



# EFFECT OF CRUDE AQUEOUS LEAVES EXTRACT OF *BRYOPHYLLUM PINNATUM* ON ANTIOXIDANT STATUS, BLOOD GLUCOSE, LIPID PROFILE, LIVER AND RENAL FUNCTION INDICES IN ALBINO RATS

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(Received 3 November 2020; Revision Accepted 2 February 2021)

## ABSTRACT

*Bryophyllum pinnatum* is an important ethnomedicinal plant. The study assessed the effect of crude aqueous leaves extract of *Bryophyllum pinnatum* (CALEBP) on fasting plasma glucose (FPG), antioxidant status, lipid profile, liver and renal function indices in albino rats. The rats were housed under standard laboratory conditions (12h light: 12h dark photoperiod),  $23 \pm 2$  °C and were given rat pellets and tap water *ad libitum*. Twenty four rats weighing 190-232g were randomized into four groups (A-D) of six rats each. Group A (control) received normal feed and water only. Groups B, C and D received orally 180, 360 and 540 mg/kg body weight respectively of CALEBP for 28 days. Serum aminotransferases, alkaline phosphatase (ALP), superoxide dismutase, catalase, FPG, lipid profile, urea, creatinine, bilirubin, proteins, malondialdehyde, glutathione (GSH) and total antioxidant capacity (TAC) and electrolytes were assessed by standard methods. Data were analyzed using one-way analysis of variance and  $p < 0.05$  was considered statistically significant. Groups C and D had significantly lower FPG ( $p = 0.030$ ;  $p = 0.01$ ) and higher ALP ( $p = 0.01$ ;  $p = 0.001$ ) compared to the controls. Group D had significantly lower creatinine ( $p = 0.03$ ) and  $K^+$  ( $p = 0.02$ ) compared to control. Group B, C and D had significantly lower GSH ( $p = 0.020$ ,  $p = 0.000$  and  $p = 0.000$ ) while group B had significantly higher TAC ( $p = 0.04$ ) compared to the controls. Dosage of extracts correlated positively with ALP ( $r = 0.705$ ,  $p = 0.000$ ) and negatively with FPG ( $r = -0.603$ ,  $p = 0.002$ ),  $K^+$  ( $r = -0.563$ ,  $p = 0.004$ ), creatinine ( $r = -0.464$ ,  $p = 0.022$ ) and GSH ( $r = -0.786$ ,  $p = 0.000$ ). *Bryophyllum pinnatum* aqueous leaves extract could lower blood glucose, potassium and creatinine levels and may increase ALP activity and GSH depletion in high doses.

**KEYWORDS:** *Bryophyllum pinnatum*, aqueous leaf extract, dosage, effect assessment, Albino rats

## INTRODUCTION

Nowadays, there is significant demand for traditional medicine (Casmir *et al.*, 2017). Traditional medicine is known for its availability, affordability, unique natural way of healing and long-lasting curative potency with

less or no side effect (Usifoh and Udezi, 2013). Globally, about 80 to 90% primary source of healthcare is provided by traditional medicine (Mafimisebi and Oguntade, 2010). Several medicinal plants have diverse phytochemicals that can enhance erythropoiesis, protein synthesis and immune defense

