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AMELIORATIVE EFFECT OF ETHANOL EXTRACT OF *ATHROSPIRA PLATENSIS* (SPIRULINA) AND *VITIS VINIFERA* L. (GRAPE) FRUIT ON DEXAMETHASONE INDUCED HYPERTENSION ON WISTA RATS

[*1]Mohammed, A.U., Appah. J[2]., Haroun.A.A[3]., [4]Bello.A., [5]Musa I.M., Sheriff, B[6].

[*1]Department of Science Laboratory Technology, Federal Polytechnic Monguno, P. M. B. 1066 Borno state Nigeria
[2,3&4]Nigerian Defence Academy Kaduna, Department of Biological Sciences Kaduna State Nigeria
[5]Department of Biological sciences, Faculty of sciences, Borno state University Borno state Nigeria
[6]Department of Agricultural and Bioenvironmental Engineering, Ramat Polytechnic, Maiduguri

Abstract: *Hypertension, a major risk factor for cardiovascular disease and global mortality, is characterized by elevated blood pressure. This study explored the therapeutic effects of ethanol extracts from Arthrospira platensis (Spirulina) and Vitis vinifera (Grape) fruit on dexamethasone-induced hypertension in Wistar rats. Fresh Spirulina and Grape samples were obtained from Maiduguri and Jos, Nigeria, and processed for extraction and phytochemical analysis. Forty Wistar rats were divided into eight groups, with hypertension induced via dexamethasone over six days and subsequently treated for five weeks. Blood pressure, heart rate, and body weight were monitored at intervals, while liver, kidney, and blood parameters were assessed to evaluate safety and toxicity. Phytochemical screening identified saponins, tannins, flavonoids, carbohydrates, and cardiac glycosides in both extracts, with triterpenes present only in Grape. The extracts demonstrated low toxicity, with LD50 values above 5000 mg/kg and 2000 mg/kg. Both significantly lowered blood pressure, improved body weight, and exhibited nephroprotective and renoprotective effects. Spirulina also synergized with the antihypertensive drug Amlodipine, suggesting its potential as a novel therapeutic agent. Histological analyses confirmed no harm to the liver, kidney, or heart, while the extracts reversed dexamethasone-induced weight loss and hypertension. These findings highlight the potential of Arthrospira platensis and Vitis vinifera as safe and effective natural remedies for hypertension and emphasize the need for further research to isolate active compounds responsible for these benefits.*

Keywords: *Hypertension, Spirulina, Grape Extract, Antihypertensive, Phytochemicals.*

INTRODUCTION

Hypertension, commonly referred to as high blood pressure, is a significant global health concern defined by specific criteria. According to the American College of Cardiology and the American Heart Association (ACC/AHA) guidelines, elevated blood pressure is characterized by a systolic pressure (SBP) between 120–129 mm Hg and a diastolic pressure (DBP) under 80 mm Hg. Stage 1 hypertension is diagnosed when SBP reaches 130–139 mm Hg or DBP rises to 80–89 mm Hg. Hypertension is the leading preventable risk factor for cardiovascular disease (CVD) and all-cause mortality globally, with its prevalence steadily increasing due to aging populations and lifestyle-related risk factors such as high sodium intake, low potassium intake, and physical inactivity.

The condition is a major health burden in both developed and developing nations. In the United States, hypertension is the most common primary diagnosis, affecting approximately 86 million adults aged 20 and older. It significantly contributes to the risk of stroke, myocardial infarction, vascular diseases, and chronic kidney disease. On a global scale, the World Health Organization (WHO) has identified hypertension as a leading cause of mortality, reflecting its pervasive impact. Notably, in populous nations like China, hypertension has emerged as the principal cause of death, emphasizing the urgent need for effective prevention and management strategies worldwide.

MATERIALS AND METHODS

PRE-EXTRACTION PROCESSES

Collection and Identification

The fresh plant material of the *Arthrospira platensis* (Spirulina) was collected from the Lake Chad basin shores of Maiduguri, Borno State. While the fresh Grapes was purchased from Building Material Market of Jos, Plateau State. Both samples were identified at the Herbarium Section of the Department of Biological Science, Nigerian Defence Academy Kaduna.

EXTRACTION PROCESSES

Arthrospira platensis (Spirulina)

The collected samples were poured on muslin cloth and placed on dry sandy soil (absorbent), the water content was drained and left with a cake-like. This was carefully transferred to plain cardboard paper and air-dried at an ambient temperature. Five hundred (500) grams of the powdered samples were used for the extraction using Soxhletation with 2.5 liters of ethanol (85%). The extract was further concentrated using a rotary evaporator at 50℃ to remove all the residual solvent and labeled as *Arthrospira platensis* extract (APE) (Fayzunnessa *et al.,* 2011).

*Vitis vinifera L. (*Grapes)

The grapes were washed well and mixed using an electric blinder for a period of (5-7 minutes). The mixture was filtered using a sieve lined with a fine muslin cloth, and then the juice produced from it was discarded, while the remaining residues were taken in a strainer and shed-dried.

