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Original Research Article

Hypolipidaemic Effect of Lycopene from Red Tomatoes (*Solanum lycopersicum* L.) and its Potential for the Prevention of Cardiovascular Diseases

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ABSTRACT

The Nutritional and therapeutic benefits of lycopene from red tomatoes and its products cannot be overemphasized. Therefore, this study aimed to evaluate the hypolipidaemic effect of lycopene in three different preparations of red tomatoes in hyperlipidemic rats. Forty male Wistar rats were used for the study. The rats were divided into four groups (A - D) of 10 animals each. Group A was used as the control and received basal home diet throughout the duration of the experiment. Groups B, C, and D were fed with hyperlipidemic diets for one month, followed by lycopene in three different preparations of red tomatoes (Raw tomatoes, Tomato juice, and Cooked tomatoes) for another one month. Body weight and growth rate of the rats were monitored. The serum lipid profiles of the rats after administration of the hyperlipidaemic diet as well as after treatment with red tomato preparations were determined following standard procedures. Results showed that lycopene reduced weight gain induced by hyperlipidaemic diet, increased faecal fat content, and significantly reduced hyperlipidaemia in rats. The cooked tomatoes had the greatest effect in lowering serum total cholesterol, low density lipoprotein, and increasing high density lipoprotein levels. This suggests that lycopene present in cooked tomatoes are more readily absorbed in the intestine and therefore achieve higher concentration in the blood. Based on the findings from this study, dietary red tomatoes rich in lycopene may play a significant role in weight reduction, and in lowering plasma cholesterol which directly or indirectly reduces the risk of cardiovascular diseases.

Keywords: Tomatoes, Lycopene, Hyperlipidemia, Cardiovascular diseases, Plasma lipids.

Introduction

A number of fruits such as tomatoes are usually considered as vegetable by nutritionists. Like every other fruit, tomatoes (*Solanum lycopersicum L.*) are classified as fruits by botanists because they are the fleshy plant parts enclosing the seeds. Despite it being among the vegetable fruits in Nigeria with high nutritional and therapeutic values, tomatoes are still less consumed in Nigerian diet compared to its consumption in American diet.[1] One way to increase tomato consumption may be to leverage on its availability and numerous health benefits.[1] Tomatoes are a rich source of nutritional compounds like vitamin C, vitamin A (as carotenoids), fibres, minerals such as potassium, and the antioxidant lycopene.[2]

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Lycopene is a major dietary carotenoid and tomato-based foods are the richest source of lycopene. It is true that there is relationship between the consumption of tomato and its derived products and their beneficial or harmful effects on human health, and in several disease conditions such as gastroesophageal reflux disease or heartburn, allergies, kidney and cardiovascular disorders, prostate cancer, irritable bowel syndrome, lycopenodermia, body aches, arthritis, and urinary problems.[3] Recent studies have affirmed that tomatoes contain minerals, vitamins, proteins, essential amino acids (leucine, threonine, valine, histidine, lysine, arginine), mono-unsaturated fatty acids (linoleic and linolenic acids), carotenoids (lycopene and β-carotenoids), and phytosterols (β-sitosterol, campesterol and stigmasterol).[3-6] It has also been re-emphasized that lycopene is the main dietary carotenoid in tomato and tomato-based food products and lycopene consumption by humans has been reported to protect against cancer, cardiovascular diseases, neurodegenerative diseases, and osteoporosis.[4,6] Tomato and its derived products have very remarkable nutritional value in addition to their prominent antioxidant, anti-inflammatory, and anticancer activities, and are generally quite safe as food.[3] Tomatoes and tomato-based sauces and juices accounts for more than 85% of the dietary intake of lycopene for most people in Nigeria.[7,11] The lycopene content of tomatoes depends on the species and increases as the fruit ripens. Other sources of lycopene include apricot, guava, watermelon, papaya and pink grape fruits.

