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ORIGINAL ARTICLE

Turmeric improves glycemic control and exhibits insulin secretagogue activity in Alloxan induced diabetic rat model.

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ABSTRACT… Objective: To analyze effects of turmeric in glycemic control and insulin secretagogue activity in alloxan induced diabetic rat model. **Study Design:** Experimental Study. **Setting:** Department of Surgery, Liaquat University of Medical and Health Sciences, Jamshoro/Hyderabad. **Period:** February 2019 to January 2020. **Material & Methods:** A sample of 100 adult male rats was selected according to inclusion criteria. Rats were grouped as negative control (group A), positive control – diabetic rats (group B), and experimental groups C – E. Group C- was diabetic rat + 100 mg ethanol extract of turmeric, Group D- was diabetic rat + 300 mg ethanol extract of turmeric, and Group E- was diabetic rat + 500 mg ethanol extract of turmeric. Overnight fasting rats were administered Alloxan 120 mg/Kg body weight intraperitoneally (i.p) by pinching abdominal wall under skin for the induction of diabetes mellitus in the rats. Blood glucose, glycated hemoglobin A1 (A1C) and serum insulin were analyzed. Statistical analysis was performed on SPSS package (ver. 21.0, IBM, incorporation, USA) at $p \leq 0.05$ (Confidence interval 95%). **Results:** Blood glucose, A1C and serum Insulin levels were improved in turmeric treated experimental rats. Significant reduction in blood glucose and A1C were found in turmeric treated rats (P=0.0001). Serum insulin levels were found increased in turmeric treated experimental groups C – E compared to positive control B (P=0.0001). **Conclusion:** Administration of turmeric significantly reduced the blood glucose and A1C with increased serum insulin levels in alloxan induced diabetic rats.

Key words: Alloxan, Diabetic Rats, Glycemic Control, Insulin.

INTRODUCTION

Turmeric plant belongs to the ginger family. Botanically, it is called the Curcuma longa.[1,2] It's a rhizome consumed for flavoring of food preparation. It has been used for various ailments in Asia since centuries back.[1,2] Turmeric is famous condiment in the Asian countries. Ancient description of using medicinal plants dates back 2500-1800 BC mentioned in the Rig Veda.[2,3] It is publicly called one of the "Golden spices" of Asia used as a prime ingredient in curry powder and cuisines. Cultivation record of turmeric plant is found 3000 BC in Harappan civilization. Turmeric is used in Unani, Siddha, and Ayurveda medicine systems. It is also used as home remedy for various ailments. Turmeric is used for wide spectrum of disorders such as for fungal infections, soothing agent for inflammation, multiple sclerosis, cataract, rheumatoid arthritis, Alzheimer's disease and inflammatory bowel disease.[2-5] Turmeric is recognized of its anti – mutagenic and anti – carcinogenic, anti – fungal, hepatoprotective, anti-coagulant, anti – fibrotic, anti –viral, anti – protozoa, anti – fertility, anti – hypertensive, anti – hyper lipidemic and anti – diabetic activity.[2-7] Turmeric is used for various ailments such as hepatitis, arthritis, a remedy for liver and stomach, toothache, bactericidal and germicidal disinfectant and deodorizing agent. It relieves cough, cold, sneezing and skin allergy.[2-7]

Anti – diabetic action of turmeric is currently of great clinical importance as the diabetes mellitus (DM) has increased exponentially. South

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East Asia is tagged as capital of DM including Pakistan.[8,9] Global prevalence of diabetes mellitus (DM) showed 463 million diabetics in 2019 that is predicted to rise to 700 million by the year 2045.[8,9] Pakistan shows 26.3% DM prevalence as reported.[8] Although various allopathic drugs are available but there is dire need of home remedies for the DM that should be simple, cheap, inexpensive and easily available. Hence there is need to re – evaluate the available herbs for their anti – diabetic potential. Keeping in view of rising prevalence of diabetes mellitus, it seems attractive to analyze the potential of simple herbal agents with fewer adverse effects. The present study was planned to analyze the effects of turmeric on blood glucose and serum insulin in Alloxan induced diabetic rats.

