

## **An Overview of Lycopene as an Anti Oxidants & the Development of Extraction Procedure of Lycopene from Regional Guava Fruit.**

Shashikant R Pattan<sup>1</sup>, Vinayak Gawade<sup>1</sup>, Utkarsha D. Gharate<sup>1</sup>, Nikita B. Wabale<sup>1</sup>, R.S.Kalkotwar<sup>1</sup>, Seema S. Vetal<sup>1</sup>, S.N. Hiremath<sup>2</sup>, Arun S. Kurhade<sup>1</sup>, Dr.U.B. Shetkar<sup>3</sup>

1. Department of Pharmaceutical Chemistry, Pravara Rural College of Pharmacy, Pravaranagar, Loni, 413736, (MS) India.

2. Department of Pharmaceutics, Pravara Rural College of Pharmacy (Women) Chincholi,

3. Dept. Of Medicine, Rural Medical College, PIMS, Deemed University, Loni

### **Summary**

Lycopene, a carotenoid without provitamin-A activity, is present in many fruits and vegetables. Lycopene has good antioxidant activity. The amount of Lycopene present in regional Guava fruit is much higher than Tomatoes. In the present work, the extraction process has been developed to extract Lycopene from Guava fruit and modify it to commercial level. Lycopene, a Carotenoid without provitamin – A activity is present in many fruit and Vegetable. It is red fat-soluble pigment found in certain plant and micro organisms, where it serves as accessory light gathering pigment and protects these organisms against the toxic effects of oxygen and light. Lycopene, one of more than 600 carotenoids found in nature, is a powerful antioxidant, probably more powerful than beta carotene. Studies show Lycopene works well together with several other antioxidants, including vitamin E and flavonoids.

**Keywords:** Lycopene, Carotenoid.

### **Address for Correspondence:**

**Dr. Shashikant R Pattan,**

Principal, Department of Pharmaceutical Chemistry, Pravara Rural College of Pharmacy, Pravaranagar.

A/P- Loni Bk. Taluka -Rahata, Dist-Ahmednagar 413736, India (MS).

E-mail- [shashipattan@yahoo.com](mailto:shashipattan@yahoo.com).

**Introduction**

Antioxidant are widely used as ingredients in dietary supplements that are used for health purposes such preventing cancer and heart disease. Lycopene is one of the Carotenoid, which has very good antioxidant property and found to be present in variety of vegetables and fruits such as tomatoes, red carrots, watermelons, papayas, gauva etc.

**SOURCES OF LYCOPENE**

<b>Vegetable Source</b>	<b>µg Lycopene per Gram Wet Weight</b>
<b>Tomato</b>	<b>8.8 – 42</b>
<b>Tomato Juice</b>	<b>86 – 100</b>
<b>Tomato Sauce</b>	<b>63 – 131</b>
<b>Tomato Ketchup</b>	<b>124</b>
<b>Watermelon</b>	<b>23 – 72</b>
<b>Pink Grapefruit</b>	<b>3.6 – 34</b>
<b>Pink Guava</b>	<b>54</b>
<b>Papaya</b>	<b>20 - 53</b>

## 1 .GUAVA FRUIT



## Scientific classification

<b>Kingdom:</b>	Plantae
<b>Division:</b>	Magnoliophyta
<b>Class:</b>	Magnoliopsida
<b>Subclass:</b>	Rosidae
<b>Order:</b>	Myrtales
<b>Family:</b>	Myrtaceae
<b>Subfamily:</b>	Myrtoideae
<b>Tribe:</b>	Myrteae
<b>Genus:</b>	<i>Psidium L.</i>
<b>Synonyms</b>	
<i>Calyptropsidium O.Berg</i> <i>Corynemyrtus (Kiaersk.) Mattos Guajava Mill. Mitropsidium Burret</i>	

**NUTRIENTS AND DIETARY ANTIOXIDANT VALUE IN GUAVAS**

<b>Food Value Per 100 g of Edible Portion</b>	<b>Value</b>
<b>Lycopene</b>	<b>5.40mg</b>
<b>Calories</b>	<b>36-50</b>
<b>Moisture</b>	<b>77-86 g</b>
<b>Dietary Fiber</b>	<b>2.8-5.5 g</b>
<b>Protein</b>	<b>0.9-1.0 g</b>
<b>Fat</b>	<b>0.1-0.5 g</b>
<b>Ash</b>	<b>0.43-0.7 g</b>
<b>Carbohydrates</b>	<b>9.5-10 g</b>
<b>Calcium</b>	<b>9.1-17 mg</b>
<b>Phosphorus</b>	<b>17.8-30 mg</b>
<b>Iron</b>	<b>0.30-0.70 mg</b>
<b>Carotene (Vitamin A)</b>	<b>200-400 I.U</b>
<b>Vitamin C (variable by species)</b>	<b>37-400 mg</b>
<b>Thiamin</b>	<b>0.046 mg</b>
<b>Riboflavin</b>	<b>0.03-0.04 mg</b>
<b>Niacin</b>	<b>0.6-1.68</b>

- ❖ Guavas are often considered superfruits, being rich in vitamins A and C, omega-3 and -6 polyunsaturated fatty acids (mainly in the seeds which must be chewed to obtain the omega fats) and especially high levels of dietary fiber.
- ❖ A single guava contains over four times the amount of vitamin C as a single orange (228 mg per 100 g serving), and also has good levels of the dietary minerals, potassium, magnesium, and an otherwise broad, low-calorie profile of essential nutrients.
- ❖ Nutritional value is greatly dependent on species, the strawberry guava notably containing only 37 mg of vitamin C per 100g serving, practically a tenth of the vitamin C found in more common varieties.
- ❖ Vitamin C content in strawberry guava, however, is still a high percentage (62%) of the Dietary Reference Intake for this vitamin.
- ❖ Guavas contain both major classes of antioxidant pigments - carotenoids and polyphenols, giving them relatively high dietary antioxidant value among plant foods.
- ❖ As pigments provide plant food their colors, guavas that are red, yellow or orange in color have more potential value as antioxidants sources than unpigmented species.