Five hundred gram (500g) of shed dried grape residue was macerated with 2.5 liters of ethanol (80%), the mixture was kept for 72 hours in a cool and dark place. Thereafter, the extract was filtered using a vacuum filtration unit and then concentrated using a rotary evaporator at 40°C, and the concentrated filtrate was labeled as *Vitis vinifera* extract (VVE) and stored at -20°C for further use.

PHYTOCHEMICAL SCREENING

Phytochemical screening involves the preliminary qualitative analysis of plant extracts to detect the presence of various secondary metabolites. In this study, both extracts were tested following the protocols described by Trease and Evans (2004). The phytochemical tests aimed to identify alkaloids, flavonoids, saponins, tannins, glycosides (including cardiac and steroidal glycosides), and terpenoids. Standard procedures were employed, ensuring reliable identification of these compounds through observable changes such as precipitate formation or color change.

To detect alkaloids, Dragendorff's test was utilized, which produced a reddish-brown precipitate, confirming their presence. For flavonoids, the Shinoda test was conducted using methanol, metallic magnesium chips, and concentrated hydrochloric acid, leading to a yellowish coloration indicative of flavonoids. Steroids and triterpenes were identified using the Liebermann-Burchard test, where acetic acid anhydride and sulfuric acid were added to the extract, resulting in color changes like blue, green, red, or orange. Saponins were confirmed by the Froth Test, where vigorous shaking of the extract with water produced a stable 2 cm foam layer.

Cardiac glycosides were identified using the Keller-Kiliani test, which yielded a purple-brown ring at the interphase and a pale green color in the upper layer. Phenolic compounds were detected by adding iron(III) chloride to the extract, resulting in blue, green, red, or purple coloration. Tannins were confirmed when ferric chloride solution produced a greenish-black precipitate. These results demonstrate the diverse array of bioactive compounds present in the extracts, which could contribute to their therapeutic potential.

Experimental Animal and Housing

Sixty (60) healthy Wistar rats (*Mus musculus*) (not less than 12 weeks old) weighing 140–240g were purchased from the Animal house of the Department of Pharmacology and Therapeutics, Faculty of Pharmaceutical Sciences, Ahmadu Bello University Zaria. Animals were housed in stainless steel cages (34 × 47 × 18 cm) lined with wood shavings.

The rats were fed on standard rat chow and water ad libitum. The animals were kept in a well-ventilated room within a temperature range of 25–30°C with ambient light and dark cycles of 10–16 hours, respectively. Rice husk was used as bedding material and changed daily. The rats were kept for seven days to acclimatize before the commencement of the experiments.

Animal grouping and dosing for dexamethasone (DEX) Induced Hypertension in Wistar rats.

The initial systolic and diastolic blood pressure (SBP and DBP) and heart rate (HR) before induction of hypertension were noted down.

Hypertension was then induced in the rats by giving 0.03 ml/kg of DEX 21-phosphate disodium salt in drinking water for six (6) days (Soto-Piña, *et al.,* 2019), while the control group received

only drinking water. Measurement of the SBP and DBP was done weekly until hypertension (SBP > 140 mmHg; DBP > 90 mmHg) was induced after six (6) weeks. The hypertensive rats were then put into eleven (11) groups of five (5) rats each and labeled I-XI for the experiment.

Experimental Design

The antihypertensive activity of the aqueous extract was evaluated by using dexamethasone-induced hypertension in rats as previously described by Soto-Piña, *et al.,* (2019). Forty (40) Wistar rats were randomly divided into eleven (8) groups of five rats each and daily treated for five consecutive weeks as described by Dzeufiet *et al.,* (2014).

Group I (negative control) was treated with normal saline (10mL/kg), while Group II-IV was treated with 50, 100, and 150 mg/kg of APE, and Groups V–VII with 50, 100, and 150 mg/kg of VVE, respectively, by oral gavage as single doses while Group IX (positive control) was treated with amlodipine (ADP) (10 mg/kg).

Meanwhile, the most effective dose (100 and 150mg/kg) of body weight of APE and VVE respectively was selected for the interactive study. Fifteen (15) healthy Wistar rat was divided into three (3) groups (n=5). Group I was treated with the combination of APE and VVE (CAVE), while group II was treated with APE and ADP (10 mg/kg), and group III was treated with VVE and ADP (10 mg/kg).

All the treatments last for five (5) weeks with daily measurement of systolic and diastolic BP as well as the heart rate at the interval of 4, 8, and 24 hours after treatment according to the method described by Sokpe *et al.,* (2020) with a little modification. During the experimental period, the body weight was assessed twice a week (Dzeufiet *et al.,* 2014)

Data Analysis

Values for parameters measured were expressed as means ± SEM. Significant differences in treatments were analyzed using one-way analysis of variance (ANOVA).

Multiple comparisons between groups were done using Dunnett's post hoc test. All statistical analyses were carried out with SPSS (16.0). Values are considered to be statistically significant at a p-value less than or equal to 0.05 ($p \leq 0.05$).