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(Udo and Ojjezeh, 2016; Udo *et al.*, 2017), lower blood glucose, triglyceride and cholesterol levels (Miguel, 2010; Howida and Abou, 2016); possess anti-inflammatory, anti-oxidative, renal and hepatic protective potentials (Feng *et al.*, 2015). *Bryophyllum pinnatum* Kurz is an important ethnomedicinal plant widely distributed in many parts of the world such as Europe, Madagascar, America, India, China, Asia and Africa (Seema, 2018). *B. pinnatum* is popularly known in English as life miracle, resurrection, or 'never die' plant. In Nigeria, it is locally known as *Oduduk mmong* (in Efik), *Abamoda* (in Yoruba), *Ugwoba* (in Igbo) and *Karan* (in Hausa). It is a fast-growing succulent perennial plant found in temperate, tropical and subtropical areas. It is also grown around houses and in gardens for both ornamental and medicinal purposes. The plant can grow to about 1.5 meter in height with leaves arranged in opposite direction (Anuradha *et al.*, 2012). Leaves have a wide spectrum of therapeutic potentials attributed to the rich phytochemicals such as flavonoids, triterpenes, alkaloids, steroids, saponins, glycosides, tannins, bufadienolides (Nagaratna and Prakash, 2015; Aprioku and Igbe, 2017). *B. pinnatum* is used traditionally to treat so many illnesses including diabetes, liver and kidney diseases, dyslipidaemia, obesity, cough, wound, ulcer, infection, anaemia (Okwu and Nnamdi, 2011; Muhammad *et al.*, 2012). However, the numerous medicinal claims of some plants have in recent times, led to indiscriminate and excessive use of *Bryophyllum pinnatum* especially in the Southeastern Nigeria without adequate knowledge of its systemic effect (Anuradha *et al.*, 2012). The incautious use of this plant may partly be due to the going-round belief among some people who rely so much on traditional and complementary medicine that herbs have minimal or no side effects compared to innumerable conventional drugs that may cause several other health issues in the body (Patel *et al.*, 2012). This belief has resulted in increasing and unwary use of *B. pinnatum* in traditional medicine. However, it is pertinent to note that some medicinal plants and herbal products could as well be toxic to organs like the liver and kidneys when not taken in safe dosages (Ghasi *et al.*, 2011; Golderg, 2018). Leaves of *B. pinnatum* contain high level of alkaloids and saponin (Ojo *et al.*, 2018) which when taken in high doses become toxic to organs (Spanou, 2010; Ghasi *et al.*, 2011). Hence, the need for continued scientific assessment of the effect of this famous medicinal plant in its crude forms often taken by the people at various doses. The aim of this study was to assess the effect of crude aqueous leaves extract of *Bryophyllum pinnatum* on antioxidant status, blood glucose, lipid profile, liver and renal function indices in albino rats.

## MATERIALS AND METHODS

### Plant Material

Fresh leaves of *Bryophyllum pinnatum* were obtained in Ikot Ekpene City Plaza, Akwa Ibom State, Nigeria in June, 2018 and were confirmed by a plant taxonomist, in the Department of Botany, University of Calabar, Calabar, Cross River State, Nigeria. The plant leaves specimens were deposited at the departmental herbarium with voucher number: Herb/ Bot./UCC/192.

### Experimental Animals

Twenty four (24) albino rats of both sexes aged 8-10 weeks; weighing between 190 to 232g were purchased from and housed in the University of Calabar animal house, Calabar, Cross River State, Nigeria. The male rats (n=12) were separated from the female rats (n=12) to avoid pregnancy. Rats were allowed to acclimatize to laboratory conditions for one week in well-ventilated cages with 12-hours light and dark cycle at room temperature (23± 2 °C). The animals were maintained on a standard feed and water *ad libitum*. Approval for the study was obtained from the Animal Research Ethics Committee of the Faculty of Allied Medical Sciences of the University of Calabar. The guidelines on the Care and Handling of Research Animals (NIS, 1985) as well as other procedures following the approval for the study were strictly adhered to.

### Extract Preparation

The fresh leaves of *Bryophyllum pinnatum* were detached from the stems, cleaned and air dried for eight days and then pulverized into powder using an electric blender. The leaf powder weighed nine hundred and thirty grams (930g) and was soaked in 2500ml of distilled water in an Erlenmeyer conical flask (3000ml) for 48 hours with intermittent shaking, 3-5 times daily. It was then filtered using muslin sieve followed by Whatman paper (size no.1), and the filtrate was evaporated to dryness using water bath at 55°C (Sanjit *et al.*, 2018). The crude aqueous leaves extract of *Bryophyllum pinnatum* (CALEBP) obtained in a pasta form weighed 62.4g which was stored at 2°C and reconstituted as at when needed for the experiment.

