgium.

PLANT COLLECTION AND EXTRACTION

Fresh samples of *Datura stramonium* were collected from Ureje quarters, Ado-Ekiti, Ekiti State, Nigeria. The fresh leaves and seeds were rinsed with distilled water and air-dried at room temperature until it was completely dry. The dried sample was homogenized using an electrical grinder. Extraction was carried out using a modified method of Ogunmoyele *et al.*, (2019). Three hundred grams (300g) of the pulverized *Datura stramonium* was weighed and soaked in distilled water for 24 hours after which it was decanted and filtered using Whatman's filter paper, the filtrate was kept secured in a container and placed in a fridge. This process was repeated until a clear filtrate was obtained indicating that most of the active component in *Datura stramonium* has been extracted. The resulting filtrate was pooled and evaporated using a water bath at 40°C. The extract was dissolved in distilled water at a concentration of 50mg/ml, 100mg/ml, 2000mg/ml, and 400mg/ml.

EXPERIMENTAL ANIMALS

Twenty-five (25) male albino rats weighing between 180g and 200g were used for this experiment. They were randomly assigned into five groups of five animals each and housed in different cages at the animal house of the College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti. Access to standard rat pellets and clean water were given ad libitum. They were allowed 14 days to acclimatize.

Ethical Approval

Approval for this study was obtained from Afe Babalola University Health Research Ethical Committee (ABUADHREC) with the number ABUADHREC/15/06/2023/2024. The principles of laboratory animal care were followed during the animal research (NIH publication #85-23, revised in 1985)

STUDY DESIGN

Experimental animals were randomly distributed into five groups of five animals each. Each group was exposed to graded doses of aqueous extract of *Datura stramonium* for twenty-eight days while the control received distilled water for the duration of the experiment. The study design is described in figure 1. below

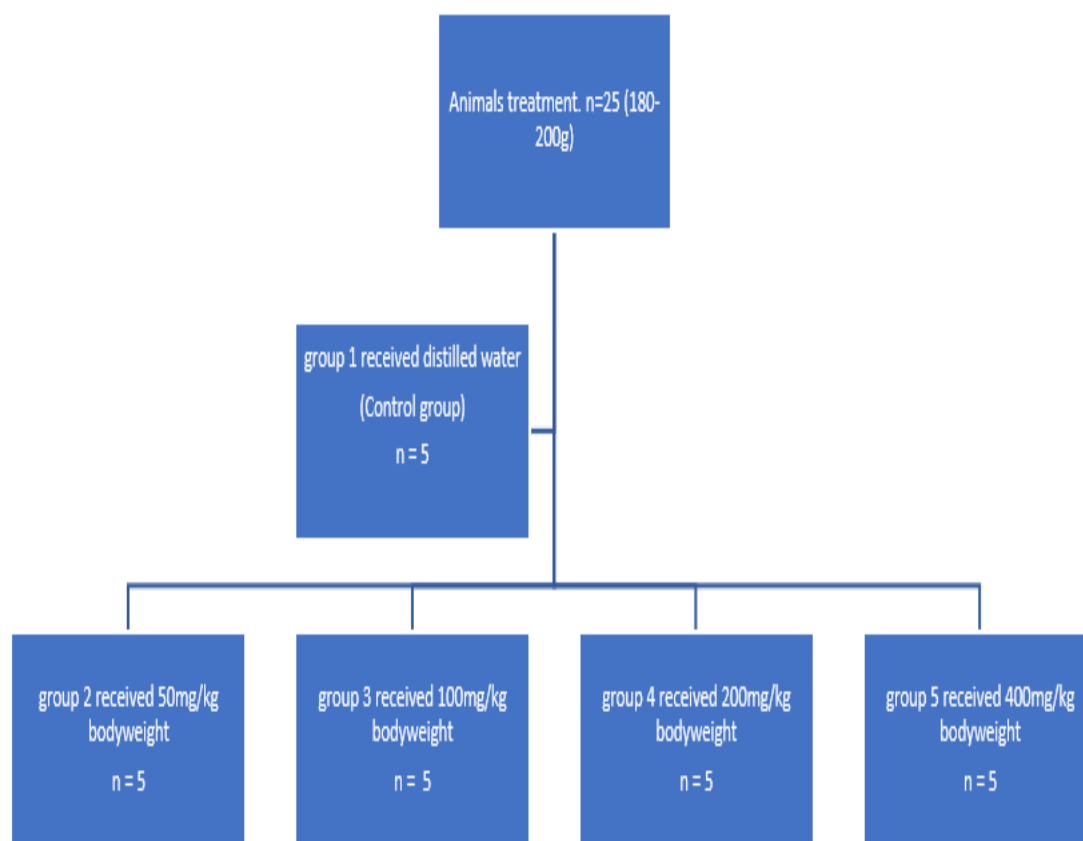


Figure 1: Animals treatment

At the expiration of the experiment, animals were sacrificed under light ether anaesthesia. Heart and kidney were harvested, rinsed in normal saline to remove blood stains, blotted dry, and then kept in the freezer until further analysed.

