

**PJN**

ISSN 1680-5194

PAKISTAN JOURNAL OF  
**NUTRITION**

**ANSI***net*

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## Oral Administration of Extract from *Curcuma longa* Lowers Blood Glucose and Attenuates Alloxan-Induced Hyperlipidemia in Diabetic Rabbits

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**Abstract:** The biochemical effects of methanol extract of *Curcuma longa* on plasma cholesterol, glucose, protein, triglyceride and creatinine levels were studied in alloxan induced diabetic rabbits. The rabbits were induced by intra-peritoneal injection of alloxan, which was prepared in proportion to the rabbit's body weight and administered per kilogram body weight of each rabbit. The animals were placed into three main groups in this study: normal, diabetic test animals and diabetic control animals. Single doses of plant extracts were used for the respective studies and the biochemical parameters were assessed from day 0 to day 12, on day 3 respectively. The results of plasma glucose levels indicated an increase from 6.6-8.0 g/L in the diabetic rabbits treated with *C. longa* extract, compared to the diabetic control which maintained a level of 6.3 g/L. Creatinine level in the test animals decreased from 264.5-94.6  $\mu\text{mol/L}$  and plasma cholesterol in the test group. However the plant extract only showed a slight decrease in the plasma triglyceride and protein levels of alloxan diabetic rabbits. Polydipsia in untreated in diabetic animals was reduced to normal in those administered the plant extract. *Curcuma longa* could be a possible source of antidiabetic chemotherapeutic agents.

**Key words:** *Curcuma longa*, hypolipidemic, antihyperglycemic, alloxan-induced diabetic rabbits

### INTRODUCTION

Diabetes is a growing global public concern. In America, over 18 million American have diabetes and the disease is the sixth leading cause of death in America. In diabetes mellitus, chronic hyperglycemia produces multiple biochemical sequelae and diabetes-induced oxidative stress play a role in the symptoms and progression of the disease (Giugliano *et al.*, 1996). Oxidative stress in cells and tissues results from increased generation of reactive oxygen species and/or from diseases in antioxidant defense potential are known to be major problems in diabetes (Quiles *et al.*, 2002). Clinical and experimental evidence have suggested that free radical mediated oxidative processes are involved in the pathogenesis of diabetic complications, especially cardiac dysfunction which may be caused by altered lipid levels and oxidation of LDL (Cai *et al.*, 2003). Hyperlipidemia with increased concentrations of cholesterol and triglycerides-carrying lipoproteins has been reported in experimental diabetes mellitus. Elevated lipid levels, especially hypercholesterolemia, might be responsible for onset development of atherosclerosis during the course of diabetes mellitus.

The therapeutic benefits of dietary constituents of plant origin have continued to attract attention for known diseases and emerging diseases. *Curcuma longa* L. is synonymous with *Curcuma domestica* Vahl. It is a perennial herb and belongs to the family Zingiberaceae. The rhizome of the *C. longa* is the source of turmeric with

a characteristic yellow colour, slight odour and bitter taste. Turmeric is used as a condiment and flavouring agents in medicines, confectioneries and in curry powder. (Abbiw, 1990; Ammon and Wahl, 1991) In the Nigerian, Chinese and Ayurvedic ethnomedicines, turmeric has been used for management of inflammation, jaundice, gastric ulcer, skin wounds, tumors and menstrual problems as well as larvicidal on *Anopheles gambiae* (Thorne Research, 2001; Arafat, 2005; Ajaiyeoba *et al.*, 2007) The major chemical constituent *C. longa* rhizome is a yellow pigment, 1,7-bis (4-hydroxy-3-methoxyphenyl) -1, 6-heptadiene-3, 5-dione, known as curcumin (diferulolylmethane). Curcumin has shown antioxidant, anti-neoplastic and anti-inflammatory properties (Lantz *et al.*, 2005; Swarnakar *et al.*, 2005; Surh, 2002). The compound has been found to protect against cisplatin-induced clastogenesis by acting as a free radical scavenger (Antunes *et al.*, 2000). Similarly, it has been reported that Curcumin has a potential protective role against cyclophosphamide-induced chromosomal breaks in rats. Kang *et al.* (2002) reported that Curcumin inhibits collagen synthesis and hepatic stellate cell activation *in-vivo* and *in-vitro* and thus may prove to be a valuable anti-fibrogenic agent.

The current study was conducted to assess the possible hypoglycemic and hypolipidemic effects of the turmeric extract in rabbits rendered diabetic by intravenous injection of 10% alloxan, using the single dose of 100 mg/kg.

## MATERIALS AND METHODS

**Plant collection, authentication and extraction:** Large quantities of *Curcuma longa* rhizomes and leaves were purchased from Oja-Oba Market in Ibadan and were identified by the Herbarium in Botany Department of the University of Ibadan Nigeria. These were air dried at room temperature in the laboratory and were powdered using the Hammer mill in Agronomy Department of the University of Ibadan. Powdered *Curcuma longa* (373 g) was Soxhlet extracted for 72 h using absolute Ethanol and the concentrated extracts were stored in sample bottles. The animals in group A were given 250 mg/kg plant extract per body weight for twelve consecutive days.