### Experimental Design

The rats were randomized into four groups (A-D) of six rats each. Animals in group A served as control and were given distilled water and normal feed only. Groups B, C and D received 180mg/kg, 360mg/kg and 540mg/kg body weight of CALEBP respectively via oral intubation for 28 days.

### Blood Sample Collection

After the last administration of the extract on the 28<sup>th</sup> day, the rats were fasted overnight but allowed access to water *ad libitum*. On the 29<sup>th</sup> day, blood sample for fasting plasma glucose was obtained by cutting the tail tip of the rat with sharp scalpel. Thereafter, each rat was placed under mild (3.8%) chloroform anesthesia in a closed desiccator and suddenly removed when reflexes were completely lost. Thoracic cavity was cut open after cervical dislocation; blood sample was obtained via cardiac puncture using 10 ml syringe and a 21 G needle into appropriately labeled sample tubes and allowed to clot before centrifugation at 3000 x g for 5 minutes using a bench centrifuge. Serum was obtained and stored at -20 °C till analyzed.

### BIOCHEMICAL ESTIMATION

**Fasting Plasma Glucose and Lipid Profile:** Fasting plasma glucose (FPG) level was estimated by the glucose oxidase method of Trinder (1969), Total Cholesterol (TC) and Triglycerides (TG) levels were estimated by the method of Allain *et al.*, (1974) and by the method of Bucolo and David, (1973) respectively. High density lipoprotein cholesterol (HDL-C) level was determined by the Precipitation and Cholesterol methods of Demacker *et al.*, (1997) and Allain *et al.*, (1974) while low density lipoprotein (LDL-C) level was calculated by using Friedewald's equation (LDL-C (mmol) = TC-HDL-C-VLDL-C) (Friedewald *et al.*, 1972). VLDL-C level was obtained by calculation using the equation (VLDL-C (mmol) = TG/2.2 provided TG was  $\leq$  4.5mmol/l (Burtis *et al.*, 2008).

**Liver Function Test:** Activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined by colourimetric method as described by Reitman and Frankel (1957) while determination of alkaline phosphatase (ALP) activity was done by the method of Rec (1972). Total and conjugated bilirubin levels were determined by the method of Jendrassic and Grof, (1938). Estimation of serum total protein and serum albumin level were done by the methods described by Tietz (1995) and by Grant (1987).

**Renal Function Test:** Electrolytes (Na<sup>+</sup>, K<sup>+</sup> and Cl<sup>-</sup>) levels were determined by using Auto ISE Analyzer (AC 9000 Series Automatic Electrolyte Analyzer) supplied by AUDICOM Medical Technology CO., LTD, China. Serum bicarbonate (HCO<sub>3</sub><sup>-</sup>) level was determined by the back titration method as described by Cheesbrough (2004); Serum creatinine and urea levels were estimated by the modified Jaffe method of Spierto *et al.*, (1979) and the Urease-Berthelot method of Blass *et al.*, (1974) respectively.

**Oxidative Stress Markers:** Catalase (CAT) and superoxide dismutase (SOD) activities were determined by methods of Aebi (1983) and Xin *et al.*, (1991) respectively. Determination of level of lipid peroxidation product, malondialdehyde (MDA) was by the method described by Wallin *et al.*, (1993), glutathione (GSH) level was determined by the method of Ellman (Ellman, 1959) while total antioxidant capacity (TAC) was determined by the ABTS method described by Miller *et al.*, (1997).

### Statistical Analysis

Statistical analysis was done using the PAWS 18, a statistical package from SPSS Inc, Chicago, USA. The results were expressed as mean  $\pm$  SD. Groups were compared using one way analysis of variance (ANOVA) and Post Hoc analysis using least significance difference (LSD). The significance level was set at 95 % confidence interval and p<0.05 was considered statistically significant.

### RESULTS

Table 1 shows a significant variation (p<0.05) in the mean value of fasting plasma glucose (FPG) among the treated groups. Groups C and D showed significantly lower (p<0.05) FPG levels compared to control. Group D showed a significantly lower (p < 0.05) FPG level compared group B. Animals in group B had significantly higher (p<0.05) LDL-C compared to control while group D had significantly lower (p< 0.05) TC and LDL-C levels than group B.