PREPARATION OF HOMOGENATE FOR HEXOKINASE, ALDOLASE, PYRUVATE KINASE AND LACTATE DEHYDROGENASE ACTIVITIES

Heart and kidney homogenates were prepared according to the method of Abdel-Hamid (2013). Ten (10) percent of the homogenate was prepared by placing 0.2g of organs in 1.8ml of 0.1 M Tris-HCl buffer (pH 7.4), this was done by 6 up and 6 down strokes at 1100rpm using a power-driven Teflon pestle in potter-Elvehjem glass homogenizing cup maintained at 4°C. The homogenate was then centrifuged at 4000rpm at 4°C for 10 minutes. The supernatant was carefully pipetted into an Eppendorf tube for the determination of hexokinase, aldolase, pyruvate kinase, and lactate dehydrogenase activities.

ENZYME ASSAYS

Hexokinase activity was determined by the method of Colowick (1973) while aldolase was evaluated based on Boyer's modification of the hydrazine assay (Jagannathan *et al.*, 1956). Activity of pyruvate kinase was determined according to the method of Buchner and Pfleiderer (1955), Lactate dehydrogenase activity was determined spectrophotometrically according to the method of Borgmann *et al.* (1974) as described in Cypress Diagnostic kit manual.

STATISTICAL ANALYSES

Results were expressed as mean±standard error of mean (SEM). Data was analysed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. $P < 0.05$ was considered statistically significant.

RESULTS

Figures 1 and 2 show that the administration of DS significantly increased hexokinase activities in both the heart and kidney when compared with the control. The effect observed in the activities appears to be dose-dependent.

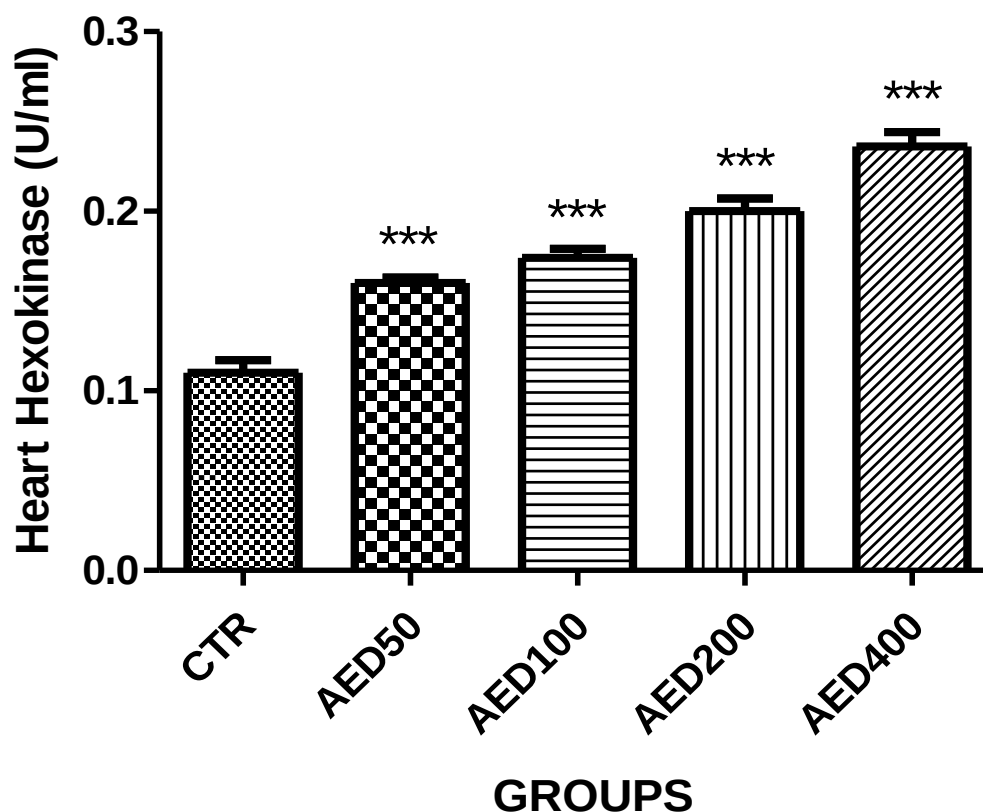


Fig. 1 Effect of DS on hexokinase activity in the heart of male albino rats that were orally exposed to graded doses of DS. Values are expressed as mean $\pm$ SEM of five determinations. ***P < 0.001 vs control.

