Tomato Cuisines: A delectable rejoinder to threat of chronic ailments?

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ABSTRACT

With the advent of modern times, stress and pollution have led to major effect on rise of death toll due to chronic diseases. Such diseases are major cause of concern for the medical society. Lycopene, a carotenoid pigment found in tomatoes and its products has antioxidant properties due to the presence of numerous double bonds. Increased consumption of lycopene containing diet has been proposed to offer a protection against many types of cancers and cardio-vascular diseases. Its potential role as nutraceutical has been suggested in many studies. The present review deals with fundamental biochemistry, bio-availability and benefits of lycopene rich diet and its relation with some chronic diseases like various forms of cancers and cardiovascular diseases.

Keywords: ROS, antioxidants, Nutraceuticals, atherosclerosis, stroke, microRNA, lncRNA, RESSAS

INTRODUCTION

Apart from genetic factors, major chronic diseases such as obesity, diabetes, hypertension, chronic fatigue syndrome (CFS), Alzheimer's disease, ischemic injury and cancer, have been linked by many authors, to modern lifestyles and environmental factors. Reactive oxygen species (ROS) may be considered as metabolic pollutants which adversely affect cellular functions. Many environmental factors and xenobiotics also function for their increased production within the cell. Aerobic cells experience a continuous exposure of "oxidative stress" due to undesirable multidirectional oxidative reactions of ROS with vital cellular components such as DNA, membranes and proteins. Some theories also propose free radicals as the main offenders for cellular senility. Main ROs are: superoxide, singlet oxygen, hydrogen peroxide, hydroxyl radical, lipid peroxyl and peroxynitrite anion. Although considered as non-essential nutrients, anti-oxidants from a wide variety of herbal sources perform scavenging free radicals and protect the cellular machinery from oxidative damage. Some antioxidant systems also exist within the cell while others are accessible through food. Main dietary antioxidants are: Vitamin C, vitamin E, polyphenols (flavanoids), carotenoids (carotenes, lutien, zeaxanthin and lycopene), manganese, iodide and selenium. The present review describes the effects of lycopenes and their role as preventive anti-oxidant and their potential use as nutraceutical from risk of several chronic diseases[1,2,3].

DIETARY SOURCES

Lycopene is one of the widely plant pigments known as carotenoids, which act as photoprotective pigments in plants. Lycopene is deep red crystalline solid pigment which was first isolated from *Tamus communis* berries in 1873 by Hartsen. Lycopene is found naturally in fruits and vegetables that have color ranging from pink, red, scarlet or deep red. Some plants like asparagus, which do not have red color at all, also contains lycopene. Major sources of lycopene are : tomato (*Lycopersicon esculentum*), gac (*Momordica cochinchinensis*), autumn olive (*Elaeagnus umbellata*), wolfberry or goji (*Lycium barbarum*), red guava (*Psidium guajava*), watermelon (*Citrullus lanatus*), rosehip (*Rosa* spp.), seabuckthorn (*Hippophae* sps.) papaya (*Carica papaya*) and surinam cherry or pitanga (*Eugenia uniflora*). Gac fruit, which has restricted distribution in Southeast Asia, is known for its very high content (350-1900 mg/kg) of lycopene. Similarly autumn olive has higher content of lycopene than raw

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tomatoes. Tomatoes are the most common source of lycopene. Content is variable according to varieties and degree of ripening. Processed tomato products such as tomato sauce, ketchups, paste, soup and sun dried tomatoes have lycopene in different concentrations, from 60-1500 mg/kg.

CHEMISTRY AND BIOSYNTHESIS

Lycopene (6E, 8E, 10E, 12E, 14E, 16E, 18E, 20E, 22E, 24E, 26E) - 2, 6, 10, 14, 19, 23, 27, 31 – octamethyldotriaconta - 2, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 30 - tridecaene) is also known as γ, γ - carotene or *all-trans* lycopene [4]. Like other carotenoids, lycopene ($C_{40}H_{56}$) is derived from terpenoid synthetic pathway in plants. It is tetraterpene made up from eight isoprene units. Since it is lipid soluble, it is synthesized within chloroplast and thylakoid membrane. Lycopene is highly unsaturated hydrocarbon having 13 = bonds. *Cis* or *trans* isomers exist due presence of such double bonds. From more natural diets, it is obtained in all-*trans* form, which is then, may be converted to some *cis*-isomers by unknown *in vivo* mechanism.