Table 2 shows a significant variation (p< 0.05) in serum alkaline phosphatase (ALP) activity among the groups. A post hoc analysis of the effect of CALEBP on liver enzymes activities showed significantly higher (p = 0.01 and p = 0.001) serum ALP activities in groups C and D when compared to control. ALP in group D was significantly higher (p = 0.010) than group B. There were no significant variations (p>0.05) in the bilirubin, total protein, albumin and globulin levels and ALT and AST activities among the treatment groups.

Table 3 shows effect of CALEBP on renal function of rats in treatment groups and control. There were significant (p<0.05) variations in serum potassium and creatinine levels among the groups. Serum K<sup>+</sup> and creatinine levels in group D were significantly lower (p = 0.02 and p = 0.03) when compared to the control group. When treatment groups were compared, groups C and D had significantly (p = 0.01; p = 0.001) lower serum potassium level than group B. Group D also had significantly (p< 0.05) lower serum creatinine level than groups B and C. A post hoc analysis showed a significantly higher (p = 0.01) urea level in group C compared to the control group.

Table 4 shows effect of the extract on oxidative stress markers. There was a significant variation ( $p < 0.05$ ) in the serum GSH level among the groups. All the treated groups (B, C and D) showed a dose dependent significantly lower ( $p = 0.020$ ,  $p = 0.000$  and  $p = 0.000$ ) serum GSH levels compared to control. The effect was prominently observed in groups C and D. There were no significant variations ( $p > 0.05$ ) in superoxide dismutase and catalase activities among the groups. Post hoc analysis showed significantly lower ( $p = 0.01$ ) MDA level in

group D when compared to group B. TAC was significantly ( $p = 0.04$ ) higher in group B compared to the control group.

Table 5 shows the correlation of dosages and some variables in the treatment groups. Results showed a significant negative correlation between dosage and FPG ( $r = -0.603$ ,  $p = 0.002$ ),  $K^+$  ( $r = -0.563$ ,  $p = 0.004$ ), creatinine ( $r = -0.464$ ,  $p = 0.022$ ) and, GSH ( $r = -0.786$ ,  $p = 0.000$ ). However, a positive significant correlation was found between the dosage of the extract and ALP ( $r = 0.705$ ,  $p = 0.000$ ).

**Table 1: Effect of crude aqueous leaves extract of *Bryophyllum pinnatum* on FPG and Lipid profile**

Parameter	Group A n = 6	Group B n = 6	Group C n = 6	Group D n = 6	F-value	P-value
FPG (mmol/L)	7.59 ± 1.16	7.07 ± 2.41	5.38 ± 1.09	4.74 ± 0.97 <sup>b, d</sup>	4.113	<b>0.020*</b>
TCH (mmol/L)	2.46 ± 0.52	2.94 ± 0.44 <sup>c</sup>	2.91 ± 0.39	2.40 ± 0.36	2.709	0.072
TRG (mmol/L)	0.44 ± 0.12	0.52 ± 0.05	0.40 ± 0.08	0.51 ± 0.13	1.739	0.191
HDL (mmol/L)	1.06 ± 0.15	1.12 ± 0.08	1.23 ± 0.31	1.03 ± 0.08	1.394	0.274
LDL (mmol/L)	1.20 ± 0.41	1.59 ± 0.38 <sup>a, c</sup>	1.51 ± 0.15	1.18 ± 0.27	2.608	0.080
VLDL (mmol/L)	0.20 ± 0.06	0.23 ± 0.03	0.18 ± 0.04	0.22 ± 0.06	1.306	0.300

**a** = value significantly higher than that of control. **b** = value significantly lower than that of group C  
**c** = value significantly higher than that of group D. **d** = value significantly lower than that of control.