## 2. PAPAYA



Scientific classification	
Kingdom:	Plantae
(unranked):	Angiosperms
(unranked):	Eudicots
(unranked):	Rosids
Order:	Brassicales
Family:	Caricaceae
Genus:	<i>Carica</i>
Species:	<i>Papaya</i>
Binomial name	<i>Carica Papaya</i>

**POTENTIAL FOOD VALUE OF PAPAYA**

<b>Energy</b>	<b>163 kJ (39 kcal)</b>
<b>Carbohydrates</b>	<b>9.81 g</b>
<b>Sugars</b>	<b>5.90 g</b>
<b>Dietary fibre</b>	<b>1.8 g</b>
<b>Fat</b>	<b>0.14 g</b>
<b>Protein</b>	<b>0.61 g</b>
<b>Vitamin A equiv.</b>	<b>328 µg (36%)</b>
<b>Thiamine (Vit. B1)</b>	<b>0.04 mg (3%)</b>
<b>Riboflavin (Vit. B2)</b>	<b>0.05 mg (3%)</b>
<b>Niacin (Vit. B3)</b>	<b>0.338 mg (2%)</b>
<b>Vitamin B6</b>	<b>0.1 mg (8%)</b>
<b>Folate (Vit. B9)</b>	<b>38 µg (10%)</b>
<b>Vitamin C</b>	<b>61.8 mg (103%)</b>
<b>Calcium</b>	<b>24 mg (2%)</b>
<b>Iron</b>	<b>0.10 mg (1%)</b>
<b>Magnesium</b>	<b>10 mg (3%)</b>
<b>Phosphorus</b>	<b>5 mg (1%)</b>
<b>Potassium</b>	<b>257 mg (5%)</b>
<b>Sodium</b>	<b>3 mg (0%)</b>
<b>Percentages are relative to US recommendations for adults.</b>	

