Original Article

# Lycopene Ameliorates Glycemic Control in Fructose Induced Diabetes Mellitus in Wistar Albino Rats



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## ABSTRACT

**Objective:** Experiment determining the blood glucose regulating effects of lycopene in high fructose fed diet (HFD) induced diabetes mellitus (DM) in Male Albino Wistar Rat.

**Study Design:** An Experimental study

**Place and Duration of Study:** This study was conducted at the Departments of Basic Medical Sciences, Suleman Roshan Medical College, Tando Adam from April 2021 to September 2021 for a period of six months.

**Materials and Methods:** Sixty male Wistar albino rats were divided into –ve and +ve controls (groups A and B) and Experimental groups – HFD induced DM treated with lycopene (groups C and D). Each group comprised 15 rats. DM was induced by feeding HFD (21% w/v) till induction of fructose. Glycemic and lipid variables were estimated by standard biochemical analysis from the blood sera of rats. Data was analyzed in SPSS 21.0 (IBM, Incorporation, USA) at 95% CI ($P<0.05$).

**Results:** Lycopene therapy improves the RBS, FBS and HbA1c% in experimental rats. Lycopene therapy also reduced the serum cholesterol, triglycerides and LDLc with rise in serum HDLc concomitantly ($P=0.0001$).

**Conclusion:** In conclusion, the lycopene therapy improves blood glucose and lipid level in high fructose diet induced diabetes mellitus in rat model.

**Key Words:** Lycopene, Fructose, Glycemic control, Lipids, Rats

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## INTRODUCTION

Herbs and phytochemicals have attracted much interest as remedy for various disorders in recent years including the scientific community. Much interest is growing to prove evidence, safety and effectiveness of herbs in complementary medicine. Herbs and phytochemicals are being analyzed in majority of scientific research studies making them available for alleviation of various metabolic disorders.[1] Accumulating information on bioactive compounds of herbs origin is gathering for the treatment of diabetes mellitus (DM), also proving their mechanisms of actions and safety, clinical use based on clinical evidence of their effectiveness.[1,2] Phytochemicals obtained from herbs and plants are recognized a potential source of newer drugs, the main example of this is the metformin. Phytochemicals are capable of lessening hyperglycemia and hyperlipidemia of DM.[2] This makes the herbs of utmost value and an interesting candidate for metabolic disorders such as the DM. Herbs as add on therapy potentiate their therapeutic effects too. One of such nutraceutic phytochemical is a β-carotenoid rich red pigmented substance called lycopene derived from tomatoes, red fruits, apricots, papaya, guavas, grape fruits, watermelons, grapes and vegetable and is also present in human plasma.[1,3] Lycopene is a linear polyene acyclic hydrocarbon isomer of β-carotene.[1,3] Certain microorganisms contain lycopene. Lycopene functions through both non-oxidative and oxidative mechanisms. Lycopene is capable of quenching the reactive oxygen species (ROS) free radicals and maintains redox homeostasis within body cells. Lycopene prevents oxidative process of proteins, DNA, phospholipids and lipids. It opposes carcinogenesis through multistage anti – oxidant

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mechanisms. Lycopene is capable of quenching and scavenging the ROS.[4,5] Lycopene has higher antioxidant activity than β-carotene. Lycopene and lycopene rich food supplements have attracted growing interest protecting against various metabolic diseases such as DM.[1] Lycopene also retards formation of advanced glycation end products (AGEs).[6,7] Evidence shows the lycopene used in combination with metformin improves the glycemic control.[1] Currently, the DM prevalence is increasing in the country due to aberrant dietary habits, obesity, urbanization and sedentary life style. Hence there is dire need to analyze the new and available herbals products of their blood glucose and lipid regulating effects and lycopene is an ideal newer agent. The present experimental study evaluated the blood glucose and lipids ameliorating effects of lycopene in fructose induced diabetes mellitus in Wistar Albino rats.

# MATERIALS AND METHODS

Ethical approval of research protocol of conducting the present experimental study was taken from the institute. Research design was completed at the Departments of Basic Medical Sciences, Suleman Roshan Medical College, Tando Adam, Sindh.

