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Curcumin Improves Serum Electrolytes and Lipid Profiles of Diabetic Wistar Rats

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Abstract

Diabetes mellitus is associated with impaired renal function, malabsorption syndrome, and acid-base disorders among others. Curcumin, a constituent of turmeric possess many health benefits including anti-inflammatory, antioxidant and anticancer properties in both in vitro and in vivo models. However, its effects on serum electrolytes and lipid profiles of diabetic rats have not been fully investigated. Hence, the present study was aimed at investigating the effect of curcumin on serum electrolytes and lipid profile of alloxan-induced diabetic Wistar rats. The animals weighing 150–180g were divided into five (5) groups of four each (n=4). Diabetes was induced using a single dose of Alloxan (150 mg/kg) intraperitoneally. Group I served as non-diabetic control and received distilled water, group II, III, IV and V were diabetic and received olive oil 1 ml/kg, glibenclamide 2 mg/kg, curcumin 50 mg/kg and curcumin 100mg/kg respectively. All administrations were done for duration of 21 days. Blood glucose level was determined using glucose oxidase principle on a weekly basis and at the end of 21 days, the animals were sacrificed, and blood samples were collected for biochemical assays. The results obtained from this study showed that there was a significant decrease ($p < 0.05$) in the blood glucose levels and a significant ($p < 0.05$) increase in potassium, sodium and urea levels in the treated groups compared with the control group. These findings show that curcumin is antihyperglycemic and can improve serum electrolytes level, which may reduce diabetes-induced kidney disorders.

Keywords: curcumin, diabetes, hyperglycemia, serum electrolyte, lipid profile

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INTRODUCTION

Diabetes mellitus (DM) affected more than 463 million people in 2019 and this figure is projected to 578 by 2030 and 700 by 2045 representing about 10.9%. A reported prevalence of 0.8% to 11% involving both rural and urban dwellers with about 2% reported in Zaria (Dahiru *et al.,* 2008). The management of diabetes places a great burden on both individuals and government. The total global expenditure on diabetes was estimated to be USD 760 billion and the figures are projected to rise to about USD 845 billion by 2045 (IDF, 2019). Diabetes mellitus (DM) is a group of chronic metabolic disorders characterized by chronic hyperglycaemia because of relative or absolute lack of insulin or the actions of insulin (Kumar and Clark, 2002). Chronic hyperglycaemia during diabetes increases non-enzymatic glycation of proteins that later leads to secondary complications (Kameswararao *et al.,* 2003). Several complications associated with diabetes become severe over time. Uncontrolled hyperglycemia is the main cause of retinopathies, neuropathies, macrovascular disease and atherosclerosis, microvascular disease, liver disease and various debilitating neuropathies that diminish the quality of life and life expectancy of patients (Kelly *et al.,* 2003;bMoura *et al.,* 2011). The electrolytes in serum include sodium (Na+), potassium (K+), calcium (Ca2+) and magnesium (Mg2+) (Goji *et al.,* 2018). These electrolytes play an important role in intermediary metabolism and cellular function, including enzyme activities and electrical gradients (Al-Rubeaan *et al.,* 2011).

In addition, hypomagnesemia and diuretic associated hypokalemia may lead to a higher incidence of DM (Goji *et al.,* 2018), mild electrolyte changes such as low Mg2+levels can predict mortality in type 2 DM and oral magnesium supplementation reduces fasting plasma glucose levels in patients with DM (Lobo, 2004). Diabetics have abnormal serum lipid profiles and increased biliary cholesterol secretion, resulting in increased cholesterol saturation of bile (Okon *et al.,* 2013).The imbalance of the circulating lipid profile is a consequence of diabetes mellitus (Colca *et al.,* 1991). This imbalance in the concentration of serum lipoproteins promotes the movement of cholesterol from peripheral tissues to the liver for catabolic excretion. In cases where this transference to the liver is high and the catabolic level is low, fat can accumulate in this organ, causing non-alcoholic fatty liver disease (NAFLD) (Carew *et al.,* 1976). Furthermore, chronically high concentrations of serum lipids associated with a low level of catabolism can create the same condition (Diehl, 1991).