RESULT

ACUTE ORAL TOXICITY STUDY (LD_{50})

The LD_{50} was estimated to be above the limit dose (5000mg/kg and 2000mg/kg body weight), as no three lethality or sign of toxicity was recorded in each extract for both tests, according to category 5 of the Global Harmonization System (GHS) of the Organization for Economic Cooperation and Development (OECD-423, 2001). Meanwhile, the ethanol extract of Spirulina and Grapes after extraction and concentration was found to produce a percentage yield of 47.4 % w/w and 18.6% w/w respectively.

PHYTOCHEMICAL CONSTITUENTS

Preliminary phytochemical screening revealed the presence of; saponins, tannins, flavonoid carbohydrates, and cardiac glycoside in both extracts as shown in Table 4.1 and Table 4.2 respectively.

Table 4.1 Qualitative tests for preliminary phytochemical screening of Ethanol extract of *Vitis vinifera* L. (Grapes fruit).

TEST	OBSERVATION	INFERENCE
CARBOHYDRATES		
Molisch test	Reddish brown ring	+
Fehling test	Brick red precipitate	+
ALKALOIDS		
Dragendoffs test	No precipitate	-
Wagners test	No precipitate	-
Picric acid test	No precipitate	-
FLAVONOIDS		
Shinoda test	Orange coloration	+
Ferric chloride test	Greenish precipitate	+
TANNINS		
NaOH test	Yellow coloration	+
Ferric chloride test	Greenish precipitate	+
SAPONINS		
Frothing test	Persistent froth	+
Haemolysis test	Haemolysis of red blood cells	+
CARDIAC GLYCOSIDE		
Keller-killiani test	Pale green color	+
Kedde test	Blue color	+
ANTHRAQUINONES		
Bontragers test	No color change	-
STEROIDS		
Salkowski test	No color change	-
TRITERPENES		
Lieberman buchard test	Pink color	+

+ = Detective/Presence while **-** = not detective/absence.

Table 4.2 Qualitative tests for preliminary phytochemical screening of Ethanol extract of *Arthrospira platensis* (Spirulina).

TEST	OBSERVATION	INFERENCE
CARBOHYDRATES		
Molisch test	Reddish brown ring	+
Fehling test	Brick red precipitate	+
ALKALOIDS		
Dragendoffs test	No precipitate	-
Wagners test	No precipitate	-
Picric acid test	No precipitate	-
FLAVONOIDS		
Shinoda test	Orange coloration	+
Ferric chloride test	Greenish precipitate	+
TANNINS		
NaOH test	Yellow coloration	+
Ferric chloride test	Greenish precipitate	+
SAPONINS		
Frothing test	Persistent froth	+
Haemolysis test	Haemolysis of red blood cells	+
CARDIAC GLYCOSIDE		
Keller-killiani test	Pale green color	+
Kedde test	Blue color	+
ANTHRAQUINONES		
Bontragers test	No color change	-
STEROIDS		
Salkowski test	No color change	-
TRITERPENES		
Lieberman buchard test	No color change	-

+ = Detective/Presence while **-** = not detective/absence.

Antihypertensive effect of ethanol extract of *Athrospira platensis* (Spirulina) and *Vitis venifera* L. (Grape fruit) in dexamethasone (DEX) Wistar rats induced high blood pressure.

Both extracts have shown a significant difference compared to normal saline (distilled water) at $p < 0.05$ of the respective doses of 50, 100, and 150 mg/kg as described in Table 4.3.

The interactive effect of ethanol extract of *Arthrospira platensis* (Spirulina) and *Vitis venifera* L. (Grape fruit) in concurrent administration with standard drugs.

There is a significant difference at $p < 0.05$ of the standard drugs and ethanol extract of *A. platensis* (Spirulina) in reducing blood pressure (BP) of Dexamethasone-induced Hypertensive Wistar rats, compared to normal saline (distilled water) at a dose of 10 and 150 mg/kg respectively (Table 4.4).

Table 4.3: Antihypertensive effects of *Athrospira platensis* (Spirulina) and *Vitis venifera* (Grape) fruit ethanol extract on body weight gain, blood pressure and heart rate

Treatment	Dose (mg/kg)	BWG (g)	DAP (mm Hg)	MAP (mm Hg)	SAP (mm Hg)	HR (BPM)
NSL	10mL/kg	76.20 ± 1.98	84.92 ± 1.40	94.46 ± 1.29	117.50 ± 1.27	352.60 ± 3.77
APE	50	74.57 ± 2.62	82.04 ± 1.36*	90.44 ± 1.39*	121.48 ± 1.66*	340.80 ± 1.95*
APE	100	75.40 ± 2.03	70.50 ± 1.14*	80.84 ± 1.05*	110.54 ± 1.9*	320.60 ± 1.88*
APE	150	74.02 ± 1.53	78.14 ± 1.55*	89.43 ± 1.52*	120.56 ± 1.74*	352.80 ± 3.01*
VVE	50	73.36 ± 1.53	84.94 ± 1.55*	85.81 ± 1.52*	112.56 ± 1.74*	352.80 ± 3.01*
VVE	100	70.57 ± 2.02	80.92 ± 1.32*	92.44 ± 1.79*	123.48 ± 1.47*	362.80 ± 1.35*
VVE	150	73.36 ± 1.53	76.94 ± 1.55*	90.81 ± 1.52*	101.56 ± 1.74*	332.80 ± 3.01*
ADP	10	75.82 ± 2.31	62.68 ± 1.54**	71.00 ± 1.41**	97.70 ± 1.37**	300.60 ± 1.30**

