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Biochemical effects of Lycopene on Lipid Parameters in high Sucrose Diet Fed Male Wister Albino Rats

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Author`s Contribution

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ABSTRACT

Objective: To determine the biochemical effects of lycopene on lipid parameters in high sucrose diet fed male Wister albino rats

Methodology: This six-month experimental study was conducted at the Department of Biochemistry, Liaquat University of Medical and Health Sciences from 1-10-2022 to 30-3-2023. The rats (150–200 g) were divided into four groups (n=15 each): Group A (negative control) received a saline placebo; Group B (positive control) received a sucrose-rich diet (SRD) only; Group C received SRD plus lycopene (40 mg/kg); and Group D received SRD plus lycopene (60 mg/kg). Lycopene was dissolved in corn oil and given daily for 28 days via intragastric intubation. Blood samples were collected after a 12-hour fast and analyzed for lipid levels (cholesterol, triglycerides, LDL, and HDL). Data were analyzed using SPSS 23.0.

Results: Rats on a high-sucrose diet had significantly higher cholesterol (168.4 mg/dl), LDL (68 mg/dl), and triglycerides (100.8 mg/dl) compared to controls (132.7 mg/dl, 48.6 mg/dl, and 70.3 mg/dl, respectively; $P < 0.001$). Lycopene supplementation lowered cholesterol (157.8 mg/dl in Group C, 149.3 mg/dl in Group D) and LDL (50.8 mg/dl in Group C, 50.4 mg/dl in Group D). HDL, which decreased with sucrose intake (25.9 mg/dl), improved with lycopene (36.1 mg/dl in Group C, 43.1 mg/dl in Group D). Triglyceride levels also reduced with lycopene (92.5 mg/dl in Group C, 79.6 mg/dl in Group D). These results suggest lycopene effectively improves lipid profiles, particularly at higher doses.

Conclusion: Lycopene demonstrated significant lipid-lowering potential, effectively reducing serum cholesterol, triglycerides, and LDL levels while increasing HDL levels. These beneficial effects suggest that lycopene could be a valuable natural option for managing hyperlipidemia, particularly in urban populations in Pakistan.

Keywords: Cholesterol, LDL, HDL, TG, lycopene, Wister albino rats

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Introduction

Pakistan, like other under developed nations, is going through a rapid change in nutritional status, which is resulting in a transfer of national nutritional status from underweight to overweight and obesity. In Pakistan, living in urban areas and high household and community wealth are linked to a shift toward overweight and obesity over underweight.[1] It has been reported that change in socioeconomic status accompany by lifestyle modification, occupation, and poor eating habits, including an increase in fat and high salt diet, smoking,

alcohol consumption, excessive use of sweet beverages and more meat intake with minimal to no physical activity is more observed in middle upper class. Due to the fact that this issue of malnutrition is not yet resolved, developing nations now are dealing with the double burden of disease with rise in the rates of diseases associated with over nutrition like diabetes mellitus, osteoarthritis and cardiovascular disease. Negative health outcomes of over nutrition outweigh the outcomes that are supposed to come due to under nutrition.[2]

