

Evaluation of the effect of lycopene on lipid profile, serum antioxidant enzymes and blood sugar level in New Zealand white rabbits

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ABSTRACT

Background: Dyslipidaemias are the major cause of increased atherogenesis. Lycopene is a pigment that imparts red colour to fruits and vegetables like tomatoes. Risk of cardiovascular diseases has been shown to decrease with dietary intake of tomatoes. Although the antioxidant and hypolipidaemic properties of tomatoes have been studied extensively, beneficial effect of pure lycopene supplement as hypolipidaemic is still debatable. So, we aimed to evaluate the effect of pure lycopene powder on lipid profile, serum antioxidant enzymes and blood sugar level in hyperlipidaemic rabbits.

Methods: Adult male New Zealand White rabbits (1.5-2.5kg) were divided into three groups of six each. Group I-High Fat Diet (HFD) (5ml/kg). Group II-HFD (5ml/kg) + lycopene (10mg/kg) orally. Group III-HFD (5ml/kg) + lycopene (20mg/kg) orally. Blood samples were taken from all rabbits for baseline estimations of serum lipids, serum superoxide dismutase (SOD) and blood sugar. Same tests were performed after six weeks.

Results: There was significant decrease in the levels of serum TC, LDL-C, TG and VLDL and an increase in serum HDL-C and antioxidant SOD with lycopene administration. However, significant increase in HDL was not seen with lycopene 10mg. TG and VLDL levels were significantly less with 20mg lycopene compared to 10mg lycopene. There was however no change in blood sugar level with lycopene.

Conclusions: Pure lycopene supplement showed significant hypolipidaemic and antioxidant activity. However, it did not show significant effect on blood glucose levels.

Keywords: Antioxidant, High fat diet, Hypolipidaemic, Lycopene, Superoxide dismutase

INTRODUCTION

The term 'cardiovascular diseases' (CVD) includes Coronary Heart Disease (CHD) (Angina pectoris, Myocardial Infarction [MI], Coronary insufficiency, Coronary death), Cerebrovascular diseases (Transient Ischemic Attacks [TIA] and stroke), Peripheral Vascular Disease (PVD), Hypertension, Congestive Heart Failure (CHF), Valvular heart disease and Congenital heart disease.¹ For all diseases of the heart as well as blood vessels, CVD is used as the collective term.² In spite of the lifestyle changes and the use of new approaches in

pharmacology to decrease the cholesterol levels, CVD still continues to be the main cause of death. It is one of the major contributors to the burden of disease globally and is projected to persist as the leading cause of mortality. Thus, CVD greatly contribute to the increasing costs of health care all over the world. Nearly 80% of the deaths due to CVD occur in the low and middle-income countries, and thus it is a major public-health challenge there.³ Because of increasing obesity and alterations in the dietary habits in both western as well as the developing countries, prevalence of CVD occurring due to atherosclerosis and diabetes is increasing at an exponential rate.⁴

Risk patterns for CVD have been characterized by multiple epidemiological investigations. In particular, the factors such as age, male sex, increased levels of low-density lipoprotein cholesterol (LDL-C), decreased levels of high density lipoprotein cholesterol (HDL-C), cigarette smoking and diabetes mellitus are the principal risk factors for CVD. Along with the lifestyle changes, genetic factors, diet and age are also considered important risk factors.¹

One of the most widespread conditions which threatening the human health and survival is atherosclerosis. Basic pathogenesis of atherosclerosis comprises of an insult to the endothelial as well as smooth muscle cells of arterial wall, by various harmful factors such as mechanical damage, viral infection and dyslipidaemia, especially abnormal oxidized low-density lipoprotein (ox-LDL), resulting in large scale chronic inflammatory and fibro-proliferative response. Progressive accumulation of fibrous elements and lipids in the large arteries occurs as a result of this pathologic process.⁵

Hyperlipidaemia or the high levels of serum triacylglycerol and cholesterol is an important risk factor for premature atherosclerosis. Hypercholesterolaemia can cause an increase in the cholesterol content of endothelial cells, platelets and polymorphonuclear leukocytes; thereby all of them become the sources of oxygen free radicals that have been implicated in pathogenesis of hypercholesterolaemic atherosclerosis.⁶

Nutrition is one of the most important environmental factors involved in the development or prevention of chronically occurring degenerative diseases.⁷ Risk of heart disease is decreased significantly in the population having the diet that is rich in fruits and vegetables.⁸⁻¹⁰