For more than four decades, several studies have been conducted to determine some pharmacological effects of curcumin (turmeric). It has been reported that it can serve as a potential therapeutic agent against several chronic diseases such as hyperglycemia, inflammation and oxidative stress (Menon and Sudheer,2007; Esatbeyoglu, 2012; Sharma *et al.,* 2014, Konak and Sener, 2019). Curcumin, also known as diferuloyl methane, is a hydrophobic polyphenol derived from the rhizome (turmeric) of the herb Curcuma longa (Anand *et al.,* 2008). Even though curcumin has been extensively studied over a long time, its potential effect on serum electrolytes and lipid profiles in diabetic rats has not been fully studied. Therefore, this research work investigated the effect of curcumin on serum electrolytes and lipid profiles of diabetic Wistar rats.

MATERIALS AND METHOD

Chemicals and drugs

All chemicals and drugs were of analytical grade. Curcumin was purchased from Arkure Health Center (Haryana, India). Alloxan was purchased from (Sigma Chemical Company St.

Louis U.S.A.). A digital glucometer (the Accu-Chek Advantage, Roche Diagnostic, Germany) was used for the determination of the blood glucose levels of the animals.

Experimental Animals

A total of twenty (20) Wistar rats of both sexes weighing between 150 to 180 grams were used for the study. The animals were housed in plastic cages under standard laboratory conditions with free access to food and water for two weeks to acclimatize in the laboratory environment before the commencement of the experiments. Ethical clearance was obtained from the Ahmadu Bello University Committee on Animal Use and Care (ABUCAUC) with approval number of ABUCAUC/2016/051.

Induction of diabetes mellitus

The animals were fasted for 12-16 h with free access to water prior to the induction of diabetes. Diabetes was induced by single intraperitoneal injection of Alloxan monohydrate (Sigma St. Louis, U.S.A.) at a dose of 150 mg/kg b w dissolved in 0.9% cold normal saline. The rats were then kept for the next 24 h on 5% glucose solution bottles in their cages to prevent hypoglycemia (Dhandapani *et al*., 2002). Animals with fasting blood glucose levels of 180 mg/dL and above were considered diabetic (Kalpana *et al*., 2011).

Experimental design:

The animals were randomly divided into five (5) groups of four (4) rats each. All administration was done orally for a duration of 21 days as follows

Group I: Normal, received distilled water
Group II: diabetic, olive oil 1 ml/kg
Group III: Diabetic, received glibenclamide (glib) 2 mg/kg (standard drug)
Group IV: Diabetic, received curcumin (cur) 50 mg/kg
Group V: diabetic, received curcumin (cur) 100 mg/kg

Estimation of Blood Glucose

The blood samples were obtained by sequential snipping of the tail. A glucometer was used to measure the blood glucose levels using glucose oxidase principle (Beach and Turner, 1958) using the digital glucometer (Accu-Check Advantage, Roche Diagnostic, Germany), (Rheney and Kirk, 2000). The blood glucose level was checked on a weekly basis.

Collection of Blood and Preparation of Serum Samples

After three weeks of treatment, blood samples were obtained from all animals in each group through cardiac puncture for evaluation of serum electrolytes. The blood sample from each animal was collected in plain tubes and allowed to clot. After clotting, the blood sample was centrifuged at 1,957 × g for 10 mins. The sera were then separated and stored at -4^0 C for serum electrolytes analysis.

Biochemical analysis

Serum electrolytes levels and estimation of serum lipid profiles were determined using colorimetric assay kits (Randox, Northern Ireland) according to manufacturer's instructions while Serum Low Density Lipoprotein (LDL) Level was estimated using the Friedewald formula

LDL-C = TC - (TGL/5 + HDL-C) (Friedewald*et al*., 1972). The level of total cholesterol, triglycerides, high and low density lipoprotein cholesterols in the serum were determined.
Where; TC: total cholesterol
HDL-C: high density lipoprotein cholesterol
LDL-C: low density lipoprotein cholesterol
TGL: triglycerides

Statistical analysis
Data obtained were expressed as mean ± standard error of mean (SEM). The data were statistically analyzed using One-way analysis of variance (ANOVA) with *Tukey's* multiple comparison post hoc tests to compare the level of significance between experimental groups. The value of $P < 0.05$ was considered as significant.