\* The mean difference is significant at  $p < 0.05$

FPG = Fasting plasma glucose, TCH = Total cholesterol, TRG = Triglycerides, HDL = High density lipoprotein, LDL = Low density lipoprotein, VLDL = Very low density lipoprotein

**Table 2: Effect of crude aqueous leaves extract of *Bryophyllum pinnatum* on liver function parameters in albino rats**

Parameters	Group A (n = 6)	Group B (n = 6)	Group C (n = 6)	Group D (n = 6)	F-value	P-value
T. Bil. (mmol/L)	5.12 ± 1.49	4.92 ± 0.85	5.09 ± 0.65	4.42 ± 1.54	1.591	0.223
C. Bil. (mmol/L)	2.87 ± 0.87	1.92 ± 1.07	1.80 ± 0.68	1.88 ± 0.81	2.013	0.145
AST (I.U/L)	152.50 ± 20.98	167.50 ± 25.18	156.00 ± 26.70	151.50 ± 14.98	0.643	0.596
ALT (I.U/L)	39.00 ± 11.17	36.83 ± 4.62	44.67 ± 10.78	43.83 ± 10.59	0.914	0.452
ALP (I.U/L)	84.67 ± 17.07	101.17 ± 28.88	126.67 ± 26.03 <sup>a</sup>	138.67 ± 17.12 <sup>a, f</sup>	6.825	<b>0.002*</b>
T. Protein (g/L)	58.50 ± 5.43	59.17 ± 6.65	61.50 ± 5.03	61.17 ± 5.56	0.338	0.763
Albumin (g/L)	37.67 ± 2.42	35.17 ± 4.60	37.83 ± 3.31	38.33 ± 4.37	0.848	0.484
Globulin (µmol/L)	20.83 ± 3.76	24.00 ± 3.58	23.67 ± 5.20	25.00 ± 4.98	0.972	0.426

**a** = significantly higher than that of control. **f** = significantly higher than that of group B. \*Significant at  $p < 0.05$

T. Bil. = Total bilirubin, C. Bil. = Conjugate bilirubin, AST = Aspartate aminotransferase, ALP = Alkaline phosphate, ALT = Alanine aminotransferase, T. protein = Total protein

**Table 3: Effect of crude aqueous leaves extract of *Bryophyllum pinnatum* on renal function parameters in albino rats**

Parameters	Group A (n = 6)	Group B (n = 6)	Group C (n = 6)	Group D (n = 6)	F-value	P-value
Na <sup>+</sup> (mmol/L)	132.17±7.17	126.33 ± 13.00	128.33 ± 5.39	121.83 ±11.41	1.169	0.346
K <sup>+</sup> (mmol/L)	4.20 ± 0.47	4.63 ± 0.86	3.42 ± 0.35	3.13 ± 0.94 <sup>d, e</sup>	5.846	0.005*
Cl <sup>-</sup> (mmol/L)	86.67 ±10.41	95.00 ±17.57	96.17 ±18.67	94.00 ± 1.90	0.573	0.639
HCO <sub>3</sub> <sup>-</sup> (mmol/L)	20.17 ± 4.49	17.17 ± 5.12	22.50 ± 7.26	18.50 ± 5.65	0.969	0.427
Urea (mmol/L)	4.68 ± 0.64	5.47 ± 0.75	6.37 ± 1.18 <sup>a</sup>	5.93 ± 1.27	2.865	0.062
Creatinine (µmol/L)	75.50 ± 16.32	82.33 ± 8.50	74.50 ±11.93	59.67 ± 6.62 <sup>b, d, e</sup>	4.168	0.019*

a = significantly higher than that of control. b = value significantly lower than that of group C  
d = value significantly lower than that of control. e = value significantly lower than that of group B

\* The mean difference is significant at p < 0.05

Na<sup>+</sup> = Sodium, K<sup>+</sup> = Potassium, Cl<sup>-</sup> = Chloride, HCO<sub>3</sub><sup>-</sup> = Bicarbonate