### *In vivo* antidiabetic assays

**Animal:** Twelve healthy male rabbits weighing between 1.10 and 1.50 kg were purchased from Sasa Market in Ibadan, Nigeria. The rabbits were fed with pellets of growers mash manufactured by Guinea Mills, Ibadan and were allowed free access to water. The animals were fed for one month and were given ascorbic acid tablets for acclimatization in the Animal House of Biochemistry Department, University of Ibadan, Nigeria. The animals were placed into three groups of four rabbits each:

- Group A: Alloxan induced diabetic rabbits given extracts of *Curcuma longa* (Test group).
- Group C: Alloxan induced diabetic rabbits without administering plant extract (Negative control).
- Group D: Normal rabbits that were not induced with alloxan and were not given plant extract (Positive control).

**Biochemical and anti-hyperglycemic assays:** Diabetes was induced in the rabbits by a single inter-peritoneal injection of 100 mg/kg of Alloxan. Blood samples were collected from the ears of the rabbits into EDTA bottles containing anticoagulant and the samples were centrifuged at 3000 rpm for 10 min to obtain plasma which was stored in a refrigerator until it was used. The plasma glucose was determined by the quantitative enzymatic hexokinase determination in plasma at 520 nm wavelength using the Sigma glucose oxidase kit. Triglycerides were analyzed using enzymatic hydrolysis of triglycerides by determining colorimetrically the glycerol produced using Randox kit. Protein concentration was determined using the photometric colorimetric test (Biuret method) available in Human kit. Measurement of creatinine clearance using difference in color intensity measured at 500 nm before and after acidification was achieved using Sigma kit. Plasma cholesterol was determined using enzymatic hydrolysis and oxidation of cholesterol with quinonemine as the indicator formed from hydrogen peroxide and 4-amino antipyrine using Randox kit.

## RESULTS AND DISCUSSION

Diabetes mellitus is associated with hyperglycemic effect, increased urinary output and weight loss and these were observed in diabetes induced by Alloxan (Weaver *et al.*, 1978). Figure 1 show mean plasma glucose level (mg/dl) in diabetic animals and diabetic rabbits administered Tumeric for 12 consecutive days. There was a significant increase in blood sugar in the group A compared to the Group D, implying an increase in plasma glucose in diabetic rabbits and a significant decrease in the plasma glucose level of test rabbits administered curcumin. This result shows *C. longa* has a possible antihyperglycemic agent, confirming previous reports on this plant (Khan *et al.*, 1990). The report of *C. longa* as a potent anti-oxidant may suggest its reaction with free radicals produced by alloxan inactivating them by activating glucokinase (WHO, 1980; Szkudelski, 2001; Weaver *et al.*, 1978). The overall effect of the presence of reactive oxygen species leads to hyperlipidemia as there is an accumulation of triglycerides and cholesterol, due to damage to pancreatic islets and liver cells. (Lenzens-Bruning and Monster, 1978). Obtained data for mean total cholesterol and total triglycerides in mg/dl in this study are shown on Fig. 2 and 3 respectively. Figure 2 showed a significant increase in total cholesterol in the diabetic control when compared to the normal and the diabetic treated rabbits and in the Tumeric treated group did not change, the cholesterol decreased significantly especially on days 9 and 12. Triglyceride level was remarkably higher on days 6-12 compared to the normal and the test rabbits and this implies that the plant drug exhibited hypolipidemic effect. *C. longa* has hypocholesteric effect by its use in treating liver disorders (Ammon and Wahl, 1991; Lewis, 1972 and Nippon, 1993) have reported that increased cholesterol level in diabetes mellitus is due to enhanced activity of HMG-CoA reductase and Cholesterol Acyl Transferase (ACAT) which are the major enzymes in cholesterol biosynthesis.

The effect of *Curcuma longa* on plasma protein concentration (g/L) at 565 nm is shown on Table 1. The result indicates a significant increase in protein concentration with regards to control ( $p < 0.05$ ) and the plant drug has slightly decreased effect on the plasma protein level in the diabetic treated rabbits (A).

The plasma creatinine level in  $\mu\text{mol/L}$  at 500 nm is shown in Table 2. There was a significant increase in the creatinine concentration with respect to the control with  $p < 0.05$ .

Diabetes causes a significant increase in creatinine synthesis. There was an increase in the value of test rabbits compared to the normal rabbits and a significant decrease in the values of treated rabbits, when compared with control especially from days 6-12.

