Trop J Nat Prod Res, December 2021; 5(12):2127-2132 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Stress Responses and Alteration in Membrane-Bound Phosphatase Activities in Wistar Rats Treated with Adrenaline: The role of *Senna occidentalis* Extract

Hassan Fatima[1,2]*, Owolabi .A. Olumuyiwa[2], Anigo .M. Kola[2], Ibrahim Sani[2], Umar I. Alhaji[2]

[1]*Department of Plant Sciences, Institute for Agricultural Research, Ahmadu Bello University, Zaria, Nigeria*
[2]*Department of Biochemistry, Ahmadu Bello University, Zaria, Nigeria*

ARTICLE INFO

Article history:
Received 05 March 2021
Revised 13 December 2021
Accepted 23 December 2021
Published online 03 January 2022

ABSTRACT

The cardiotoxic effect of Adrenaline has been recounted in several studies but its effect on membrane-bound phosphatase has not been known yet. The study assessed the biochemical changes and the alterations in membrane-bound phosphatase activities after the administration of adrenaline in Wistar rats. Adult rats were treated with Adrenaline (Adr) 2 mg/kg body weight and its effect on creatine kinase-MB, lactate dehydrogenase (LDH) and electrolyte levels (Na^+, K^+, Ionized Ca, Total Ca, Mg^{2+}, PO_4) were evaluated. Other parameters investigated include the activities of sodium/potassium adenosine triphosphate (Na^+-K^+-ATPase), calcium and magnesium dependent adenosine triphosphate (Ca^{2+} - Mg^{2+}- ATPase). An impairment in the activities of sodium/potassium adenosine triphosphate (Na^+-K^+-ATPase), calcium and magnesium dependent adenosine triphosphate (Ca^{2+} - Mg^{2+}- ATPase) in the vascular tissues of adrenaline treated rats was recorded. Administration of propranolol and Coffee Senna (*S. occidentalis*) extract was able to reverse the changes in a dose-dependent manner. The result also revealed a significant rise ($P<0.05$) in the levels of serum creatine kinase-MB and lactate dehydrogenase (LDH) after adrenaline treatment, a significant decrease in serum electrolytes (sodium, calcium, magnesium, phosphate ions), and an insignificant decrease in the levels of potassium ions compared to controls. The changes could be an outcome of the alteration in transmembrane transport mechanisms.

***Keywords*:** Stress, Adrenaline, *S. occidentalis*, Na^+-K^+-ATPase, Ca^{2+} - Mg^{2+}- ATPase.

Introduction

Stress is a generic concept that describes a situation that disturbs the body's balance between a living organism and its environment, including both physiological and psychological factors.[1,2] The reactions associated with stress results in the secretion of a series of hormones which includes glucocorticoids, mainly cortisol.[2] Organism can adapt to stressing stimuli as it is constant in human life.[3] The biomarkers of stress are present in patients with essential hypertension, in similar ways cardiovascular diseases together with acute and chronic psychological substrates are usually mediated by the sympathetic nervous system.[4] Stress response refers to the systemic nonspecific response followed by the exposure to strong stimulation or chronic stress, this includes, severe trauma, burn, shock, infection, major surgery or improper environment, that disturbs organisms and damage their physical and psychological health.[5] The pathogenesis of stress induced disorder remains complicated and diverse under different stress exposure, however.[5] When living organisms are exposed to environmental stress, they triggers shielding responses ensuing within side the activation of defensive processes.[6] In the event that the exposure happens at low portions, the protective effects overwhelms the adverse effects of the exposure; this adaptive situation is referred to as "hormesis."[6]

*Corresponding author. E mail: fatiado24@gmail.com
Tel: 08059662455

Citation: Fatima H, Owolabi OA, Anigo KM, Ibrahim S, Umar IA. Stress Responses and Alteration in Membrane-Bound Phosphatase Activities in Wistar Rats Treated with Adrenaline: The role of *Senna occidentalis* Extract. Trop J Nat Prod Res. 2021; 5(12):2127-2132. doi.org/10.26538/tjnpr/v5i12.14

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

Environmental, physical, and nutritional hormetins lead to the stimulation and strengthening of the maintenance and repair systems in cells and tissues.[6] Catecholamines are stress hormones that include adrenaline, noradrenaline and dopamine. Adrenaline and noradrenaline are released by the adrenal glands as part of the rapid fight-or-flight response to stress.[7] Similarly, adrenaline has powerful, dose-dependent effects on the cardiovascular system, it increments myocardial contractility, pulse and cardiac output.[8]