### 3. TOMATO



#### Scientific classification

**Kingdom:** Plantae

**(unranked):** Angiosperms

**(unranked):** Eudicots

**Order:** Solanales

**Family:** Solanaceae

**Genus:** *Solanum*

**Species:** *lycopersicum*

**Binomial name:** *Solanum lycopersicum L.*

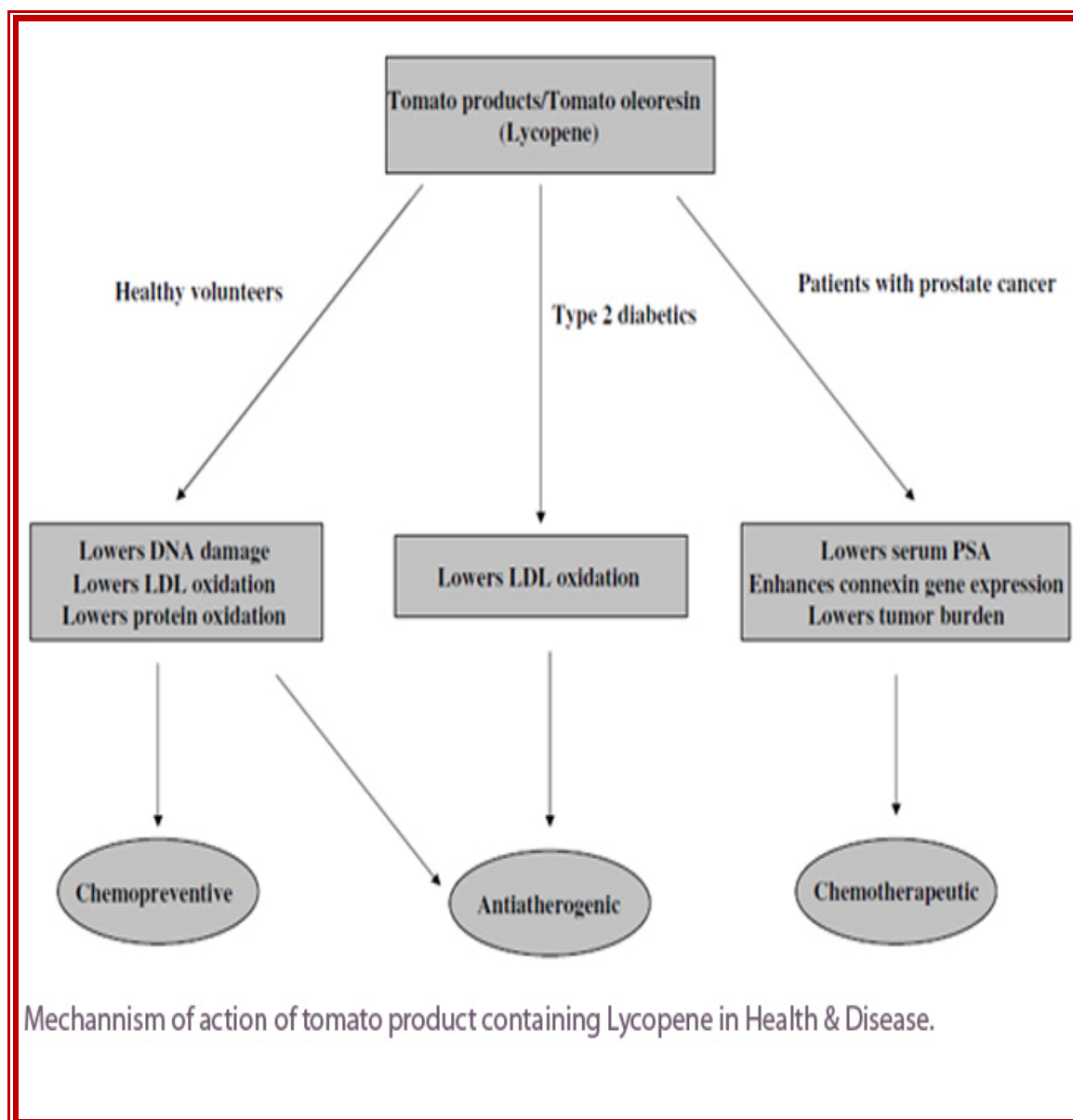
#### Synonyms

*Lycopersicon lycopersicum*  
*Lycopersicon esculentum*



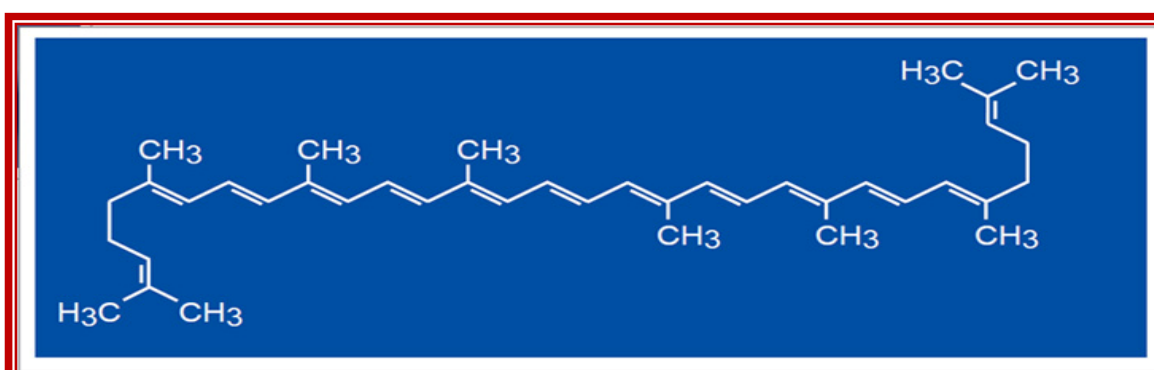
**CHEMICAL COMPOSITION OF LYCOPENE EXTRACT FROM TOMATO**

<b>Compound</b>	<b>Content [%]</b>	
	<b>Min</b>	<b>Max</b>
<b>Unsaponifiable matter</b>	<b>13.4</b>	<b>31.4</b>
<b>Lycopene</b>	<b>4.9</b>	<b>15</b>
<b>Phytoene</b>	<b>0.5</b>	<b>1.1</b>
<b>Phytofluene</b>	<b>0.4</b>	<b>0.9</b>
<b>β-Carotene</b>	<b>0.1</b>	<b>0.5</b>
<b>Tocopherols</b>	<b>1</b>	<b>3.0</b>
<b>Sterols</b>	<b>1.5</b>	<b>2.5</b>