Tomatoes, unlike other fruits and vegetables where nutritional contents such as vitamin C are diminished upon cooking, the cooking of tomatoes increases the absorption of lycopene.[7,12] For example, lycopene in tomato paste is four times more bio-available than in fresh tomatoes.[7] For this reason, tomato sauce is a preferable source of lycopene as opposed to raw tomatoes. Consequently, processed tomato products such as pasteurized tomato juice, soup or cooked tomatoes contain the highest concentration of bio-available lycopene. Cooking and crushing tomatoes and serving in oil-rich dishes greatly increase the assimilation of lycopene from the digestive tract into the blood stream. Lycopene is fat-soluble, so oil aids its absorption from the gastro-intestinal tract. Dietary source and wet weight of tomatoes as well as distribution of lycopene in body tissues are presented in tables 1 and 2, respectively (Table 1 and Table 2). Lycopene has strong antioxidant properties. Anti-oxidants have diseases-fighting properties that protect cells from damage by free radicals. Anti-oxidants work by neutralizing the free radicals generated during oxidative metabolism. Anti-oxidants may also help to keep the immune system healthy and reduce the risk of cancer and other chronic degenerative diseases.[7,11,12]
The objective of the present study is to evaluate the nutritional and therapeutic effectiveness of red tomatoes extract as a strong antioxidant in the reduction of plasma lipids (hyperlipidemia) and prevention of cardiovascular diseases (CVDs) in rats.

Materials and Methods

Preparation of basal home diet
Fresh red tomatoes, eggs, dried fish, maggi spice, palm oil, cassava, yams, cocoyams and garri (cassava flakes) were used in preparing the basal home meals.

Preparation of high lipid (hyperlipidaemic) diet
High lipid diet was prepared by mixing 1 g cholesterol, 0.5 g bile salt, and 10 g egg yolk with 100 g of the basal home diet.

Animals
Forty-four (44) male Wistar rats (one month old) were obtained from University of Calabar Medical School Animal House, Department of Biochemistry. The animals were kept in well-ventilated cages and acclimatized to the laboratory condition for 4 weeks. They were fed with the basal home diet 8 hourly and allowed accesses to drinking water *ad libitum*. The animals were weighed and their mean weight was recorded.

Ethical consideration
The animals were handled following the international guidelines for the handling and care for experimental animals. Ethical approval for the conduct of the experiment was obtained from Department of Biochemistry, University of Calabar with voucher number CRS/MH/HREC/021/Vol.V1/214.

Experimental design
Out of the 44 rats, 4 died before the commencement of the experiment, the remaining 40 rats were grouped into four groups (A – D) of 10 rats per group. The experiment was divided into three phases.

Phase 1: Rats in all the groups (A – D) were fed with the basal home diet for one month. The rats were weighed at the end of the 4th week and their mean weight was recorded.

Phase 2: Rats in group A were used as the control, and were fed with the basal home diet only, while rats in groups B – D (test groups) were fed with the high lipid diet together with basal home diet for another one month. At the end of the 4th week, the animals were weighed and their mean weight was recorded.

Phase 3: Rats in group A (control) continued to receive the basal home diet, while rats in the test groups were fed as follows; Group B: Basal home diet mixed with grinded raw fresh red tomatoes, Group C: Basal home diet mixed with tomato juice, Group D: Basal home diet mixed with cooked tomatoes. All the administrations were done for another one month. At the end of this phase, the rats were also weighed and their mean weight recorded.

Determination of serum lipid profile
At the end of each phase (phase 2 and phase 3), the rats were fasted overnight, and blood samples were collected from five randomly selected rats from each group for serum lipid profile. The blood samples were analyzed for total serum cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), and very low-density lipoprotein (VLDL) following standard procedures.

Data Collection and Analyses
The mean weight of each group before and after the test diet was estimated. The mean serum total cholesterol, LDL, HDL and VLDL were estimated and recorded. The mean group faecal fat content was also estimated and recorded. The growth rate was calculated as the ratio of the weight gained during the treatment period and the number of days in the treatment period (Equation 1).

$$\text{Growth rate (g/day)} = \frac{\text{Final weight} - \text{initial weight}}{\textit{Number of days treated}} \quad \textit{Equation} - 1$$

The mean weight increase was expressed as the percentage of the initial weight. Initial and final body weight of each rat was measured and the mean weight for each group determined. Mean weight increase or decrease was calculated as the percentage of the ratio of the weight gain to initial body weight (Equation 2).

$$\textit{Mean weight increase}(\%) = \frac{\textit{Final weight} - \textit{initial weight}}{\textit{Initial weight}} \; X \; \frac{100}{1} \quad \textit{Equation} - 2$$

Statistical analysis
Statistical analysis was done using SPSS version 22. Data were expressed as mean ± standard deviation (SD). Differences between means across the groups were determined using the student t-test, and P-value of less than or equal to 0.05 ($P \leq 0.05$) was regarded as significant at 95% confidence level.