The P-type ATPase, Na^+, K^+-ATPase (sodium pump) and the $Ca^{2+}Mg^{2+}$-ATPase (calcium pump) are involved in a variety of fundamental cellular functions and they catalyzes the active transport of cations and phospholipids across biological membranes.[9] The membrane bound sodium pump is an electrogenic transmembrane ATPase which exchanges Na^+ and K^+ ions across the plasma membrane in the expense of ATP hydrolysis.[10–12] Furthermore, the Na^+, K^+-ATPase operates at a fraction of maximal pumping capacity under resting condition, but when the demand for ion transport increases during exercise or food intake it can be significantly activated.[13] Mutations in the pump genes encoding alpha subunit isoforms have extreme physiological results, causing very unmistakable, regularly neurological infections. The distinctions in the pathophysiological impacts of transformations further underline how the active boundaries, guideline and proteomic collaborations of the Na, K-ATPase isoforms are upgraded for the individual cell needs.[11] However, the calcium pump (Ca^{2+} -ATPase or SERCA) which is found in the endoplasmic reticulum (ER) of all eukaryotic cells is a film transport protein that keeps up with the low cytosolic calcium level that empowers an immense range of flagging pathways and physiological cycles like synaptic transmission, muscle constriction and fertilization.[14] Because of its prominent role in many physiological processes, SERCA dysfunction is associated to diseases presenting various degrees of severity which includes heart failure[15], cancer[16], cellular challenges as well as in neurodegenerative conditions[17] and its

transport activity can be repressed by a variety of compounds with different chemical structures.[18]

P-type ATPases have been studied through a wide range of techniques, and research has gained very significant insight on their transport mechanism and regulation. Generally, ion homeostasis can affect an organ's natural function, diseased or healthy.[19] There are indications that adrenaline could result in cardiac toxicity and decrease the level of membrane-bound phosphatase, nevertheless, little is known about these relationships. Our assessment of literature revealed no study on the activities of membrane-bound phosphatases in cardiac tissues of adrenaline-administered rats. The parameters of cardiac toxicity; creatine-kinase, lactate dehydrogenase and transmembrane ionic movement after the administration of adrenaline in Wistar rats were investigated. The roasted seeds of Coffee Senna (*S. occidentalis*) are commonly used by local people as a coffee substitute and in curing several diseases.[20] Assessing the effect of *S. occidentalis* extract may throw some light on the mechanism of action of the extract. Since cellular membrane are among the first focuses for restorative or toxic exercises, the membrane bound phosphatase exercises are astounding model frameworks for elucidation of impacts initiated by various medications and natural poisons.[21]

Materials and Methods

Chemicals and reagents

ATP and Adrenaline were obtained from Sigma Chemical Co., St. Louis, MO, USA. All other chemicals used were of analytical grade. Standard enzymatic kits for estimation of serum parameters were commercially purchased.

Animals and treatment

Male Wistar rats, weighing 150-180g, were obtained from Department of Physiology and Pharmacology, Faculty of pharmaceutical sciences, Ahmadu Bello University, Zaria, Kaduna State, Nigeria and housed in the Departments Animal Center. Rats were housed individually in cages, in a room with 12-hour dark/light cycle. Rats were allowed free access to tap water and were fed with commercial grower's mash (PLS Feeds, Zaria, Kaduna State, Nigeria) throughout the experiment. The animal care and experimental protocols were in accordance with nationally approved guidelines. Animals were deprived of food but allowed free access to tap water for 24 hours prior to experiments.

Plant material

Fresh seeds of *Senna occidentalis* were gathered during the rainy season (July, 2011) from Bida in Niger State, longitude 30° East of the Greenwich meridian and latitude 0900° and 1130° North of the equator. The plant was authenticated and deposited with a voucher number 1047, at the Herbarium Unit of the Department of Biological Sciences, Ahmadu Bello University, Zaria.

Preparation/Extraction of plant material

The seeds of *Senna occidentalis* was shade dried, roasted at 210°C for 15 mins.[22] The coarse powdered seeds (50 g), was extracted with 2 L of 80% methanol in H_2O (v/v) by maceration for 3 days. The extract obtained was evaporated to dryness using rotary evaporator.

Acute toxicity studies

Acute toxicity of *S. occidentalis* methanolic extract was carried out using modified Lorke's method.[23] The oral median lethal dose was calculated using the formula:

$LD_{50} = \sqrt{}$minimum toxic dose × maximum tolerated dose.

Experimental design

Experimental animals were starved of food and water for 24 h and administered 2 mg/kg body weight of adrenaline intraperitoneally.[24] *Senna occidentalis* was the test group, while the negative control group was treated with saline (0.9% NaCl). Propranolol (40 mg/kg body weight) per rats was used as a positive control.

Animal Groupings

The rats were divided into seven groups (n=5 in each group).

Group 1: Normotensive rats that received normal saline only

Group 2: Adrenaline (2 mg/kg body weight) treated rats (AIR).

Group 3: Received adrenaline (2 mg/kg) and treated with propranolol (40 mg/kg).

Group 4: Received adrenaline (2 mg/kg) and treated with *Senna occidentalis* extract (125 mg/kg)

Group 5: Received adrenaline (2 mg/kg) and treated with *Senna occidentalis* extract (250 mg/kg).

Group 6: Received adrenaline (2 mg/kg) and treated with *Senna occidentalis* extract (500 mg/kg).

Group 7: Normotensive rats that received *Senna occidentalis* extract (500 mg/kg).

The extract was administered for seven days.

