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ORIGINAL ARTICLE

Curcuma longa modulates Islet β-cell function and insulin resistance in diabetic rat.

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ABSTRACT… Objective: To analyze modulating effect of Curcuma longa on Pancreatic Islet β-cell function and insulin resistance in alloxan induced diabetic rat model. **Study Design:** Experimental study. **Setting:** Department of Anatomy, Pharmacology and Pathology, SRMCH, T. Adam. **Period:** February 2019 to January 2020. **Material & Methods:** One hundred adult male rats were selected according to criteria and grouped A to E. Group A and B was negative and positive control rats, and C –E were diabetic experimental rats. Alloxan (120 mg/Kg body weight) was injected intraperitoneally (i.p) to induce diabetes mellitus. Curcuma longa was used in doses of 200, 300 and 500 mg/d for 28 days. Body weight, blood glucose, HbA1c, insulin and C-peptide were estimated. Insulin resistance (HOMA-IR) and β- cell function (HOMA-β) were calculated by formulae. Data was analyzed on SPSS package ver. 21.0 (IBM, incorporation, USA) ($p \leq 0.05$). **Results:** Twenty eight days therapy of Curcuma longa extract ameliorates blood glucose, A1C, serum Insulin levels and C-peptide levels. Insulin resistance (HOMA-IR) was found improved and β- cell function (HOMA-β) was augmented in in Curcuma longa treated experimental rats ($P=0.0001$). **Conclusion:** Administration of Curcuma longa positively modulates the Islet β-cell function and insulin resistance in alloxan induced diabetic rats.

Key words: Alloxan, Curcuma Longa, Islet β-cell, Insulin Resistance.

INTRODUCTION

Incidence and prevalence of diabetes mellitus (DM) has rapidly increased over last three decades. DM has become epidemic of non-communicable diseases. Estimates of IDF show a burden of 425 diabetics in 2017 that is estimated to project to 629 million by the year 2045, indicating total 45% rise over the globe.[1,2] DM has put an incredible burden of mortality and morbidity on the health cost all over the globe. Diabetic therapy with fewer side effects is a challenge in the medical field. Available anti – diabetic drug therapy show severe adverse drug effects related to the gut, liver, kidneys, and more over the hypoglycemia. Available oral anti – diabetic drugs are not safe in pregnancy.[1,3] Hence, it is need of searching newer drug agents for DM that may be more efficient with least or no adverse effects.[3] Numerous herbs and plants have been analyzed of anti – diabetic potential. Already 80% of World population depends on plants and herbs for medications. Research on medicinal plants is on climax in several countries.

Some countries have 35% of drugs of natural origin and ethno botanical information already proved anti diabetic potential of herbs and plants.[1,4] Curcuma longa is a herb plant that yields turmeric powder. Curcuma longa is a rhizome traditionally used in food preparation for taste and flavor purpose. Beside food consumption, it has been used for various diseases through the World since ancient times.[5-7] Curcuma long is termed as the "Golden spices" of Asia because of its wide consumption in curry powder and cuisines. Curcuma longa shows the anti – microbial, anti – inflammatory, wound healing, anti – oxidant, hepatoprotective, and anti – neoplastic potential.[8] Blood glucose regulating effect of Curcuma longa has been observed.[9]

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Anti – diabetic potential of ethanolic extract of Curcuma longa was noted in alloxan – rendered diabetic rat model but the research studies are still contradictory.[1,10] Research on anti – diabetic herbs and plants are on rise because the DM is increasing exponentially. Pakistan ranks 5th position in South East Asia that is now declared as the capital of DM.[5] Pakistan, with DM prevalence of 23%[5], show more demanding vigorous research on new anti - diabetic herbs for better glycemic control that should be available easily and cost effective with few adverse effects.

The present study was planned to analyze the modulating effect of Curcuma longa on Pancreatic Islet β-cell function and insulin resistance in alloxan induced diabetic rat model.