**Table 4: Effect of crude aqueous leaves extract of *Bryophyllum pinnatum* on oxidative stress markers in albino rats**

Variable	Group A (n = 6)	Group B (n = 6)	Group C (n = 6)	Group D (n = 6)	F-value	P-value
SOD (I.U/L)	70.85 ±5.67	77.75 ±10.59	69.13 ± 8.68	71.63 ±10.60	1.019	0.405
CAT (I.U/L)	7.83 ± 2.9	8.78 ± 2.97	6.60 ± 1.21	7.10 ± 1.90	0.949	0.436
MDA (nmol/L)	1.07 ±0.10	1.22 ± 0.27	1.05 ± 0.16	0.92 ± 0.08 <sup>e</sup>	3.091	0.050
GSH (mmol/L)	2.65 ± 0.23	2.10 ± 0.57 <sup>d</sup>	0.78 ± 0.29 <sup>d, e</sup>	1.18 ± 0.32 <sup>d, e</sup>	30.410	0.000*
TAC (mmol/L)	0.66 ± 0.32	1.15 ± 0.42 <sup>a</sup>	0.94 ± 0.42	0.95 ± 0.36	1.701	0.009

a = value significantly higher than that of control. d = value significantly lower than that of control e = value significantly lower than that of group. \*The mean difference is significant at p < 0.05 SOD = Superoxide dismutase, CAT = Catalase, MDA = Malondialdehyde, GSH = Glutathione, TAC = Total Antioxidant capacity

**Table 5: Correlation of dosage of CALEBP and some indices in treated albino rats**

Parameter	Index	r-value	p-value
Dosage (mg/kg)	Fasting plasma glucose	-0.603	0.002*
	Alkaline phosphatase	0.705	0.000*
	Potassium	-0.563	0.004*
	Creatinine	-0.464	0.022*
	Glutathione	-0.786	0.000*

\* is significant at p < 0.05

## DISCUSSION

This study assessed the effects of crude aqueous leaves extract of *Bryophyllum pinnatum* on blood glucose, lipid profile, antioxidant status; liver and kidney function indices in albino rats. In this present study, result showed that oral administration of the plant extract to albino rats for 28 days; significantly lower ( $p < 0.05$ ) FPG levels compared to controls. The reduction in FPG may be due to the phytochemical(s) contained in the extract. Studies have shown that phyto-constituents such as glycosides, alkaloids, flavonoids and carotenoids have potent anti-diabetic effects (Nusrath *et al.*, 2011). Quantitative photochemical analyses of leaves of *B. pinnatum* revealed significant presence of glycosides, alkaloids and flavonoids (kaempferol and quercetin) (Ajiboye *et al.*, 2018). Kaempferol and quercetin are bioactive plant constituents with an effective hypoglycemic effect (Aransiola *et al.*, 2014). This finding is in line with Nagaratna and Prakash (2015) who recorded a significant reduction ( $p < 0.05$ ) in blood glucose level when 200 mg/kg body weight of aqueous leaves extract *B. pinnatum* was administered to rats orally for 28 days. In Traditional Medicine Practice, this wonderful plant has also been employed in the treatment of dyslipidaemia. Although studies have reported cholesterol lowering properties of aqueous extract of this plant and also supported the reason for its usage in treating high serum cholesterol level (Adekunle *et al.*, 2016), result of the present study showed a non-significant decrease in the total cholesterol level compared to controls.

Levels of  $\text{Na}^+$ ,  $\text{Cl}^-$  and  $\text{HCO}_3^-$  varied insignificantly while serum urea level was only significantly higher ( $p < 0.05$ ) only in group B compared to controls. The serum or plasma levels of urea and creatinine are clinically significant sensitive markers in assessing the diseases of kidney function. When glomerular filtration rate (GFR) and renal clearance functions decreased, toxic waste including urea and creatinine accumulates in the blood. Although urea is affected by many factors, measurement of both serum or plasma creatinine and urea give a better indicator of renal function (Nusrath *et al.*, 2011). Hence, significantly higher serum urea level without a corresponding higher serum creatinine level as seen in this present study in group B may be due to the unstable nature of urea level in the blood. Creatinine is a nitrogenous waste product produced from the metabolism of creatine phosphate in skeletal muscle and its excretion is solely renal and in the absence of disease, is relatively constant compared to urea (Bolarin, 2010). Measurement of creatinine level is recommended in preference to plasma urea