Carotenoids are fat soluble natural pigments that are synthesized by the plants. These carotenoids are responsible for imparting bright colours to the vegetables and fruits. Carotenoids may protect the low-density lipoproteins (LDL) from undergoing oxidation, a process that is implicated in atherosclerosis development. Role of antioxidants present in the diet, such as β -carotenes, vit. C and vit. E in prevention of disease, has, in the recent years, received much attention, and extensive work has been done on them.¹¹

In the recent years, attention has been shifted from these antioxidants to lycopene, which is a carotenoid that lacks provitamin A activity owing to the absence of β -ionone ring. It occurs in many vegetables and fruits such as guava, papaya, apricots and watermelon, but tomatoes and tomato products, in varying different forms, are the main source of lycopene in the developing and developed countries. The risk of chronic ailments such as CVD and cancer has been shown to be decreased with consumption of tomatoes and tomato products containing lycopene.^{12,13}

Lycopene is an antioxidant that is known to provide protection against cellular damage which is caused by the

reactive oxygen species (ROS). Although the beneficial properties of lycopene are thought to be primarily due to its antioxidant properties, evidences are accumulating that suggest the possibility of involvement of other mechanisms too, such as modulation of intercellular gap junction communication, hormonal and immune systems and metabolic pathway.¹³

Lycopene may have considerable therapeutic potential as an antioxidant, but is not used as hypolipidaemic agent in coronary heart disease. Although there have been extensive studies on the antioxidant and hypolipidaemic properties of tomatoes and processed tomato products for the prevention of CVD, the beneficial effects of pure lycopene supplement as an antioxidant and hypolipidaemic is still debatable. In spite of the spotlight on lycopene, it may not have protective actions on its own. It may only be functioning as a marker for other active substances present in the tomatoes, or it may be working along with other phytonutrients in giving the health benefits. Thus, in the present study, we aimed to evaluate the hypolipidaemic, hypoglycaemic and antioxidant effects of pure lycopene powder in the hyperlipidaemic rabbits.

METHODS

Male New Zealand White rabbits (n = 18) weighing 1.5-2.5kg were used for the study. Rabbits were housed individually in standard stainless-steel cages at 24°C with a 12hrs light: dark cycle. They were allowed free access to food and tap water. The studies were carried out in accordance with the guidelines given by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi (India). The study was approved by Institutional Animal Ethics Committee (IAEC) of Dr. D. Y. Patil Medical College, Pimpri, Pune. The rabbits were allowed to acclimatize for one week after which blood samples were collected from all rabbits, and they were then divided into three different groups (n= 6) and fed one of the following diets for 6 weeks with normal rabbit chow. Group 1 - High fat diet (HFD) 5ml/kg, Group 2-HFD 5ml/kg + lycopene 10mg/kg, Group 3-HFD 5ml/kg + lycopene 20mg/kg body weight.

High fat diet: Constituted a mixture of coconut oil (from Marico Industries, Mumbai) and vanaspati ghee (from Hindustan Lever Ltd, Mumbai) procured from market.

Lycopene: Lycopene powder was procured from Zenith Nutrition (Bengaluru). The Quality analysis of lycopene was done from Bio-gen Extracts Pvt. Ltd. Bengaluru.

Method of preparation of HFD: Edible coconut oil and vanaspati ghee mixed together in the ratio of 2:3 respectively v/v as per method of Shyamala MP et al.¹⁴

Method of inducing hyperlipidemia: HFD, consisting of coconut oil and Vanaspati ghee, in a ratio of 2:3 v/v, at a dose of 5ml/kg body weight; was fed to all the animals

orally once daily, in addition to normal rabbit chow for 6 weeks. In addition to the above diet, lycopene was given orally once daily with a feeding tube in the dose of 10 mg/kg to second group of 6 rabbits and 20mg/kg to the third group of 6 rabbits, in addition to the above diet for 6 weeks. Blood was collected after overnight fasting from all the animals at baseline and after six weeks, as described below for the estimation of serum lipid profile, superoxide dismutase (SOD) and Blood sugar levels (BSL).

The levels of serum total cholesterol (TC), HDL-C, LDL-C, triglycerides (TG) and very low-density lipoproteins (VLDL) were estimated manually on spectrophotometer to study the hypolipidaemic activity of lycopene. Serum SOD levels were estimated manually on spectrophotometer to study the antioxidant effect of lycopene. BSL were estimated by Optimum Xceed glucometer. All the above analyses were done before and after 6 weeks in all three groups.

