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ORIGINAL ARTICLE

Effect of curcuma longa on atherogenic index of plasma in alloxan induced diabetic rats.

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ABSTRACT… Objective: To determine effects of Curcuma longa (CL) on the glycemic control, blood lipids and atherogenic index of plasma (AIP) in alloxan induced diabetic male Wistar albino rat model. **Study Design:** Experimental study. **Setting:** Department of Basic Medical Sciences, Suleman Roshan Medial College, Tando Adam, Sindh. **Period:** February 2019 to January 2021. **Material & Methods:** A sample of 100 rats was divided into negative controls (C^-), positive (diabetic) control (C^+), and experimental groups D, E and F. DM was induced by injecting Alloxan (120 mg/Kg body weight) intraperitoneally (i.p) to overnight fasting rats. Diabetic groups D, E, and F were treated with ethanol extract of Curcuma longa 100 mg, 300 mg and 500 mg orally daily for six weeks. Blood samples were collected for biochemical analysis. Atherogenic Index of Plasma (AIP) was calculated by log TAG/HDLc. Data analyzed on SPSS package (ver. 21.0, IBM, incorporation, USA) ($p \leq 0.05$). **Results:** Significant improvement in glycemic status and blood lipids was observed in Curcuma longa treated groups D, E and F ($P=0.0001$). Atherogenic index of plasma (AIP) in negative (C^-) and positive (C^+) control was 0.08 ± 0.03 and 1.11 ± 0.1 respectively ($P=0.0001$) that improved in Curcuma longa treated groups D, E and F noted as; 0.77 ± 0.3, 0.68 ± 0.3 and 0.62 ± 0.4 respectively. **Conclusion:** Present study found ethanolic extract of Curcuma longa improves the glycemic control, lipid profile and atherogenic index of plasma (AIP) in alloxan induced diabetic rat model.

Key words: Atherosclerosis, Curcuma Longa, Glycemic Control, Lipid Profile.

INTRODUCTION

Curcuma longa (turmeric) is a tropical plant that grows in suitable climate. It is perennial herb of ginger family. Herb grows up to one meter high. Leaves are oblong and tufted. Yellow turmeric is obtained from the rhizome (roots). Rhizomes are first boiled, then dried and ground into powder. It is cultivated extensively in Asian subcontinent, including Pakistan, China, India, etc.[1] Most active component of turmeric is the curcumin that comprises 2 – 8% of it. Curcuma longa contains polyphenol extracted by ethanol extraction. Curcuma long has been used for several purposes. Traditionally, it is used as flavoring and coloring agent for food in Asian cuisine. It is also used as flavoring agent for yogurt, butter, cheese and other kinds of food.[1,2] Previous studies revealed anti-inflammatory and anti-oxidant activity of Curcuma longa.[2] Other studies reported Curcuma longa modulates the cell enzymes and induces angiogenesis.[3] Historical use of Curcuma longa is notable in the ancient writings of Asia. Dose limiting toxicity of Curcuma longa derived curcumin was first published in 2001, when it was reported eight grams of it consumed for 3 months showed no toxic effects to humans.[1] A study[4] used turmeric daily for four weeks to healthy subjects and reported no changes in fasting plasma glucose and blood lipid levels.[5] A previous animal study[6] proved significant decrease in kidney dysfunction and oxidative stress and concluded the Curcuma longa protects against the diabetic nephropathy. Sedentary life style of decreased physical activity and increased calorie intake has resulted in overweight and obesity with increased metabolic syndrome and diabetes mellitus.

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Obesity is proved of causing insulin resistance, dyslipidemia, and inflammatory responses along with metabolic disorders.[1] Food of low glycemic load and index (GI) and rich in dietary fibers and whole grains are good for preventing diabetes mellitus and metabolic syndrome. Dyslipidemia is a common metabolic derangement of diabetes mellitus with atherogenic tendency that increases the risk of peripheral arterial disease, coronary artery disease, cerebrovascular accidents, etc.[1,3]

The present experimental study was conducted to analyze the effects of Curcuma longa on the glycemic control, blood lipids and atherogenic index of plasma (AIP) in alloxan induced male Wistar albino rat model.

MATERIAL & METHODS

The present experimental study was conducted at the Department of Basic Medical Sciences, Suleman Roshan Medical College, Tando Adam, Sindh. Study was approved by the Research Ethical Committee. Study was conducted from February 2019 to January 2021.