MATERIAL & METHODS

The present experimental study was conducted at the Department of Surgery, Liaquat University of Medical and Health Sciences, Jamshoro/ Hyderabad. Study proposal was approved by the Ethical Review Committee (ERC). The study was carried out from February 2019 to January 2020.

A sample of 100 adult male rats was selected according to inclusion criteria. Body weight 150 – 200 grams, male rats, Wistar albino strain, feeding well and moving around the cage were inclusion criteria. Sick, lazy rats and female gender were exclusion criteria. Animals were housed in animal house under standard conditions; 12/12 dark/light cycle, proper ventilation and feeding. Rats were selected as negative control (group A), positive control – diabetic rats (group B), and experimental groups C – E. Group C- was diabetic rat + given 100 mg ethanol extract of turmeric daily orally, Group D- was diabetic rat + given 300 mg ethanol extract of turmeric daily orally, and Group E- was diabetic rat + given 500 mg ethanol extract of turmeric daily orally. Alloxan was dissolved in normal saline (citrate buffer, pH 4.5). Overnight fasting rats were administered Alloxan 120 mg/ Kg body weight intraperitoneally (i.p) by pinching abdominal wall under skin for the induction of diabetes mellitus in the rats.[10] A rat attained blood glucose ≥250 mg/dl at 72 hours was labeled as successful DM induction. Negative controls were given normal saline placebo therapy and positive control (group B) was left untreated. Diabetic rats were given 10% DW to prevent hypoglycemia during early induction period of DM. Ethanol extract of turmeric was prepared as cited.[11]

Dry rhizomes of turmeric were crushed into fine powder. It was packed into thimble of filter paper. Later on, it was transferred to Soxhlet extractor. 5 batches of 200 grams each were subjected to 99.9% ethanol for continuous extraction. Procedure was performed at 60^0C for 48 hours till solvent became colorless in the siphon tube. Around 8 – 10 cycles took place for 200 gram powder. Flasks were added with small porcelain pieces to prevent bumping of solvent. Obtained solvent was distilled off. It was heated to evaporate using magnetic stirrer to yield a concentrated thick extract. This was diluted with Tween – 80. Ethanol extract of turmeric was ready to use for experiment purpose. Turmeric therapy was continued for 28 days. Body weight was measured on electronic weigh scale.

Blood sampling was performed from retro-orbital venous plexus using capillary tube as lancet inserted below the eyeball. Blood glucose was detected by hexokinase method, glycated hemoglobin A1 (A1C) was measured by colorimetric method and presented as %. Serum insulin was measured by Elisa assay method using commercial assay kits. Data variables were saved in a pre – structured proforma and blood findings were kept confidential by the principal investigator. Data was entered in Microsoft Excel sheet. Statistical analysis was performed on SPSS package (ver. 21.0, IBM, incorporation, USA). Numerical variables were analyzed by one – way analysis variance (1- ANOVA). Statistical level of significance of a data variable was taken at $p \leq 0.05$ (Confidence interval 95%).

RESULTS

Blood glucose, A1C and serum Insulin levels were improved in turmeric treated experimental rats as shown in Table-I. Highly significant reduction in blood glucose and A1C were in high turmeric treated rats (P=0.0001). Serum insulin levels were found increased in experimental groups C

– E compared to positive control B (Figure-1-4).

DISCUSSION

The present experimental study reports for the first time on the insulin secretagogue potential of turmeric powder in Alloxan induced diabetic male rats. Allopathic arsenal of anti – diabetic drugs have many adverse drug effects, hence need for safe herbal preparations is always demanding. Turmeric is known food flavoring condiment consumed in routine diet and is reported possess many medicinal properties hence interest is growing in researching its anti – diabetic effect on scientific grounds. In present study, we found a significant efficacy of turmeric on the glycemic control and insulin secretion.