MATERIAL & METHODS

The present experimental study was conducted at the Department of Anatomy, Pharmacology and Pathology, SRMCH, T. Adam. The study was carried out from February 2019 to January 2020. Study proposal was approved by the Ethical Review Committee (ERC). 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 C. longa daily orally, Group D- was diabetic rat + given 300 mg C. longa daily orally, and Group E- was diabetic rat + given 500 mg C. longa daily orally. Negative controls were given normal saline placebo therapy and positive control (group B) was left untreated. C. longa therapy continued for 28 days. 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. Insulin resistance (HOMA-IR) was decreased and concomitant rise in β- cell function (HOMA-β).[10,11] 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) $p \leq 0.05$ (Confidence interval 95%).

RESULTS

Body weight, Random (RBG) and fasting blood glucose (FBG) and HbA1c were improved. Serum insulin and C-peptide levels were found elevated in Curcuma longa treated diabetic rats significantly (P=0.0001). Insulin resistance (HOMA-IR) was decreased and concomitant rise in β- cell function (HOMA-β) was observed in Curcuma longa treated experimental rats (P=0.0001) (Table-I).

	Group A	Group B	Group C	Group D	Group E	P
Body weight (g)	292.2±50.1	206.1±32.0	234.5±31.1	271.5±37.1	238.5±39.1	0.0002
RBS (mg/dl)	120.9±9.7	407.9±97.7	291.1±49.9	286.±48.3	195.2±21.1	0.0001
FBS (mg/dl)	88.6±17.5	247.5±56.3	248.5±42.9	221.1±32.0	202.1±71.4	0.0003
HbA1c (%)	5.21±0.5	9.28±1.35	8.29±0.78	7.70±0.99	7.67±1.21	0.0005
Insulin (μU/L)	11.4±0.7	3.72±0.84	4.96±1.01	5.29±0.63	6.20±0.79	0.0001
C-peptide (mg/dl)	2.11±0.62	0.55±0.41	1.30±0.46	1.33±0.38	1.47±0.39	0.0003
HOMA-IR	0.64±0.31	5.28±0.46	3.92±0.70	2.58±0.83	1.78±0.74	0.0001
HOMA-β	95.4±5.96	29.4±17.7	27.67±7.50	30.67±9.13	45.4±9.71	0.0001

Table-I. Body weight, Glycemic control, Insulin resistance and β-cell function (n=100)