Adult male albino rats of Wistar strain were purchased for the experiment purpose. 100 rats were selected according to criteria of 150 – 200 gram body weight, male albino rats, Wistar strain, feeding well and mobile in the cages. Female rats, sick and lazy male rats were excluded. Conditions of animal house were standardized. 12/12 hour dark/light cycle was maintained with proper ventilation and standard feed to the rats. Rats were divided equally into negative (non-diabetic) controls (C^-), positive (diabetic) control (C^+), and experimental groups D, E and F. DM was induced by injecting Alloxan (120 mg/Kg body weight) intraperitoneally (i.p) to overnight fasting rats. Normal saline (citrate buffer, pH 4.5) was used for alloxan solution. Alloxan was injected by pinching ventral abdominal wall skin. Induction of diabetes mellitus in the rats was defined as random blood glucose ≥200 mg at 72 hours.[7] Experimental diabetic rats were given 10% DW for prevention of hypoglycemia up to 72 hours. Diabetic positive control (C^+) was untreated given placebo (N/S 0.9%) orally daily. Diabetic groups D, E, and F were treated with ethanol extract of Curcuma longa 100 mg, 300 mg and 500 mg orally daily.

Ethanolic extract of Curcuma longa was prepared.[8] Rhizomes of turmeric were dried, boiled and crushed into fine powder. Powder was mixed in ethanol and packed into thimble and filter paper. Extract was put into the Soxhlet extractor. 99.9% ethanol was used for continuous extraction. Five batches of 200 grams each were put into absolute alcohol. This procedure took place at 60^0C continued for 48 hours till solvent appeared colorless in the siphon tube. 200 grams powder was cycled for eight to ten times. Bumping of solvent was prevented by adding small pieces of porcelain into the flasks. Solvent was distilled off. Heating was done for evaporation by the magnetic stirrer to get concentrated thick extract. Tween – 80 was added to dilute the extract. Ready Curcuma longa was kept sealed in glass bottles and dose was given to rat groups for 6 weeks. Rats were weighed on electronic weight scale to get body weight that was noted. At the end of experiment period the blood samples were collected. Retro – orbital venous plexus was approached by using capillary tube behind eye ball and sufficient blood samples were taken into tubes. Random blood glucose (RBG), glycated hemoglobin A1 (A1C), blood lipids – S. cholesterol, triglycerides (TAG), LDL and HDL were estimated biochemically. Atherogenic Index of Plasma (AIP) was calculated by log TAG/HDLc. Values of 0.3 – 0.1 as low risk, 0.1 – 0.24 as medium risk and >0.24 as high risk of atherogenic tendency.[9] A proforma was designed for saving the results of rat groups.

Data variables were saved in Microsoft Excel sheet from the proforma. Data analyzed on SPSS package (ver. 21.0, IBM, incorporation, USA). Continuous variables (for example; RBG, A1C, blood lipids) were analyzed using Student's t-test at 95% Confidence interval ($p \leq 0.05$).

RESULTS

Significant improvement in glycemic status and blood lipids were observed in Curcuma longa treated groups D, E and F ($P=0.0001$) (Table-I). Atherogenic index of plasma (AIP) was calculated as log TAG/HDLc shown in Table-I. AIP in negative (C^-) and positive (C^+) control was 0.08 ± 0.03

and 1.11 ±0.1 respectively (P=0.0001). AIP was decreased in Curcuma longa treated groups D, E and F found as; 0.77±0.3, 0.68±0.3 and 0.62±0.4 respectively (Table-I and Figure-1).

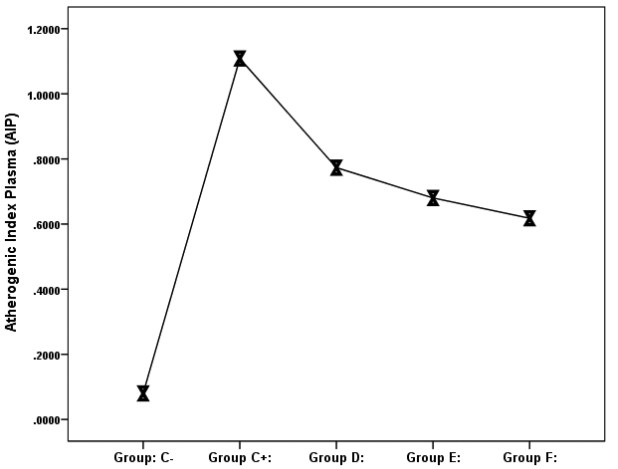

Figure-1. Figure showing the Atherogenic Index Plasma.