	Body Weight (g)	Blood Glucose (mg)	A1C (%)	Insulin (U/L)	F-Value	P-Value
Group A- Control	235.6±26.4	114.7±10.7	4.41±1.13	2.4±0.38	4.2	0.044
Group B – Diabetic control	202.2±31.3	257.9±51.2	10.9±0.82	0.63±0.4	49.3	0.039
Group C – Diabetic+ Turmeric (100 mg)	202.1±21.8	215.5±32.5	8.1±1.19	1.45±0.53	81.1	0.035
Group D – Diabetic+ Turmeric (300 mg)	216.3±23.9	198.7±15.9	7.4±1.14	1.74±0.26	42.7	0.0001
Group E – Diabetic+ Turmeric (500 mg)	209.3±26.1	176.3±13.3	6.4±0.76	1.77±0.27	45.7	0.0001

Table-I. Body weight, glycemic control and insulin in control and experimental rats. (n=100)

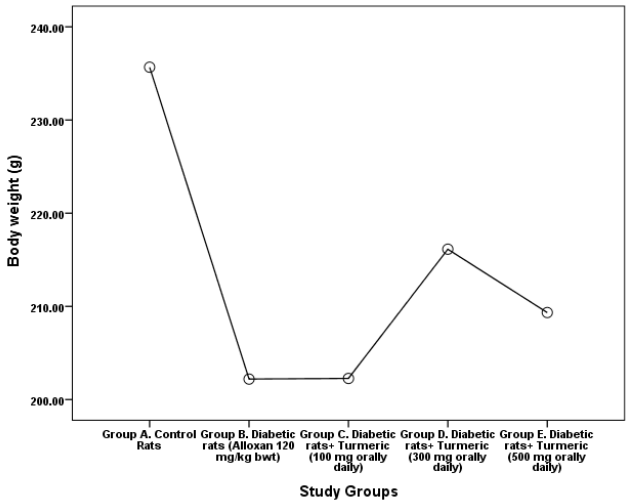

Figure-1. Body weight in animal groups.

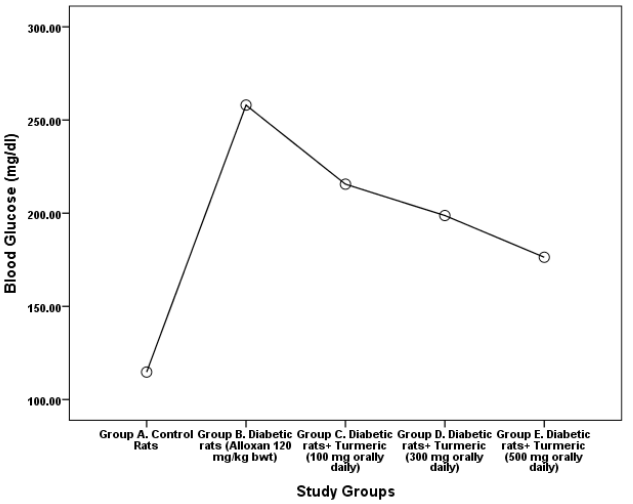

Figure- 2. Blood glucose in animal groups.

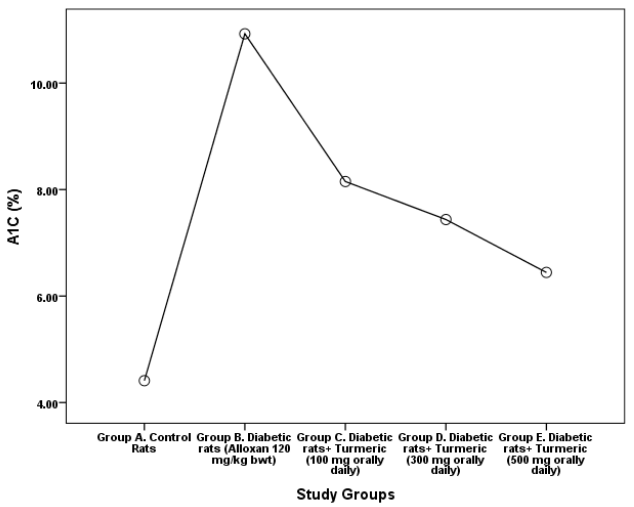

Figure-3. A1C (%) in animal groups.