Each value represents a mean ± SEM; n = 5; *p < 0.05: significantly different compared to normal saline (distilled water); **p < 0.05: significantly different compared to extract treatment (APE and VVE) at the respective doses of 50, 100 and 150 mg/kg; NSL = normal saline (10 mL/kg); APE = *Arthrospera platensis* ethanol extract at the respective doses of 50, 100 and 150 mg/kg; VVE = *Vitis vinifera* L. ethanol extract at the respective doses of 50, 100 and 150 mg/kg; BWG = body weight gained; DAP = diastolic arterial blood pressure, MAP = mean arterial blood pressure, SAP = systolic arterial blood pressure, HR = heart rate, ADP = Amlodipine (10 mg/kg).

Table 1.4 Interactive effect of concurrent administration of ethanol extract of *Arthrospira platensis* (Spirulina), *Vitis vinifera* L. (Grape) fruit with Standard drug.

Treatment	**Dose (mg/kg)**	**BWG (g)**	**DAP (mm Hg)**	**MAP (mm Hg)**	**SAP (mm Hg)**	**HR (BPM)**
NSL	10mL/kg	76.20 ± 1.98	76.92 ± 1.40	90.46 ± 1.29	117.50 ± 1.27	362.60 ± 3.77
APE+VVE	100+150	54.14 ± 1.62	76. 03 ± 1.71*	90.34 ± 1.35*	120.23 ± 1.63**	350.82 ± 1.25*
APE+ADP	100+10	72.18 ± 1.03	70.50 ± 1.07*	84.46 ± 1.15*	110.30 ± 1.42**	339.26 ± 1.16*
VVE+ADP	150+10	56.46 ± 2.02	80.92 ± 2.12	93.70 ± 1.79	123.43 ± 1.70	353.30 ± 2.30

Each value represents a mean ± SEM; n = 5; *p < 0.05: significantly different compared to normal saline (distilled water); **p < 0.05: significantly different compared to extract treatment (VVE and ADP) at a dose of 150 and 10 mg/kg; NSL = normal saline (10 mL/kg); APE+ADP = *Arthrospera platensis* ethanol extract and Amlodipine at the dose of 100 and 10 mg/kg; VVE+ADP = *Vitis vinifera* L. ethanol extract and Amlodipine at the dose of 150 and 10 mg/kg; BWG = body weight gained; DAP = diastolic arterial blood pressure, MAP = mean arterial blood pressure, SAP = systolic arterial blood pressure, HR = heart rate, ADP = Amlodipine (10 mg/kg).

Safety Assessment.

The safety of ethanol extract of Spirulina and Grapes was assessed, by employing the treatment of dexamethasone-induced hypertensive model.

The results of these findings show that there is no noticeable detrimental effect on the hematological profile as indicated in Table 4.5 and 4.6 of the group treated with *Arthrospira platensis* and *Vitis vinifera* at a dose of (100+150mg/kg) body weight, compared with the group treated with *Arthrospira platensis* and Amlodipine at a dose of (100+10mg/kg) body

weight as well as the group treated with a concurrent administration of *Vitis vinifera* and Amlodipine at a dose of (150+10mg/kg) body weight (Table 4.7).

Arthrospira platensis extract (APE) administration also did not affect kidney function parameters. The result of the urinalysis also revealed the reversal of proteinuria caused by the induction of hypertension in the APE and Amlodipine-treated rats (Table 4.8 and Table 4.9)

Table 4.5: Effect of *Atrhospera platensis* (Spirulina) ethanol extract on full blood count.

