

THERAPEUTIC POTENTIAL OF BUCHHOLZIA CORIACEA IN MODULATING HAEMATOLOGICAL AND ELECTROLYTE PARAMETERS IN DIABETIC RATS

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Abstract. Diabetes mellitus is a metabolic disorder associated with hyperglycemia and various systemic complications. This study investigated the potential therapeutic effects of methanolic and flavonoid-rich extracts of *Buchholzia coriacea* leaves on haematological and electrolyte parameters in streptozotocin (STZ)-induced diabetic rats. A total of 30 male albino rats were divided into six groups: negative control, positive control, metformin-treated group (50 mg/kg), flavonoid-rich extract-treated groups (60 and 100 mg/kg), and methanolic extract-treated group (100 mg/kg). Diabetes was induced by a single intraperitoneal injection of STZ (45 mg/kg body weight). The extracts were orally administered for two weeks, and various haematological and electrolyte indices were analyzed. Results showed that the methanolic extract at 100 mg/kg significantly improved kidney electrolytes and serum electrolyte balance, particularly Na⁺, K⁺, and Cl⁻. Haematological analysis revealed that the flavonoid-rich extract at 60 mg/kg significantly increased platelet count and maintained white blood cell balance, indicating immunomodulatory properties. These findings suggest that methanolic and flavonoid-rich extracts of *B. coriacea* may offer therapeutic potential for managing diabetes-related complications, such as immune dysregulation and electrolytes imbalance. Further studies are recommended to isolate and characterize the active compounds responsible for these effects and explore their mechanisms of action.

Keywords: *diabetes, methanolic extract, flavonoid-rich extract, metformin, kidney*

Introduction

Type I diabetes, also known as insulin-dependent diabetes mellitus (IDDM), is an autoimmune disorder in which the immune system targets and destroys the insulin-producing β -cells of the pancreas. Consequently, individuals with IDDM require insulin therapy and face a heightened risk of developing ketosis (Sarkar et al., 2019). On the other hand, Type II diabetes mellitus, or non-insulin-dependent diabetes mellitus (NIDDM), accounts for approximately 90% of all diabetes cases and affects around 5% of the global population. This form of diabetes is most commonly seen in obese adults and is characterized by tissue resistance to insulin and an insufficient compensatory response from pancreatic β -cells. This dysfunction leads to increased glucose production by the liver and reduced glucose uptake by the body's tissues. Initially, Type II diabetes is managed through dietary changes and oral hypoglycemic agents, but many patients eventually progress to requiring insulin therapy, a stage referred to as insulin-dependent Type II diabetes (Riddle, 2021). The seeds of *Buchholzia coriacea* have been reported to have many ethnomedical uses and are utilized traditionally in Nigeria for healing and a wide range of clinical conditions. Okolie et al. (2015) conducted an evaluation of the anti-diabetic properties and phytochemical composition of aqueous and methanolic extracts derived from *Buchholzia coriacea* seeds in diabetic rats induced

with alloxan and was found to lower the animals' blood glucose levels. This was partially ascribed to the fact that it was used in traditional folk medicine to treat and manage diabetes.

Review of literature

Research in both clinical settings and animal models has demonstrated that GLP-1-based treatments can enhance kidney function by improving renal blood flow (RBF), increasing urine output, preventing elevations in plasma creatinine levels, minimizing tubular necrosis, boosting renal interstitial fluid levels, and improving the glomerular filtration rate (GFR). These therapies also exhibit cytoprotective and anti-inflammatory effects (Glastras et al., 2016; Jensen et al., 2015; Fujita et al., 2014; Yang et al., 2013; Crajoinas et al., 2011; Moreno et al., 2002). Previous study by Ugwu et al. (2018) on the extracts of *Buchholzia coriacea* revealed decrease in kidney uric acid and creatinine levels in rats induced with CCl₄ whereas Lapshak et al. (2016) found no significant changes in urea and creatinine levels in rats treated with the aqueous seed extract of *Buchholzia coriacea*. This study sought to identify the mechanism of action by which *Buchholzia coriacea* elicits its health benefits. Therefore, this study sought to investigate the impact of methanolic and flavonoid-rich extracts of *Buchholzia coriacea* leaf on haematological and electrolytes parameters of diabetic-treated rats induced with streptozotocin.