Serum and Tissue preparation

After the experimental period, the animals were sacrificed by cervical separation after an overnight fast. Blood tests were gathered from the jugular vein into lithium heparinized sample bottles and centrifuge at 3000 x g for 10 min, stored at 4°C, and used within 12 h of collection. The hearts were quickly excised, cleared of connective tissue, washed in ice-cold isotonic saline, blotted with filter paper and weighed. Part of the organs was sectioned for histopathological examination and the rest was homogenized in ice-cold 0.25 M sucrose solution (1:5, w/v) as previously reported.[25] The samples were kept frozen at -20°C until analysis.

Extraction of enzyme

10% of heart homogenate was prepared in ice- cold 0.25 M sucrose and centrifuged at 3000 x g for 15 mins and the supernatant so obtained was centrifuged at 12,000 x g for 30 min in a refrigerated ultracentrifuge. The supernatant was again subjected to further centrifugation at 35,000 x g for 30 min. The resultant pellet so obtained corresponded to heavy microsomal fraction.[26] The pellet was then resuspended in cold 0.25 M sucrose and used as the enzyme source.

Biochemical assays

Assay of cardiac marker enzymes

The serum of all animals was assessed for their cardiac marker enzyme levels using commercial kits and measured spectrophotometrically.[27]

Assay of serum electrolytes

Intracellular concentrations of total magnesium and calcium were measured by atomic absorption spectrophotometry and those of sodium, ionized calcium, phosphate and potassium by ion selective electrode freshly.[28]

Assay of membrane bound enzymes

Estimation of Na^+/K^+-ATPase

The homogenate was used for the assays of the membrane-bound phosphatases. The activities of Na^+/K^+-ATPase were estimated according to the procedure of [29].The activity of the enzyme was expressed as μmoles of inorganic phosphate (Pi) liberated/min/mg protein. The reaction mixture contains 1.0 mL of 184 mM Tris-buffer (pH-7.5) and 0.2 mL of each of the reagents (50mM MgSO4, 600 mM NaCI, 50 mM KCI, 1 mM EDTA, 40 mM ATP). The reaction was mixed and incubated at 37°C for 10 mins and the reaction was commenced by the addition of 0.1 mL of homogenate. The assay medium was incubated for 15mins. After incubation the reaction was terminated by the addition of 1.0 mL of 10%TCA. The enzyme source was added to control tubes after the addition of 10% TCA. The contents were centrifuged and the phosphorous content in the supernatant was estimated spectrophotometrically.[30]

The reaction was arrested by the addition of 1 mL of cold 10% TCA. The tubes were centrifuged and the phosphorous content in the supernatant was estimated by [30] using commercial diagnostic kit. The activity of Na^+/K^+-ATPase was expressed as mmoles of phosphorous liberated/h/mg protein.

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Estimation of Ca^{2+}-ATPase

Ca^{2+}-ATPase activity was assayed according to the method of[31], 0.1ml each of all reagents (125 mM Tris-HCI buffer, 50mM CaCI2, 10mM ATP) was added in a test tube and mixed well. Then 0.1ml of distilled water and 0.1 mL enzyme source was again added and mixed well. The reaction mixture was incubated for 15 mins at 37^0C. After incubation, the reaction was stopped by the addition of 1.0ml of 10% TCA. The enzyme source was added to control tubes after the addition of 10% TCA. The contents were centrifuged and the phosphorus content in the supernatant was estimated spectrophotometrically by [30] the ammonium molybdate method, based on the modified.[32] The activity of the enzyme was expressed as μmoles of inorganic phosphate (Pi) liberated/min/mg protein.

Estimation of Mg^{2+}-ATPase

The assay of the activities of Mg^{2+}-ATPase was evaluated by the method of.[33] It was initiated by the addition of 0.1ml homogenate to an incubation medium containing 0.1ml of distilled water and 0.1ml each of the reagents (375 mM Tris-HCI buffer, pH-7.6, 25 mM $MgCI_2$, 10 mM ATP). The reaction mixture was incubated for 15 mins at 37^0C. After incubation, the reaction was stopped by the addition of 0.1 mL of 10%TCA. The enzyme source was added to control tubes after the addition of 10% TCA. The contents were centrifuged and the phosphorus content in the supernatant was estimated spectrophotometrically by [30] the ammonium molybdate method, based on the modified.[32] The activity of the enzyme was expressed as μmoles of inorganic phosphate (Pi) liberated/min/mg protein.

Total protein

Total Protein levels in the tissue homogenate were determined by the method of [34]using bovine serum albumin as a standard.

Statistical analysis

Data were analyzed using the generalized linear model procedure (proc GLM) of statistical analysis system.[35] Results were expressed as mean ± SEM. Differences between means were separated using Duncan multiple range test (DMRT). A probability value of 0.05($P < 0.05$) was considered as significant.