Estimations

All the reagents for the estimations were of analytical grade and were purchased from Erba Mannheim.

Estimation of lipid profile

Estimations of the levels of serum TC, HDL and TG were done manually on spectrophotometer. Estimations of the levels of LDL and VLDL were done according to Friedewald's equation.¹⁵

$$\text{LDL} = \text{TC} - \text{HDL} - (\text{TG}/5)$$

$$\text{VLDL} = \text{TG}/5$$

Estimation of serum superoxide dismutase levels

Measurements of serum SOD levels were done by using the method of Marklund S.¹⁶

Estimation of blood sugar levels

BSL were estimated by using the optimum Xceed glucometer, by putting a drop of blood on the test strip, which was then inserted into the glucometer.

Statistical analysis

The statistical analysis of the study was done using the statistical package Graph Pad Prism Version 8.0.1 (2018) for Windows. Student's paired 't' test was used to compare the measurements taken at baseline and at 6 weeks, within each group.

Results were expressed as mean±SD and statistical significance between means was analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. Value of p<0.05 was considered statistically significant.

RESULTS

Table 1 shows the effect of HFD on the lipid profile, SOD and BSL after 6 weeks in group 1. Compared to baseline, there was significant increase in serum TC, LDL, TG and VLDL and significant decrease in HDL and SOD levels. However, there was no significant difference in BSL.

Table 1: Effect of HFD on lipid profile, SOD and BSL after 6 weeks in the HFD group.

Parameter	Mean±SD		p value
	Baseline levels	After 6 weeks	
TC (mg/dL)	106.3±5.01	222.4±17.2	<0.0001 *
HDL (mg/dL)	36.62±5.1	23.74±3.22	<0.0001 *
LDL (mg/dL)	51.47±5.522	169.1±14.37	<0.0001 *
TG (mg/dL)	90.93±3.121	149.7±11.89	<0.0001 *
VLDL (mg/dL)	18.19±0.6241	29.94±2.378	<0.0001 *
SOD (mg/dL)	3.238±0.1406	2.322±0.1422	<0.0001 *
BSL (Units)	98.5±3.78	98.33±1.86	0.9395

* p<0.05

Table 2 shows the effect on serum levels after six weeks on all parameters in all three groups. Table 2 and Figure 1 show the multiple comparisons between all lipid parameters after six weeks between group-1 Vs group-2, group-1 Vs group 3 and group 2 Vs group 3 using ANOVA followed by Tukey's test of multiple comparisons. They show statistically significant decrease in serum TC, LDL, TG and VLDL levels in group 2, when compared with group 1. However, there was no significant difference in

serum HDL levels in group 2 when compared with group 1. They also show statistically significant decrease in serum TC, LDL, TG and VLDL and statistically significant increase in serum HDL levels in group 3 when compared with group 1. They also show statistically significant decrease in serum TG and VLDL levels in group 3 when compared with group 2. However, they also show that there was no statistically significant difference in serum TC, LDL and HDL levels in group 3, when compared with group 2.

Table 2: Multiple comparisons of parameters after 6 weeks across the groups.

Parameter	Mean ± SD		
	Group 1: (HFD)	Group 2: (HFD + Lycopene 10mg/kg)	Group 3: (HFD + Lycopene 20mg/kg)
TC (mg/dL)	222.4±17.2	160.7±5.511 *	145.8±4.505 *
HDL (mg/dL)	23.74±3.22	28.26±3.628	30.43±2.781 *
LDL (mg/dL)	169.1±14.37	107.5±3.403 *	94.17±5.082 *
TG (mg/dL)	149.7±11.89	124.7±3.657 *	106.1±4.647 * #
VLDL (mg/dL)	29.94±2.378	24.95±0.7313 *	21.21±0.9295 * #
SOD (mg/dL)	2.322±0.1422	03.00±0.07924 *	02.81±0.2 *
BSL (Units)	98.33 ± 1.86	98.83±4.021	99.00±3.16

*Significant as compared to the HFD group. # Significant as compared to the HFD + Lycopene 10mg/kg group.