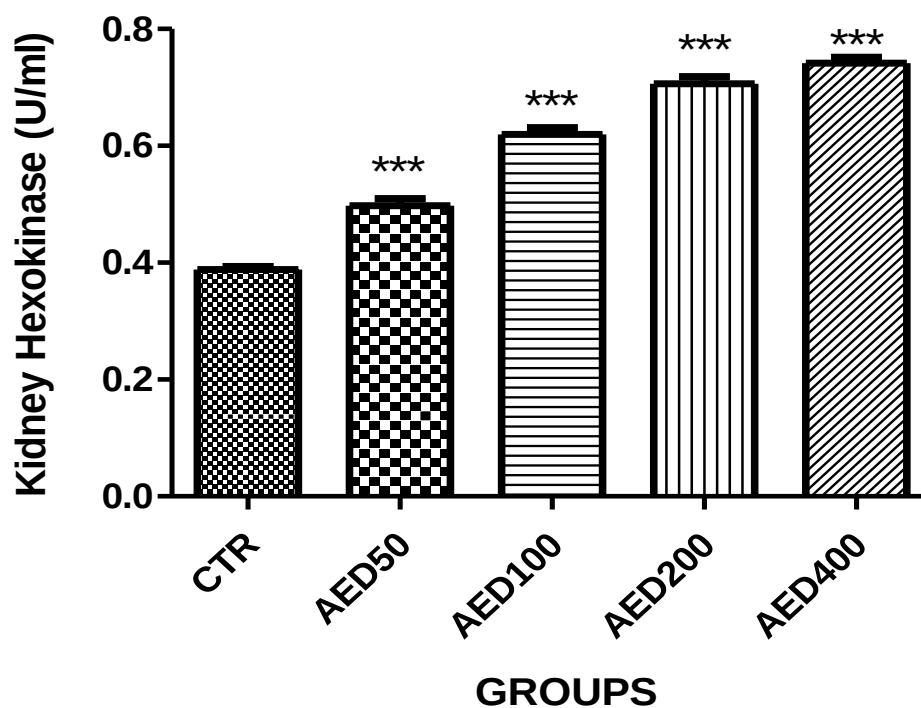


Fig. 2 Effect of DS on hexokinase activity in the kidney of rats that were orally exposed to graded doses of DS. Values are expressed as mean $\pm$ SEM of five determinations. ***P < 0.001 vs control.