Parameter	APE (50mg/kg)	APE (100mg/kg)	APE (150mg/kg)	Positive control (10mg/kg)	Negative control (10mg/kg)
WBC ($x10^3$/uL)	10.03 ± 1.22	9.08 ± 0.51	10.60 ± 0.32	11.48 ± 1.36	10.10 ± 0.79
RBC ($x10^{63}$/uL)	8.16 ± 0.31	7.77 ± 0.56	8.01 ± 0.14	8.02 ± 0.30	8.16 ± 0.17
HGB (g/dL)	13.73 ± 0.84	12.96 ± 1.02	13.14 ± 0.17	13.30 ± 0.11	13.35 ± 0.16
HCT (%)	45.03 ± 1.48	42.86 ± 1.63	44.66 ± 1.28	43.40 ± 1.58	44.35 ± 0.16
MCV (fL)	55.22 ± 0.70	54.96 ± 1.14	55.72 ± 0.97	54.15 ± 0.59	14.20 ± 0.80
MCH (pg)	18.02 ± 0.53	17.98 ± 0.36	17.68 ± 0.26	17.93 ± 0.58	54.23 ± 0.82
MGHC (g/dL)	31.62 ± 0.58	31.74 ± 0.51	30.72 ± 0.65	32.08 ± 1.05	54.23 ± 0.84
PLT ($x10^3$/uL)	614.17 ± 90.97	802.20 ± 78.86	668.00 ± 77.60	700.25 ± 118.89	693.50 ± 92.47
LYM %	65.40 ± 2.61	69.74 ± 3.01	65.64 ± 2.52	67.05 ± 1.88	65.05 ± 1.86
LYM ($x10^3$/uL)	6.58 ± 0.92	6.30 ± 0.39	9.56 ± 0.33	7.75 ± 1.12	6.68 ± 0.57
RDW_SD (fL)	29.08 ± 0.65	26.56 ± 3.39	30.48 ± 0.66	30.70 ± 1.19	28.13 ± 0.63
RDW_CV (%)	14.73 ± 0.70	13.10 ± 0.97	14.10 ± 0.72	16.03 ± 1.95	13.35 ± 0.93
PDW (fL)	10.17 ± 0.20	10.16 ± 0.61	10.40 ± 0.74	10.73 ± 0.59	9.78 ± 0.09
MPV (fL)	7.75 ± 0.13	8.90 ± 0.93	7.86 ± 0.29	7.63 ± 0.17	7.80 ± 0.17
P_LCR (%)	10.77 ± 0.76	12.68 ± 0.26	12.24 ± 1.73	11.00 ± 0.98	11.10 ± 0.90

All values were expressed as mean ± SEM followed by one-way ANOVA with Dunnett's post hoc test (n=5). Statistically, there is no significant difference ($p \leq 0.05$) WBC= White blood cell; RBC= Red blood cell; HGB= Haemoglobin; HCT= Haematocrit; MCV= Mean Cell Volume; MCH= Mean Cell Haemoglobin; MCHC: Mean Cell Haemoglobin Concentration; PLT= Platelet; LYM= Lymphocyte; RDW= Red Cell Distribution Width; SD= Standard Deviation; CV= Coefficient of Variation; PDW= Platelet Distribution Width; MPV= Mean Platelet Volume; P_LCR= Platelet Large Cell Ratio.

Table 4.6: Effect of *Vitis vinifera* (Grape) fruit ethanol extract on full blood count.

Parameter	VVE (50mg/kg)	VVE (100mg/kg)	VVE (150mg/kg)	Positive control (10mg/kg)	Negative control (10mg/kg)
WBC ($x10^3$/uL)	10.10 ± 1.20	11.08 ± 0.51	14.60 ± 0.32	9.48 ± 1.36	10.10 ± 0.79
RBC ($x10^{63}$/uL)	10.16 ± 0.32	7.77 ± 0.56	8.01 ± 0.14	8.02 ± 0.30	8.16 ± 0.17
HGB (g/dL)	15.70 ± 1.84	12.96 ± 1.02	13.14 ± 0.17	13.30 ± 0.11	13.35 ± 0.16
HCT (%)	45.12 ± 1.48	42.86 ± 3.63	44.66 ± 1.28	43.40 ± 1.58	14.35 ± 0.16
MCV (fL)	56.23 ± 1.70	54.96 ± 1.14	55.72 ± 0.97	54.15 ± 0.59	54.20 ± 0.80
MCH (pg)	20.21 ± 1.53	17.98 ± 0.36	17.68 ± 0.26	17.93 ± 0.58	54.23 ± 0.82
MGHC (g/dL)	31.62 ± 1.52	31.74 ± 0.51	30.72 ± 0.65	32.08 ± 1.05	54.23 ± 0.84
PLT ($x10^3$/uL)	611.12 ± 90.97	802.20 ± 78.86	668.00 ± 77.60	700.25 ± 118.89	693.50 ± 92.47
LYM %	67.42 ± 2.61	69.74 ± 3.01	65.64 ± 2.52	67.05 ± 1.88	65.05 ± 1.86
LYM ($x10^3$/uL)	7.51 ± 0.93	7.35 ± 0.47	9.56 ± 0.33	8.74 ± 1.12	7.67 ± 0.57
RDW_SD (fL)	30.18 ± 0.65	28.52 ± 2.39	33.42 ± 0.66	33.70 ± 1.19	30.14 ± 0.65
RDW_CV (%)	16.73 ± 0.70	15.10 ± 0.97	15.10 ± 0.73	18.03 ± 1.94	15.36 ± 0.95
PDW (fL)	11.16 ± 0.20	11.14 ± 0.61	11.42 ± 0.74	11.72 ± 0.59	10.73 ± 0.09
MPV (fL)	8.74 ± 0.13	9.92 ± 0.93	8.85 ± 0.30	8.62 ± 0.18	8.82 ± 0.18
P_LCR (%)	11.78 ± 0.75	13.68 ± 0.25	13.26 ± 1.73	12.02 ± 0.98	12.11 ± 0.92