Sucrose is commonly consumed by the urban population as sugar in tea, sweets, etc. The other names for sucrose are cane sugar and table sugar.[3] Metabolic syndrome is a serious medical condition that can lead to a number of non-communicable chronic diseases. Elevated triacylglycerides ≥150 mg/dl, decreased ≤ HDL 40 mg/dl in men and ≥ 50 mg/dl in women, hypertension (systolic blood pressure [SBP] ≥130 mmHg or diastolic blood pressure [DBP] ≥ 85 mmHg), and hyperglycemia are the major clinical features of metabolic syndrome.[4] The risk of metabolic syndrome rises with age. . The metabolic syndrome (MetS) is not a disease itself. Instead, it's a collection of risk factors, including obesity, increased blood pressure, raised blood sugar levels, and abnormal lipid parameters. Obesity, insulin resistance, hormonal imbalance etc. Polycystic ovarian syndrome (PCOS), smoking and unhealthy lifestyle are the major risk factors of metabolic syndrome.[5] Atherosclerosis, often known as plaque buildup in the arteries, can be caused by these causes. This is when chemicals like lipids, cholesterol, and others are deposited in intima of artery walls. More than 60% of people with type 2 diabetes mellitus (T2DM) die due to cardiovascular diseases. Hyperglycemia and dyslipidemia are important risk factors for all cardiovascular events. Evidence suggests that endothelial dysfunction is an important factor in the development of pathology in large vessels under hyperglycemic conditions. Elevated hyperglycemia and high fatty acids stimulate pro-inflammatory cytokine levels and oxidative stress through reactive oxygen synthesis. As a result, the arteries become hardened, narrowed and blocked which first lead to rise in blood pressure and ultimately to total ischemia of supplied organ if not treated.[6]

About 30% of the world's population is dealing with overweight and obesity, the prevalence is still steadily increasing worldwide. Pakistan has ranked 9th in the world's most obese nations' ratings.[7] Many herbs are currently being studied and have been studied for their effects on regulating blood sugar and blood lipids. One such herbal remedy is lycopene. Lycopene is a naturally occurring red carotenoid compound of fruit and plant origin. It is a non-vitamin A β-carotenoid with many biological effects.

is found in tomatoes, watermelon, apricots, guava and grapefruit etc,[8] 9.04 mg of lycopene can be obtained from 100 ml of tomato juice. Lycopene is taken to prevent and treat cardiovascular diseases and even cancers. Supplementation with lycopene reduces the risk of coronary heart disease, most likely due to lycopene's outstanding antioxidant properties. Lycopene is a potent antioxidant it kills reactive oxygen species that are produced in our body and also preserve and promote the precursors of antioxidants. Lycopene intake significantly reduces oxidized LDL levels in humans. Lycopene also inhibits cholesterol synthesis by inhibiting enzymes mainly Hydroxy Methyl Glutaryl Co-A (HMG Co-A) reductase enzyme which is a rate controlling enzyme in the endogenous synthesis of cholesterol.[9] Lycopene lowers LDL cholesterol levels, improves HDL cholesterol levels and minimizes the risk of coronary atherosclerosis. The antioxidant, antihyperlipidemic, antidiabetic, anticancer and antihypertensive potential of lycopene has been very well reported.[10]

Currently, hyperlipidemia is on the rise, and available drugs are effective but have many significant side effects. Therefore, natural nutraceuticals such as lycopene need to be explored to address the growing metabolic health challenges in the country. Available antihyperlipidemic drugs have shown serious side effects. Therefore, there is a gap in research for new herbal medicines that are safer and more effective without side effects that control blood sugar and lipid levels. One of the herbs that have been studied and researched for hyperlipidemia is lycopene. This study is designed to analyze the biochemical effects of lycopene on lipid parameters in a high-sucrose diet treated male Wistar Albino rats.

Methodology

An experimental study was done during 6 months from 1-10-2022 to 30-3-2023 at Department of Biochemistry Liaquat University of Medical and Health Sciences Jamshoro. Adult male albino Wistar rats with body weight 150- 200gm body weight and on sucrose diet were incorporated. Female rats, sick rats and Rats with different body weight were excluded. The rats were randomly divided into 4 groups. The study included four groups of rats, divided into control and experimental groups, with each group consisting of 15 rats (n=15). The