## LYCOPENE CHEMISTRY

### Structure of Lycopene

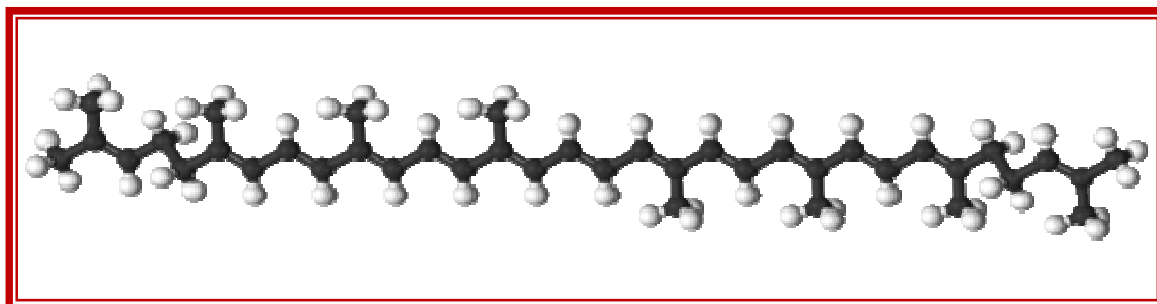


### 3 Dimensional Structure of Lycopene:

**Synonyms-** psi-carotene, all trans Lycopene, lycopersicon, solanorubin.

**Common name(s)-** Rhodopurpurin

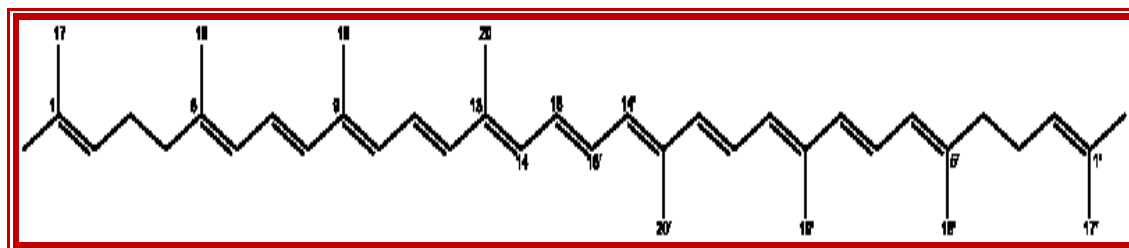
IUPAC Name :  $\psi,\psi$ -carotene



### PIGMENT BIOCHEMISTRY LYCOPENE

Properties	
Molecular formula	$C_{40}H_{56}$
Molar mass	$536.87 \text{ g mol}^{-1}$
Appearance	Deep red solid
Melting Point	$172-173^{\circ}\text{C}$
Solubility in Water	Insoluble

❖ **Chemical structure:**



❖ **Main absorbance wavelength:**

~470 nm

❖ **Natural sources:**

tomatoes, red carrots, watermelons, papayas, Gauvas etc.

❖ **Related compounds:**

carotenoid, e.g.  $\beta$ -carotene

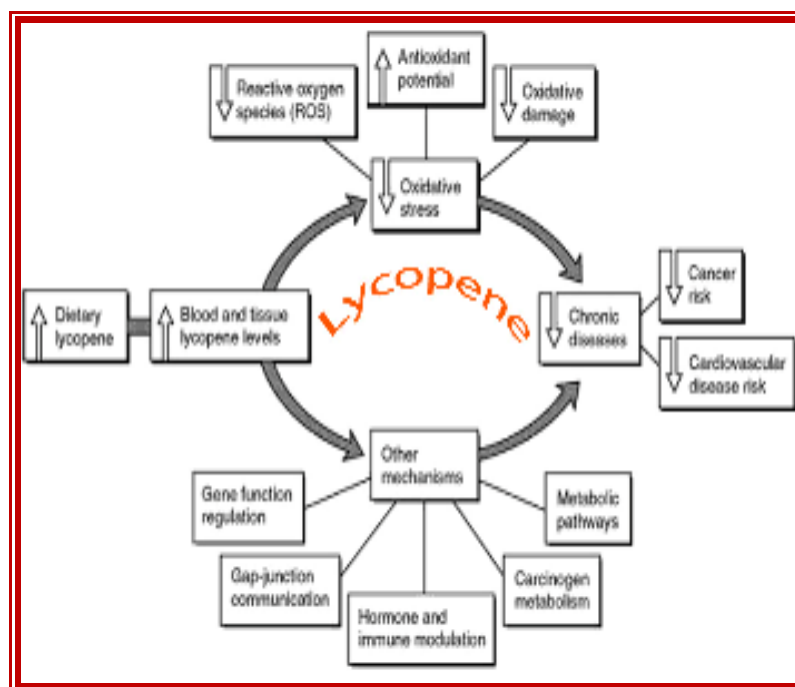
### DIETARY ANTIOXIDANT IN BIOLOGICAL SYSTEM

- ❖ The term antioxidant [also antioxygen ] originally referred specifically to a chemical that prevented the consumption of molecular oxygen.
- ❖ An antioxidant is a chemical that reduces the rate of particular oxidation reactions in a specific context, where oxidation reactions are chemical reactions that involve the transfer of electrons from a substance to a oxidizing agent.
- ❖ Antioxidants are particularly important in the context of organic chemistry and biology.
- ❖ All living organisms maintain a reducing environment inside their cells, all cells contain complex systems of antioxidants to prevent chemical damage to the cells' components by oxidation.
- ❖ Antioxidants are widely used as ingredients in dietary supplements that are used for health purposes such preventing cancer and heart disease.

### **MECHANISM OF ACTION OF ANTIOXIDANT**

- Free radicals have been implicated in the causation and progress of several diseases e.g. atherosclerosis and CHD, cancer, respiratory diseases.
- Dietary consumption of a variety of nutrient antioxidant [vit.C and E. Beta carotene, Lycopene] is desirable since each antioxidant targets certain types of damaging free radicals.
- Free radicals are the molecules or molecular species containing one or more unpaired electrons with independent existence. e.g.  $H_2O_2$ ,  $OH\cdot$ .
- Free radicals are highly reactive and are capable of damaging all types of biomolecules (Proteins, lipids, carbohydrates, nucleic acid) and have been implicated in the causation of many diseases eg. Cardiovascular diseases cancer inflammatory diseases.
- To eradicate the harmful effects of free radicals, the aerobic cells have developed antioxidant defense mechanism.

### **PROPOSED MECHANISMS FOR THE ROLE OF LYCOPENE IN CHRONIC DISEASE**



**Fig: MECHANISM OF ACTION OF LYCOPENE**

- Lycopene acts in many different ways in the body. It works as an antioxidant and it may help reduce DNA damage.
- Furthermore, Lycopene inhibits prostatic IGF-I signaling, IL-6 expression (interleukin), and androgen signaling. Moreover, Lycopene improves communication between cells, and induces phase II drug metabolizing enzymes.
- A cellular and molecular study have shown Lycopene to be one of the most potent antioxidants and has been suggested to prevent carcinogenesis and atherogenesis by protecting critical biomolecules such as DNA, proteins, lipids and low density lipoproteins (LDLs).
- Lycopene, because of its high number of conjugated double bonds, exhibits higher singlet oxygen quenching ability compared to b-carotene or a-tocopherol.