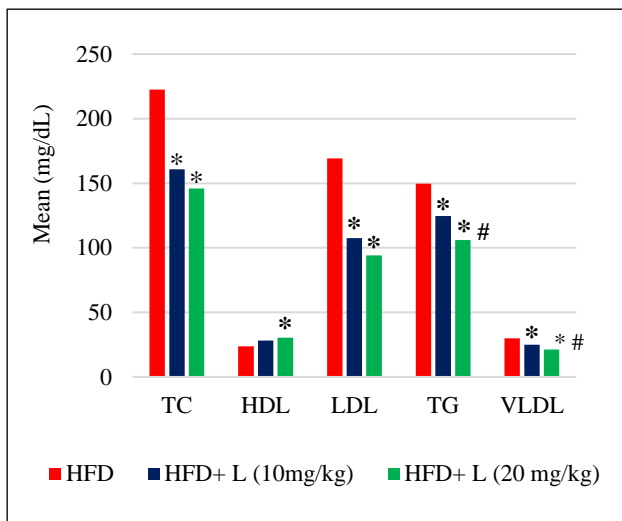


Figure 1: Effect of lycopene on lipid profile.

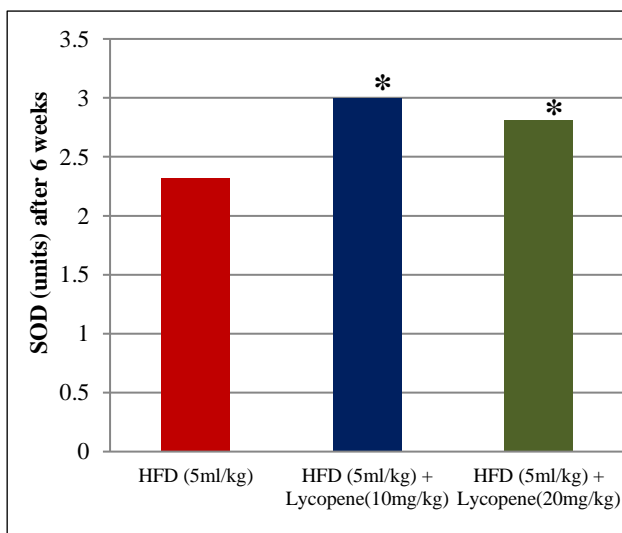


Figure 2: Effect of lycopene on serum superoxide dismutase.

Table 2 and Figure 2 show the multiple comparisons between serum SOD levels after six weeks between group

1 Vs group 2, group 1 Vs group 3 and group 2 Vs group 3 using ANOVA followed by Tukey’s test of multiple comparisons. They show statistically significant increase in serum SOD levels in group 2 and statistically significant increase in serum SOD levels in group 3, when compared with group 1. However, they also show that there was no significant difference in serum SOD levels in group 3 when compared with group 2.

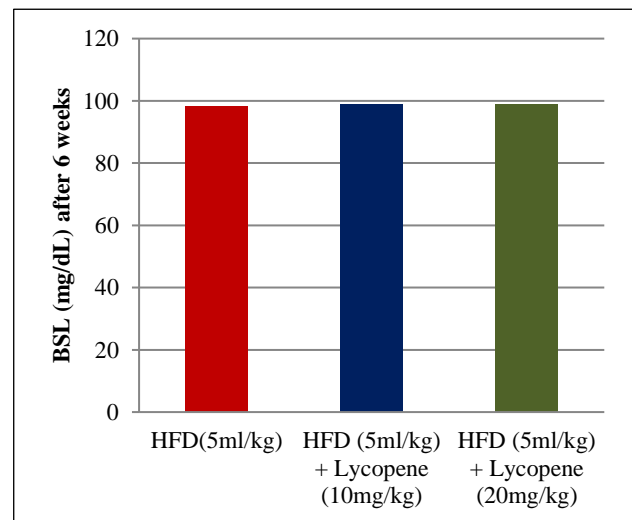


Figure 3: Effect of lycopene on blood sugar.

Table 2 and Figure 3 show the multiple comparisons between BSL after six weeks between group 1 Vs group 2, group 1 Vs group 3 and group 2 Vs group 3 using ANOVA followed by Tukey’s test of multiple comparisons. They show that there was no statistically significant difference in BSL in group 2 and group 3, when compared with group 1. They also show that there was no statistically significant difference in BSL in group 3, when compared with group 2.