control group was further categorized into Group A, which served as the negative control and received 0.9% normal saline (N/S) as a placebo, and Group B, the positive control, which was given a sucrose-rich diet (SRD) for 28 days but remained untreated. The experimental group received both SRD and Lycopene supplementation for 28 days. Group C was administered Lycopene at a dose of 40 mg/kg body weight (BW), while Group D received a higher dose of Lycopene (60 mg/kg BW). The experiment aimed to evaluate the effects of Lycopene therapy in combination with a sucrose-rich diet over the study period. At the post-experiment phase, all rats underwent blood sampling procedures. After 12 hours of fasting, blood samples were collected via cardiac puncture using EDTA and plain tubes. The serum was separated from the clotted blood by centrifugation at 5000 rpm for 15 minutes within 1 hour of collection, after which the supernatant was harvested and stored at -80°C for the analysis of blood lipids, including triglycerides, cholesterol, low-density lipoproteins (LDL), and high-density lipoproteins (HDL). For Lycopene administration, Lycopene (purity >90%) was dissolved in 0.5 mL corn oil and given via intragastric intubation for 28 consecutive days. For sucrose feeding, sucrose was dissolved in pure water at a concentration of 30 g/L, and 10 mL of this 30% sucrose solution was administered daily in drinking water for 28 consecutive days. Data was analyzed on SPSS 23.0 version. Continuous/numerical variables serum cholesterol, triglycerides, low density lipoproteins and high density lipoproteins were compared among control and experimental groups analyzed by one - way Analysis of variance (ANOVA) taking p-value P<0.05 as significant.

Results

The serum cholesterol levels varied significantly among the groups ($p < 0.001$). The negative control (Group A) had the lowest cholesterol (132.7 mg/dl), while the positive control (Group B) showed the highest (168.4 mg/dl). Lycopene supplementation reduced cholesterol levels, with Group C (40 mg/kg) at 157.8 mg/dl and Group D (60 mg/kg) at 149.3 mg/dl, indicating a dose-dependent cholesterol-lowering effect. Table I

Table I: Serum Cholesterol levels in Controls and Experimental groups. (n=4)

Groups	Mean±SD	SEM	P-Value
Group A. Negative control	132.7±2.1	0.7	<0.001
Group B. Positive control	168.4±2.2	0.7	
Group C. Lycopene40mg/kg	157.8±1.2	0.4	
Group D. Lycopene60mg/kg	149.3±1.9	0.6	

The negative control group (Group A) exhibited the highest HDL concentration (46.6 mg/dl), whereas the positive control group (Group B), which followed a sucrose-rich diet without intervention, recorded the lowest value (25.9 mg/dl). Among the experimental groups, Group C (40 mg/kg Lycopene) displayed an HDL level of 36.1 mg/dL, while Group D (60 mg/kg Lycopene) had a higher HDL concentration of 43.1 mg/dl. Table II

Table II: HDL in Controls and Experimental groups. (n=4)

Groups	Mean± SD	SEM	P-Value
Group A. Negative control	46.6±1.8	0.6	<0.001
Group B. Positive control	25.9±1.1	0.4	
Group C. Lycopene40mg/kg	36.1±1.5	0.5	
Group D. Lycopene60mg/kg	43.1±1.6	0.5	

The negative control group (Group A) had an LDL level of 48.6 mg/dl, while the positive control group (Group B), which followed a sucrose-rich diet without treatment, showed the highest LDL level (68 mg/dl). Lycopene supplementation helped lower LDL levels, with Group C (40 mg/kg) at 50.8 mg/dl and Group D (60 mg/kg) at 50.4 mg/dl, indicating significant protective effects of Lycopene in reducing LDL levels ($p < 0.001$). Table III

Table III: LDL in Controls and Experimental groups. (n=4)

Groups	Mean±SD	SEM	P-Value
Group A. Negative control	48.6±2.7	0.9	<0.001
Group B. Positive control	68±3.2	1.1	
Group C. Lycopene 40mg/kg	50.8±2.9	0.9	
Group D. Lycopene 60mg/kg	50.4±3.8	1.3	

The negative control group (Group A) had the lowest TG level (70.3 mg/dL), while the positive control group (Group B), which followed a sucrose-rich diet without treatment, exhibited the highest TG level (100.9 mg/dl). Lycopene supplementation resulted in a dose-dependent reduction in TG levels, with Group C (40 mg/kg) at 92.5 mg/dL and Group D (60 mg/kg) at 79.6 mg/dl, suggesting a significant potential lipid-lowering effect of Lycopene ($p < 0.001$). Table IV

