

Lycopene: Redress for Prostate Cancer

Sai Venkata Vedavyas Pisipati*, Harshavardhan Pathapati, Ganesh Bhukya, Suresh Nuthakki, Baburao Chandu, SreeKanth Nama and RajDev Adeps

Donbosco P.G. College of Pharmacy, 5th Mile, Pulladigunta, Kornepadu (V), Vatticherukuru (M), Guntur, Andhra Pradesh, Pin-522017, India.

ABSTRACT

Lycopene, a carotenoid is what that gives red colour to some fruits like pomegranate, tomato, papaya etc... People with a sound diet of lycopene may have a less risk of cancers especially prostate cancer which is most impedent for the males of age 40-50 years. So, in countries of north America and Europe food contains much of the lycopene supplements. In accordance with the American journal of epidemiology 2002 studies implies that men with crushed serum lycopene levels are more divulged to prostate cancer and those with sound diet of lycopene have a less risk of prostate cancer. In a care study conveyed by The British journal of urology, men with prostate cancer are subjected to surgery and the tumour is detonated. Amongst the men half a set were supplemented with lycopene supplements and half were not. Those subjected with lycopene supplements have less bone pains and live longer than those not supplemented. This paints a picture about importance of lycopene in treatment of prostate cancer. This article evokes the importance of lycopene and its way of destroying the cancer. Lycopene reduces the risk of cancer by diverging its effect on the plasma Insulin like growth factor, on Connexins, and the most acceptable one, by quench of free radicals.

KEY WORDS

Lycopene, Insulin like growth factor, Anti oxidant, conjugated bonds, Prostate cancer, Connexins.

received on 18-04-2012
accepted on 04-05-2012
available online 15-05-2012
www.jbclinpharm.com

1. INTRODUCTION:

Lycopene also commonly called as rhodopurpurin is a polyunsaturated hydrocarbon and is a tetraterpene tacked with eight isoprene units which has carbon and hydrogen only as the building blocks. It has a molecular formula $C_{40}H_{56}$ with a molar mass 536.87 gmol⁻¹[1] and is insoluble in water. Its eleven conjugated bonds afford it the deep red colour and are creditworthy for its antioxidant property[1]. The chemical structure of lycopene was shown in fig.1. Its deep red colour and non-toxicity evokes it as a good food supplement.

The eleven conjugated double bonds yeilds its anti oxidant activity. Only Trans forms are available in nature inspite of its stability and all the cis-forms are unstable. The cis-forms are available in sound in the human serum and all the trans-forms are converted to cis forms in the body.

A study published in the American Journal of Epidemiology in 2002[2] suggests that low concentrations of serum lycopene may be more strongly associated with aggressive prostate cancer. In their discussion, researchers state that their findings imply that disease progression may be especially susceptible to the protective effects of lycopene. This study was of particular importance because it included large numbers of US African Americans and they concluded that the results apply to this racial group. Among 72 studies identified, 57 reported that higher tomato intake or blood lycopene levels reduced the risk of cancer at a defined anatomic site; 35 of these associations were statistically significant. 23 the evidence for a benefit was strongest for cancers of the prostate, lung, and stomach[3].

According to European journal of clinical nutrition Supplementa-tion of tomato products, containing lycopene, has been shown to lower biomarkers of oxidative stress and carcinogenesis in healthy and type II diabetic patients, and prostate cancer patients, respectively. Processed to-mato products like tomato juice, tomato paste, tomato puree, and tomato ketchup and tomato oleoresin have been shown to provide bio- available sources of lycopene, with consequent increases in plasma lycopene levels versus baseline. Dietary fats enhance this process and should be consumed together with food sources of lycopene.

In congitation, a bird's eye view on prostate cancer must be essayed; Prostate cancer, seen in the prostate gland present in male reproductive system. The prostate cancer cells are very slow growing. Despite their slow growing some cancers may be aggressive. The cancer may metastasize into other parts of the body especially into the bones and lymph nodes. This may cause some potential symptoms. Pictorially the deviation between the affected prostate and normal prostate gland is shown in fig 2.

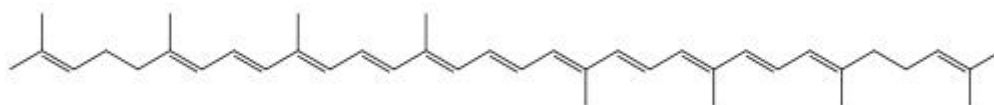
Prostate cancer have following groundses such as, Erectile dysfunctioning, Painful ejaculation.