All values are expressed as mean ± SEM followed by one-way ANOVA with Dunnett's post hoc test (n=5). Statistically, there is no significant difference ($p \leq 0.05$) WBC= White blood cell; RBC= Red blood cell; HGB= Haemoglobin; HCT= Haematocrit; MCV= Mean Cell Volume; MCH= Mean Cell Haemoglobin; MCHC: Mean Cell Haemoglobin Concentration; PLT= Platelet; LYM= Lymphocyte; RDW= Red Cell Distribution Width; SD= Standard Deviation; CV= Coefficient of Variation; PDW= Platelet Distribution Width; MPV= Mean Platelet Volume; P_LCR= Platelet Large Cell Ratio.

Table 4.7: Effect of *A. platensis* ethanol extract on liver and kidney function in Dexamethasone-induced Hypertensive Wistar rats.

Parameter	APE (50mg/kg)	APE (100mg/kg)	APE (150mg/kg)	Positive control (10mg/kg)	Negative control (10mg/kg)
ALP (U/L)	130.3 ± 7.88	152.9 ± 11.09	134.7 ± 31.22	--	149.5 ± 24.80
Total protein (g/L)	67.62 ± 0.85	69.44 ± 1.13	76.86 ± 1.50	71.65 ± 1.52	66.76 ± 2.61
Albumen (g/L)	30.80 ± 0.84	29.46 ± 0.63	32.28 ± 1.21	32.87 ± 0.90	31.38 ± 1.31
AST (U/L)	155.9 ± 14.58	155.5 ± 16.47	145.3 ± 10.54	168.7 ± 4.615	148.5 ± 15.42
ALT (U/L)	40.20 ± 1.62	41.33 ± 2.40	38.50 ± 4.11	31.75 ± 1.63	40.13 ± 4.70
GGT (U/L)	5.0 ± 0.0	5.0 ± 0.0	5.0 ± 0.0	5.0 ± 0.0	5.0 ± 0.0
TBIL (µmol/L)	3.84 ± 0.25***	4.82 ± 0.40***	4.50 ± 0.20***	9.12 ± 0.10	11.07 ± 0.28
Urea (mmol/L)	6.90 ± 0.58	6.92 ± 0.41	7.04 ± 0.42	--	7.78 ± 0.32
Creatinine (µmol/L)	88.44 ± 2.57	88.13 ± 2.77	96.02 ± 3.13	--	83.84 ± 3.77
Na (mmol/L)	143.6 ± 0.39	143.7 ± 0.70	144.4 ± 0.55	142.9 ± 0.47	143.3 ± 1.07
K (mmol/L)	4.90 ± 0.16	5.43 ± 0.08	5.21 ± 0.18	5.86 ± 0.29	5.65 ± 0.43
Cl (mmol/L)	101.9 ± 0.64	103.2 ± 0.76	104.1 ± 0.75	99.8 ± 0.90	102.4 ± 0.38

All values were expressed as mean ± SEM, followed by one-way ANOVA with Dunnett's multiple comparison post hoc test (n = 5). ***$p \leq 0.05$ as compared to the negative control ALP= Alkaline Phosphatase; T= Total; AST= Aspartate Aminotransferase; AL= Alanine Aminotransferase; GGT- c= Glutamyl transferase; Na= Sodium; K: Potassium; Cl= Chloride.

Table 4.8: Effect of *A. platensis* ethanol extract on urine content in Dexamethasone-induced hypertensive Wistar rats.

Parameter	APE (50mg/kg)	APE (100mg/kg)	APE (150mg/kg)	PC (10mg/kg)	NC (10mg/kg)
Leukocyte	Trace	Trace	Trace	Trace	Trace
Urobilinogen	Trace	Trace	Trace	Trace	Trace
Bilirubin	-	-	-	-	-
Blood	-	-	-	-	-
Nitrite	-	-	-	-	-
Ph	9.04 ± 0.13	9.70±0.03	8.76 ± 0.42	8.62 ± 0.40	8.72 ± 0.46
SG	1.03 ± 0.01	1.03 ± 0.01	1.04 ± 0.01	1.04 ± 0.01	1.02 ± 0.01
Protein	++	++	++	++	++
Glucose	-	-	-	-	-
Ketones	-	-	-	-	-

The values are expressed as mean ± SEM (n = 5). SG= Specific gravity; PC= Positive control; APE= *Arthrospira platensis;* NC= Negative control, while - = Negative

Table 4.9: Effect of *Vitis vinifera* ethanol extract (VVE) on liver and kidney function in Dexamethasone-induced Hypertensive Wistar rats.