- cis-Lycopene has been shown to predominate in both benign and malignant prostate tissues, suggesting a possible beneficial effect of high cis-isomer concentrations, and also the involvement of tissue isomerases in in-vivo isomerization from all trans to cis form .
- The 9-cis b-carotene is a better antioxidant than its all-trans counterpart, no such mechanistic data have been reported in case of individual Lycopene isomers.
- At a physiological concentration of 0.3mmol/l, Lycopene has been shown to inhibit growth of non-neoplastic human prostate epithelial cells in vitro, through cell cycle arrest which may be of significant implications in preventing benign prostate hyperplasia, a risk factor for prostate cancer.
- Lycopene has also been shown to significantly reduce LNCaP human prostate cancer cell survival in a dose-dependent manner and this antineoplastic action may be explained by increased DNA damage at high Lycopene concentrations (45mM), whereas lower levels of Lycopene reduced malondialdehyde formation, with no effects on DNA.
- Physiologically attainable concentrations of Lycopene have been shown to induce mitochondrial apoptosis in LNCaP human prostate cancer cells, although no effects were observed on cellular proliferation or necrosis.
- As evident from in vitro and animal studies, purified Lycopene may inhibit prostate cancer growth only at higher concentrations, in comparison with tomato antioxidant supplementation.
- The inhibitory effects of Lycopene on MCF7 human mammary cancer cell growth, owing to interference in IGF-1 receptor signaling and cell cycle progression.

- Thus, interference in androgen metabolism, and inhibition of growth factors and cytokine activity, appear to be the major pathways through which Lycopene inhibits prostate and breast cancer growth.
- Studies using human and animal cells have identified a gene, connexin 43, correlated with reduced indexes of neoplasia, and whose expression is unregulated by Lycopene and which allows direct intercellular gap junctional communication, thereby reducing the rate of proliferation.
- Lycopene has also been shown to interfere in lipid metabolism, lipid oxidation and corresponding development of atherosclerosis.
- Lycopene treatment has been shown to cause a 73% suppression of cellular cholesterol synthesis in J-774A.1 macrophage cell line, and augment the activity of macrophage LDL receptors.
- Oxidized LDLs are highly atherogenic as they stimulate cholesterol accumulation and foam cell formation, initiating the fatty streaks of atherosclerosis.
- LDL susceptibility to oxidative modifications is decreased by an acyl analog of platelet-activating factor (PAF), acyl-PAF, which exerts its beneficial role during the initiation and progression of atherosclerosis.
- A combination of purified Lycopene (5mmol/l) with  $\alpha$ -tocopherol in the concentration range of 1–10mmol/l resulted in a significant greater inhibition of in vitro LDL oxidation, than the expected additive individual inhibitions.



- In this study, purified Lycopene was also shown to act synergistically with other natural antioxidants like the flavonoid glabridin, the phenolics rosmarinic acid and carnosic acid, and garlic in inhibiting LDL oxidation in vitro.
- These observations suggest a superior antiatherogenic characteristic of tomato oleoresin over pure Lycopene.
- The combination of Lycopene with other natural antioxidants, as in tomatoes, may be more potent in inhibiting lipid peroxidation, than Lycopene per se.
- Interestingly, whereas limited in vitro studies show convincing antioxidant and anticarcinogenic effects of Lycopene, animal studies and several clinical trials report beneficial effects following consumption of tomato products containing Lycopene.
- There exists limited in vivo data on the effects of Lycopene per se. In this review, we will summarize the effects of Lycopene supplementation, as tomato products or purified Lycopene, on biomarkers of oxidative stress and carcinogenesis in clinical trials, with supporting epidemiological observations on dietary and plasma Lycopene levels and the reduced incidence of certain types of cancer.

### **EXTRACTION METHOD OF LYCOPENE (FROM GUAVA)**



- **Principle.**

- Guava paste is dehydrated with methanol & Lycopene is extracted from residue with methanol carbon tetrachloride.
- The crude product is crystallized twice from benzene by the addition of methanol giving Lycopene of 98-99% purity.
- Further purification is achieved by a chromatographic procedure using calcium hydroxide as adsorbent.

### **EXTRACTION PROCEDURE (FOR GUAVA FRUIT)**

- Canned guava paste 50mg in 3litre wide mouth bottle is dehydrated by adding 65ml methanol.
- The mixture is immediately shaken vigorously to prevent formation of hard lumps.
- A small sample of suspension is tested by hand if it has a glutinous consistency more methanol is added to main portion to avoid possible clogging of filters.
- The mixture is allowed to stand for 1-2 hrs & is then shaken.
- The thick suspension is filtered on Buchner funnel.
- The yellow filtrate is discarded.
- The dark red cake is returned to bottle & shaken with mixture of 35ml methanol & 35ml carbon tetrachloride.
- The stopper of the bottle must fit well & should be lifted for a moment after the mixing, to release built a pressure, brief shaking followed by opening of bottle as repeated until no more excess pressure is noticed.
- The suspension is shaken for 10-15 minutes & separate by filtration on large Buchner funnel.
- The filtration consists of a lower dark red carbon tetrachloride phase & orange aqueous methanolic layer.
- The slightly colored guava residue is crushed by hand to form uniform powder.
- It is re-extracted with 35 ml of each solvent as describe the suspension is filtered.
- The filtrate is combined with the methanol layer is transferred to 2ltr. White emulsion appears as upper phase.