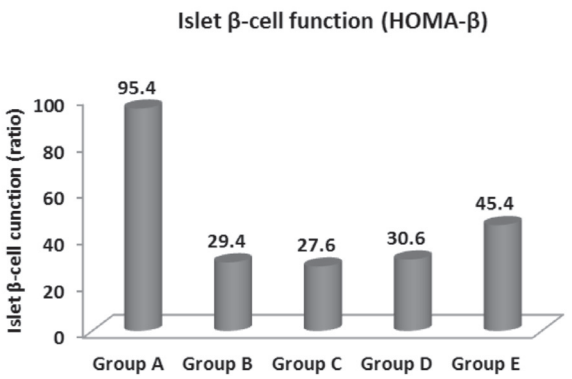

Figure-1. Islet β-cell function in controls and experimental rats

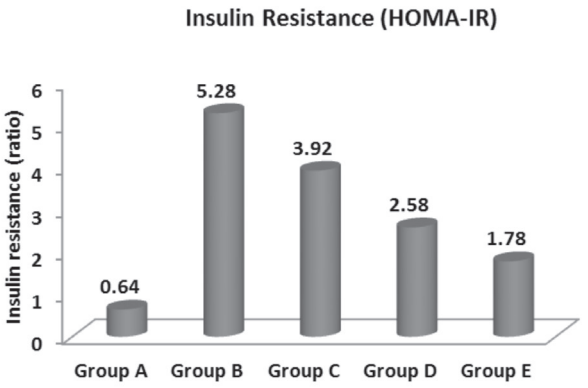

Figure-2. Insulin resistance in controls and experimental rats

DISCUSSION

The present experimental study reports for the first time on the Body weight, Random (RBG) and fasting blood glucose (FBG) and HbA1c were improved. Serum insulin and C-peptide levels were found increased in Curcuma longa treated diabetic rats significantly (P=0.0001). Findings are consistent with previous studies.[12,13] In present study, the Insulin resistance (HOMA-IR) was decreased and concomitant rise in β- cell function (HOMA-β) was observed in Curcuma longa treated experimental rats (P=0.0001). The findings are in agreement with previous studies.[14,15] In present study, the insulin resistance (HOMA-IR) in negative control (A) was 0.64±0.31, positive control (B) as 5.28±0.46 and experimental groups C – E was found as 3.92±0.70, 2.58±0.83 and 1.78±0.74 respectively (P=0.0001), while the Islet β- cell function (HOMA-β) negative control (A) was 95.4±5.96, positive control (B) as 29.4±17.7 and experimental groups C – E was found as 27.67±7.50, 30.67±9.13 and 45.4±9.71 respectively (P=0.0001). The findings are supported by previous studies.[14,15] It has been debated that the allopathic anti – diabetic drugs often cause serious drug related adverse effects hence there is need of searching of herbal preparations that has been proved in the present study. Curcuma longa is a commonly used food condiment for flavoring purpose and has proved medicinal potential in particular the anti – diabetic activity that needs scientific experiment for making it available for this purpose.[12-15] In present animal study, the anti- diabetic potential of Curcuma longa was observed significantly in terms of improved Islet β- cell functioning and mitigation of insulin resistance (HOMA-IR). The findings are in line with previous studies.[15,16] Curcuma longa mitigated the insulin resistance with improved Islet β- cell functioning that corrected the glycemic control of experimental rats (Table-I).

In present study, the insulin secretion was boosted by Curcuma longa therapy that is consistent with previous studies.[16,17] In present study, the islet β – cell functioning was found preserved in Curcuma longa treated rats that is in full agreement with a previous study[18] as they concluded the glycemic effect was better in those with preserved islet β – cell mass in pancreas. In present study, the Curcuma longa improved the glycemic index in dose – dependent fashion. The islet β – cell function and insulin resistance show improvement at doses of 200, 300 and 500 mg of Curcuma longa (P=0.0001) (Table-I). But higher dose of Curcuma longa extract showed better therapeutic efficacy that is in agreement with Santoshkumar et al[19] as they found significant glucose lowering effects at high Curcuma longa dose of 500 mg/Kg body weight. Other previous studies[20,21] reported the glycemic control is improved due to anti – oxidant and anti – inflammatory effects of Curcuma longa that is different from the present study as we could not measure oxidants/antioxidant and inflammatory mediators due to financial issues. Curcuma longa combats oxidative injury[22] that might contribute to its glycemic improving effect that is not consistent

with present study. Improved glycemia and insulin resistance of present study is also supported by a previous obese diabetic mice model study.[23]

We found elevated serum insulin levels in high dose fed rats (Table-I) that is caused by stimulation of β – cell function, this is in keeping with previous studies.[24,25] In summary, we found improved β-cell function (HOMA-β) with reduction in Insulin resistance (HOMA-IR) and significant correction of glycemic indices. It is concluded the Curcuma longa exhibits excellent stimulation of β – cells functioning and mitigation of insulin resistance that may be exploited for treating type 2 diabetic subjects but this needs large scale studies. Only limitation of present diabetic rat study is other parameters of insulin resistance and glycemic control were not analyzed, however the findigns are worth to report for better diabetic control through herbal remedy. Further studies – both animal and clinical are recommended with large sample size.

CONCLUSION

The present study shows the Curcuma longa positively modulates the Islet β-cell function and insulin resistance. Curcuma longa exhibits excellent stimulation of β – cells functioning and mitigation of insulin resistance that may be exploited for treating type 2 diabetic subjects but this needs large scale studies.

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1	Rasheed Ahmed Soomro	Literature review, Study conception, Exp. Animal gloves.	
2	Samreen Pandhiani	Drug dose, Curemme longa experimental.	
3	Aftab Abbasi	Animal intubation, Drug+Diet feelia.	
4	Hina Mawani	Animal gloupins, feequis + Sampling.	
5	Abdul Majid	Animal gloupsis, blood sampling.	
6	Asim Mehmood	Albanucene verious	
7	Kashif Rasheed Shaikh	Data analysis.	