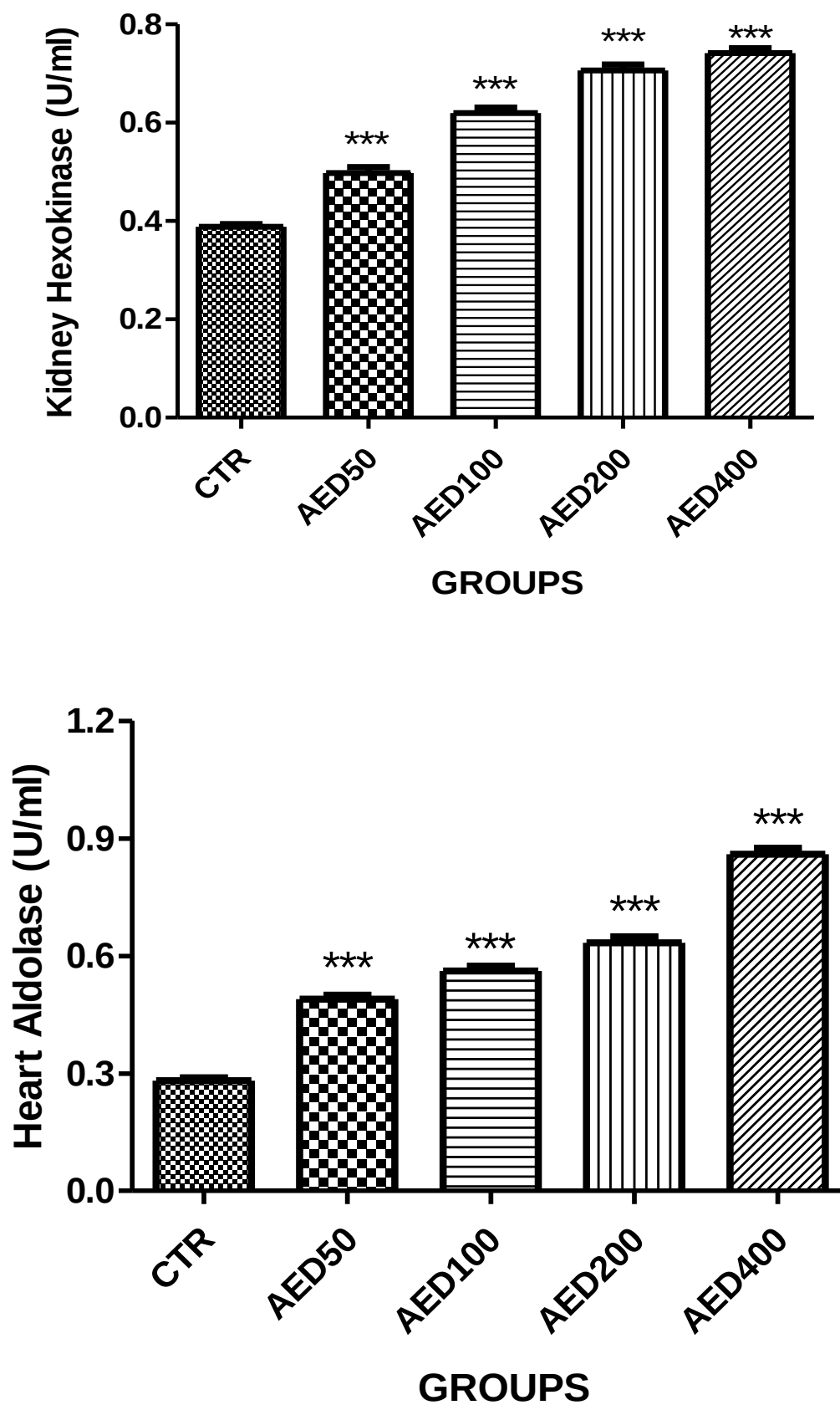


Fig. 3 Effect of DS on aldolase activity in the hearts of rats that were orally exposed to graded doses of DS. Values are expressed as mean $\pm$ SEM of five determinations. ***P< 0.001 vs control.

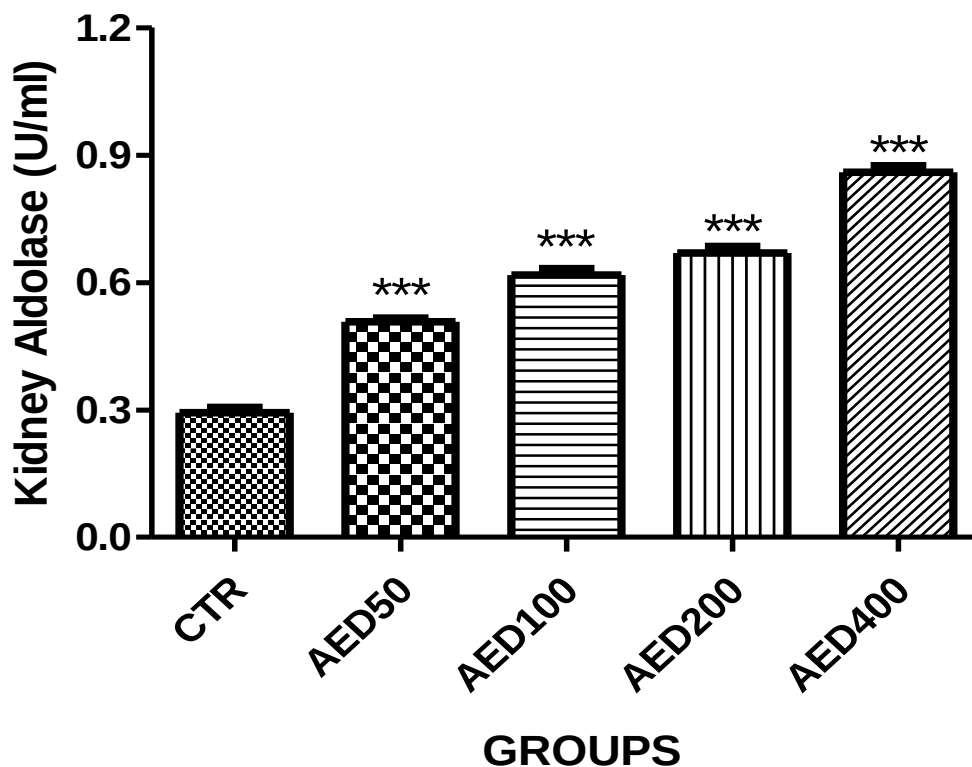


Fig. 4 Effect of DS on aldolase activity in the kidney of rats that were orally exposed to graded doses of DS. Values are expressed as mean±SEM of five determinations. ***P< 0.001 vs control.