DISCUSSION

Tomato is one of the most commonly consumed fruits/vegetables worldwide. Average annual approximate consumption in America of fresh tomatoes has been

estimated to be 8kg per person and that of processed tomato products is 31kg per person.¹⁷

Growing evidence from various in vitro experiments as well as from epidemiological and intervention studies on the cardiovascular benefits of lycopene prompted us to investigate the impact of pure lycopene supplementation on diet-induced hyperlipidaemia in adult male New Zealand rabbits.

In our study, hyperlipidaemia was induced by administering high fat diet to New Zealand white rabbits as described by Shyamala MP et al.¹⁴ The authors stated that hyperlipidaemia is the result of an oxidative abuse due to free radicals, formed by the interaction of high fat diet.

In the present study, we have used New Zealand white rabbits for induction of diet-induced hyperlipidaemia as they are the most commonly used animal model for the same.

The advantage of this species is that although they have low plasma TC concentration and HDL is the dominant lipoprotein, VLDL becomes the major plasma lipoprotein when exposed to high cholesterol diet.¹⁸

In our study, the hypolipidaemic, hypoglycaemic and antioxidant activity of pure lycopene powder 10mg/kg and 20 mg/kg body weight was evaluated in the rabbits fed with HFD.

We observed that, as compared to the baseline, daily oral administration of HFD in the dose of 5ml/kg for 6 weeks resulted in significant increase in serum TC, LDL, TG and VLDL; significant decrease in the levels of serum HDL and antioxidant SOD but no significant difference in BSL (Table 1).

Compared to baseline levels, there was significant difference in the serum lipid profile, SOD and BSL with the administration of lycopene in the dose of 10mg/kg and 20mg/kg along with HFD.

Pairwise comparison between the groups was done using ANOVA followed by Tukey's test of multiple comparisons and the following results were obtained (Table 2).

Compared to the HFD group, with the administration of lycopene 10mg/kg along with HFD, there was significant decrease in the levels of serum TC, LDL, TG and VLDL (Table 2, Figure 1), significant increase in serum SOD levels (Table 2, Figure 2), but no significant difference in the levels of serum HDL (Table 2, Figure 1) and BSL (Table 2, Figure 3).

Compared to the HFD group, with the administration of lycopene 20mg/kg along with HFD, there was significant decrease in the levels of TC, LDL, TG and VLDL (Table 2, Figure 1). significant increase in the levels of serum

HDL (Table 2, Figure 1) and SOD (Table 2, Figure 2), but no significant difference in BSL (Table 2, Figure 3).

Compared to the administration of lycopene 10mg/kg along with HFD, with the administration of lycopene 20mg/kg along with HFD, there was significant decrease in the levels of TG and VLDL (Table 2, Figure 1), but no significant difference in the levels of TC and LDL (Table 2, Figure 1), SOD (Table 2, Figure 2) and BSL (Table 2, Figure 3). This shows dose dependent activity of lycopene on serum HDL, serum TG and VLDL level (Table 2, Figure 1).

An inverse association between the consumption of tomatoes and tomato products with the prevalence of CVD has been indicated by clinical epidemiological studies. Tomatoes have a plethora of ingredients. The carotenoid lycopene has attracted lot of attention for its potentially beneficial cardiovascular effects in the recent years. Located mainly in tomato peels, lycopene contributes to the red colour of tomatoes. Cell culture studies have suggested a number of underlying mechanisms for protective cardiovascular actions of lycopene. These include inhibition of proliferation of smooth muscle cells and foam cell formation, prevention of injury to the endothelial cells, modulation of cholesterol metabolism and the inhibition of LDL oxidation and decrease of pro-inflammatory cytokines.¹⁹

A number of clinical studies have indicated an inverse correlation of circulating plasma lycopene levels with adverse cardiovascular parameters. In the Rotterdam study, higher lycopene serum levels were seen to be modestly associated with reduced aortic calcification.²⁰ Lorenz M et al, have reported a correlation between elevated plasma lycopene levels and decreased intima-media thickness in the carotid artery, a parameter of early stage of atherosclerosis.¹⁹ An inverse relationship was observed between the circulating plasma lycopene levels and arterial stiffness. The impact of lycopene on blood cholesterol levels in clinical intervention studies appears to be dose-dependent.