Materials and Methods

All procured chemicals and reagents employed in this study were of analytical quality. Fresh leaves of *Buchholzia coriacea* were harvested from Commander Camp, Odode-Idanre, in Ondo State, Nigeria. The plant was identified and authenticated by Dr. O. Obembe from the Herbarium of the Department of Plant Science and Biotechnology, Adekunle Ajasin University, Akungba-Akoko, Ondo State, Nigeria. It was assigned the voucher number PSB-250, and a reference sample was deposited in the Herbarium for future documentation (*Figure 1*). The fresh leaves of *Buchholzia coriacea* were thoroughly rinsed with water, air-dried at room temperature for several weeks, and subsequently ground into a fine powder using a grinding machine. The powdered material was then stored for further analysis. The methanol extract was prepared following a modified version of the method described by Lapshak et al. (2016). A ratio of 1:4 (w/v) was used, combining 500 g of powdered leaves with 2000 ml of absolute methanol. The mixture was left to soak for 72 hours, then filtered through cheesecloth, and the resulting filtrate was air-dried. A portion of the methanol extract was dissolved in a water and diethyl ether mixture at a 1:5 ratio within a separating funnel and allowed to stand overnight. The aqueous layer was separated and further partitioned with n-butanol for 24 hours. The n-butanol layer was then separated and treated with 1% KOH. Following this, the KOH layer was isolated, acidified using dilute HCl, and partitioned again with water-saturated n-butanol. The resulting flavonoid-rich n-butanol extract was freeze-dried at 45°C. The presence of flavonoids in the sample was verified using the method outlined by Sofowora (1993).



Figure 1. *Buchholzia coriacea* tree with fruits.

For this study, thirty male Wistar rats weighing between 80-145 g were obtained from Ajibode, Ibadan, Oyo State, Nigeria. The animals were housed in cages under controlled laboratory conditions in the animal facility of the Department of Biochemistry at Adekunle Ajasin University, Akungba-Akoko, Ondo State, Nigeria. Prior to the start of the treatment, the rats were acclimatized for 14 days with unrestricted access to tap water and standard feed. Diabetes was induced in the rats by administering an intraperitoneal injection of streptozotocin (STZ) at a low dose of 45 mg/kg body weight, following an overnight fast. Two days following the STZ injection, blood glucose levels were measured using a portable glucometer (Gluco-Plus Inc., Quebec, Canada) with blood samples obtained from the tail vein. Rats with a fasting blood sugar (FBS) level exceeding 200 mg/dl were considered diabetic (Ajiboye et al., 2016). Over a period of two weeks, the rats were given varying doses of the extract orally, as described by Fakoya et al. (2024). Metformin (50 mg/kg) was used as the control treatment. After two weeks of treatment, the rats were anaesthetized with diethyl ether and subsequently euthanized via cervical dislocation. Blood samples were drawn into EDTA and plain tubes for haematological and serum analyses. Tissues were excised with a sterile scalpel, excess fat was removed, and the tissues were rinsed with normal saline to eliminate any blood residues. They were then weighed and stored at -4°C for electrolyte analysis.

Blood samples for serum were allowed to stand at room temperature for 30 minutes to enable clotting. Once clotting occurred, the samples were centrifuged at 3000 x g for 15 minutes. The clot settled at the bottom of the tubes, and the serum (supernatant) was carefully aspirated using a Pasteur pipette. The serum was then properly labelled and stored at -5°C for subsequent analysis. Electrolyte concentrations, including Calcium and Sodium, were measured using the method outlined by Trinder (1951). Potassium concentration was assessed according to the procedure of Henry (1974), while Chloride levels were determined using the method described by Marshall et al. (2020). Determination of bicarbonate was carried out following the procedure described in a commercially available kit with the method of Young (1997). Haematological assessment of blood cell parameters was carried out following standard protocols. White blood cells and platelets were counted visually using an improved Neubauer counting chamber (Doyle, 2006). Monocyte and granulocyte concentrations were determined using an auto-analyzer (Doyle, 2006). The results are presented as means±standard error of the mean from three independent observations. A one-way analysis of variance

(ANOVA) was conducted, followed by Tukey's post-hoc multiple range test. Data analysis was performed using GraphPad Prism 6.0, with statistical significance established at $p < 0.05$.

Results and Discussion

Following the induction of diabetes with streptozotocin and treatment with a 100 mg/kg dose of methanol extract from Buchholzia coriacea leaves, as previously outlined in Fakoya et al. (2024), the results for the electrolytes parameters were presented in tables. Haemolytic analysis data were also presented in tables below.