Results and Discussion

The changes in biochemical and physiological parameters occurring a long time after stress are not yet elucidated.[36]But, it is believed that stress have negative impacts on health and disease risk, although the exact mechanisms by which this occurs, as well as the implications for treatments and clinical recommendations, have not been examined in-depth.[7] There are factors which are dependent on the stress response being pathologic, including individual adapting abilities, life history, seriousness, and span of the stressor.[7] Lately, more attention has been received on the role of catecholamine-induced cardiac toxicity, elevated levels of circulating catecholamines on oxidation induce cardiac dysfunction and sudden cardiac death through the formation of aminochrome, development of oxidative stress, and occurrence of intracellular Ca^{2+} overload, while, high doses of adrenaline causes myocardial cell damage.[37]Beta-blockers act to inhibit β-adrenergic signaling and propranolol, also a beta-blocker has been prescribed for the treatment of hypertension, including anxiety.[7]

The administration of adrenaline to rats increased cardiotoxicity manifested by elevation in the levels of cardiac injury markers i.e., serum LDH and CK-MB levels (Table 1). Values of CK-MB in the stressed group (untreated AIR) were significantly elevated ($p<0.05$) compared to all other groups. No significant differences were observed between groups treated with 125 mg/kg extract and normotensive control. Lower values were recorded in groups treated with propranolol and groups treated with extract at 250 mg/kg. The negative control group recorded a significant increase ($p<0.05$) in LDH values compared to others. Groups treated with 500mg/kg body weight of extract and positive control group had values similar to that of normotensive rats. Treatment with propranolol, 125 mg/kg and 250 mg/kg body weight of extracts also had similar values. The extracts dose-dependently reversed the stress-induced increases in serum CK-MB and LDH activities. It was observed that treatment at different concentration of the extract also showed a significant ($p<0.05$) decrease in enzyme activities. Increase in such enzymes could suggest leakage as a result of toxicity induced by adrenaline treatment. The results also indicate that *S. occidentalis* seed extract has the tendency to reduce the leakage of the elevated cardiac marker enzymes. Previous findings have also demonstrated that an injection of adrenaline or isoproterenol, a *beta*-adrenergic agonist, increases plasma CK, LDH activities in rats and dogs.[38]

The results of serum electrolytes are presented in Table 2. A significant decrease ($P<0.05$) in the level of sodium was observed in negative control group compared to the normotensive group and significant differences were observed in rats treated with 250 mg/kg body weight of extract and the propranolol treated group. However, there was a significant increase ($P<0.05$) in sodium level for AIR treated with 500 mg/kg body weight when compared to other groups and no significant difference ($P<0.05$) in potassium ion concentration in normal and experimental rats. Adrenaline treated rats with propranolol and the positive control group showed a significant decrease ($P<0.05$) in the level of ionized calcium concentrations compared to all other groups. A significant decrease ($P<0.05$) was also observed in the treatment groups (125, 250, 500 mg/kg) compared with the negative control. There was a significant increase ($P<0.05$) between the negative control and all other groups in total calcium level. Treatment with 125 mg/kg body weight of extract had similar value for total calcium ion with the normotensive group rats, AIR treatment with propranolol, 250; 500 mg/kg body weight of extract and the positive control all showed a significant decrease when compared to normotensive group. The levels of magnesium ion concentration were significantly decreased ($P<0.05$) in negative control group compared to all others, treatment with 250 mg/kg body weight and positive control exhibited similar values. A significant decrease ($P<0.05$) was observed between groups treated with 500 mg/kg weight of extract and positive control group compared to normotensive groups in phosphate ion level. Treatment with propranolol, 125 and 250 mg/kg body weight of extract also showed a significant decrease. This demonstrate that the use of *S. occidentalis* extract may attenuate the electrolyte changes in the early phase of cardiac toxicity.

Table 1: The levels of creatine kinase and lactate dehydrogenase of Wistar rats treated with adrenaline.

S/N	Groups	CK-MB (IU/L)	LDH (IU/L)
1	Normotensive Rats	410.52 ± 26.3^{b}	180.66 ± 7.03^{b}
2	Untreated AIR	496.06 ± 13.07^{a}	207.44 ± 11.28^{a}
3	AIR + 40 mg/kg Propranolol	377.79 ± 22.54^{bc}	188.13 ± 5.52^{ab}
4	AIR + 125 mg/kg Extract	413.36 ± 8.36^{b}	194.86 ± 10.1^{ab}
5	AIR + 250 mg/kg Extract	383.00 ± 10.7^{bc}	189.78 ± 6.10^{ab}
6	AIR + 500 mg/kg Extract	353.36 ± 14.81^{cd}	173.74 ± 6.41^{b}
7	Normal Rats+500 mg/kg Extract	327.36 ± 6.99^{d}	169.89 ± 5.54^{b}

Data are expressed as mean ± SEM. Values with different superscripts along the column are significantly different ($P < 0.05$). AIR (Adrenaline-Induce Rats). CK=Creatine kinase-MB, LDH=Lactate Dehydrogenase.