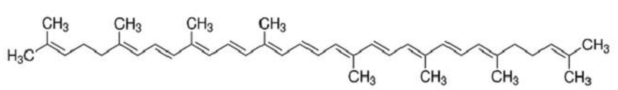

Figure 1. Structure of Lycopene

Lycopene can be synthesized by the mevalonic acid or by the methyl-erythritol phosphate pathway in plants. Like other terpenoids, biosynthesis start with formation of five-carbon units of isopentenyl pyrophosphate (IPP) and its isomer, dimethyl allyl pyrophosphate (DMAPP). Three molecules of IPP and one of DMAPP in the presence of the enzyme geranylgeranyl pyrophosphate synthase forms a 20 carbon terpenoid, geranylgeranyl pyrophosphate (GGPP). Apart from carotenoids, GGPP is also a precursor of gibberellins and chlorophylls. Two molecules of GGPP are joined (head to head) by phytoene synthase (PSY) enzyme to form phytoene (C_{40}). Phytoene is a molecule with nine double bonds, is further desaturated to lycopene which contains 13 double bonds by phytoene desaturase (PDS) enzyme. In bacteria, conversion of phytoene to lycopene is a single step process catalyzed by carotene desaturase (CRTI). In plants this process is completed in three steps catalyzed by PDS, ζ-carotene desaturase (ZDS) and carotenoid isomers (CRTISO) respectively.

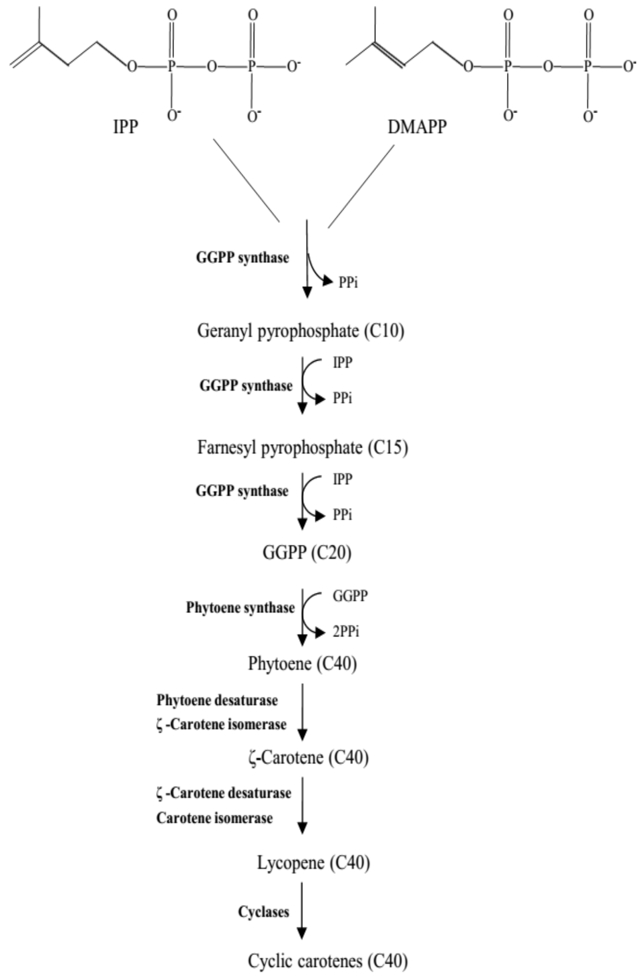

Figure 2. Biosynthesis of lycopene[10]