The effect of B. coriacea extracts on kidney electrolytes in STZ-induced diabetics rats

The kidney electrolyte levels of Na^+ and Ca^{2+} in the treated rats showed a significant increase ($p < 0.05$) in those given 100 mg/kg body weight of methanol extract from Buchholzia coriacea leaves, compared to both the positive and negative control groups. However, there was no significant difference when compared to the metformin-treated group for Na^+ levels. No significant difference was observed in the level of bicarbonate ion in the kidney when compared to the negative control. However, there was a significant increase when compared to both metformin and flavonoid-treated groups, as outlined in Table 1. This result suggests that the methanol extract of Buchholzia coriacea (M100) has a positive effect on maintaining electrolyte balance in diabetic rats, particularly in the sodium, calcium, and bicarbonate levels. The flavonoid extracts also show some potential effects, but to a lesser extent compared to the methanol extract. The positive control group (P-CTR) shows signs of electrolyte imbalance, which is common in diabetic conditions.

Table 1. The effects of B.coriaceae extracts on kidney electrolytes in STZ-Induced diabetic rats.

S/N	Group	Na^+ (mg/dL)	Ca^{2+} (mg/dL)	HCO_3^- (mg/dL)
1	N-CTR (negative/normal control)	97.140±9.833 ^{cd}	14.142±1.799 ^a	247.5758±23.333 ^g
2	P-CTR (positive control)	97.509±0.665 ^d	34.837±2.099 ^c	134.576±3.807 ^d
3	MET(metformin group)	127.122±4.339 ^e	30.047±0.174 ^b	160.606±14.675 ^e
4	FL2 (60mg/kgb.w flavonoid)	81.444±6.447 ^c	51.946±5.792 ^d	122.159±27.227 ^{cd,e}
5	FL1 (100mg/kgb.w flavonoid)	55.500±9.911 ^{ab}	55.191±1.417 ^d	170.076±5.953 ^e
6	M100 (100mg/kgb.w methanol extract)	124.556±8.898 ^e	91.531±6.822 ^e	242.045±8.529 ^{f,g}

Note: ^aValues with different superscripts are significantly different ($p < 0.05$), while values with the same superscripts do not show a significant difference.

The effects of B. coriacesa extracts on serum electrolytes in STZ-induced diabetics rats

Serum electrolyte levels of K^+ and Ca^{2+} in the treated rats showed a significant increase ($p < 0.05$) in those administered 100 mg/kg body weight of methanol extract from Buchholzia coriacea leaves, compared to the positive control. However, no significant difference was observed when compared to the metformin-treated group for Ca^{2+} levels. Serum chloride ion level was significantly lowered in the plant extract treated group compared to the positive control, although this value was higher than that of the negative control. Serum chloride ion level of rats administered with 100 mg of methanol extract of Buchholzia coriacea leaf was significantly higher than those of metformin and flavonoid-treated groups, as outlined in Table 2. The results suggest that Buchholzia coriacea extracts (both flavonoid-rich and methanol extracts) help regulate

serum electrolyte imbalances in STZ-induced diabetic rats. The flavonoid-rich extracts (FL1 and FL2) increased calcium and potassium levels, while the methanol extract (M100) elevated chloride levels. These findings indicate that the plant extracts may restore electrolyte balance disrupted by diabetes, potentially offering protective effects on kidney and cardiovascular health. The extracts could serve as a natural remedy for managing diabetes-related electrolyte disturbances, with further studies needed to explore their clinical applications.

Table 2. The effects of *B.coriaceae* extracts on serum electrolytes in STZ-induced diabetic rats (serum electrolytes of rat after treatment).

S/N	Group	Na ⁺ (mg/dL)	Ca ²⁺ (mg/dL)	HCO ₃ ⁻ (mg/dL)
1	N-CTR (negative/normal control)	16.029±0.828 ^a	145.075±16.125 ^b	122.113±6.331 ^b
2	P-CTR (positive control)	37.635±2.814 ^d	248.101±14.022 ^d	1068.618±24.006 ^f
3	MET(metformin group)	26.653±2.002 ^c	88.450±4.497 ^a	165.529±28.630 ^b
4	FL2 (60mg/kgb.w flavonoid)	43.332±0.239 ^e	182.558±17.031 ^c	197.561±11.308 ^{b,c}
5	FL1 (100mg/kgb.w flavonoid)	46.738±1.871 ^f	284.457±10.079 ^e	145.041±17.804 ^b
6	M100 (100mg/kgb.w methanol extract)	25.003±1.051 ^c	137.752±14.900 ^b	261.301±12.134 ^d

Note: ^aValues with different superscripts are significantly different ($p < 0.05$), while values with the same superscripts do not show a significant difference.