Table 2 shows that Curcumin reduced the total protein concentration as it significantly reduced the creatinine

Table 1: The effect of *Curcuma longa* on plasma protein concentration (mg/dl) in alloxan diabetic rabbits

Grouping	Days				
	0	3	6	9	12
A(Curcuma)	8.2995±0.651	6.1505±0.460	6.595±0.325	8.025±0.0813	5.910±0.834
C Diabetic control	6.6385±0.428	5.260±1.117	6.270±0.191	6.300±0.0235	6.304±0.486
D (normal)	5.93±1.183	5.39±1.183	5.39±1.183	5.39±1.183	5.39±1.183

Table 2: Effect of *Curcuma longa* on creatinine level (µm/dl) of alloxan diabetic rabbits

Grouping	Days				
	0	3	6	9	12
A(Curcuma)	264.550±57.350	421.650±8.950	112.130±7.680	104.890±40.070	94.584±29.74
C Diabetic control	403.55±22.800	343.55±94.58	360.63±134.61	361.130±140.134	384.64±8.290
D (normal)	130.880±24.59	130.880±24.59	130.880±24.59	130.880±24.59	130.880±24.59

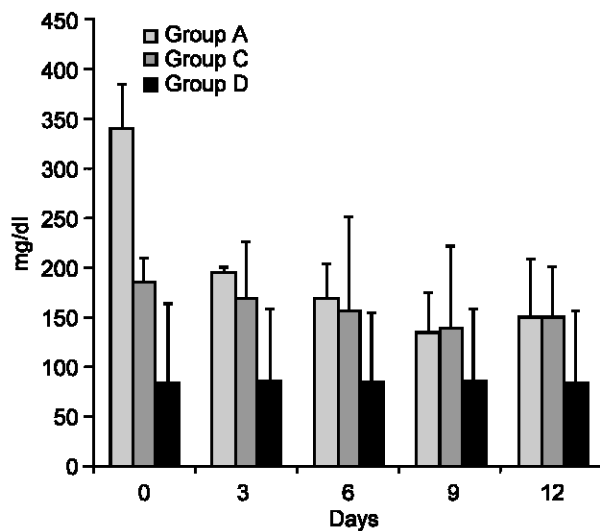


Fig. 1: Effect of curcuma longa on plasma glucose level in alloxan-diabetic rabbits

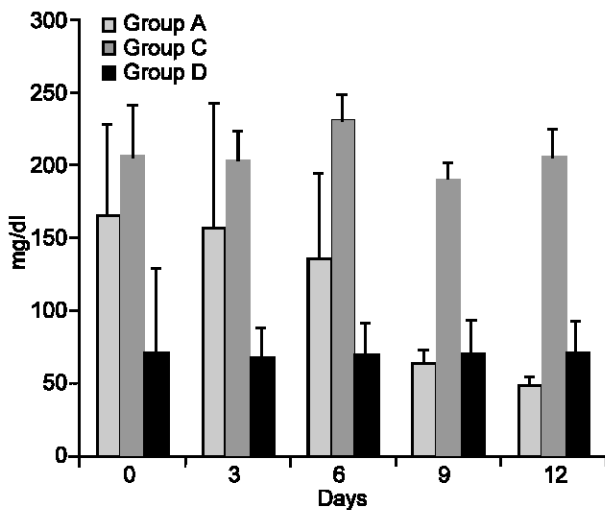


Fig. 2: Effect of curcuma longa on plasma cholesterol of alloxan diabetic rabbits plasma cholesterol in mg/dl

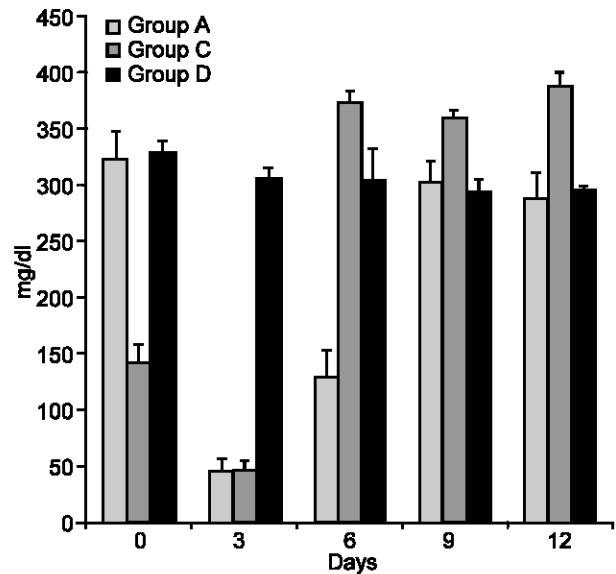


Fig. 3: Effect of curcuma longa on plasma triglyceride levels in alloxan diabetic rabbit (Tg in mg/dl)

level of alloxan diabetic rabbits, thus implying hypoprotein properties.

Diabetes is associated with polyphagia (increased appetite), polydipsia (increased thirst), polyuria (increased urine) as well as general inactivity. These symptoms were markedly reduced in dietetic rabbits treated with Tumeric. Diabetes has no cure, but effective control of blood sugar levels is beneficial especially in terms of prolonging life and reducing some long term complications. We have shown in this study to *C. longa* reduces plasma glucose level in diabetic rabbits as well as secondary symptoms that accompany diabetes such as hypercholesterolemia and hyperlipidemia.

#### ACKNOWLEDGEMENTS

The author for correspondence is grateful to TWAS for postdoctoral fellowship in Centres of Excellence in the South, utilized in HEJ Research Institute of Chemistry, University of Karachi, Karachi, Pakistan, where this work

was presented as poster in 9<sup>th</sup> International Symposium on Protein-Structure function relationships held in the same institute in January 2007.

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