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Table 2: Extracts of *Senna occidentalis* seeds with serum electrolytes levels of Wistar rats treated with adrenaline

S/N	Groups	Na^+ (mmol/l)	K^+ (mmol/l)	Ionized Ca (mmol/l)	Total Ca (ppm)	Mg^{2+} (ppm)	PO_4 (mmol/l)
1	Normotensive Rats	166.0 ± 3.03^{a}	11.6 ± 0.34^{a}	2.48 ± 0.03^{a}	407.63 ± 29.4^{a}	10.04 ± 0.47^{a}	2.08 ± 0.08^{a}
2	Untreated AIR	150.0 ± 8.74^{bc}	10.66 ± 0.49^{a}	2.44 ± 0.02^{ab}	284.24 ± 28.2^{c}	7.11 ± 0.65^{d}	2.03 ± 0.14^{ab}
3	AIR + 40 mg/kg Propranolol	162.75 ± 2.06^{abc}	11.33 ± 0.21^{a}	2.36 ± 0.02^{c}	355.80 ± 28.9^{ab}	8.35 ± 0.73^{bcd}	1.88 ± 0.06^{abc}
4	AIR + 125 mg/kg Extract	160.75 ± 4.53^{abc}	11.88 ± 0.84^{a}	2.41 ± 0.01^{bc}	414.53 ± 7.04^{a}	9.71 ± 0.44^{ab}	1.72 ± 0.16^{bcd}
5	AIR + 250 mg/kg Extract	156.33 ± 7.97^{abc}	11.73 ± 0.72^{a}	2.43 ± 0.03^{bc}	371.74 ± 18.6^{ab}	8.77 ± 0.38^{abc}	1.67 ± 0.10^{cd}
6	AIR + 500 mg/kg Extract	148.40 ± 2.14^{c}	11.48 ± 0.65^{a}	2.39 ± 0.01^{bc}	313.60 ± 14.5^{bc}	7.67 ± 0.37^{cd}	1.50 ± 0.03^{d}
7	Normal Rats + 500 mg/kg Extract	$161.0 \pm 2.74b^{ac}$	11.55 ± 0.39^{a}	2.35 ± 0.02^{c}	350.11 ± 8.1^{abc}	8.97 ± 0.42^{abc}	1.51 ± 0.07^{d}

Data are mean ± SEM. Values with different superscripts along the column are significantly different ($P<0.05$). AIR (Adrenaline-Induced Rats).

The effect of adrenaline administration, sufficient to achieve its pathophysiological levels resulted in a significant decrease in the level of Mg^{2+}.[39] Hence a diminished concentration of extracellular free Mg^{2+} results in an expanded Ca^{2+} influx and expanded the concentration of intracellular free Ca^{2+}.[39] This effect was abolished by simultaneous infusion of propranolol.[39] Hypomagnesemia builds potassium discharge, and hypokalemia is hard to cure with simultaneous hypomagnesemia in light of the fact that the sodium-potassium-ATPase pump requires the presence of magnesium ions.[40] A non-significant reduction was observed in serum K^+ level. Similar alteration in serum K^+ level in early myocardial infarction was observed by couple of researchers.[41]Catecholamines cause hypokalemia and increases the arrhythmic risk; however the Na^+ K^+ATPase pump was stimulated via β_2 receptors and potassium was shift into the intracellular compartment by adrenaline.[42]Hypocalcemia occurred after the administration of high-dose adrenaline, this induces the opening of Ca^{2+} channels which increases calcium influx and elevates intracellular calcium even further.[43] Treatment with *S. occidentalis* extract normalized this effect. Hyponatremia may be due to increased catecholamine or a consequence of hypomagnesemia which causes inadequate activities of Na^+,K^+ ATPase thereby resulting in intracellular accumulation of sodium.[44] Dysregulation of the phosphorus homeostasis basically influences cellular metabolism, musculoskeletal and cardiovascular capacities.[45]Treatment of adrenaline into healthy male subjects reduced the plasma concentrations of both potassium and phosphate to a similar extent, in a dose-dependent manner, an effect which was prevented by the administration of propranolol.[46] It thus seems that low and high but even high-normal phosphate levels have harmful effects on cardiac function. Hypophosphatemia due to transcellular shift may be caused by increased catecholamine action and adrenaline is the main hypophosphatemia catecholamine. High serum levels of catecholamines, either endogenous (e.g., in septic patients) or exogenous, improves the intracellular shift of phosphate, that is utilized for the formation of phosphate-containing intermediates of the glycolytic metabolism.[47] Results of membrane bound phosphatases in the heart tissues are presented in Table 3. The activities of Na^+K^+ATPase, Ca^{2+} ATPase, Mg^{2+} ATPase were significantly diminished in adrenaline-induced rats (Group II) when compared with control rats (Group I). The activities of these enzymes were reverted to near normal in *S. occidentalis* extract administered rats (Group IV, V, VI, and VII). No significant change was observed in propranolol (positive control) rats (Group III) as compared to the negative control group (Group II). Membrane bound ATPases plays an important role in the contraction and relaxation of the cardiac muscle by maintaining the normal ion levels inside the myocyte. The cardiac function is being affected by changes in the properties of these ion pumps.[48] The effect of catecholamines in acute and chronic stress is balanced by magnesium. However, Mg^{2+} together with ATP can greatly stimulate the release of catecholamine from adrenal medullary granules. Neither ATP nor Mg^{2+} alone may have any effect on the release of catecholamine.[39] The effects of Ca^{2+}, which causes the release of catecholamine from the granules, are inhibited in the presence of ATP and Mg^{2+}.[39] Na^+,K^+-ATPase is sensitive to a great number of different groups of analytes, including cardiovascular drugs, biologically important elements, heavy metals, organic solvents and some toxic organic compounds.[49] Reduced activities of Mg^{2+} ATPase and Na^+/K^+ ATPase may be responsible for ionic imbalance caused by adrenaline which damages the membranous proteins. Since Ca^{2+}-ATPase is an extrusion pump; a drop in its activity may lead to an increase in intracellular calcium accumulation.[50]However, it was reported that inhibition of Ca^{2+}- ATPase induced perturbation of cell calcium homeostasis and its effect may associate with a marked increase in Ca^{2+} permeability.[51] Previous studies have shown a dynamic regulation of ATPases in the regulation of vascular smooth muscle tone and endothelial function in addition to alterations in cations metabolism.[52,53]