The effects of *B. coriacea* extracts on some haemolytic indices in STZ-induced diabetics rats

White blood cells (WBC), Lymphocytes (LYMP), Granulocytes (GRA) and Platelets (PLT) levels revealed a significant increase ($p < 0.05$) in rats administered with 100 mg of methanol extract of *Buchholzia coriacea* leaf when compared to negative control and metformin-treated groups (except GRA) but were significantly lowered when compared to the positive control and flavonoids treated groups as showed in *Table 3*. The results suggest that *Buchholzia coriacea* extracts, especially flavonoids and methanol extracts, influence haematological parameters in STZ-induced diabetic rats. The extracts significantly reduced WBC and GRA, indicating a potential anti-inflammatory effect. The flavonoid-treated groups, particularly at 60 mg/kg, showed increased platelet counts, suggesting a possible role in regulating platelet activity. These findings highlight the therapeutic potential of *Buchholzia coriacea* in managing immune response and haematological disturbances in diabetes.

Table 3. The effects of *B. coriacea* extracts on some Haemolytic Indices in STZ-Induced diabetic rats (white blood cells, lymphocytes, granulocytes and platelets of rats after treatment).

S/N	Group	WBC ($\times 10^9/L$)	LYMP ($\times 10^9/L$)	GRA($\times 10^9/L$)	PLT($\times 10^9/L$)
1	N-CTR (negative/normal control)	1.700±0.577 ^b	1.133±0.348 ^a	0.333±0.145 ^a	21.300±4.304 ^a
2	P-CTR (positive control)	12.733±1.241 ^f	9.883±0.324 ^e	2.533±0.203 ^{b,c}	149.000±7.550 ^e
3	MET(metformin group)	0.538±0.085 ^a	0.680±0.171 ^a	1.667±0.240 ^{b,c}	59.867±5.081 ^b
4	FL2 (60mg/kgb.w flavonoid)	12.033±1.490 ^f	7.717±0.421 ^d	1.933±0.318 ^b	472.000±36.373 ^f
5	FL1 (100mg/kgb.w flavonoid)	13.783±1.566 ^f	7.767±1.676 ^{c,d,e}	4.667±0.176 ^f	254.000±14.434 ^d
6	M100 (100mg/kgb.w methanol extract)	6.000±0.964 ^d	3.733±0.348 ^b	1.267±0.176 ^b	153.000±15.588 ^c

Note: ^aValues with different superscripts are significantly different ($p < 0.05$), while values with the same superscripts do not show a significant difference.

The effects of *B. coriacea* extract on percentage lymphocytes and granulocytes in STZ-induced diabetics rats

The percentage lymphocytes of rats administered with 100mg/kg of methanol extract of *Buchholzia coriacea* leaf were significantly higher than those of metformin and flavonoids (100 mg/kg b.w) treated groups, while the percentage granulocytes were significantly lower than those of metformin and flavonoid (60 mg/kg b.w) treated groups as outlined in *Table 4*. The results suggest that *Buchholzia coriacea* extracts, particularly the flavonoid and methanol extracts, have an impact on the distribution of lymphocytes and granulocytes in STZ-induced diabetic rats. The metformin group showed a significant reduction in lymphocyte percentage and an increase in granulocyte percentage, indicating a possible shift in immune response. The flavonoid-treated group (100 mg/kg) exhibited a lower percentage of lymphocytes compared to the positive control group, which suggests a potential modulating effect on lymphocyte count. Overall, *Buchholzia coriacea* extracts might influence immune cell distribution, with the flavonoid and methanol extracts showing promising effects in altering lymphocyte and granulocyte levels in diabetes-induced rats.

Table 4. The effects of *B. coriacea* extracts on percentage lymphocytes and granulocytes in STZ-Induced diabetic rats (percentage lymphocytes and granulocytes of rat after treatment).