What may be the mechanisms behind the cholesterol lowering effects of lycopene? Increase in the faecal cholesterol excretion, along with decreased activity of liver HMG CoA reductase was shown after dietary lycopene intake in rabbits suggesting a decrease in the intestinal cholesterol absorption and biosynthesis.²

Human intervention studies have yielded inconsistent results for lycopene's effects on the plasma lipid levels. In a study by Fuhrman B, dietary supplementation of lycopene (60mg/day) to six men for a period of three months caused significant 14% decrease in their plasma LDL cholesterol concentrations.²¹

In a meta- analysis of intervention trials, Reid K found that lycopene may keep the cholesterol as well as blood pressure in healthy range.²² In this study, researchers

identified 12 studies of at least two weeks duration, which involved supplementation with lycopene to help with high cholesterol levels and high blood pressure.

However, Engelhard YN, reported that in mild hypertensive patients, no effects on blood lipid levels were obtained after daily supplementation for eight weeks with a tomato extract containing 15 mg lycopene.²³

A meta-analysis of human intervention trials reported significant decrease in total cholesterol and LDL only in the doses equal to or more than 25mg lycopene daily. Lycopene in doses less than 25mg per day had no effect on serum cholesterol levels. HDL cholesterol remained unchanged by lycopene intake, irrespective of the dosage.²²

Oxidative stress has been assumed to mediate the atherosclerotic dysfunction. Reactive oxygen species (ROS) including superoxide (O₂⁻), hydrogen peroxide (H₂O₂), hydroxyl radical (OH⁻), and peroxynitrate (ONOO⁻) have oxidant property and contribute to the oxidative stress. Normal function of the endothelium is characterized by a balance between nitric oxide (NO) and other antioxidants. Potent vasodilator and antioxidant NO, as a scavenger of superoxide ions, antagonizes the vasoconstrictive properties of ROS. Lycopene has antioxidant activity by increasing the bioavailability of NO, by decreasing the lipid peroxidation and ROS production.²⁴

In our study, with the administration of lycopene, significant increase was seen in the levels of SOD as a marker of its antioxidant effect. (Table 2. Figure 2) This finding correlates with the previous study by Subhash K.²⁶ SOD arguably is the most crucial antioxidant of the body, as it disarms the highly reactive superoxide, that is the most dangerous free radical. It reduces the radical superoxide (O₂⁻) so as to form H₂O₂ and O₂. Even though H₂O₂ is a pro-oxidant compound too, enzyme catalase and glutathione peroxidase subsequently convert it to simple water and oxygen. Hence, lycopene, the novel SOD boosting supplement, by strengthening the primary antioxidant system of the body, may offer protection from free radicals and may play a protective role by decreasing the oxidative stress that is implicated in atherosclerosis and other life-threatening diseases.

In a study by Rao AV, fifty known chronic osteoarthritis patients were given tomato juice (200ml) per day, along with normal diet and specific treatment for one month.¹³ Measurements of malondialdehyde, SOD, reduced glutathione, vit. E, vit C and beta carotene were taken before and after the oral supplementation of tomato juice. Results showed that, lycopene in tomato juice as a source of natural antioxidant, along with specific treatment, brought antioxidants levels to the normal in osteoarthritis cases, which prevents or minimizes further oxidative damage.

There was however no significant difference in the fasting blood sugar levels with HFD and both the doses of lycopene 10mg/kg and 20mg/kg. (Table 1, Table 2, Figure 3). This suggests that though lycopene has hypolipidaemic and antioxidant effects, it lacks the hypoglycaemic activity.

CONCLUSION

We have observed the hypolipidaemic and antioxidant effects with the administration of lycopene orally once daily for six weeks in the dose 10mg/kg and 20mg/kg body weight. It is of interest that there was a dose related decrease in the serum TG levels and this was also reflected in the serum VLDL levels. Since there is no effective drug available at present to decrease the serum TG levels, lycopene can be further evaluated in clinical settings. Also, more experimental studies to establish the therapeutic dose and clinical studies to evaluate the role of lycopene in comparison with statins in patients of mild hyperlipidaemia need to be conducted.