Table 3: Extracts of *Senna occidentalis* seeds on the activities of membrane-bound phosphatase in Wistar rats treated with adrenaline.

S/N	Groups	Na^+ K^+ ATPase	Ca^{2+} ATPase	Mg^{2+} ATPase
1	Normotensive Rats	8.05 ± 0.29^{a}	10.44 ± 1.36^{a}	11.62 ± 0.67^{a}
2	Untreated AIR	3.46 ± 1.06^{b}	7.20 ± 0.42^{b}	6.31 ± 0.54^{c}
3	AIR + 40mg/kg Propranolol	6.67 ± 0.45^{a}	7.29 ± 0.92^{b}	5.72 ± 0.60^{c}
4	AIR + 125mg/kg Extract	6.23 ± 0.56^{a}	9.48 ± 0.90^{ab}	9.31 ± 1.06^{ab}
5	AIR + 250mg/kg Extract	4.18 ± 0.64^{b}	8.64 ± 1.00^{ab}	8.47 ± 0.83^{bc}
6	AIR + 500mg/kg Extract	3.50 ± 0.53^{b}	8.06 ± 0.93^{ab}	7.90 ± 1.09^{bc}
7	NormotensiveRats+500mg/kg Extract	4.18 ± 0.64^{b}	7.36 ± 0.15^{b}	8.52 ± 0.86^{bc}

Values are mean ± SEM. Values with different superscripts along the column are significantly different ($P < 0.05$). AIR (Adrenaline-Induce Rats). Activities were expressed as µmoles of Pi liberated/min/mg protein.

Conclusion

In summary, the results indicate that administration of adrenaline alters electrolyte and membrane-bound phosphatase activities. A significant increase in CK-MB and LDH values were also seen .Accordingly, the administration of *S. occidentalis* significantly ameliorate the cardiotoxic effect of adrenaline and the activities of the membrane-bound phosphatase as well as the cardiac markers, and electrolyte levels were restored to near normal, suggesting theβ-adrenergic effect of the extract.

Conflict of Interest

The authors declare no conflict of interest.

Author's Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgements

The authors wish to thank Dr Musa Bashir for providing us with his expertise in preparation for our experiment. Unreserved appreciation and thanks also to Ali Sani Suleiman for his timely help in induction and restraining of the animals.