2. PROSTATE CANCER SPIFFLICATING ACTIVITY OF LYCOPENE:

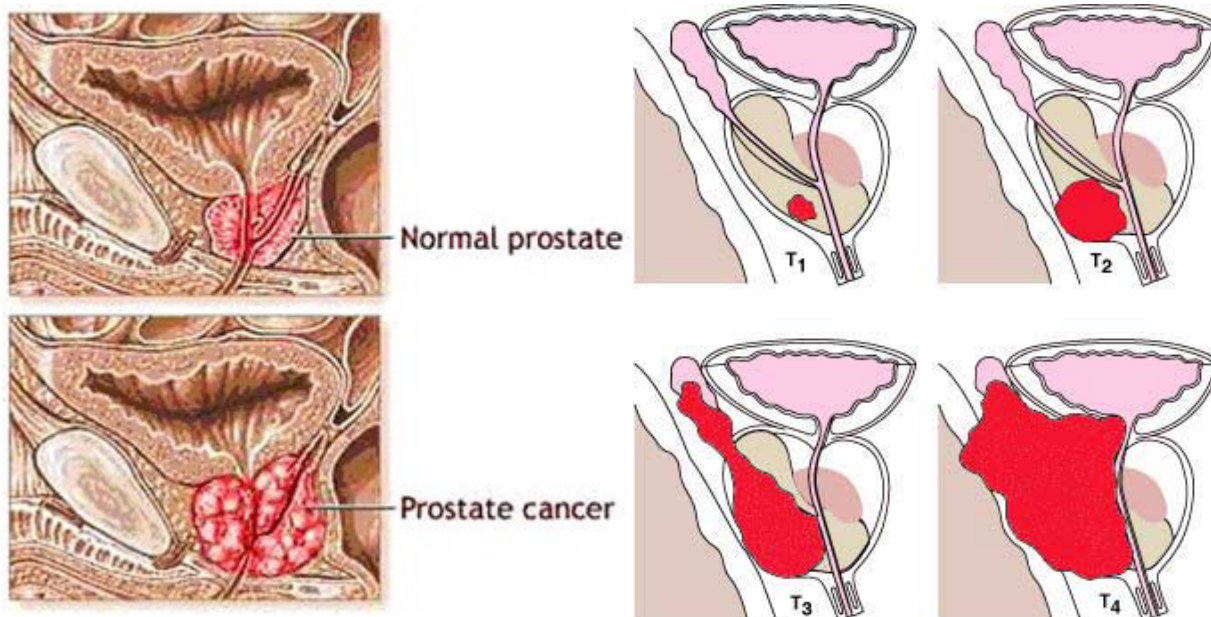
Lycopene's mechanism of action were explicated by three theories:

2.1. The first one reads as; lycopene reduces the Insulin Growth factor[2] levels which plays a key role in the tumour formation. It is elicited as,

Figure1: Skeletal Formula of Lycopene⁽¹⁾.



*Corresponding Author E-mail: manivedavyas.pisipati@gmail.com

Figure 2: Normal prostate and Cancer Prostate representation pictorially.

Insulin growth factor and growth hormone are colligated with each other. When growth hormone is secreted from the anterior pituitary part it induces the production of Insulin Like Growth Factor (IGF) by the liver and secretion of IGF inhibits the secretion of GH by feedback mechanism. IGF are proteins of high sequence similarity with the insulin [3] and has two cell surface receptors, IGF-1 & IGF-2 of which, IGF-1 is postulated here now. The theme of this article is not to highlight the structure and chemistry of IGF, but only to enlighten its role in the cell-proliferation and preventing apoptosis.

2.1.1. General Physiology Of INSULIN LIKE GROWTH FACTOR-1:

IGF-1 is a protein also called as Somatomedin C, is encoded by IGF-1 gene and the actions elicited by it are called as Non Suppressable Insulin Like Activity (NSILA). It is required in the childhood growth and cell proliferation.

IGF-1 evokes its activity by its binding to IGF-1 receptor (IGF1R), a Tyrosine Kinase Receptor which broaches intracellular signaling. IGF1 is the most virile stimulator of Akt signaling pathway [3-5] which is useful in cell proliferation and an inhibitor of programmed cell death i.e. apoptosis. Akt, also known as protein kinase B [5] is a serine/threonine protein kinase that fiddles a critical role in cell cycle and cell proliferation as follows:

Bcl-2 associated death protein (BAD) is involved in the cell apoptosis [6] and forms a heterodimer with B cell lymphoma 2 (Bcl-2) by triggering a Bax triggered apoptosis. Thus cell apoptosis is evoked. The de-phosphorylated BAD is active and evokes apoptosis. The Akt phosphorylates the BAD and thus dissects the BAD from the Bcl2 associated heterodimer complex thus inactivating its function of apoptosis [6].

2.1.2. Forbiddance of IGF1 activity by LYCOPENE:

As lycopene lowers the IGF1 levels in the body [7-10], the Akt signalling pathway is not activated and thus the BAD associated with Bcl2 complex is not dephosphorylated and thus BAD hetero dimer elicits its activity of apoptosis.

2.2. The second theory of action of Lycopene is as follows

Lycopene reduces the gap-junctional communication between the prostate cells. Thus, cells with increased junctional communication grow slower than those with reduced junctional communication.