Table 1: Dietary sources and wet weight of tomato

Dietary sources	Wet weight (mg/g)
Raw tomato	8.8 – 42.0
Tomato juice	86 – 100
Tomato sauce	63 – 131
Tomato pink	20 – 54
Tomato puree	<0.1 – 7.8

(Source)[7]

Table 2: Distribution of Lycopene in body tissues/organs

Tissues	Wet weight (μg/g)
Liver	1.28 – 5.72
Kidney	0.15 – 0.62
Adrenal gland	1.90 – 21.40
Ovary	0.25 – 0.28
Adipose tissue	0.20 – 1.30
Lung	0.31
Colon	0.75
Breast	0.78
Skin	0.42

(Source)[7]

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Results and Discussions

Body weights of rats after feeding with basal home diet

The mean body weights of the rats in the different groups after feeding with basal home diets for four weeks are shown in Table 3. There was no significant difference in the mean weight among the four groups ($p = 0.491$).

Effect of hyperlipidemic diet and tomato preparations on body weight and growth rate of Wistar rats

Table 4 shows the effect of hyperlipidemic diets on mean body weight and growth rate of Wistar rats. The rats treated with hyperlipidemic diets showed an increase in mean body weight of 34.91 ± 0.13, which was significantly higher compared to that of the control with mean body weight increase of 20.53 ± 0.02 ($p < 0.05$). Also, there was an increase in the percentage growth rate of rats treated with hyperlipidemic diets (0.99 g/day). This was significantly higher when compared with the rats administered the basal home diets only (control), which showed a growth rate of 0.58 g/day ($P < 0.05$). In view of the above, the hyperlipidaemic diet produced significant increases in the body weight as well as the growth rate compared to the control ($P < 0.05$).

The effect of the three different preparations of red tomatoes on body weight and growth rate of Wistar rats are presented in Table 5. The rats treated with the three different tomatoes preparation showed a significant weight decrease when compared with the control ($P < 0.05$). The percentage mean weight decrease was seen more with the group treated with cooked tomatoes (13.63 ± 0.25%), followed by the group treated with tomato juice (13.05 ± 0.30%) and the least was seen with the group treated with raw tomatoes (12.27 ± 0.13%) when compared with the control (0.93 ± 0.30%). Similarly, there was a significant decrease in growth rate in the treatment groups when compared to the control ($P < 0.05$).

The increase in body weight after feeding with high fat diet for one month could be attributed to the ability of this diet to contribute to body fat, and consequently resulting in hyperlipidemic effect. This observation is in tandem with the work of Burton-Freeman *et al*. (2011) who reported that hyperlipidemia induced by exogenous dietary fat contribute to excessive weight gain and obesity if not controlled.[1] The findings from this study have shown the nutritional and therapeutic benefit of tomatoes a major source of lycopene, therefore suggesting the ability of this substance (lycopene) in reducing body weight in obesity.

Effect of hyperlipidemic diet and tomato preparations on serum lipid profile in Wistar rats

Table 6 shows the effect of hyperlipidemic diets on serum lipid profile. Feeding of the rats with hyperlipidaemic diet resulted in a significant increase in serum total cholesterol and LDL in all the treatment groups compared to the control group ($p < 0.05$). However, there were no significant differences in serum HDL and VLDL between the treatment groups and the control group ($p > 0.05$). The arterogenic index or TC/HDL ratio was also significantly higher in the hyperlipidaemic groups (B, C, and D) compared to the control (Group A).