References

1. König U, Visser EK, Hall C. Indicators of stress in equitation. Appl Anim Behav Sci [Internet]. 2017; 190(2):43-56.
2. Ramírez-alvarado ED, López-luna A, Alejandra B, Martínez S, Flores- JA, Torre D, Ortega-Hernández Z , Moreno-Longoria J, Hugo S. Rol Of Cortisol In Cellular Stress. Int J Pharm Sci Invent. 2020; 9(I):30-36.
3. Daian MR, Petroianu A, Alberti LR. Current Knowledge on Psychic Stress in Surgical Procedures. Open J Biol Sci. 2016; 1:007-13.
4. Esler M. Mental stress and human cardiovascular disease. Neurosci Biobehav Rev [Internet]. 2017; 74:269-276.
5. Du J, Li M, Huang Q, Liu W, Li W qun, Li Y jian, Gong Z Cheng. The critical role of microRNAs in stress response: Therapeutic prospect and limitation. Pharmacol Res. 2019; 142:294-302.
6. Rossnerova A, Izzotti A, Pulliero A, Bast A, Rattan SIS, Rossner P. The molecular mechanisms of adaptive response related to environmental stress. Int J Mol Sci. 2020; 21(19):1-15.
7. Kelly RR, Mcdonald LT, Jensen NR, Sidles SJ, Amanda LC. Impacts of Psychological Stress on Osteoporosis : Clinical Implications and Treatment Interactions. Front Psychiatry. 2019; 10(200):1-21.
8. Verberne AJM, Korim WS, Sabetghadam A, Llewellyn-Smith IJ. Adrenaline : insights into its metabolic roles in hypoglycaemia and diabetes. Br J Pharmacol. 2016; 173:1425-1437.
9. Dao TT, Sehgal P, Tung TT, Vuust J, Nielsen J, Palmgren M, et al. Demethoxycurcumin Is A Potent Inhibitor of P-Type ATPases from Diverse Kingdoms of Life. PLOS. 2016; 11(9):1-19.
10. Ghosh B and Lepore ASGM. Understanding the Dysfunction of Na+/K+-ATPase in Rapid-Onset Dystonia Parkinsonism and Amyotrophic Lateral Sclerosis. In: Chakraborti S., Dhalla N. (eds) Regulation of Membrane Na+-K+ ATPase. Adv Biochem Heal Dis [Internet]. 2016; 15:145-157.
11. Clausen MV, Hilbers F, Poulsen H. The structure and function of the Na,K-ATPase isoforms in health and disease. Front Physiol. 2017; 8:1-16.
12. Pivovarov AS, Calahorro F, Walker RJ. Na^+ / K^+ - pump and neurotransmitter membrane receptors. Invertebr Neurosci [Internet]. 2019; 19(1):1-16.
13. Pirkmajer S and Chibalin AV. Na, K-ATPase regulation in skeletal muscle. Am J Endocrinol Metab. 2016; 311(1):E1–31.
14. Primeau JO, Armanious GP, Fisher MLE, Young HS. The SarcoEndoplasmic Reticulum Calcium ATPase. In: Harris J., Boekema E. (eds) Membrane Protein Complexes: Structure and Function. Subcell Biochem. 2018; 87:229-258.
15. Goico A, Chandrasekaran M, Herrera CJ. Novel developments in stress cardiomyopathy : From pathophysiology to prognosis. Int J Cardiol [Internet]. 2016; 223:1053-1058.
16. Patergnani S, Danese A, Bouhamida E, Aguiari G, Previati M, Pinton P, Giorgi C . Various Aspects of Calcium Signaling in the Regulation of Apoptosis, Autophagy, Cell Proliferation, and Cancer _ Enhanced Reader. Int J Mol Sci. 2020; 21(8323):1-27.
17. Chami M and Checler F. Alterations of the Endoplasmic Reticulum (ER) Calcium Signaling Molecular Components in Alzheimer's Disease _ Enhanced Reader. Cells. 2020; 9(2577):1-23.
18. Tadini-Buoninsegni F, Smeazzetto S, Gualdani R, Moncelli MR. Drug interactions with the Ca2+-ATPase from Sarco(Endo)plasmic reticulum (SERCA). Front Mol Biosci. 2018; 5(APR):1-8.
19. Themistocleous SC, Yiallouris A, Tsioutis C, Zaravinos A, Johnson EO, Patrikios I. Clinical significance of P - class pumps in cancer (Review). Oncol Lett. 2021; 22(658):1-18.
20. Yadav JP, Arya V, Yadav S, Panghal M, Kumar S, Dhankhar S. Fitoterapia Cassia occidentalis L .: A review on its ethnobotany , phytochemical and pharmacological profile. Fitoterapia [Internet]. 2010; 81(4):223-230.
21. Vasić V, Momić T, Petković M, Krstić D. Na+,K+-ATPase as the target enzyme for organic and inorganic compounds. Sensors. 2008; 8(12):8321-8360.
22. Olapade AA and Ajayi OA. Effect of roasting regime on phytochemical properties of Senna occidentalis seeds. Int J Food Stud. 2016; 5(2):203-211.
23. Lorke D. A New Approach to Practical Acute Toxicity Testing. Arch Toxicol. 1983; 54:275-276.
24. Radaković M, Borozan S, Djelić N, Ivanović S, Miladinović DĆ, Ristanić M, Spremo-Potparevic B, Stanimirovic Z. Nitroso-oxidative stress, acute phase response, and cytogenetic damage in wistar rats treated with adrenaline. Oxid Med Cell Longev. 2018; 2018(1805354):1-12.
25. Olatunji LA and Soladoye AO. Effect of increased calcium intake on cardiac and vascular Na +-K+-ATPase activity in oral contraceptive-treated female Sprague-Dawley rats. Indian J Exp Biol. 2006; 44(11):875–879.
26. Davis PW. Inhibition of renal Na+, K+-activated adenosine triphosphatase activity by ethacrynic acid. Biochem Pharmacol. 1970; 19(6):1983-1989.
27. Ali F, Ali S, Naqvi S, Bismillah M, Wajid N. ScienceDirect Comparative analysis of biochemical parameters in diabetic and non-diabetic acute myocardial infarction patients. Indian Heart J [Internet]. 2016; 68(3):325-331.
28. Ballentine R and Burford D. Determination of Metals (Na , K , Mg , Ca , Mn , Fe , Co , Cu , Zn). Meth Enzymol. 1957; 3:1002-1035.
29. SL B. Sodium-potassium activated adenosine triphosphatase and cation transport. Membr Ion Transp EE Bittar, ed London Intersci Publ Ltd,. 1970. 257-263 p.
30. Fiske CH and Subbarow Y. The colorimetric determination of phosphorus. J Biol Chem. 1925; 66:375-400.
31. Hjerten S and Pan H. Agarose suspension electrophoresis. The. Biochim Biophys Acta,. 1983; 728:281-288.
32. Daly JA and Ertingshausen G. Direct method for determining inorganic phosphate in serum with the "CentrifiChem". Clin Chem. 1972; 18(3):263-265.
33. Ohnishi T, Suzuki T, Suzuki Y, Ozawa K. A comparative study of plasma membrane Mg^{2+}-ATPase activities in normal, regenerating and malignant cells. Biochim Biophys Acta. 1982; 684(1):67-74.
34. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem. 1951; 193:265-275.
35. Nshinyabakobeje S. Using SAS PC with WINDOWS 95, 98,