DISCUSSION

The present experimental rat study first time analyzed the efficacy of ethanolic extract of Curcuma longa on the glycemic control, lipid profile and atherogenic index of plasma (AIP) in alloxan induced diabetic rat model. We observed significant improvement in Curcuma longa treated experimental groups D, E and F (P=0.0001). Atherogenic index of plasma (AIP) was calculated as log TAG/HDLc[9] shown in Table-I. AIP in negative (C^-) and positive (C^+) control was 0.08±0.03 and 1.11 ±0.1 respectively (P=0.0001) compared to significant decrease in Curcuma long treated groups D, E and F found as; 0.77±0.3, 0.68±0.3 and 0.62±0.4 respectively (Table-I and Figure-1). The findings suggest the Curcuma longa prevents atherogenic tendency in alloxan induced diabetic rats. The findigns of present study are supported by previous studies.[10-12] Majeed et al[11] analyzed the anti – atherosclerotic and anti – inflammatory effects of 12 weeks curcumin therapy and reported positive effects on the serum cholesterol, TAGs, LDLc, HDLc and AIP. The findings of above study are in agreement with the present study. Wojcik et al[12] analyzed the underlying molecular mechanism of C. longa curcumin on type 2 diabetes and cancer. They reported the C. longa curcumin mitigated the hyperlipidemia and risk of atherosclerosis and oncongenesis in their study. Ghelani et al[10] examined the efficacy of C. longa curcumin on liver lipids and adenine induced renal injury in rat model. Previous studies[13,14] had reported similar finding of hypocholesterolemia and AIP and effect was produced through inhibition of hepatic HMG-CoA reductase enzyme. The findings of hypolipidemic effect and AIP of above study is in agreement with the present study. Another study[15] reported the C. longa curcumin increases hepatic clearance of cholesterol through stimulation of CYP7A1 enzymatic activity in the liver through its gene expression. Other previous study[16] conducted on mice model, demonstrated reduction of LDLc cholesterol through up regulation of LDLc receptors in the macrophages. Ghelani et al[10] reported the C. longa curcumin supplementation decreases serum TAGs, hepatic TAGs, and serum VLDLc similar to present study.

	Group C^-	Group C^+	Group D	Group E	Group F	P
Body weight (g)	178.5±15.5	183.3±14.1	175.3±13.1	178.3±13.9	176.4±14.3	0.95
RBG (mg/dl)	125.1±7.2	409.1±146.5	285.1±61.7	280.6±60.5	198.0±23.0	0.003
A1C (%)	5.11±0.6	8.66±0.72	8.14±0.7	7.09±0.78	6.49±0.50	0.016
S. Cholesterol (mg/dl)	108.9±2.4	216.7±52.5	203.3±24.1	173.5±52.3	150.1±37.1	0.018
S. triglycerides (mg/d)	83.0±20.5	179.4±31.1	174.4±26.7	159.5±19.3	154.3±26.5	0.015
Serum LDL (mg/d)	80.9±17.8	178.7±25.3	127.3±56.3	114.3±44.9	106.5±36.5	0.001
Serum HDL (mg/d)	44.2±3.3	24.3±1.3	25.8±1.3	30.2±3.2	34.2±5.9	0.001
AIP	0.08±0.03	1.11 ±0.1	0.77±0.3	0.68±0.3	0.62±0.4	0.0001
Group C^- → negative control, Group C^+ →positive control						

Table-I. Glycemic control, Blood Lipids and Atherogenic Index Plasma of rats. (n=100)

The findings of present study are also supported by previous studies.[14,17,18] Seo et al[19] reported the C. longa curcumin decreases blood lipids and AIP through up regulation of skeletal muscle lipoprotein lipase (LPL) activity in db/db mice. Prabu et al[20] reported that a C. longa curcumin decreased blood lipids and AIP through induction of plasma LPL activity in arsenic intoxicated rat model. We found similar blood lipid findigns that could be due to the increased tissue and plasma LPL enzyme induction by the C. longa. Ratio of TAGs to HDLc is a useful indicator of cholesterol homeostasis and AIP in the arterial wall[10-12] and this has been found ameliorated by six weeks C. longa therapy in present study. Zhao et al[20] conducted study in mice model. They C. long curcumin ameliorated HDLc abnormalities through induction of lecithin cholesterol acyl transferase (LCAT). Evidence based findings of present research show the Curcuma longa as an excellent anti – hyperlipidemia and anti – hyperglycemia agent. Curcuma longa may be used to modify the blood lipids fractions in general and atherogenic index plasma in particular to mitigate the risk of atherosclerosis in diabetic population.

Limitations of present research is the animal study design hence findings are not generalizable clinical settings. Future studies with type 2 diabetic subjects are recommended.

CONCLUSION

The present study found ethanolic extract of Curcuma longa improves the glycemic control, lipid profile and atherogenic index of plasma (AIP) in alloxan induced diabetic rat model. Further studies are recommended, both animal and clinical studies to make this herbal remedy available for preventing the atherosclerosis.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Samreen Pandhiani	Drug dose, encume long departb.	
2	Aftab Abbasi	Animal lumins, Animal scorepes, blood sampling.	
3	Hina Mawani	Animal lesions lit review, Animal samples.	
4	Abdul Majid	Animal groups, blood sampling, Performed analysis.	
5	Asim Mehmood	Animal groups, alternagive draft performed.	
6	Rasheed Ahmed Soomro	Interpretation of blood samples.	
7	Kashif Rasheed Shaikh	Data analysis.	