6. DISCUSSION

As stated by Silaste ML,

tomato is one of the most widely consumed fruits/vegetables all over the world. It has been estimated that in America the average annual consumption of fresh tomatoes is approximately 8 kg per person and that of processed tomato products is 31 kg per person.”

In our study, hyperlipidaemia was induced by administering high fat diet to New Zealand White rabbits as described by Shyamala MP et al. who 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.

As per Singh V,

the advantage of this species is that although they have low plasma cholesterol concentration and HDL is the dominant lipoprotein, VLDL becomes the major class of plasma lipoprotein when exposed to cholesterol rich diet.”

In our study, the hypolipidaemic, hypoglycaemic and antioxidant activity of pure lycopene powder 10 mg/kg and 20 mg/kg body weight was evaluated in the rabbits fed with high fat diet. Similarly, the effect of pure lycopene powder 10 mg/kg and 20 mg/kg on serum nitric oxide levels was evaluated.

In our study, daily oral administration of high fat diet in a dose of 5 ml/kg for 6 weeks resulted in highly significant increase in serum total cholesterol, LDL, triglycerides and VLDL, whereas there was a highly significant decrease in the level of serum HDL and antioxidant SOD as compared with the baseline levels. However daily oral administration of high fat diet in a dose of 5 ml/kg for 6 weeks did not result in any significant difference in BSL as expected, since this animal model is not used to induce hyperglycaemia. Serum nitric oxide levels, as compared to baseline levels, were not significantly altered.

Administration of lycopene orally once daily in the dose of 10 mg/kg resulted in highly significant difference as compared to baseline levels in the lipid profile and blood antioxidant SOD. Administration of lycopene in the dose of 10 mg/kg led to significant
difference in BSL, as compared to baseline levels. However, administration of lycopene in the dose of 10 mg/kg did not cause any significant difference as compared to baseline levels in the serum nitric oxide levels.

Administration of lycopene orally once daily in the dose of 20 mg/kg led to highly significant difference as compared to baseline levels in the lipid profile, blood antioxidant SOD and BSL. However, administration of lycopene in the dose of 20 mg/kg did not cause any significant difference as compared to baseline levels in the serum nitric oxide levels.

Pairwise comparison between the groups was done using Tukey’s test of multiple comparisons and the following results were obtained:

There was a highly significant decrease in the levels of TC, LDL, TG and VLDL with the administration of lycopene 10 mg/kg, as compared to the HFD group. There was a highly significant increase in the levels of serum SOD with the administration of lycopene 10 mg/kg, as compared to the HFD group. There was a significant increase in the levels of serum nitric oxide with the administration of lycopene 10 mg/kg, as compared to the HFD group. However, there was no significant difference in the levels of serum HDL with the administration of lycopene 10 mg/kg, as compared to the HFD group. Similarly, there was no significant difference in BSL with the administration of lycopene 10 mg/kg, as compared to the HFD group.

There was a highly significant decrease in the levels of TC, LDL, TG and VLDL with the administration of lycopene 20 mg/kg, as compared to the HFD group. There was a highly significant increase in the levels of serum HDL, SOD and nitric oxide with the administration of lycopene 20 mg/kg, as compared to the HFD group. However, there was no significant difference in BSL with the administration of lycopene 20 mg/kg, as compared to the HFD group.

There was a highly significant decrease in the levels of TG and VLDL with the administration of lycopene 20 mg/kg, as compared to the administration of lycopene 10 mg/kg. However, there was no significant difference in the levels of TC, HDL, LDL, SOD, BSL and nitric oxide with the administration of lycopene 20 mg/kg, as compared to the administration of lycopene 10 mg/kg.
Since, in the case of blood sugar levels, p-value was greater than 0.05 as per the ANOVA test, there was no significant difference in the blood sugar level between the three treatment groups.

Mulkalwar S$^{12}$ stated that “Clinical epidemiological studies indicate that the consumption of tomatoes and tomato products is inversely associated with the prevalence of CVD. Tomatoes contain a plethora of ingredients.” As stated by Lorenz M$^{113}$ “during recent years, the carotenoid lycopene has attracted much attention for its potentially beneficial cardiovascular effects. It is located mainly in tomato peels and contributes to the red colour of tomatoes. A number of underlying mechanisms for protective cardiovascular actions of lycopene have been suggested in cell culture studies. These include inhibition of smooth muscle cell proliferation and foam cell formation, prevention of endothelial cell injury, modulation of cholesterol metabolism and inhibition of LDL oxidation and decrease of pro-inflammatory cytokines.”

As per Klipstein-Grobusch K$^{114}$ “a number of studies have shown an inverse correlation of circulating plasma lycopene levels with adverse cardiovascular parameters in humans. In the Rotterdam study, higher lycopene serum levels were modestly associated with reduced aortic calcification.” Lorenz M et al$^{113}$ stated that “elevated plasma levels of lycopene correlated with decreased intima-media thickness in carotid artery, a parameter of early stage of atherosclerosis. An inverse relationship between circulating plasma lycopene levels and arterial stiffness was observed. The impact of lycopene on blood cholesterol levels in human intervention studies appears to be dose-dependent.”