- If the emulsion is reddish it is stirred with glass rod until the droplets of carbon tetrachloride join the lower layer.
- The phases are separated and carbon tetrachloride is wash with water.
- The carbon tetrachloride solution is drain in 1ltr. Erlenmeyer flask and dried over anhydrous sodium sulphate.
- The extract is poured in 1lit RBF.
- The solvent is evaporated with water pump to about 5 ml in water bath as 60°C.
- The solution is transferred to similar flask of 10 ml capacity using few ml of carbon tetrachloride.
- The solvent is removed completely in vacuum leaving a dark oily residue which is diluted with few ml of benzene and evaporated again to remove carbon tetrachloride completely.
- The partly crystalline dark residue is transferred with 1 ml benzene to a 25 ml of Erlenmeyer flask.
- The flask is immersed in hot water.
- Boiling methanol is added in portion using dropper to benzene solution with stirring until 1 ml methanol has been introduced.
- The crystals of crude Lycopene begin to appear.
- The crystallization is completed by keeping the liquid at room temperature and then in ice water after 1 to 2 hrs. The crystals are collected on small Buchner funnel and washed with 2ml boiling methanol.
- The Lycopene crystals are transferred to 10ml centrifuge tube the last portion being removed from funnel with small quantity of boiling benzene.

- Benzene is added to centrifuge tube to make up volume to 1ml. the crystal are dissolved by dipping tube in to hot water and stirring the contents when clear solution is obtained, boiling methanol is introduced in small portion with dropper.
- The solution is stirred with glass rod until crystals begin to appear.
- The centrifuge tube is kept at room temperature for short time then in ice bath more methanol is added in small portion with stirring to cold solution.
- The volume of methanol present should not exceed 1ml the mixture is allowed to stand for two hours in ice bath and crystals separated by brief but strong centrifuging.
- The mother liquor is decanted.
- The crystals are treated in centrifuged tube with 1ml boiling methanol.
- The mixture is stirred and methanol is removed by centrifuging before its cools.
- The methanol is decanted and washing is repeated at least two times more, if crystallization and purification were satisfactory long red Lycopene prisms are observed under microscope.
- The centrifuge tube and its contents are dried in vacuum at room temperature for few hours and then weighed yield which is depend on quality of guava pastes about 15mg.

### **BIOAVAILABILITY OF LYCOPENE**

- Although 90% of the Lycopene in dietary sources is found in the linear, all-trans conformation, human tissues (particularly liver, adrenal, adipose tissue, testes and prostate) contain mainly cis-isomers. A dietary supplementation of tomato puree for 2 weeks in healthy volunteers led to a completely different isomer pattern of plasma Lycopene in these volunteers, versus those present in tomato puree. 5-cis, 13-cis and 9-cis-Lycopene isomers, not detected in tomato puree, were predominant in the serum

- Analysis of plasma Lycopene in male participants in the Health Professionals Follow-up Study revealed 12 distinct cis-isomers and the total cis-Lycopene contributed about 60–80% of total Lycopene concentrations.
- Studies conducted with lymph cannulated ferrets have shown better absorption of cis-isomers and their subsequent enrichment in tissues.
- Physiochemical studies also suggest that cis-isomer geometry accounts for more efficient incorporation of Lycopene into mixed micelles in the lumen of the intestine and into chylomicrons by the enterocyte.
- Cis-isomers are also preferentially incorporated by the liver into very low-density lipoprotein (VLDL) and get secreted into the blood.
- Research has shown convincing evidence regarding the isomerization of all trans-Lycopene to cis-isomers, under acidic conditions of the gastric juice.
- Incubation of Lycopene derived from capsules with simulated gastric juice for 1 min showed a 40% cis-Lycopene content, whereas the levels did not exceed 20% even after 3hr incubation with water as a control.
- However, when tomato puree was incubated for 3hr with simulated gastric juice, the cis-Lycopene content was only 18%, versus 10% on incubation with water.
- Thus, gastric pH and food matrix influence isomerization and subsequent absorption and increased bioavailability of cis-Lycopene.
- The process of cooking which releases Lycopene from the matrix into the lipid phase of the meal increases its Bioavailability, and tomato paste and tomato puree are more bioavailable sources of Lycopene than raw tomatoes.
- Dietary fat has been shown to promote Lycopene absorption, principally via stimulating bile production for the formation of bile acid micelles.

- Consumption of tomato products with olive oil or sunflower oil has been shown to produce an identical bioavailability of Lycopene, although plasma antioxidant activity improved with olive oil consumption, suggesting a favorable impact of monounsaturated fatty acids on Lycopene absorption and its antioxidant mechanism
- In an attempt to study Lycopene metabolism, developed a physiological pharmacokinetic model to describe the disposition of Lycopene, administered as a tomato beverage formulation at five graded doses (10, 30, 60, 90 or 120mg) in healthy men.
- Blood was collected before dose administration and at scheduled intervals until 672hr. The overall results of this study showed that independent of dose, 80% of the subjects absorbed less than 6mg of Lycopene, suggesting a possible saturation of absorptive mechanisms.