Table IV: TG in Controls and Experimental groups. (n=4)

Groups	Mean±SD	SEM	P-Value
Group A. Negative control	70.3±3.8	1.3	<0.001
Group B. Positive control	100.9±4.9	1.6	
Group C. Lycopene40mg/kg	92.5±3.4	1.1	
Group D. Lycopene60mg/kg	79.6±3.8	1.3	

Discussion

The present experimental study investigated the curative effects of Lycopene in a high-sucrose-fed rat model to evaluate its lipid lowering potential. Rats in the experimental groups were given a high-sucrose diet, and after the successful induction of hyperlipidemia, Lycopene was administered to assess its lipid-lowering effects. Previous studies have reported a significant reduction in hyperlipidemia with Lycopene supplementation, supporting its role in lipid metabolism regulation.

One such study conducted on male mice fed a high-fat diet divided them into two groups, where one received Lycopene supplementation while the other did not. After 19 weeks, the Lycopene-treated group exhibited markedly lower serum cholesterol and LDL levels, along with a notable increase in HDL levels, compared to the control group.[13] These findings align with the results of our study. A previous study on 256 healthy broiler chicks investigated the hypocholesterolemic effects of Lycopene, with doses of 100, 200, and 400 mg/kg. After the experimental period, blood analysis revealed a significant dose-dependent reduction in serum cholesterol, triglycerides, and low-density lipoproteins (LDL). These findings support the results of our current study, reinforcing the potential of Lycopene in managing lipid-related disorders and improving metabolic health.[14]

Our findings were also supported by the Mirahmadi M et al.[15] In aligns to this study A study conducted by Syeda Nuzhat Fatima Zaidi on 24 albino Wistar rats evaluated the effects of Lycopene supplementation on lipid profiles in thioacetamide-induced liver cirrhosis. The study found that thioacetamide exposure led to decreased HDL cholesterol (HDLc) levels, while LDL cholesterol (LDLc), total cholesterol, and triacylglyceride levels increased significantly. After six weeks of Lycopene therapy, a marked reduction in serum LDLc, cholesterol, and triacylglyceride was observed, along with a significant rise in HDLc levels.[16] Consistently another study which was conducted on 32 individuals aged 40-65 years with moderate hyperlipidemia (TGs >150 mg/dl and HDLc 130-160 mg/dl) evaluated the effects of Lycopene supplementation. Participants were divided into two groups, where one received docosahexaenoic acid (DHA) alone, while the other received DHA combined with 7 mg of Lycopene. After a two-week trial, the analysis of serum cholesterol, triglycerides, and LDL cholesterol (LDLc) revealed a significant reduction in all three parameters.[17] Additionally a meta-analysis including 12 trial arms (n=781) demonstrated a significant increase in HDLc levels in the Lycopene-treated group compared to the control group. These findings align with the results of our present study, further reinforcing the positive impact of Lycopene on lipid metabolism and its potential role in improving cardiovascular health.[18] Based on evidence from previous studies, Lycopene has demonstrated significant lipid-lowering potential and may be considered a therapeutic option for managing hyperlipidemia conditions.

However, this study has certain limitations, including the use of an animal model and a small sample size, which may affect the generalizability of findings. Future research should focus on human clinical trials with larger sample sizes to further validate the efficacy and safety of Lycopene in hyperlipidemia management.

Conclusion

It is concluded that Lycopene possess lipid lowering and blood glucose lowering potential and were found effective in lowering serum cholesterol, triglycerides, low density lipoprotein and elevating the serum high density lipoproteins. These biological effects may be utilized for hyperlipidemia conditions prevailing in urban population of Pakistan. This herbal remedy is safe, effective, easily available and inexpensive for use by community.

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