On the other hand, when the hyperlipidaemic rats were fed with the different tomato preparations, we noticed a significant decrease in serum total cholesterol and LDL in the group treated with cooked tomatoes (Group D) compared with the control group ($p < 0.05$), whereas, in the other two groups B and C which were treated with raw tomatoes and tomato juice, respectively, there was no significant difference in their TC and LDL levels and that of the control (Group A) (($p > 0.05$). For the serum HDL, a significant increase was observed only in the group treated with the cooked tomatoes. For the VLDL, there was no significant difference between the treatment groups and the control. It is important to note that the groups treated with tomato juice and cooked tomatoes (Groups C and D) exhibited a significant reduction in the arterogenic index (TC/HDL) compared to the control group (Table 7).

The increase in serum total cholesterol induced by the hyperlipidaemic diet could be due to increased activity of lipoprotein lipase induced by the presence of dietary fats in the gastrointestinal tract. The increased activity of the enzyme lipase increases the absorption of digested fats and consequently increase the serum total cholesterol, low density lipoprotein, decrease the high-density lipoprotein and increase very low-density lipoprotein. A similar observation has been reported in different studies which showed that feeding male rats with hyperlipidemic diets increase the serum total cholesterol, low density lipoprotein, decrease high density lipoprotein and increase very low-density lipoprotein.[2,4,7,11]

The findings from this study have demonstrated the activity of lycopene present in red tomatoes in lowering the serum total cholesterol, low density lipoprotein, and in increasing high density lipoprotein levels by inhibiting the activity of lipoprotein lipase and indirectly reducing the digestion and absorption of dietary fats induced by the hyperlipidemic diet. It is important to note that Lycopene has no effect on very low-density lipoprotein because of the high concentration of triglycerides and low cholesterol content in the very low-density lipoprotein. This is relevant in the prevention and efficient management of hyperlipidemia. The ratio of total cholesterol to HDL (TC/HDL) decreased among the intervention groups with the lowest seen in group D treated with cooked tomatoes. The lower the TC/HDL ratio, the more protective is lycopene to the heart. This agrees with the findings from several studies which highlighted the importance of lycopene in the management of noncommunicable diseases (NCDs) and obesity.[3,5-8,11,12] This study have contributed to existing literature of the use of appropriate diets in the prevention and efficient management of hyperlipidemia which is a major risk factor for cardiovascular diseases.

Table 3: The mean weights of rats after feeding with basal home meals for one month (n = 40)

	Weight (g)				
	Group A	**Group B**	**Group C**	**Group D**	**P-value**
	71.00	81.20	91.10	86.14	
	90.10	82.40	87.30	92.20	
	67.30	75.30	85.00	90.10	
	88.20	87.40	86.10	87.20	
	93.10	90.50	90.45	99.54	
	91.00	90.46	90.60	90.35	0.491
	80.32	80.50	85.00	80.45	
	82.00	84.51	83.10	80.20	
	79.30	80.25	80.02	80.35	
	96.50	78.50	75.50	76.00	
Mean	84.64	83.58	85.40	85.23	

Values are Mean ± Standard deviation (SD)

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Effect of tomato preparations on faecal fat content

Table 8 shows the percentage mean faecal fat content in male Wistar rats treated with the three different tomato preparations. There was a significant increase in the faecal fat content between the treatment groups when compared with the control ($P < 0.05$). The greatest increase in faecal fat content was observed in the groups treated with cooked tomatoes (Group D), followed by tomato juice (Group C), and lastly, the raw tomatoes (Group B).

This observation indicates that lycopene aid in the excretion of dietary fats in faeces by reducing the digestion and absorption of dietary fats from the guts, which help in weight reduction especially in obesed patients.

Conclusion

The evaluation of the effectiveness of three preparations of tomatoes has indicated that cooked tomatoes have the greatest effect in reducing hyperlipidaemia. This could be due to the fact that lycopene present in cooked tomatoes is more readily absorbed from the intestine and thus achieve a higher concentration in the blood. In addition, the findings from the study suggest that lycopene could be used as weight reducing agent since it lowers the intestinal fat absorption and increases faecal fat content. Furthermore, consumption of diets rich in red tomatoes would decrease Low Density Lipoprotein (LDL), increase High Density Lipoprotein (HDL), and protect cellular fat molecules which will eventually lead to a significant reduction in cardiovascular symptoms such as artherosclerosis, a condition responsible ischaemic heart disease in humans. Therefore, dietary red tomatoes rich in lycopene may play a significant role in the reduction of plasma cholesterol and directly or indirectly be effective in the management of cardiovascular diseases. Arising from the foregoing, the authors recommend the consumption of tomatoes and tomato-based products especially in its cooked form. However, further studies is needed to substantiate the claims made in this study.