### **STABILITY OF LYCOPENE**

- Lycopene is susceptible to chemical changes such as oxidation followed by degradation or isomerization when exposed to light, heat and oxygen.
- Lycopene present in extracted material from Guava fruit was shown to be stable under storage at 4°C and room temperature when tested over a time period ranging from 01 to 37 months.
- Lycopene stability was assessed for extracted material from Guava fruit using spectrophotometer and HPLC.

## **PHARMACOKINETICS**

- Lycopene is available in nutritional supplements in the form of an oleoresin, in phospholipids complexes and in oils.
- In foods, Lycopene exists as part of a matrix (in chloroplasts or chromoplasts) within the vegetables or fruit.
- The efficiency of absorption of Lycopene from supplements and foods is variable.
- The efficiency of absorption of Lycopene from tomatoes, in which Lycopene is tightly bound within the matrix, is low.
- It is much higher in processed tomato products.
- The improved availability of Lycopene from processed foods is due to its release from the ruptured plant cells following the mechanical and thermal processing, as well as heat induced-trans to cis isomerization.
- Cis-Lycopene is reported to be more bioavailable than trans-Lycopene.
- Lipids increase the absorption of Lycopene.

## **DISTRIBUTION OF LYCOPENE IN HUMAN BODY**

- For example, the combination of tomato sauce and olive oil delivers more absorbable Lycopene than tomato sauce without oil.
- Lycopene from supplements or from the matrices of foods is either solubilized in the lipid core of micelles (formed from bile salts and dietary fat) in the lumen of the small intestine or forms clathrate complexes with conjugated bile salts.
- Micelles and clathrate complexes deliver Lycopene to the enterocytes.



Lycopene is released from the enterocytes into the lymphatics in the form of

chylomicrons.

<b>Tissue</b>	<b>nmol/g</b>
<b>Liver</b>	<b>1.28–5.72</b>
<b>Kidney</b>	<b>0.15–0.62</b>
<b>Adrenal</b>	<b>1.9–21.6</b>
<b>Testes</b>	<b>4.34–21.4</b>
<b>Ovary</b>	<b>0.25–0.28</b>
<b>Adipose</b>	<b>0.2–1.3</b>
<b>Lung</b>	<b>0.22–0.57</b>
<b>Colon</b>	<b>0.31</b>
<b>Breast</b>	<b>0.78</b>
<b>Skin</b>	<b>0.42</b>

- Lycopene is transported by the lymphatics to the general circulation via the thoracic duct.
- In the circulation, lipoprotein lipase hydrolyzes much of the triglycerides in the chylomicrons, resulting in the formation of chylomicron remnants.
- Chylomicron remnants retain apolipoproteins E and B48 on their surfaces and are mainly taken up by hepatocytes and to lesser degrees by other tissues.
- Within hepatocytes, Lycopene is incorporated into lipoproteins.

- Lycopene is released into the blood from the hepatocytes in the form of very-low density lipoproteins (VLDL) and low-density lipoproteins (LDL).
- In the plasma, VLDL is converted by lipoprotein lipase to LDL.
- Lycopene is transported in the plasma predominantly in the form of LDL
- This report details the findings of a single-dose Phase I pharmacokinetic and toxicity study of a food-based formulation of Lycopene in healthy adult male subjects.
- Five dosing groups (n=5 per group) were sequentially treated with increasing doses of Lycopene ranging from 10 to 120mg. Blood samples were collected for a total of 28 days (672hr) after administration of single doses of Lycopene.
- The mean time ( $t_{max}$ ) to reach maximum total Lycopene concentration ( $C_{max}$ ) ranged from 15.6 to 32.6hr.
- The  $C_{max}$  for total Lycopene ranged between 4.03 and 11.27 $\mu$ g/dl (0.075–0.210 $\mu$ m). Mean AUC 0–96 and elimination half-life for total Lycopene ranged from 214 to 655 $\mu$ g h/dl (3.986–12.201 $\mu$ mol h/l) and 28.1 and 61.6hr, respectively.
- The changes observed in Lycopene exposure parameters (e.g.,  $C_{max}$  and AUC 0–96) were not proportional to increments in dose, with larger increases observed at the lowest end of the dosing range (10–30 mg).
- Chylomicron Lycopene was measured during the first 12 h with the differences observed among the dosing groups not reaching statistical significance.
- These findings may reflect a process of absorption that is saturable at very low dosing levels or may be explained by the large interindividual variability in attained Lycopene concentrations that were observed within each dosing group.

- Pharmacokinetic parameters for trans- and cis-Lycopene isomers were calculated and are reported here.
- The formulation was well tolerated with minimal side effects, which were mainly of gastrointestinal nature and of very low grade.

### **MARKETED PRODUCT'S**

#### **Prostate Power Rx**

Formulated by Ray Sahelian, M.D.

With Saw Palmetto, Pygeum, Stinging Nettle, Lycopene and important Ingredients for support of normal prostate size.

Prostate Power Rx is carefully formulated with important herbs and nutrients to provide optimal prostate health.





## DOSE SCHEDULE OF LYCOPENE

### ❑ For Exercise – Induced asthma

#### ❖ Adult (Aged 18 or Older)

- A dose of 30 milligrams daily by month has been reported in scientific studies.

#### ❖ Children (Younger than 18 Years)

- The Dosing and Safety of Lycopene have not been studied thoroughly in children and Lycopene cannot be recommended for any use.