BIOCHEMISTRY, BIOAVAILABILITY & METABOLISM

Due to higher association of lycopenes to the food fibers and their lipid solubility, they are difficult to absorb through the gastro intestinal tract. Its absorption is largely dependent on the presence of fats in diet. So bile acids and emulsification of fats is required for their absorption. Aging and dietary fibers reduce the bio-absorption of lycopene. Presence of dietary fats in this way, enhance their bioavailability. Clinical conditions or drugs which reduce fat content in intestine, also negatively affect lycopene absorption. A sucrose ployester Olestra™, which is used as fat substitute in foods which normally have high fat content, is also have been used to demonstrate the effect of fat on absorption of lycopene. Lycopene is known to be carried into the blood stream with chylomicrons and LDLs. Food processing is known to increase its *cis* isomeric configuration. As contrary to beta-carotene, lycopene bioavailability is increased with heating during processing or cooking. Since lycopene formulations are highly expensive, some novel encapsulation techniques have been proposed to enhance its bioavailability. Lycopene loaded O/W (oil in water) emulsions can be produced. Similarly lycopene nanoparticles can be prepared by precipitation and RESSAS (rapid expansion of supercritical solution into aqueous solution) techniques. Lycopene can also be encapsulated using cyclodextrins.

THERAPEUTIC APPLICABILITY OF LYCOPENE

Antioxidant properties of lycopene have been demonstrated in vitro and cell cultures. Lycopene acts as H_2O_2 (hydrogen peroxide) and NO_2 (nitrogen dioxide) quenchers. Presence of numerous conjugated double bonds and its hydrophobic nature, attributes to antioxidant properties of lycopene. Numerous studies have suggested its role as a nutraceutical preventive measure for chronic diseases like various forms of cancer, heart diseases and diabetes. Diet related epidemiological and statistical studies have shown that tomato rich diet has protective effect against cancers of prostate, lungs and stomach. However, less significant effect has been shown for cancers of cervix, breast and colon. Several evidences suggest that lycopene and alpha carotene rich diet is associated with reduction of risk of cancers of prostate and lungs. A large body of research reports, however inconclusive, is available for the mode of action of lycopene. Most of *in vitro* studies in cancer cell line show that lycopene acts by reducing the effect of IGF-1 (insulin like growth factor 1) and arrests the cell cycle in G0/G1 phase by inhibiting phosphorylation of some key proteins. High serum levels of IGF-1 are found in several types of cancers. Apart from IGF-1, lycopene is also known to modify the levels of various growth factors like PDGF (vascular endothelial growth factor), EGF (epidermal growth factor) and PDGF (platelet-derived growth factor). Various signal transduction receptors and effector protein phosphorylation are affected by lycopene supplementation in diet[5]. Some of them are: PDGF R-beta (vascular endothelial growth factor receptor –β), ERK1/2 (extracellular signal regulated kinase 1/2), p38, and JNK (c-Jun N-terminal kinase). However, such evidences have been considered as “insufficient” for an approval of ‘qualified labeling’ by FDA.

LDLs (Low density lipoproteins) are modified by oxidation and such LDLs are known to be associated with CVDs (cardio-vascular diseases) [6]. Lycopene and other food related anti-oxidants have been suggested to have protective functions. Studies have shown a reduction of risk if the diet is supplemented with lycopene. Some epigenetic changes such as DNA methylation of promoter regions of some genes are associated with atherosclerosis. Such genes are superoxide dismutase, estrogen receptors and nitric oxide synthase [7,8,9]. Reports have identified links between LINE-1 methylation in heart diseases and modified levels of LDL [10]. Epigenetic regulation of CVD and stroke has been implicated by *micro-RNAs* and *long non-coding RNAs* (lncRNAs). Antioxidants work by suppressing the inflammatory markers in endothelium and influence development of CVDs. However, role of lycopene in such cases is remained to be established.

CONCLUSION

Free radicals have damaging effects on vital cellular components and a diet supplemented with antioxidants like lycopene and carotenes may have a protective role in chronic diseases. Tomatoes and its processed food products like sauces and ketchups are highly enriched with lycopene. Mediterranean diet is considered as beneficial for risk reduction of cancers as it contains tomatoes in most of its recipes. The highest amount of evidence existed for its role against cancers especially those of prostate and lungs. However, such studies are insufficient to reach any conclusion about the specific role of lycopene. The molecular bases of such claims are to be tested for its target sites of action and extant of protection it may confer, if any.

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