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REFERENCES

1. Riccioni G, Mancini B, Di Ilio E, Bucciarelli T, D'Orazio N. Protective effect of lycopene in cardiovascular disease. *Eur Rev Med Pharmacol Sci.* 2008;12:183-90.
2. Verghese M, Richardson JE, Boateng J, Shackelford LA, Howard C, Walker LT et al. Dietary lycopene has a protective effect on cardiovascular disease in New Zealand White male rabbits. *J Biol Sci.* 2008;8(2):268-77.
3. Chhetri S, Khan A, Rathore NS, Ishaq F, Chandel AS, Malhotra D. Effect of lovastatin on lipoprotein lipid peroxidation and antioxidant status in inflammation induced hyperlipidaemic rats. *J Chem Pharm Res.* 2011;3(3):52-63.
4. Zimmet PZ, Lefebvre P. The global NIDDM epidemic. *Diabetologia.* 1996;39:1247-48.
5. Min-Yu H, Yi-Lin L, Chong-He J, Zhao-Qian L, Shu-Lin Q, Yi-Ming H. Comparison of lycopene and fluvastatin effects on atherosclerosis induced by a high fat diet in rabbits. *Nutrition.* 2008;24:1030-38.
6. Abdelhalim MAK. The potential influence of high cholesterol diet-induced oxidative stress on composition and properties of red blood cells in rabbits. *Afr J Microbiol Res.* 2010;4(9):836-43.
7. Iannelli P, Zarilli V, Varicchio E, Tramontano D, Mancini FP. The dietary antioxidant resveratrol affects

- redox changes of PPAR α activity. *Nutr Met Cardiovas Dis.* 2007;17(4):247-56.
8. Willet W. Coffee and coronary heart disease. A new problem with old brew? *Ann Epidemiol.* 1994;4(6):497-98.
 9. Mazza G, Kay CD, Cottrell T, Holub BJ. Absorption of anthocyanins from blueberries and serum antioxidant status in human subjects. *J Agric Food Chem.* 2002;50(26):7731-37.
 10. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH collaborative research group. *N Eng J Med.* 1997;336(16):1117-24.
 11. Sies H, Stah W. Vit E, C, beta carotene and other carotenoids as antioxidants. *Am J Clin Nutr.* 1995;62;1315-21.
 12. Gerster H. The potential role of lycopene for human health. *J Am Coll Nutr.* 1997;16(2):109-26.
 13. Rao AV, Agarwal S. Role of antioxidant lycopene in cancer and heart disease. *J Am Coll Nutr.* 2000;19(5):563-69.
 14. Shyamala MP, Venukumar MR, Latha MMS. Antioxidant potential of *Syzygium aromaticum* (Gaertn.) Linn (cloves) in rats fed with high fat diet. *Ind J Pharmacol.* 2003;35:99-103.
 15. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18(60):499-502.
 16. Marklund S, Marklund G. Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. *Eur J Biochem.* 1974;47:469-74.
 17. Silaste M-L, Alfthan G, Aro A, Kesaniemi A, Horkko S. Tomato juice decreases LDL cholesterol levels and increases LDL resistance to oxidation. *Br J Nutr.* 2007;98:1251-58.
 18. Singh V, Tiwari RL, Dikshit M, Barthwal M. Models to study atherosclerosis: a mechanistic insight. *Curr Vasc Pharmacol.* 2009;7:75-109.
 19. Lorenz M, Fechner M, Kalkowski J, Frohlich K, Trautmann A, Bohm V et al. Effects of lycopene on the initial state of atherosclerosis in New Zealand White rabbits. *PLoS ONE.* 2012;7(1):e30808.
 20. Klipstein-Grobusch K, Launer LJ, Geleijnse JM, Boeing H, Hofman A et al. Serum carotenoids and atherosclerosis. The Rotterdam Study. 2000;148:49-56.
 21. Fuhrman B, Elis A, Aviram M. Hypercholesterolaemic effect of lycopene and beta carotene is related to suppression of cholesterol synthesis and augmentation of LDL receptor activity in macrophages. *Biochem Biophys Res Commun.* 1997;233:658-62.
 22. Ried K, Fakler P. Protective effect of lycopene on serum cholesterol and blood pressure: Meta-analyses of intervention trials. *Maturitas.* 2011;68(4):299-310.
 23. Engelhard YN, Gazer B, Paron E. Natural antioxidants from tomato extract reduce blood pressure in patients with grade I hypertension. A double-blind placebo-controlled pilot study. *Am Heart J.* 2006;(5):100e1-100eb.
 24. Tandon V, Bano G, Khajuria V, Parihar A, Gupta S. Pleiotropic effects of statins. *Indian J Pharmacol.* 2005;37(2):77-85.
 25. Subhash K, Bose C, Agrawal BK. Effect of short-term supplementation of tomatoes on antioxidant enzymes and lipid peroxidation in type II diabetes. *Ind J Clin Biochem.* 2007;22(1):95-8.

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