Table 4: The effect of hyperlipidemic diet on mean body weight and growth rate of male Wistar rats (n = 40)

Parameters	Control	Hyperlipidemic diet
Initial weight (g)	84.64 ± 1.23	84.73 ± 1.24
Final body weight (g)	102.02 ± 0.10	114.31 ± 1.20
Mean weight increase (%)	20.53 ± 0.02	34.91 ± 0.13
Growth rate (g/day)	0.58	0.99

Values are Mean ± Standard deviation (SD)

Table 5: The effect of dietary supplement with the three (3) different tomato preparations on body weight of hyperlipidemic rats (n = 40)

Parameter	Group A (control)	Group B (raw tomatoes)	Group C (tomato juice)	Group D (cooked tomatoes)
Initial weight (g)	114.36 ± 0.35	114.36 ± 0.50	114.00 ± 0.45	114.56 ± 0.32
Final weight (g)	115.42 ± 0.05	100.32 ± 0.32	99.12 ± 0.50	98.94 ± 0.23
Diff. in Mean weight (g)	1.06 ± 0.30	-14.04 ± 0.23	-15.18 ± 0.40	-15.62 ± 0.23
% Mean weight increase	0.93 ± 0.30	-12.27 ± 0.13	-13.05 ± 0.30	-13.63 ± 0.25
Growth rate	0.03 ± 0.00	-0.41 ± 0.00	-0.43 ± 0.01	-0.45 ± 0.01
ANOVA	0.32	0.2	0.2	0.2
T-test	P < 0.05	P < 0.05	P < 0.05	P < 0.05

Values are Mean ± Standard deviation (SD)

Table 6: The effect of hyperlipidemic diets on lipid profile of male Wistar rats

Parameter	Value (mg/dL)				
	Group A	Group B	Group C	Group D	P-value
TC	190.00 ± 0.20	220.00 ± 0.42	222.00 ± 0.80	225.00 ± 0.64	0.02
LDL	380.00 ± 0.30	440.00 ± 0.45	448.00 ± 0.23	450.00 ± 0.33	0.01
HDL	45.00 ± 0.10	40.00 ± 0.23	40.00 ± 0.50	39.00 ± 0.32	0.32
VLDL	150.00 ± 0.10	160.00 ± 0.24	160.00 ± 0.50	161.00 ± 0.25	0.22
TC/HDL	4.22 ± 0.10	5.50 ± 0.25	5.55 ± 0.40	5.77 ± 0.20	0.01

Values are Mean ± Standard deviation (SD)

Table 7: The effect of dietary supplementation with the three different tomato preparations and atherogenic index of hyperlipidemic rats (n = 40)

Parameters (mg/dL)	Group A (control)	Group B (raw tomatoes)	Group C (tomato juice)	Group D (cooked tomatoes)
TC	220.0 ± 0.23	195.0 ± 0.03	190.0 ± 0.02	160.0 ± 0.03*
LDL	400.0 ± 0.24	395.0 ± 0.04	390.0 ± 0.02	360.0 ± 0.05*
HDL	45.00 ± 0.02	46.00 ± 0.04	48.00 ± 0.10	54.00 ± 0.30*
VLDL	160.0 ± 0.32	155.0 ± 0.30	155.0 ± 0.35	154.0 ± 0.23
TC/HDL	4.88	4.24	3.96*	2.96*
T-test	P > 0.05	P > 0.05	P < 0.05	P < 0.05

Values are Mean ± Standard deviation (SD); *Significant difference compared to control

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Table 8: Percentage mean faecal fat content in Wistar rats following dietary supplementation with the three different tomato preparations (n = 40)

Parameters (mg/100%)	Group A (control)	Group B (raw tomatoes)	Group C (tomato juice)	Group D (cooked tomatoes)	P-value
Crude fat	10.0 ± 0.01	25.0 ± 0.30*	32.0 ± 0.13*	65.0 ± 0.21*	0.01

Values are Mean ± Standard deviation (SD)
* Represents statistical significant difference compared to the control ($P < 0.05$)

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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