As shown in figure 3 and 4, aldolase activities were significantly increased by the administration of graded doses of *Datura stramonium*. The effects observed are dose-dependent with the highest dose, 400mg/kg body weight having the most significant effect on aldolase activities in the heart and kidney

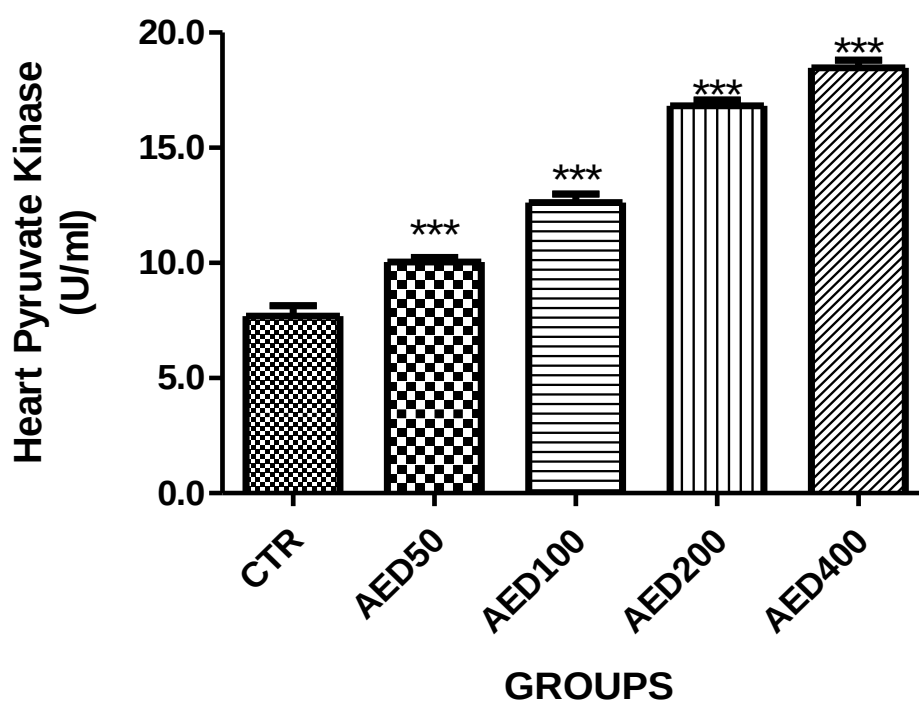


Fig. 5 Effect of DS on pyruvate kinase activity in the heart of male albino rats that were orally exposed to graded doses of DS. Values are expressed as mean±SEM of five determinations. ***P< 0.001 vs control.

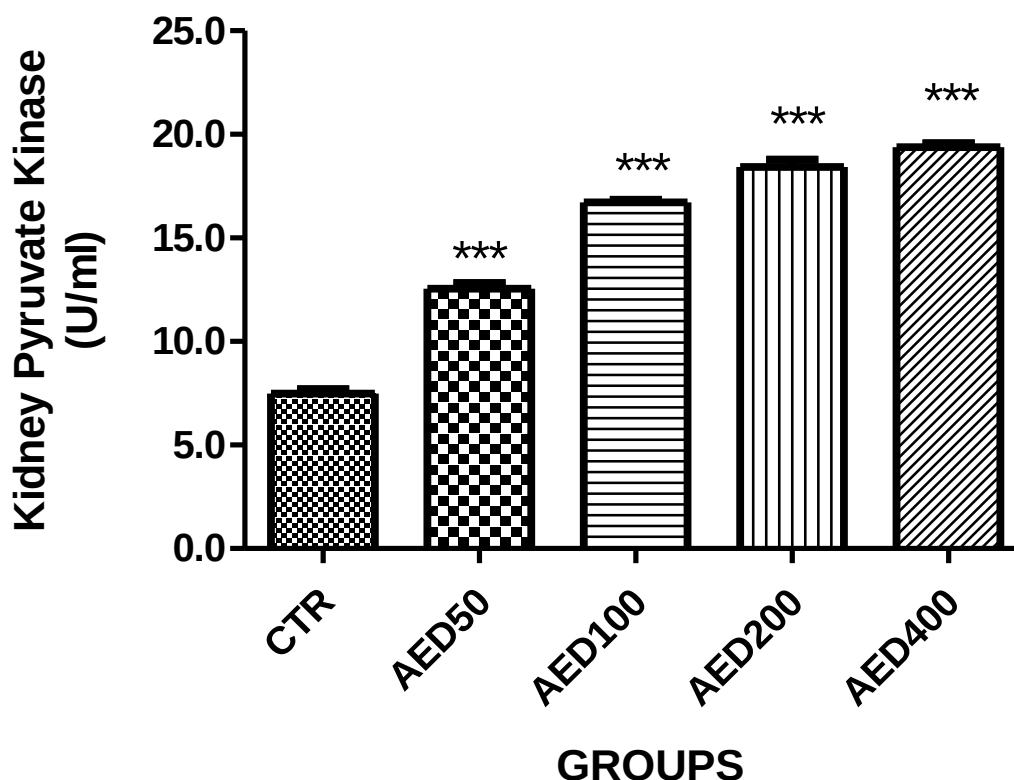
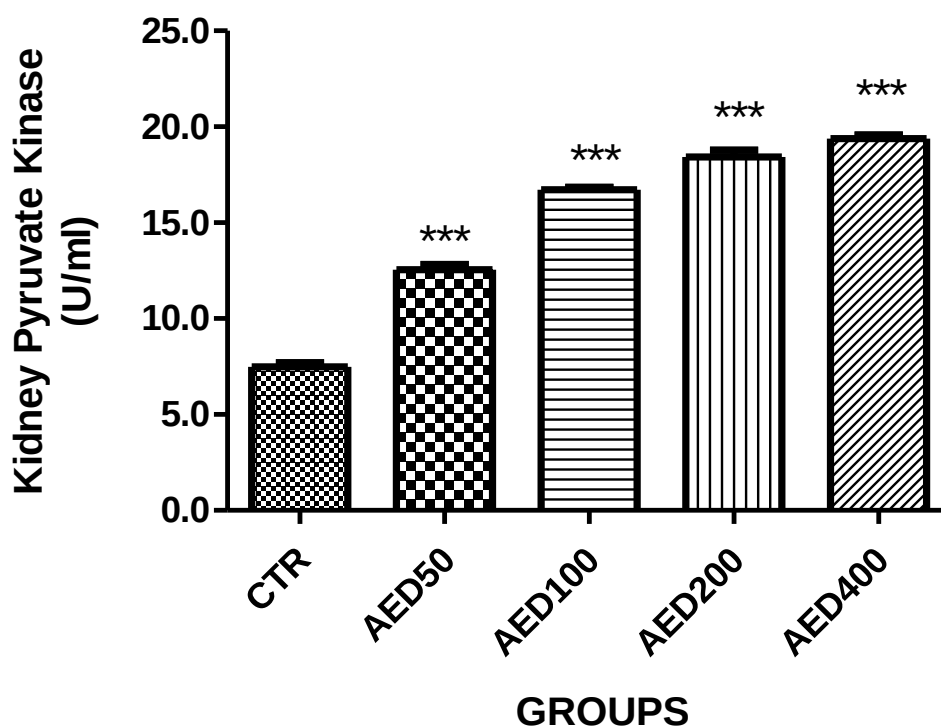