Experimental study was conducted at the Animal house of Sindh Agriculture University. We purchased rats from the Animal house (SAUT) of Albino rats of Wistar strain. Experiment was conducted from the April 2021 to September 2021. Sixty male albino of Wistar strain were purchased according to the inclusion and exclusion criteria. Albino rats of 150 – 200 grams, male gender, moving in the cages and eating properly, with proved diabetes mellitus (DM) induction with high fructose diet (HFD – 21% w/v) were included. Fructose was given in dose of 10 g/kg bwt diluted in water to give – 21% w/v solution.[8] Present study strictly excluded the female rats, lazy and not feeding properly male rats. Rats not developing DM with HFD (21% w/v). Experimental rats were handled according to the NIH, USA guidelines for animals. Animals were housed in stainless steel – cages provided with proper feeders and drinkers within the cages. Temperature was maintained at 25 ± 3 °C. Light/dark cycles of 12/12 hours were maintained. Experiment lasted for eight weeks. Feeds and water was available ad – libitum in the cages. Negative control (group – A) were given normal chow diet. Positive control (group B) was given normal diet + HFD. Experimental rats group C and D were fed normal chow diet fortified with HFD and treated with lycopene 4 and 8 mg/kg/day[9] p.o. respectively. Lycopene was got from the pharmacy department of institute. Therapy continued for eight weeks. After the experiment was over, the rats were handled carefully for the blood sampling. A lancet was delicately inserted behind the eye ball and blood coming from the retro orbital venous plexus was collected into the sterilized tubes. 2 ml blood was taken into tubes. Sera were stored at -20$^0$C. Blood glucose, glycated hemoglobin A1, serum creatinine, and blood lipids were analyzed in post graduate laboratory. Data was saved in proforma that was designed with research protocol. Results were entered in Microsoft Excel sheet. Data values were entered in SPSS 21.0 for statistical analysis. One – way analysis of variance, descriptive statistics, and post Hoc Bonferroni test analyzed the continuous result variables. Resutls were presented in tables as mean+/- SD. 95% CI (P<0.05) was used for data analysis of statistically significant.

# RESULTS

Lycopene therapy ameliorates the random blood glucose (RBS) and fasting blood glucose (FBS) and the glycated hemoglobin A1 (HbA1c) (%) in experimental rats (table – 1).

**Table No.1: Glycemic control in different rat groups**

| Parameter | Rat groups | | | | |
|---|---|---|---|---|---|
| | A | B | C | D | P |
| RBS (mg/dl) | 118.4±3.7 | 264.3±28.1 | 229.5±23.0 | 209.7±14.1 | 0.0001 |
| FBS (mg/dl) | 65.5±7.3 | 258.1±29.3 | 172.1±21.3 | 133.1±19.1 | 0.0003 |
| HbA1c (%) | 4.7±0.7 | 8.7±0.7 | 7.6±0.5 | 6.75±0.5 | 0.0001 |

**Table No.2: Blood lipid profile in different rat groups**

| Parameter | Rat groups | | | | |
|---|---|---|---|---|---|
| | A | B | C | D | P |
| Total Cholesterol | 121.9±9.9 | 388.1±29.3 | 267.1±15.1 | 193.1±17.7 | 0.0001 |
| Triglycerides | 175.2±17.1 | 401.1±12.1 | 353.3±30.7 | 252.1±25.1 | 0.0003 |
| LDLc | 119.5±9.3 | 263.1±27.5 | 235.9±26.1 | 163.5±11.3 | 0.0001 |
| HDLc | 40.9±1.2 | 23.2±1.7 | 25.1±1.8 | 37.3±3.1 | 0.0001 |

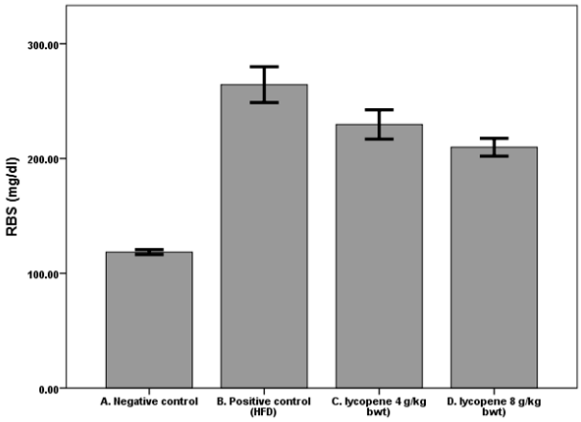


**Figure No.1: Random blood glucose (RBS) (mg/dl)**

RBS in positive control group B was 264.3±28.1 mg/dl that was decreased by lycopene therapy in experimental

groups C and D significantly noted as 229.5±23.0 and 209.7±14.1 mg/dl respectively (P=0.0001). FBS in positive control group B was 258.1±29.3 mg/dl that was decreased by lycopene therapy in experimental groups C and D significantly noted as 172.1±21.3 and 133.1±19.1 mg/dl respectively (P=0.0003). HbA1c in positive control B was 8.7±0.7% that was decreased to 7.6±0.5 and 6.75±0.5 in experimental groups C and D (P=0.0001). Lycopene therapy also reduced the serum cholesterol, triglycerides and LDLc with rise in serum HDLc concomitantly (P=0.0001).