S/N	Group	LYMP (%)	GRAN (%)
1	N-CTR (negative/normal control)	67.167±5.862 ^{c,d}	28.250±3.262 ^{b,c}
2	P-CTR (positive control)	69.800±2.646 ^{c,d}	20.167±1.953 ^a
3	MET (metformin group)	53.533±2.373 ^a	37.250±1.761 ^d
4	FL2 (60mg/kg flavonoid)	69.233±3.733 ^c	25.050±0.144 ^b
5	FL1 (100mg/kg flavonoid)	53.400±5.947 ^{a,b}	19.550±4.474 ^a
6	M100 (100mg/kg methanol extract)	63.300±3.835 ^c	22.700±0.462 ^a

Note: ^aValues with different superscripts are significantly different ($p < 0.05$), while values with the same superscripts do not show a significant difference.

Diabetes mellitus is a group of metabolic conditions marked by consistently high blood sugar levels. This persistent high blood sugar leads to symptoms such as frequent urination, excessive thirst, and increased hunger (Balaji et al., 2019). If not properly managed, diabetes can lead to various complications. Acute issues may include diabetic ketoacidosis and nonketotic hyperosmolar coma, while severe long-term consequences can encompass heart disease, stroke, kidney failure, foot ulcers, and eye damage (Balaji et al., 2019). Data obtained from this study shows that *B. coriacea* methanolic leaf extract has the potential to boost the immune system of diabetic treated rat by improving the antibodies which will help to mitigate against the antigens produced from diabetic-induced rat. In the kidney of the rat administered with *B. coriacea* extract, an increase in several parameters of the electrolytes (Na^+ , Ca^{2+} and HCO_3^-) with concurrent increases in some serum electrolyte parameters (K^+ , Ca^{2+} and Cl^-) was noted. This report was in contrast to the findings of Lapshak et al. (2016), who recorded no significant influence on the serum electrolytes when rats were administered aqueous seed extract of *Buchholzia coriacea*. This observation might be a result of the differences in the method of extraction used, which might affect the concentration of the phytochemicals in the extract presumed to be responsible for any changes. The hypoglycaemic effects of phytochemical constituents such as alkaloids and flavonoids have been reported (Lapshak et al., 2016; Oladele et al., 1995); it is conceivable to predict that some of these phytochemical constituents of plants are presumably responsible for the glucose-lowering potential of the methanol extract of *Buchholzia coriacea* leaf observed in this study..

Conclusion

Based on the findings, it can be concluded that *Buchholzia coriacea* extracts, particularly flavonoid and methanol extracts, have beneficial effects in modulating immune response and improving haematological parameters in STZ-induced diabetic rats. The results suggest that the extracts may help regulate the balance between lymphocytes and granulocytes, potentially enhancing immune function and reducing inflammation associated with diabetes. These results provide evidence that *Buchholzia coriacea* extracts, especially the flavonoid and methanol preparations, may offer therapeutic potential for managing diabetes-related complications, such as immune dysregulation and liver and kidney dysfunction. However, further studies are required to better understand the underlying mechanisms of action and confirm the clinical relevance of these findings.

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Conflict of interest

The authors confirm that there is no conflict of interest involve with any parties in this research study.

REFERENCES

- [1] Ajiboye, T.O., Mohammed, A.O., Bello, S.A., Yusuf, I.I., Ibitoye, O.B., Muritala, H.F., Onajobi, I.B. (2016): Antibacterial activity of *Syzygium aromaticum* seed: Studies on oxidative stress biomarkers and membrane permeability. – *Microbial Pathogenesis* 95: 208-215.
- [2] Balaji, R., Duraisamy, R., Kumar, M.P. (2019): Complications of diabetes mellitus: A review. – *Drug Invention Today* 12(1): 98-103.
- [3] Crajoinas, R.O., Oricchio, F.T., Pessoa, T.D., Pacheco, B.P., Lessa, L.M., Malnic, G., Girardi, A.C. (2011): Mechanisms mediating the diuretic and natriuretic actions of the incretin hormone glucagon-like peptide-1. – *American Journal of Physiology-Renal Physiology* 301(2): F355-F363.
- [4] Doyle, D. (2006): William Hewson (1739-74): the father of haematology. – *British Journal of Haematology* 133(4): 375-381.
- [5] Fakoya, A., Orole, R.T., Akingbemila, A.A., Elekan, A.O., Okoh, E.F., Olusola, A.O. (2024): Effects of Flavonoid-Rich Extract of *Buchholzia Coriacea* Leaf on Streptozotocin-Induced Changes in Rats. – *Biomedical Journal of Scientific & Technical Research* 57(3): 49371-49376.
- [6] Fujita, H., Morii, T., Fujishima, H., Sato, T., Shimizu, T., Hosoba, M., Tsukiyama, K., Narita, T., Takahashi, T., Drucker, D.J., Seino, Y. (2014): The protective roles of GLP-1R signaling in diabetic nephropathy: possible mechanism and therapeutic potential. – *Kidney International* 85(3): 579-589.
- [7] Glastras, S.J., Chen, H., McGrath, R.T., Zaky, A.A., Gill, A.J., Pollock, C.A., Saad, S. (2016): Effect of GLP-1 receptor activation on offspring kidney health in a rat model of maternal obesity. – *Scientific Reports* 6(1): 12p.
- [8] Henry, R.J. (1974): *Clinical Chemistry, Principles and Techniques*. – Harper and Row, Hagerstown, Medical Department 1629p.