Fig. 6 Effect of DS on pyruvate kinase activity in the kidney of male albino rats that were orally exposed to graded doses of DS. Values are expressed as mean $\pm$ SEM of five determinations. ***P< 0.001 vs control.

Figure 5 shows the activity of pyruvate kinase in the heart of male rats exposed to graded doses of aqueous extract of *Datura stramonium*. A significant increase was observed in the activities of the enzyme at all doses. Figure 6 also revealed a significant increase in the activity of pyruvate kinase activity in the kidney of male rats exposed to aqueous extract of *Datura stramonium*.



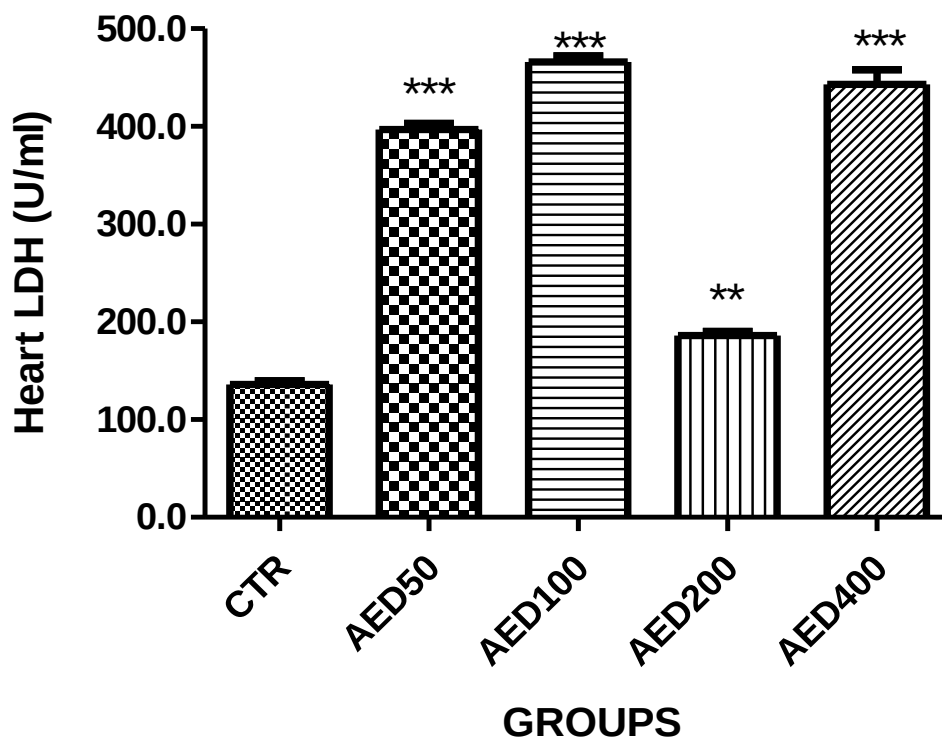


Fig. 7 Effect of DS on lactate dehydrogenase activity in the heart of male albino rats that were orally exposed to graded doses of DS. Values are expressed as mean±SEM of five determinations. ***P< 0.001 vs control.