RESULTS
A significant decrease ($p < 0.05$) was observed in the fasting blood glucose level in the curcumin-treated groups (50 and 100 mg/kg b.w.) compared to the control group (Table 1). The curcumin-treated groups showed significant ($p < 0.05$) decrease in fasting blood glucose levels (104.25 ± 3.90 and 93.25 ± 4.48) after 21 days of administration, when compared to the control group treated with olive oil (220.00 ± 7.22).

Table 1: Effect of Curcumin on fasting blood glucose levels

Groups	day 0 (mg/dl)	day 7 (mg/dl)	day 14 (mg/dl)	day 21 (mg/dl)
Normal	91.75 ± 4.97	95.25 ± 2.14	93.25 ± 2.69	94.00 ± 2.08
Control	301.25 ± 9.24*	217.50 ± 6.60*	222.00 ± 13.48*	220.00 ± 7.22b
Glib 2 mg/kg	305.75 ± 6.73*	134.50 ± 3.62#	156.25 ± 5.51*#	93.75 ± 3.84#
Cur 50 mg/kg	321.25 ± 6.73*	245.75 ± 4.87*	191.50 ± 5.81*#	104.25 ± 3.90#
Cur 100 mg/kg	314.00 ± 9.40*	287.25 ± 5.53*	238.50 ± 1.85*	93.25 ± 4.48#

Values having superscripts letters are significant *,# = p < 0.05 significant. *= compared to normal, # = compared to control

A significant increase in serum potassium, sodium and urea level in the 100 mg/kg bw was observed in the curcumin-treated group compared to the control group (Table 2). The curcumin-treated groups showed significant ($p < 0.05$) increase in the 100 mg/kg dose of curcumin (7.90 ± 0.28), (124.00 ± 2.68) and (58.99 ± 1.79) compared to (6.79 ± 0.26), (77.00 ± 2.52) and (33.60 ± 1.25) in potassium, sodium and urea concentration, respectively, after 21 days of administration.

Table 2: Effect of Curcumin on serum electrolytes levels.

Groups	K (mmol/L)	Na (mEq/L)	UREA (mg/dL)	CREA (μmol/L)
Normal	6.41 ± 0.27	116.25 ± 2.72	33.60 ± 1.25	44.20 ± 0.00
Control	6.79 ± 0.26	77.00 ± 2.52	57.58 ± 2.69	44.20 ± 0.00
Glib 2 mg/kg	8.22 ± 0.18a	67.00 ± 1.46a	36.15 ± 1.24b	48.10 ± 2.86
Cur 50 mg/kg	7.37 ± 0.47	78.50 ± 1.94a	48.99 ± 1.79b	48.00 ± 3.00
Cur 100 mg/kg	7.90 ± 0.28	124.00 ± 2.68b	44.71 ± 1.61b	44.55 ± 0.35

Values having different superscripts letters are significant [a,b]= $p < 0.05$ significant. a = compared to normal and b= compared to control

A significant ($p < 0.05$) decrease and increase in the level of serum triglycerides and HDL cholesterol at 100 mg/kg bw and 50 mg/kg bw curcumin administration, respectively, was observed compared to the control group (Table 3) indicating that curcumin at both doses affects lipid profiles. The curcumin-treated groups showed no significant ($p < 0.05$) increase or decrease in all treated groups compared to the control.

Table 3: Effect of curcumin on serum lipid profile levels.

Groups	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
Normal	2.59 ± 0.00	0.97 ± 0.12	0.43 ± 0.12	1.97 ± 0.15
Control	2.59 ± 0.00	1.10 ± 0.19	0.25 ± 0.00	2.11 ± 0.04
Glib 2 mg/kg	2.59 ± 0.00	0.85 ± 0.05	0.26 ± 0.00	2.16 ± 0.01
Cur 50 mg/kg	2.59 ± 0.00	0.82 ± 0.02	0.34 ± 0.08[a]	2.09 ± 0.08
Cur 100 mg/kg	2.59 ± 0.00	0.80 ± 0.00[a]	0.27 ± 0.01	2.16 ± 0.01

Values having superscripts letter is significant [a] $p < 0.05$ significant. a = compared to control.