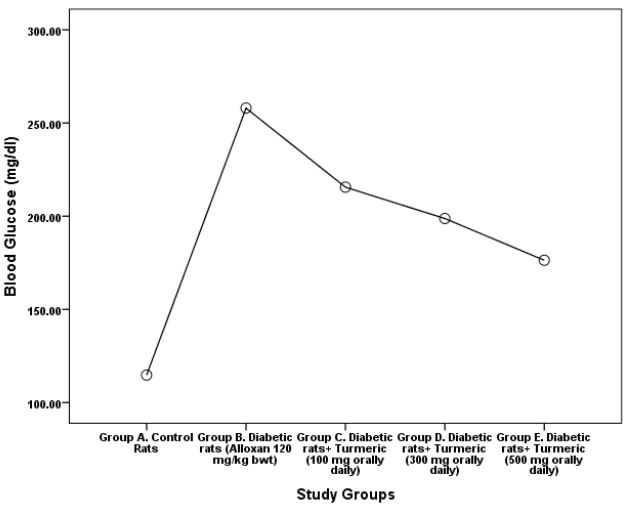

Figure-4. Insulin level in animal groups.

Turmeric efficacy was dose dependent, with prominent insulin secretagogue activity observed in high dose turmeric treated rats (P=0.0001). Serum insulin in turmeric experimental groups C, D and E were noted as 1.45±0.53, 1.74±0.26 and 1.77±0.27 U/L respectively compared to 0.63±0.4 U/L in positive control and 2.4±0.38 U/L in negative control (P=0.0001). Turmeric administration to diabetic rats increased the post – prandial serum insulin concentration that ameliorated the glycemic control. The findings are in agreement with previous studies.[12,13]

DM is a much common health disorder and its prevalence has increased too much hence there is need to search for alternative herbs in addition to the available allopathic drug therapy which have many adverse effects. Turmeric has been used for diabetes mellitus since Vedic time period.[14] A previous study[15] reported the therapeutic effect of turmeric is prominent in those with preserved islet β – cell mass in pancreas hence it is useful for the type 2 diabetic subjects. In present study, glycemic control and insulin secretagogue activity was noted in 100, 300 and 500 mg dose, but the effect was highly significant in high turmeric dose (P=0.0001) (Table-I). The findings are in agreement with Santoshkumar et al[2] that found significant glucose lowering potential at higher turmeric dose (500 mg/Kg body weight). Previous studies[2,12] have reported anti – inflammatory, anti – oxidant and anti – neoplastic activity of turmeric. A previous study[16] reported amelioration of glycemic control with 1 gram of turmeric administered to diabetic rats for 3 weeks; the finding is in keeping with our present study. Another study[17] reported the curcumin, an active component of turmeric, improved the renal functions in diabetic rats and anti – oxidant potential of it was also observed. They observed decrease in creatinine and creatinine clearance in diabetic rats when curcumin (15 – 30 mg/Kg) was given for 2 weeks.

Turmeric is reported to combat oxidative injury in an in – vitro human endothelial cell model.[18] A previous study[19] reported improved glycemic control and insulin sensitivity in obese diabetic mice model. The findings support the observations of present study. In present study, we observed the short time potential of turmeric on the blood glucose, A1C and serum insulin concentrations. Findings of present study prove the insulin secretagogue potential of turmeric in diabetic rats given for 4 weeks and glycemic control was improved significantly. Insulin secretagogue action of turmeric is induced through stimulation of β – cell function that is in agreement with a previous study.[20] The findings are in line with the present study. We conclude the turmeric exhibits excellent glucose regulating activity through insulin secretagogue effect on the β – cells of pancreas. Limitation of present experimental study is the animal study design and short turmeric therapy duration hence findings are pre – clinical. Further studies are recommended.

CONCLUSION

The present study shows that the ingestion of turmeric significantly reduced the blood glucose and A1C with increased serum insulin levels in alloxan induced diabetic rats. Findings indicate the turmeric may have insulin secretagogue action on pancreas. Turmeric may be used as add on therapy in diabetics, however, this demands clinical trials.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Asim Mehmood	Study concept, Animal experiment, Data collection.	
2	Rasheed Ahmed Soomro	Study design, Allonum dose, Sample collection.	
3	Samreen Pandhiani	Literature review, Study design, Drug dosage.	
4	Aftab Abbasi	Arrival Graphic feeding, exp.	
5	Hina Mawani	Arrival Graphic experiment, Data collection.	
6	Abdul Majid	Biochemical acquistion.	
7	Kashif Rasheed Shaikh	Drug dose, exp.	