- [9] Jensen, E.P., Poulsen, S.S., Kissow, H., Holstein-Rathlou, N.H., Deacon, C.F., Jensen, B.L., Holst, J.J., Sorensen, C.M. (2015): Activation of GLP-1 receptors on vascular smooth muscle cells reduces the autoregulatory response in afferent arterioles and increases renal blood flow. – *American Journal of Physiology-Renal Physiology* 308(8): F867-F877.
- [10] Lapshak, L.J., Domkat, L.C., Nansah, L.S. (2016): The effect of aqueous extract of *Buchholzia coriacea* seeds on some biochemical parameters in normal and alloxan-induced diabetic rats. – *International Journal of Biochemistry Research and Review* 11(1): 1-10.
- [11] Marshall, W.J., Lapsley, M., Day, A., Shipman, K. (2020): *Clinical chemistry*. – Elsevier Health Sciences 432p.
- [12] Moreno, C., Mistry, M., Roman, R.J. (2002): Renal effects of glucagon-like peptide in rats. – *European Journal of Pharmacology* 434(3): 163-167.
- [13] Okolie, A., Obiudu, I.K., Agbafor, K.N., Unaegbu, M., Engwa, G.A., Obiudu, C.V. (2015): Anti-diabetic property and phytochemical composition of aqueous and methanol extracts of *Buchholzia coriacea* seeds in alloxan-induced diabetic rats. – *Journal of Medical Sciences* 15(5): 241-245.
- [14] Oladele, S.B., Ayo, J.O., Aduadi, A.O. (1995): Medicinal and physiological properties of flavonoids, coumarin derivatives and anthraquinones of plant origin. – *West African Journal of Pharmacology and Drug Research* 11: 134-144.
- [15] Riddle, M.C. (2021): The current schemes of insulin therapy: pro and contra. – *Diabetes Research and Clinical Practice* 175: 10p.
- [16] Sarkar, B.K., Akter, R., Das, J., Das, A., Modak, P., Halder, S., Sarkar, A.P., Kundu, S.K. (2019): Diabetes mellitus: A comprehensive review. – *Journal of Pharmacognosy and Phytochemistry* 8(6): 2362-2371.
- [17] Sofowora, A. (1993): *Medicinal plants and traditional medicine in Africa*. Ibadan. – Nigeria: Spectrum Books Ltd 98p.
- [18] Trinder, P. (1951): A rapid method for the determination of sodium in serum. – *Analyst* 76(907): 596-599.
- [19] Ugwu, G.C., Okanya, C.L., Egbuji, J.V., Okwo, J.I., Nnamonu, E.I., Eyo, J.E. (2018): Comparative nephroprotective effects of extracts of *Buchholzia coriacea* on some biochemical parameters in carbon tetrachloride-induced toxicity in *Rattus norvegicus*. – *Dhaka University Journal of Pharmaceutical Sciences* 17(2): 227-235.
- [20] Yang, H., Li, H., Wang, Z., Shi, Y., Jiang, G., Zeng, F. (2013): Exendin-4 ameliorates renal ischemia-reperfusion injury in the rat. – *Journal of Surgical Research* 185(2): 825-832.
- [21] Young, D.S. (1997): Effects of drugs on clinical laboratory tests. – *Annals of Clinical Biochemistry* 34(6): 579-581.