measurement since it is a better pointer of over-all renal function and progression in renal failure (Nusrath *et al.*, 2011). Therefore, the progression of kidney damage is characterized generally by low GFR, significant increases in both blood urea and creatinine levels with a decrease concentration of serum electrolytes (Ossman *et al.*, 2014; Mahendra *et al.*, 2016). The significantly lower ( $p < 0.05$ ) serum creatinine and potassium levels in groups C and D when compared to control, are indications of absence of kidney damage or dysfunction. Based on this result, it could also be suggested that the CALEBP either enhanced potassium intracellular uptake or up-regulated GFR and increase volume of urine, leading to increase urinary excretion of potassium and creatinine in a dose dependent manner. Marked hypokalaemia is an abnormally low serum or plasma potassium level which can be caused by factors including diuretic therapy such as Furosemide, Ethacrynic acid and Thiazides (Bolarin, 2010). Leaves extract of *B. pinnatum* has been reported of having diuretic properties (Patil *et al.*, 2009; Uhegbu *et al.*, 2017). Thus, the significantly lower ( $p < 0.05$ ) serum potassium levels observed at dosages of 360mg/kg and 540 mg/kg body weight of CALEBP may be due to diuretic potential of the plant. This present result is in line with the findings of Biswas *et al.*, (2011) and Dabur *et al.*, (2012).

Results of oral administration of CALEBP at the dosages used in this present study showed no significant variation in AST and ALT activities among the groups. However, conjugated bilirubin level increased insignificantly ( $p > 0.05$ ) while total bilirubin decreased but not significant compared to controls. AST and ALT are markers of hepatic damage. Bilirubin is a byproduct of haemoglobin breakdown. It binds to albumin and is transported to the hepatocytes for conjugation and subsequent excretion into bile. Thus, damage to hepatocytes prevents normal conjugation of bilirubin and its excretion into bile ducts, resulting in marked hyperbilirubinaemia (Adi and Alturkmani, 2013). The nonsignificant decrease ( $p > 0.05$ ) in the serum total bilirubin concentration of the treated group compared to the control group may suggest normal bilirubin conjugation and hepatic excretory function. Result of this study also revealed that serum albumin, globulin and total protein concentrations were not significantly different from controls. Albumin and globulins (except gamma immunoglobulins are synthesized in the liver. Consequently, significantly low serum or plasma levels of these analytes indicate impaired proteins synthesis due to massive loss of hepatocytes involved in albumin and globulin synthesis to injury (Ogunka-Nnoka *et al.*, 2017). In summation, significantly lower

albumin and total protein concentrations, elevated liver enzymes activities and bilirubin level are affirmation of liver injury (Abdulazees *et al.*, 2014; Ogunka-Nnoka *et al.*, 2017). In this present study, the assayed liver function indices with the exception of ALP in the treated groups were not significantly varied from the control group. This result, therefore, suggests that the plant extract did not inflict damage on the integrity of the hepatocytes membrane. However, significantly higher ( $p < 0.05$ ) ALP activities observed in group C and D may be due to a negative interaction of the bioactive constituent(s) of the plant extract on the hepatobiliary cells. Leaves of *B. pinnatum* contain high amount of alkaloids (Ojo *et al.*, 2018). According to Abdulazees *et al.*, (2014), the amine (NH) and hydroxyl (OH) functional groups of alkaloid could interfere with nucleic acid and protein synthesis in the liver thereby leading to liver dysfunctions and elevated ALP activity. Based on this findings, it could be posited that post hepatic (hepatobiliary) cells may be more susceptible to injury than hepatic cells. This finding agrees with the reported of Abdulazees *et al.*, (2014).