2000, and WINDOWS NT. Vol. 302/602, Biometry & Statistics 302/602, 2002; 1-59p.
36. Shkurashivska S and Ersteniuk H. The effect of adrenaline on the mineral and trace element status in rats. Open Life Sci. 2019; 14(1):158-164.
37. Dhalla NS. Formation of Aminochrome Leads to Cardiac Dysfunction and Sudden Cardiac Death. Circ Res. 2018; 123:409-411.
38. Van Belle H, Verheyen W, Ver Donck K, Janssen PAJ, Robertson JIS. Prevention of Catecholamine-Induced Cardiac Damage and Death with a Nucleoside Transport Inhibitor. J Cardiovasc Pharmacol. 1992; 20:173-178.
39. Kostov K and Halacheva L. Role of Magnesium Deficiency in Promoting Atherosclerosis , Endothelial Dysfunction , and Arterial Stiffening as Risk Factors for Hypertension. Int J Mol Sci. 2018; 19(1724):1-23.
40. Whang R, Flink EB, Dyckner T, Wester PO, Aikawa JK, Ryan MP. Magnesium Depletion as a Cause of Refractory Potassium Repletion. Arch Intern Med. 1985; 145(9):1686-1689.
41. Abraham AS, Rosenman D, Meshulam Z, Zion M, Eylath U. Serum, lymphocyte, and erythrocyte potassium, magnesium, and calcium concentrations and their relation to tachyarrhythmias in patients with acute myocardial infarction. Am J Med. 1986; 81(6):983–988.
42. Urso C, Canino B, Brucculeri S, Firenze A, Caimi G. Analysis of electrolyte abnormalities and the mechanisms leading to arrhythmias in heart failure . A literature review. Clin Ther. 2016; 167(4):e85-91.
43. Kodavanti PRS, Cameroo JA, Yallapragada PR, Desaiah D. Effect of Chlordecone (Kepone @) on Calcium Transport Mechanisms in Rat Heart Sarcoplasmic Reticulum. Pharmacol Toxcol. 1990; 67: 227-234.
44. Hulting J. In hospital Ventricular Fibrillation and its Relation to Serum Potassium. Acta Med Scand Suppl. 1981; 647:109-116.
45. Kritmetapak K and Kumar R. Phosphate as a Signaling Molecule. Calcif Tissue Int. 2019; 108:16-31.
46. Ljunghall S, Joborn H, Rastad J, Åkerstrom G. Plasma Potassium and Phosphate Concentrations—Influence by Adrenaline Infusion, β-blockade and Physical Exercise. Acta Med Scand. 1987; 221(1):83-93.
47. Megapanou E, Florentin M, Milionis H, Elisaf M, Liamis G. Drug‐Induced Hypophosphatemia : Current Insights. Drug Saf [Internet]. 2020; 43(3):107-210.
48. Yogeeta SK, Gnanapragasam A, Senthilkumar S, Subhashini R, Devaki T. Synergistic salubrious effect of ferulic acid and ascorbic acid on membrane-bound phosphatases and lysosomal hydrolases during experimental myocardial infarction in rats. Life Sci. 2006; 80(3):258-263.
49. Vasić VM, Čolović MB, Krstić DZ. Mechanism of Na+/K+-ATPase and Mg2+-ATPase inhibition by metal ions and complexes. Hem Ind. 2009; 63(5A):499-509.
50. Auer J, Weber T, Berent R, Lamm G, Eber B. Serum potassium level and risk of postoperative atrial fibrillation in patients undergoing cardiac surgery. J Am Coll Cardiol. 2004; 44(4):938-939.
51. Hazarika A and Sarkar SN. Effect of isoproturon pretreatment on the biochemical toxicodynamics of anilofos in male rats. Toxicol . 2001;165(2–3):87-95.
52. Krug LM and Berk BC. Na+,K+-adenosine triphosphatase regulation in hypertrophied vascular smooth muscle cells. Hypertens. 1992; 20(2):144-150.
53. Makynen H, Kahonen M, Arvola P, Wuorela H, Vapaatalo H, Porsti I. Dietary calcium and magnesium supplements in spontaneously hypertensive rats and isolated arterial reactivity. Br J Pharmacol. 1995; 115(8):1455-1462.