Parameter	VVE (50mg/kg)	VVE (100mg/kg)	VVE (150mg/kg)	Positive control (10mg/kg)	Negative control (10mg/kg)
ALP (U/L)	132.03 ± 7.86	154.09 ± 12.13	136.5 ± 3.23	--	150.05 ± 2.83
Total protein (g/L)	63.62 ± 0.82	69.44 ± 1.20	68.85 ± 1.52	73.67 ± 1.53	68.77 ± 2.63
Albumen (g/L)	32.82 ± 0.85	30.47 ± 0.64	36.31 ± 1.23	34.76 ± 0.12	33.40 ± 1.32
AST (U/L)	157.10 ± 16.58	157.15 ± 16.47	147.30 ± 10.56	170.60 ± 4.15	150.50 ± 16.43
ALT (U/L)	43.23 ± 1.64	43.36 ± 2.42	40.51 ± 4.13	33.74 ± 1.62	42.13 ± 4.72
GGT (U/L)	5.0 ± 0.0	5.0 ± 0.0	5.0 ± 0.0	5.0 ± 0.0	5.0 ± 0.0
TBIL (µmol/L)	4.86 ± 0.25***	6.82 ± 0.40***	6.51 ± 0.20***	11.13 ± 0.10	13.15 ± 0.27
Urea (mmol/L)	8.92 ± 0.58	8.94 ± 0.41	8.14 ± 0.42	--	8.78 ± 0.35
Creatinine (µmol/L)	89.54 ± 2.54	89.13 ± 2.77	96.02 ± 3.14	--	83.85 ± 3.76
Na (mmol/L)	146.6 ± 0.39	146.17 ± 0.50	148.4 ± 0.75	145.9 ± 0.47	143.13 ± 1.14
K (mmol/L)	4.12 ± 0.16	5.53 ± 0.05	5.22 ± 0.16	5.86 ± 0.28	5.67 ± 0.45
Cl (mmol/L)	101.9 ± 0.64	103.12 ± 0.76	104.12 ± 0.73	98.18 ± 0.90	106.14 ± 0.36

All values were expressed as mean ± SEM, followed by one-way ANOVA with Dunnett's multiple comparison post hoc test (n = 5). ***p ≤ 0.05 as compared to the negative control ALP= Alkaline Phosphatase; T= Total; AST= Aspartate Aminotransferase; ALT= Alanine Aminotransferase; GGT= Glutamyltransferase; Na= Sodium; K: Potassium; Cl= Chloride.

DISCUSSION

Vascular tone is regulated by the endothelium that lines the inside of blood arteries. It does this by releasing several mediators and preserving a balance between vasoconstriction and vasorelaxation. Particularly, arterial relaxation and cardiovascular homeostasis are regulated by nitric oxide (NO) produced by endothelial nitric oxide synthase (eNOS) in endothelial cells (Son et al., 2010; Kim et al., 2011; and In et al., 2018).

In many cardiovascular disorders, poor endothelium-dependent vasodilation is linked to decreased nitric oxide (NO) levels. Conversely, because structural and functional alterations in the vascular endothelium led to hypertension, there is a correlation between vasorelaxation and hypertension (In et al., 2018).

Phytochemical compounds are various bioactive chemicals present in plants' parts and are beneficial to humans (Muhamad *et al.,* 2021). The preliminary phytochemical screening in the current study revealed that *Vitis vinifera* (Grape) fruit, contains phytochemical compounds such as; carbohydrates, flavonoids, cardiac glycoside, tannins, triterpenes, and saponins and it is consistent with the work of Hassan *et al.,* (2015) and Arora *et al.,* (2016).

Additionally, Raja *et al.,* (2020) also reported that the methanol extract of *Vitis vinifera* showed the presence of glycosides, phytosterol, saponins, tannins, flavonoids, and terpenoids which is in agreement with the current findings. Thus, in respective of the solvent used, the extract still possesses the presence of the above compounds.

On the other hand, the study revealed the presence of; carbohydrates, flavonoids, tannins, saponins, and cardiac glycoside with the absence of triterpenes from the preliminary phytochemical screening of ethanol extract of *Arthrospira platensis* (Spirulina). This is in agreement with the work of Marikani *et al.,* (2014); and El-Chaghaby *et al.,* (2019).

However, the current study revealed the absence of alkaloids, anthraquinones and steroids in both extracts and it is inconsistent with the findings of Thangaraj *et al.,* (2022), who reported the presence of; alkaloids, terpenoids, flavonoids, tannins, polyphenols, saponins, cardiac glycoside and quinones in methanol extract of spirulina. A report from Chen, *et al.,* (2014), revealed that these phytochemicals have antioxidant activity with health protection ability.

The study revealed that *Arthrospira platensis* is independent of dose-related effects, but *Vitis vinifera* shows a dose-dependent effect for body weight reduction. Thus, this may be attributed to the decrease in blood pressure when compared with the normal control group. This is in line with the findings of Park *et al.,* (2016), who reported that grape seed extract significantly reduced systolic blood pressure by 5.6% and diastolic blood pressure by 4.7% after 6 weeks of supplementation in subjects with mildly elevated blood pressure.