❑ For Atherosclerosis

❖ Adult (Aged 18 or Older)

- A dose of 1.243 grams of 6 % Lycopene daily by mouth has been reported in scientific studies.

❑ For enhancement of Immune function

❖ Adult (Aged 18 or Older)

- A dose of 13.3 milligrams of Lycopene daily by mouth has been reported in scientific studies.

❑ For Sun Protection

❖ Adult (Aged 18 or Older)

- A dose of 8 milligrams of Lycopene in combination with other antioxidant taken by mouth for 12 weeks has been studied for sun protection.

❑ For Infertility

❖ Adult (Aged 18 or Older)

- A dose of 2000 micrograms has been taken by mouth

### **SAFETY ISSUES OF LYCOPENE**

- Lycopene is to be a safe supplement, as evidenced by the fact that felt comfortable giving it to pregnant women.
- One evaluation of the literature concluded that long term use of Lycopene should be generally safe in doses up to at least 75 mg. per day.
- Maximum safe dosages for Young Children's, pregnant or nursing women or those with severe or kidney diseases have not been established.

➤ Note :

- ✚ Pregnant women should consult with a Physician before taking any herbs or supplement of Lycopene.

## **POTENTIAL DANGERS OF LYCOPENE**

### **☐ Allergies**

- People with allergies to Lycopene itself should avoid use.

### **☐ Side Effect**

- No Side effect has been reported from eating Lycopene based products. However, the safety of Lycopene supplements have not been well studied in humans.

## **DRUG INTERACTION**

- Interactions with drugs, supplements and other herbs product have not been thoroughly studied.
- Lycopene may increase the cholesterol – lowering effects of drugs such as Lovastatin (Mevacor) or use of drugs such as Lovastatin may decrease levels of Lycopene in the blood. This possible interaction has not been well studied.

- Other Drugs such as Cholestyramine (Questran, Prevalite) and Colestipol (Cholestid) as well as Nicotine and Alcohol.
- Red palm oil may increase blood level of Lycopene.

## USES OF LYCOPENE

### ❑ Blocks growth of cancer cells, Prevent heart disease

- ❖ Guava is a special carotenoid called Lycopene. For a long time, Lycopene took backseat to a related compound called beta-carotene. Lycopene even more powerful than beta-carotene. Lycopene may reduce lipid by inhibiting enzyme macrophage 3-hydroxy3-methyl glutaryl coenzyme reductaseA & by enhancing low LDL degradation.

### ❑ Cancer

- ❖ Oxidative stress is recognized as one of the major contributors to increased risk of cancer, and in chemical assays Lycopene is the most potent antioxidant among various common carotenoids. Lycopene has been found to inhibit proliferation of several types of human cancer cells. Carotenoid-containing plant products, such as Lycopene, exert a cancer protective effect via a decrease in oxidative and other damage to DNA in humans.



### ❑ Prostate Cancer

- ❖ High consumption or high circulating concentrations are associated with a reduction in risk of prostate cancer. Dietary Lycopene intake and both serum insulin-like growth factor-1 (IGF-1) levels and risk of prostate cancer. Lycopene prior to surgery has the potential to decrease the growth of prostate cancer. Lycopene inhibit human cancer cell growth by interfering with growth factor receptor signaling and cell cycle progression, specifically in prostate cancer cells.

### ❑ Breast Cancer

- ❖ Some studies have found a significant inverse association between Lycopene in breast tissue and breast cancer risk. Lycopene has been found to inhibit breast cancer tumors more efficiently

### ❑ Pancreatic cancer

- ❖ Dietary intake of Lycopene is associated with reduced pancreatic cancer risk.
- ❖ Although fruits and vegetables have been implicated in the etiology of pancreatic cancer, the role of phytochemicals in these food groups has received little attention to date.
- ❖ In this study, we investigated the possible association between dietary carotenoids and pancreatic cancer risk.
- ❖ The results of this study suggest that a diet rich in tomatoes and tomato-based products with high Lycopene content may help reduce pancreatic cancer risk.

#### ❑ **Other Hormone-related Cancers**

- ❖ Intake of dietary Lycopene may also play a role in the prevention of ovarian and cervical cancers. Lycopene intake was significantly and inversely associated with risk for ovarian cancer, predominantly in postmenopausal women. Women with higher levels of Lycopene in the blood were found to have a 33-percent decreased risk of developing cervical cancer.

#### ❑ **Diabetes**

- ❖ A study investigated the relationship between hyperglycemia and serum carotenoids, including Lycopene, and intake of vegetables and fruits rich in carotenoids, including Lycopene might be a protective factor against hyperglycemia.

#### ❑ **Other Clinical Indications**

- ❖ Studies have also investigated the relationship and/or use of Lycopene for cataracts, malaria, digestive-tract cancers, immune modulation, Alzheimer's disease. Patients with HIV infection or inflammatory diseases may have depleted Lycopene serum concentrations more clinically oriented research is indicated.

### CONCLUSION

The Lycopene, a precursor of carotenoid, present in regional Guava fruit is much higher than Tomatoes although it has been reported to be present in many of the fruits & vegetables having good antioxidant activity. Its antioxidant property is also investigated for cataracts, malaria, digestive-tract cancers, immune modulation, Alzheimer's disease. Lycopene is reported for its antiviral activity, blocking the Viral growth, It is also Suggested for Enzyme inhibition of Chronic diseases. Thus Lycopene is found to be promising additive ,and major component in Drug Discovery process.

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