Although flavonoids are used by plants defense against disease, they are nowadays considered as a potent antioxidant in human diet (Ezejindu, 2013). A quantitative phytochemicals evaluation of leaves of *B. pinnatum* revealed the presence of flavonoids in high abundance (Casmir *et al.*, 2017). Flavonoids are plant secondary metabolites which have ability to scavenge free radicals and thus prevent oxidative damage (Adeleke *et al.*, 2018). In this present study, serum antioxidant enzymes activities of superoxide and catalase in the treated groups were comparable with the control group. SOD and CAT are universal enzymes of aerobes and are involved in primary defense of cells against free radicals. SOD protects cells against oxygen free radical by dismutation of the intensely reactive superoxide anion to molecular oxygen and hydrogen peroxide while catalase then detoxifies hydrogen peroxide to water and so preventing cells from oxidative damage (Nayana *et al.*, 2012). Disturbance in the ratio of oxidants to antioxidants, wherein the equilibrium is skewed to the left, favours accumulation of excess reactive oxygen and nitrite free radicals with consequence damage to plasma membrane, proteins and DNA. On the other hand, adequate antioxidants or strong antioxidant system neutralizes any oxidative free radicals (Nayana *et al.*, 2012). Our result also showed marked decrease in MDA level in group D compared to control group. MDA is a by-product of lipid peroxidation (Hassan, 2010) and a significant concentration of it in the blood results from a weak antioxidant system, incapable to mop up excessive free radicals (Lawal *et*

*al.*, 2017). The decreased level of MDA observed in this study suggests the ability of the extract to prevent cells membrane from lipid peroxidation via its antioxidant and free radical scavenging activity. Concentrations of reduced glutathione (GSH) were significantly lower ( $p = 0.000$ ) in all the treated groups (B, C and D) compared to control group. The effect may be due to the phytochemical constituent(s) of the plant extract, which may also suggest inhibitory effects of CALEBP at the dosages used in this present study, on the de novo synthesis of serum GSH. Inhibition of glutathione synthetase (GS) or gamma-glutamyl cysteine synthetase ( $\gamma$ -GCS) results in significant depletion of glutathione level (Ujowundu *et al.*, 2012; Couto *et al.*, 2013). The significantly lower GSH level may also be due to its vital role as an antioxidant and its involvement in phase two detoxification process as well as a substrate for glutathione peroxidase enzyme. Meanwhile, the exact mechanism underlying the significantly lower levels of serum GSH in the CALEBP treated groups compared to the control group is not fully clear. Plants with potent antioxidants potentials can replenish or boost up antioxidant capacity of plasma by adding to the endogenous antioxidants (Samaniego-Sanchez *et al.*, 2011; Xinsheng and Jose, 2012). In this present study, CALEB significantly increased ( $p < 0.05$ ) total antioxidant capacity (TAC) at a dosage of 180mg/kg. TAC is the measure of both the enzymatic and non enzymatic antioxidants of the body (Xinsheng and Jose, 2012). Therefore, significant depletion of one or more of the antioxidants that make up the antioxidant system may lower the total anti-oxidant capacity of the plasma. GSH is an essential and the most abundant non-enzyme antioxidant in the plasma. Significant decrease of GSH concentration as seen in this study may also be the reason for the lower TAC observed in groups C and D when compared to significant increase of TAC in group B. Negative significant correlations between dosage of CALEBP with FPG, GSH,  $K^+$  and creatinine levels as well as positive significant correlation between dosage of CALEBP and ALP suggest dose-dependent effects of leaves of *Bryophyllum pinnatum* on the assayed parameters.

## CONCLUSION

We therefore conclude that crude aqueous leaves extract of *Bryophyllum pinnatum* (CALEBP) could significantly lower blood glucose, creatinine and potassium levels; deplete serum glutathione and may also cause higher alkaline phosphatase activity in a dose dependent manner. Dosage with glucose, creatinine, potassium and glutathione levels are indirectly proportional while dosage and alkaline

phosphate activity are directly proportional to each other.

### COMPETING INTERESTS

The authors declare that there is no conflict of interest for the manuscript.

### ACKNOWLEDGEMENT

The authors acknowledge the effort and contributions of the technical staff of the Department of Medical Laboratory Science, University of Calabar, Cross River State and Deridam Research Institute, Uyo, Akwa Ibom State, Nigeria.

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