APPENDIX I: HISTOLOGICAL RESULT

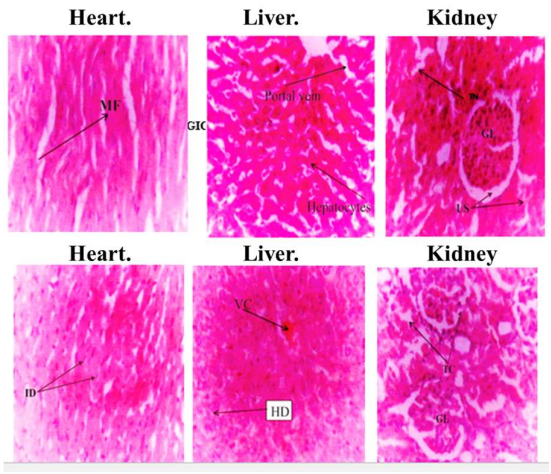

Figure 1: Micro Photography of Heart, Liver and Kidney. Haematoxylin/Eosin and Masson Trichrome staining; x400; n= 5; APE = *Arthrospera platensis* ethanol extract of the most effective dose. MF= Muscle fiber; I =Intercalated disc; CV = Vascular Congestion; GL = Glomeruli; TC = Tubular Clarification; HD = Hepatocytes Degeneration; US = Urinary space; T = Tubules.

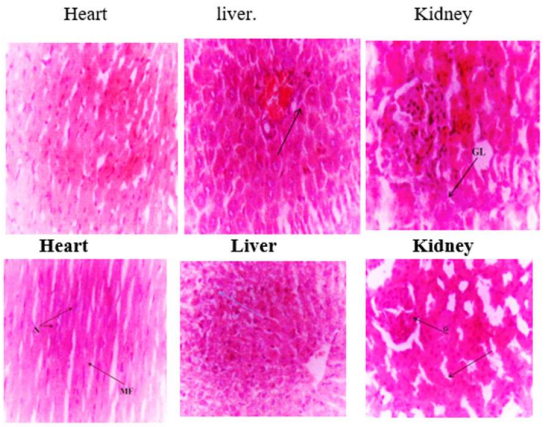

Figure 2: Micro Photography of Heart, Liver and Kidney. Haematoxylin/Eosin and Masson Trichrome staining; x400; n= 5; APE = *Arthrospera platensis* ethanol extract of the most effective dos; N= nuclei; MF= Muscle fiber and GL = Glomeruli.

CONCLUSION

The LD_{50} was estimated to be above the limit dose (5000mg/kg and 2000mg/kg) body weight, indicating that both extracts are practically non-toxic. The preliminary phytochemical screening revealed the presence of; saponins, tannins, flavonoids carbohydrates and cardiac glycoside with the absence of alkaloids, anthraquinones, and steroids in both extracts. Conversely, triterpenes is present only in *vitis vinifera* ethanol extract as presented in table 4.1 and table 4.2. This is in line with the findings of Manjula *et al.,* (2022), who reported the absence of alkaloids, anthraquinones, and steroids in the ethanol extract of spirulina, and the

work of Raja, *et al.,* (2020), who reported a similar absence in the ethanol extract of *Vitis vinifera* (Grapes) Fruit.

The antihypertensive effect of ethanol extract of *Arthrospira platensis* (Spirulina) and *Vitis vinifera* (Grape) fruit was determined in dexamethasone-induced high blood pressure Wistar rats and the results suggested that both extracts could be beneficial in improving hypertension through their ability to lower systolic and diastolic blood pressure. Thus, this could be attributed to the intrinsic effects of the phytochemical constituents present in both extracts. Additionally, both extracts demonstrated promising nephron and reno-protective effects as well as improvement in the treatment of dexamethasone-induced hypertension in Wistar rats.

Nevertheless, both extracts have also shown depressed dexamethasone-induced high blood pressure and weight loss with a subsequent decrease in blood pressure as well as an equal increase in body weight.

Thus, the improvement of body weight gain following the administration of the extracts could be due to the carbohydrate present in both extracts and the increase in insulin sensitivity, coupled with the subsequent increase in glucose uptake.

The result indicated a good synergistic effect between *Arthrospira platensis* and Amlodipine (standard drugs).

Thus, this showed the agonistic effect of the extract with the standard drugs in reducing high blood pressure treatment of hypertension. Additionally, this indicated that spirulina can be used as a lead in the search for a novel agent for the treatment of hypertension.

The safety assessments of both extracts showed no detrimental effect on the liver, kidney, and heart in dexamethasone-induced hypertensive Wistar rats.

RECOMMENDATIONS

. Further studies should be carried out to determine the active compounds responsible for ameliorating the high blood pressure and improved treatment of hypertension.

2. It is also recommended that, further investigation should be carried out on selective toxicity effect of the extracts in-vitro.

3. Notwithstanding, the potentiality of incorporating *Vitis vinifera* (Grape) fruit with *Atrhospera platensis* (Spirulina) extracts as a functional ingredient in food products and beverages to enhance their antihypertensive capacity is worth of exploring.

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