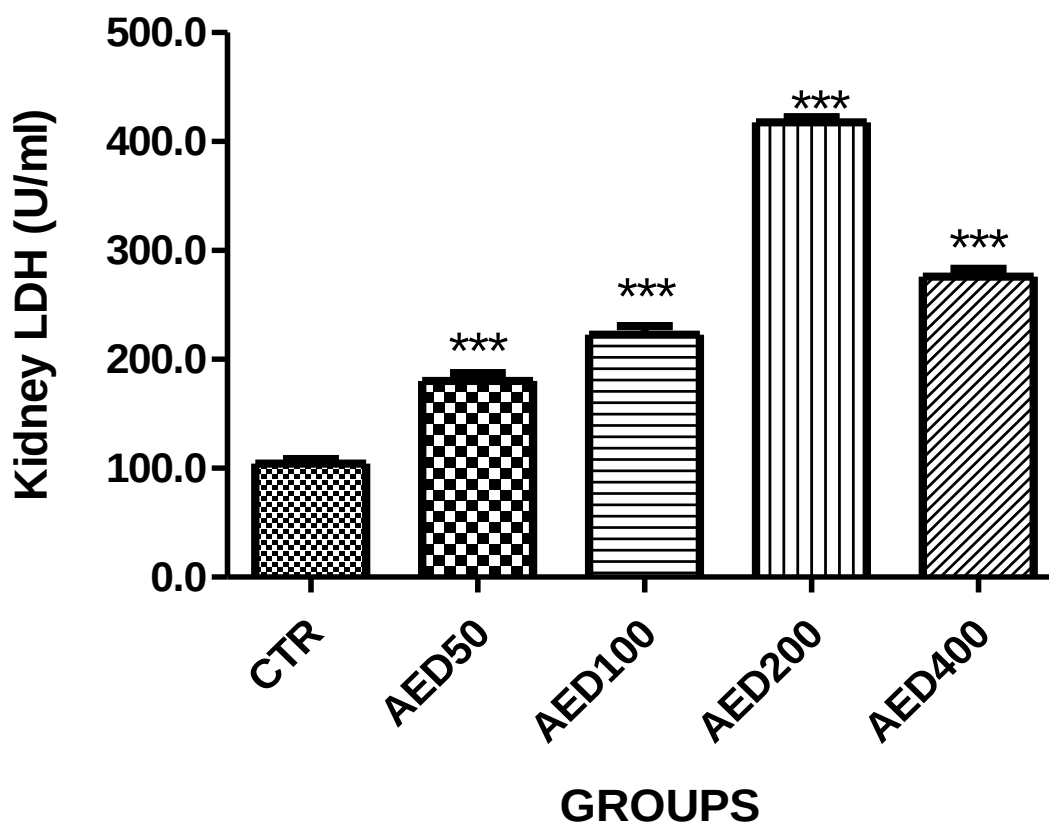


Fig. 8 Effect of DS on lactate dehydrogenase activity in the kidney of male albino rats that were orally exposed to graded doses of DS. Values are expressed as mean±SEM of five determinations. ***P< 0.001 vs control.

The activity of lactate dehydrogenase was significantly increased by the administration of an aqueous extract of *Datura stramonium* as observed in figures 7 and 8. The increase observed however was not dose-dependent as observed in hexokinase, aldolase, and pyruvate kinase. The highest increase in lactate dehydrogenase activity observed in the heart was at the dosage of 100mg/kg bodyweight closely followed by 400mg/kg bodyweight. However, the highest activity of the enzyme in the kidney was observed at 200mg/kg bodyweight.

DISCUSSION

The effect of aqueous extract of *Datura stramonium* on some glycolytic enzymes was evaluated in this research work. *Datura stramonium* has been used since time immemorial to treat some diseases and ailments. Several research works have corroborated this unique plant's pharmacological and toxicological properties. Extensive research work has been conducted in order to determine the phytochemicals components which might be responsible for both the pharmacological and toxicological activities of the plant. According to Bharkta and Lalita (2013), the pharmacological activities of *Datura stramonium* include but are not limited to antiasthmatic, antimicrobial, antifungal, anti-inflammatory, and anticancer. Its usage also includes the treatment of organophosphate poisoning and others. Kerchner and Farkas (2020) also stated that *Datura stramonium* is renowned for its anticholinergic activities resulting in vasodilation, suppressed salivation, blurred vision, psychosis, and tachycardia. These toxicological activities are due to the presence of atropine, a secondary metabolite found in the plant. Scopolamine is another secondary metabolite found in *Datura stramonium* and has been shown to be antimuscarinic and a smooth muscle relaxant.