Multiple studies on lycopene pertaining to its cardiovascular benefits led to the present study to evaluate the effect of pure lycopene powder in hyperlipidaemic male New Zealand White rabbits.

As stated by Tandon V$^{115}$ “there is an assumption that oxidative stress mediates atherosclerotic dysfunction. ROS including superoxide (O2-), hydroxyl radical (OH-), hydrogen peroxide (H2O2) and peroxynitrate (ONOO-) have oxidative property and contribute to oxidative stress. Normal endothelial function is characterized by a dynamic balance between nitric oxide (NO) and other antioxidants. As a scavenger of superoxide ions, the potent vasodilator and antioxidant NO, antagonizes the vasoconstrictive
properties of ROS. Lycopene possesses antioxidant activity by increasing the NO bioavailability, by reducing lipid peroxidation and ROS production.”

What are the mechanisms behind the cholesterol lowering effects of lycopene? Verghese M² stated that “increased faecal cholesterol excretion, together with reduced liver HMG CoA reductase activity was shown after dietary lycopene intake in rabbits suggesting decreased intestinal cholesterol absorption and biosynthesis.”

However, clinical intervention studies of lycopene on lipid profile have yielded inconsistent outcomes. Fuhrman et al¹¹⁶ reported that “dietary supplementation of lycopene (60 mg/day) to six men for a 3-month period resulted in significant 14 % reduction in their plasma LDL cholesterol concentrations.”

In addition, Ried K¹¹⁷ in a meta- analysis of intervention trials found that “lycopene may keep cholesterol as well as blood pressure in healthy range.” In this study, researchers identified 12 studies lasting at least 2 weeks in duration, which involved supplementing with lycopene to help with high cholesterol levels and high blood pressure.

In a study done by Rao SV¹¹⁸ reported that “fifty known chronic osteoarthritis patients were given a glass of tomato juice (200ml) per day, along with normal diet and specific treatment for one month. Malondialdehyde, reduced glutathione, SOD, vit. C, vit E and beta carotene were measured before and after tomato juice oral supplementation. The results showed that, lycopene in tomato juice as a source of natural antioxidant, along with specific treatment, brought antioxidants to the normal in osteoarthritis cases, which prevents or minimizes further oxidative damage.”

However, Engelhard YN¹¹⁹ reported that “no effects on blood lipid levels were obtained after supplementation with a tomato extract containing 15 mg lycopene daily for 8 weeks in mild hypertensive patients.”

Ried K¹¹⁷ stated that “meta-analysis of human intervention trials revealed significant reduction in total and LDL cholesterol only at doses of more than or equal to 25 mg lycopene daily. Doses of less than 25 mg lycopene had no effect on serum cholesterol levels. HDL cholesterol was not changed by lycopene intake independently of dosage given.”
In our study, with the administration of lycopene, there was a significant increase in the levels of SOD as a marker of its antioxidant effect. This finding is in common with the previous study by Subhash K. who stated that “SOD is arguably body’s most crucial antioxidant as it is responsible for disarming the most dangerous free radicals of all, the highly reactive superoxide. It reduces the radical superoxide (O$_2^-$) to form H$_2$O$_2$ and O$_2$. Although H$_2$O$_2$ is also a pro-oxidant compound, it is subsequently converted by enzyme catalase and glutathione peroxidase to simple water and oxygen. So, by strengthening the body’s primary antioxidant system, this novel SOD boosting supplement may offer the powerful free radical protection and may play a protective role in reducing the oxidative stress implicated in atherosclerosis and other life-threatening diseases.”

In our study, there was a significant increase in the levels of serum nitric oxide with administration of lycopene 10 mg/kg as compared to high fat diet. There was a highly significant increase in the levels of serum nitric oxide with administration of lycopene 20 mg/kg as compared to high fat diet. These findings suggest the effect of lycopene on the vascular tone and hence the blood pressure. Dalbeni A. stated that “lycopene increases NO generation and release, as shown by the increase in NO and nitrite/nitrate concentrations, by preventing peroxynitrate formation. Lycopene has biological activity, blunting the increase in cell migration induced by VEGF-A, Possibly through NO depended modulation of VEGF signalling system. The potential of lycopene bioactivity should be further investigated in the setting of vascular inflammation and pathological angiogenesis.”

Thus, we have observed the hypolipidaemic effect with the administration of lycopene orally once daily for six weeks in the dose 10 mg/kg and 20 mg/kg body weight. Probable mechanism of hypolipidaemic effect of lycopene may be due to its antioxidant effect and nitric oxide may also have a role in this action.

It is of interest that there was a dose related decrease in the serum triglycerides levels and this was also reflected in the serum very low density lipoproteins levels. Since there is no effective drug available at present to decrease the serum triglycerides levels, lycopene can be further evaluated in clinical settings.