DISCUSSION

Hyperglycemia is associated with many complications including micro and macrovascular disorders, electrolytes imbalance, dyslipidemia, inflammation and memory loss (Johnson *et al*., 2012; Omigie and Agoreyo, 2014; Yakubu and Nwodo, 2015; Khanduker *et al.,* 2017). Curcumin is beneficial in reducing hyperglycemia by significantly ($p < 0.05$) decreasing the fasting blood glucose level after 21 days. The decrease may be because of an increase in tissue uptake of glucose via activation of glucose transporters. This result corroborates findings of Garkuwa *et al*. (2017), who reported a decrease in fasting blood glucose level of alloxan-induced diabetic Swiss albino mice following administration of curcumin. In addition, Odesanmi *et al.* (2020) reported the antihyperglycemic effect of turmeric extracts on alloxan-induced diabetic rats.

Hyperglycemia has been associated with an imbalance in electrolytes level (Khanduker *et al.,* 2017). These electrolytes are important in many physiological processes, which include controlling of fluid levels, acid-base balance, nerve conduction, blood clotting, muscle contraction, amongst others (Husain *et al.,* 2009; Khanduker *et al.,* 2017). Diabetes is associated with hyponatraemia due to decreased plasma tonicity, hypervolemia, hypertriglyceridemia. Results obtained from this study (Table 2) showed significant ($p < 0.05$) decrease in the plasma sodium concentration in the control group and this increase may be as a result of an increase in plasma tonicity due to hyperglycaemia and subsequent movement of water from the cells. The decrease in sodium level observed in the control group (Table 2) was significantly improved in the 100 mg/kg bw curcumin treated group where serum sodium level significantly ($p < 0.05$) increased compared to the control as observed on Table 2. This change might be because of the antihyperglycaemic effect of curcumin as seen in table 2. The increase in sodium concentration shows that the tonicity of the plasma was restored, and the sodium ion may have helped in the sodium-glucose co-transport system, suggesting an increase in renal glucose absorption. Diabetes is associated with both increase and decrease in serum potassium level. An increase in serum potassium levels is associated with the redistribution of potassium due to increase in plasma tonicity, whereas a decrease in its level is due to an increase in gastrointestinal and renal loss of potassium. The findings of this study indicated no significant increase in serum

potassium level and may be because of the antihyperglycemic effect of curcumin as shown in Table 1. The increase in potassium concentration also suggests that curcumin helps reverse diabetes-induced malabsorption syndrome, where potassium shift and renal loss of potassium due to osmotic diuresis are the leading cause of hypokalemia in patients with diabetes (Liamis *et al.,* 2014). Serum urea and creatinine are markers of diabetic nephropathy, where levels are increased in uncontrolled hyperglycaemia (Ashraf *et al.,* 2013; Bamanikar *et al.,* 2016). In Table 2, it is observed that serum urea was significantly ($p < 0.05$) increased in the control group compared to the normal and curcumin-treated groups. This result indicated that both doses of curcumin had improved the glomerular filtration of urea. No significant difference was observed in the serum creatinine levels across the different treatment groups.

Diabetes mellitus has been associated with impaired lipid metabolism, increased levels of triglycerides, total cholesterol, increased and decreased half-life of LDL and HDL cholesterols respectively (Jain *et al.,* 2016; Bhuyar, 2017). Findings from this study did not show any significant difference in the serum levels of total cholesterol, LDL and HDL cholesterols across the groups. Although reduction and increase in the level of triglycerides and HDL cholesterol, respectively, were not significant, the reduction triglycerides and increase in HDL signify potential benefits of this substance on serum lipid profiles. This result agreed with findings of Hussein *et al.* (2014), who also reported the hypolipidemic effect of curcumin in hyper-cholestrolemic rats.

CONCLUSION

This study suggests that curcumin possesses antihyperglycemic effect and improve serum electrolytes (sodium, potassium and urea) and lipid profiles (triglycerides and HDL) levels. Further studies are recommended to establish the mechanism through which curcumin acts to improve these physiological parameters.

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