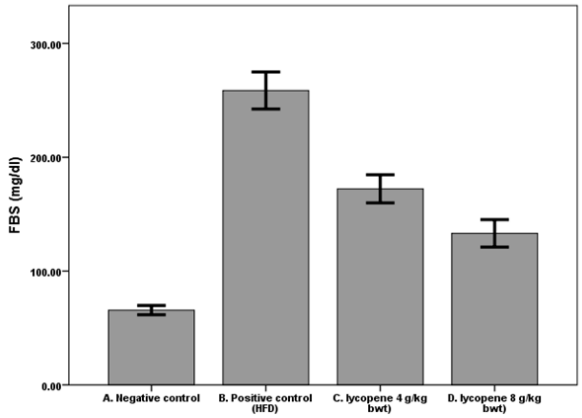


**Figure No.2: Fasting blood glucose (RBS) (mg/dl)**

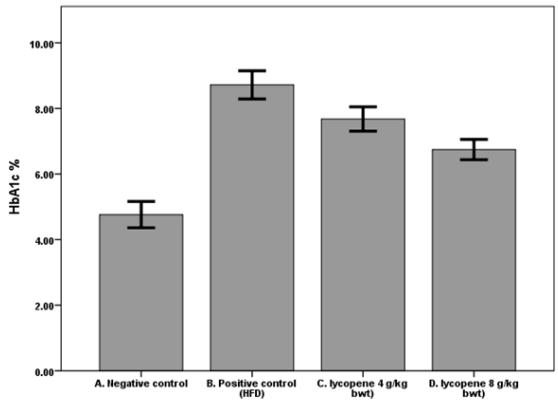


**Figure No.3: Serum Glycated HbA1 (HbA1c) (%)**

# DISCUSSION

The present experimental study determined blood glucose and lipid regulatory effects of lycopene in high fructose fed diet Wistar Albino male diabetic rat model positively. The present study proves glucose and lipid lowering effects of lycopene in HFD induced diabetes mellitus. The findings are in agreement with previous studies.[10-12] Present study is the first from our institute reporting on the topic. Prevalence and incidence of DM is increasing in the country hence there is dire need innovation in the diabetic therapy beside allopathic drug therapy. Rising DM populations in Pakistan has raised its position to fifth rank and high prediction for the future.[13,14] Lycopene is red pigmented fruit and vegetable derived agent that has proved astonishing results in previous studies.[1,3] Lycopene is present in tomatoes and tomato – products, grapefruits, pink guava, minestrone soup, pizza, spaghetti, etc.[1,3] Present study consumed lycopene in doses of 4 and 8 g/Kg bwt in HFD rats that proved noticeable biological potential on blood glucose and lipid levels. Leh et al[15] (2021) reported the lycopene intake in diabetic population in doses of 0.04 and 0.05 mg/Kg bwt and reported highly significant pharmacological effects on blood lipids and glucose. The findings of above study are concordant to present study. A previous study[1] proved lycopene rich yogurt therapy positively lessened the hyperglycemia, dyslipidemia and oxidative markers in diabetic rats. Lycopene combined with curcumin produced highly significant lipid and glucose regulatory effects in another study. They also reported dampening of oxidative stress.[16] The present study provides scientific insights on the potential of lycopene as therapeutic agent; the findings are supported by previous study. Lycopene has gained much scientific attention and research interest against the metabolic syndrome and associated grave complications like diabetes mellitus.[17,18] Supporting the present study, previous studies[19,20] found improvement in glucose intolerance and insulin resistance in HFD mice model. A recent review[21]reported lycopene maintained pancreatic function and metabolic defects in in – vivo models. Ozmen et al[22] witnessed the lycopene prevents the vacuolization and loss of insulin cells in pancreatic Islets in diabetic rats. Lycopene therapy increased circulating insulin levels with improved glycemia and dyslipidemia. Lycopene therapy attenuated dyslipidemia in a previous study[23], has been witnessed. The findigns of above studies are in line keeping with present study. Lycopene has also been proved as scavenger of reactive oxygen species (ROS), $HO^-$, $OCl^-$, and other species.[1,24-26] Anti-oxidative effects of lycopene have been proved in another previous study.[27] The findings of above studies are matchless to our present study as the oxidative status was not detected due to financial issues. Considering literature, it shows lycopene is an interesting panacea against development of DM and its complications. Findings of present study reinforces the need for future animal and human studies investigating the lycopene effects scientifically. Extrapolating the results of present study, it is inferred lycopene is a nutraceutical herb of prime importance for the diabetes mellitus. Lycopene is an herbal nutraceutic agent that needs further research to make it available for the DM therapy.[1,3] Findings of lycopene therapy of present study, prove glycemic and lipid regulatory potential that may be exploited for clinical use, however, this needs further research. Lycopene may then be used as alternative add – on therapy for diabetes mellitus.

# CONCLUSION

In conclusion, the lycopene therapy improves blood glucose and lipid level in high fructose diet induced diabetes mellitus in rat model. Euglyemic and hypolipidemic potential of Lycopene is a very important finding that demands further clinical research making it conveniently available as an alternative add – on therapy for diabetes mellitus. Future studies are recommended to validate the finding of present study.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design of Study: | Jawad Mumtaz Sodhar |
| Drafting: | Shagufta Memon, Majid Ali Hingoro |
| Data Analysis: | Palwasha Abbasi, Mashal Siddiqui, Umair Ali Soomro |
| Revisiting Critically: | Jawad Mumtaz Sodhar, Shagufta |
| Final Approval of version: | Jawad Mumtaz Sodhar |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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