Datura stramonium is another narcotic that is commonly abused; the roots, leaves, and entire plant can be consumed to have euphoric and hallucinatory effects, especially in adolescents and young adults (Tranca *et al.*, 2017). Intoxication due to the abuse of this plant has been reported by many researchers and physicians. Luigi *et al.* (2014) claim that two patients who consumed a significant number of *Datura stramonium* seeds noticed a rapid gain in strength and energy as well as some violent compulsion. Two cases of teenage *Datura stramonium* intoxication were reported by Sean and Anthony (2015). Both patients had to be restrained because they were too belligerent to be sedated. The cases of four adolescents were also reported in 2008 by Tannis *et al.*, the patients all seemed to have excessive energy and behaved irrationally from *Datura* intoxication and had to be restrained and sedated. These researchers also reported increases in heart rate, blood pressure, and some other parameters. This study was carried out to investigate the activities of some of the glycolytic enzymes because of the burst in energy reported by these researchers after *Datura stramonium* intoxication.

It was discovered that all the enzymes that were investigated in the heart and kidney significantly increased due to the administration of an aqueous extract

of *Datura stramonium*. Hexokinase is the first enzyme in the glycolytic pathway. It catalyzes the irreversible phosphorylation of glucose. Activities of the enzyme after *Datura stramonium* administration increased in all the doses administered. Increased activity of hexokinase literally means increased glycolysis hence increased energy production. This same pattern was seen in aldolase and pyruvate kinase activities. Aldolase is the fourth enzyme in the glycolytic pathway, it cleaves fructose 1,6-bisphosphate into a molecule of glyceraldehyde-3-phosphate and dihydroxyl acetone phosphate. Dose-dependent increases were observed in the activities of heart and kidney aldolase in all the experimental groups. Pyruvate kinase catalyzes the last step in glycolysis under aerobic conditions. It catalyzes the irreversible conversion of phosphoenol pyruvate to pyruvate with the concomitant generation of ATP. The activity of pyruvate kinase in the heart and kidney was significantly increased by all the administered doses when compared to the control. The increases observed appeared to be dose-dependent, especially in the heart.

Lactate dehydrogenase activity also significantly increased in both compartments, although the increases observed were not dose-dependent. 100mg/kg and 400mg/kg body weight produced the highest effect in the heart while 200mg/kg body weight produced the highest effect in the kidney. Lactate dehydrogenase converts pyruvate into lactate under anaerobic conditions with the concomitant reduction of NAD⁺ to NADH. This is in tandem with the findings of Maibam *et al.*, 2012 and Ahmad *et al.*, 2012 that an increase in lactate dehydrogenase activities was observed in various compartments of rats and mice after the administration of *Datura stramonium*.

Bamlaku and Gedefaw (2020), Belayneh *et al.*, 2019, Oladipo *et al.*, 2019, Ali Email Al-Snafi (2017), and Shobha *et al.*, 2014 reported the antidiabetic activities of different parts of *Datura stramonium*. The antidiabetic effect could be due to the upregulation of glycolytic enzymes thereby increasing the rate of conversion of glucose to pyruvate which will inadvertently reduce the blood glucose level. Olagunju *et al.*, 1999 corroborated these findings in their research on *Plumbago Zeylanica*. They reported that the hyperglycaemic effects of the root extract of **plumbago Zeylanica** were due to the down-regulation of some key glycolytic enzymes in the plumbago Zeylanica treated rats when compared with the control. The excessive energies reported by the physicians (Sean and Anthony, 2015, Luigi *et al.*, 2014 and Tannis *et al.*, 2008) regarding patients intoxicated by *Datura stramonium* consumption can also be a result of up-regulation of glycolytic enzymes leading to the generation of ATP. This upregulation of glycolytic enzymes might ultimately transmit to the Krebs cycle and the electron transport chain enzymes.

CONCLUSION

The present study revealed that crude aqueous extract of *Datura stramonium* was able to upregulate the activities of glycolytic enzymes in the heart and kidney of male albino rats. This might be the mechanism behind the

anti-diabetic properties of *Datura stramonium* and the excessive energies reported by physicians after *Datura* intoxication.

Author Contributions

Owolabi O. V. designed the study, Omiyale B.O., Owolabi O.V., Osesusi E. T carried out the bench work: Oni J.O, and Olojo F. O and Alli Smith Y.R. analyzed the data: Owolabi O.V, Fidelix A. and Kolawole O.D prepared the first draft of the manuscript, Enye L.A. and AlliSmith Y.R reviewed the final draft of the manuscript. All authors read and approved the final manuscript.

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