2.2.1. CONNEXINS-The Gap Junctional Proteins:

Connexins are the gap junctional proteins [11]. There are different types of connexins such as, Cx33, 43, 50, 40, 33 [11] etc., of which each one has its own importance, but the one that is mired for cell proliferation is Cx43 [11], also known as Gap junction Alpha-1 protein [11]. This protein is encoded by GJA1 gene. The encoded protein forms a part of gap junctions between cells and are involved in the cell to cell diffusion of low molecular weight materials.

Studies of Zangh Y. et al on connexin 43 shows that cx43 expression levels influence the cell proliferation. Their studies conveyed that increased expression of Cx43 reduced the fibroblast proliferation and reduced expression of Cx43 increased proliferation [2].

In 2002, Kucuk and others discussed the effects of lycopene supplementation on localized prostate cancer patients. They've once again proved that was previously discussed by Zhang et al that lycopene increases the Gap junctional communication by the increasing expression of connexin 43 gene. 27 other studies also have essayed that upregulation of connexin gene 43 has been achieved by lycopene that increases gap junctional communication between tumour cells and thus reduces cell proliferation [2].

2.3. The third explication of mechanism of action of lycopene is its antioxidant property [13-17]. Lycopene is a potent antioxidant and the antioxidant property of lycopene is due to the eleven conjugated bonds in its structure. Free radicals are the by-product of cells. The free radicals can react with the cells and cause efficient damage to the cells. Studies of Chadstone shows that absence of Betaionone ring in the lycopene give it anti oxidant ability. It induces the Phase II detoxification enzymes that can eliminate the free radicals and thus essaying its anti oxidant activity. Lycopene has twice as high as beta-carotene ability to quench the free radicals. This is the most acceptable explication on the mechanism of action of lycopene. A review article in the "Journal of the American College

Figure 3: Food supplement for lycopene.

of Nutrition” explains that free radicals and cellular oxidative damage are associated with a number of chronic diseases of aging. Lycopene is very efficient at finding, capturing and cleaning up free radicals from the cellular environment thus preventing cancer.

3. OTHER IRREFUTABLE EFFECTS OF LYCOPENE [17]:

- Studies prove that it has been useful in lowering of hypertension, in particular mild hypertension.
- Naturally lycopene is useful in the production of vitamin A. So, it is also helpful in the improved eyesight.
- Lycopene it increases the High Density Lipid levels (HDL) which are useful for the absorption of Lower Density Lipids (LDL), thereby preventing atherosclerosis, hypercholesterolemia. As an anti oxidant it also helps cholesterol from being oxidised.
- Lycopene is also useful in treating oral leukoplakia, a condition which is precancerous mucous membrane condition, which is manifested by white patches.

4. FOOD SUPPLEMENTS FOR LYCOPENE [1] :

Lycopene, found in many fruits and vegetables especially in tomatoes and watermelon, which may play an important role in reducing risks of prostate cancer (fig. 3).

Other types of supplements such as those found in Acai, Goji, Noni, Pomegranate, Curcumin, Soy extracts, Artichoke, Asparagus, Barley grass, etc. Some of the sources rich in lycopene were shown in Table 1.

5. HANDINESS AND DOSAGE:

- Lycopene is formulated along with the multivitamins. They are formulated as capsules. An intake of 5-10 mg [17], few times a week is ample for the one who doesn't take much more vegetables or fruits. But, for those who have a decent diet of fruits and vegetables there isn't any need of running for the dietary supplements of lycopene.

6. RATIOCINATION:

Lycopene which is a carotenoid pigment has good irrefutable role in prevention of prostate cancer. Pragmatical approaches have adapted and leavened its vitality.

Table 1: List of food supplements and the amount of lycopene in Microgram/Gram wet weight [1].

Source	Microgram/gram wet wt
Gac	2000-2,300
Raw Tomato	8.8-42
Water melon	23-72
Pink Grape fruit	3.6-34
Pink Guava	54
Papaya	20-53
Apricot	<0.1

So considering all the above essays it is to be noted that lycopene consumption is important to prevent the carcinogenesis and it is proved in various studies as stated above. This article evokes that it is better to have lycopene supplements than to have a surgery and that is proved in the studies stated. Thus "PREVENTION MAY BE BETTER THAN CURE"

REFERENCES:

1. <http://en.wikipedia.org/wiki/lycopene>.
2. www.vitaminherbuniversity.com/topic.asp?categoryid=3&topicid=1096#top.
3. Michael N. Pollak, Eva S. Schernhammer, Susan et al... Insulin Like Growth Factors And Neoplasia. Nature Reviewers Cancer 4 July 2004; 505-518.

4. George Davey Smith, David Gunnell, Jeff Holly. A Potential Mechanism linking the Environment with Cancer. *BMJ* 2000; 321:347
5. Constantine S Mitsiades, Nicolas Mitsiades, Vassiliki Poulaki, et al.....Activation Of NF-kB And Upregulation Of Intracellular anti apoptotic Proteins Via The IGF/Akt Signalling In Human Multiple Myeloma Cells: Therapeutic Implications. *Oncogene* 2002; 21: 5673-5683.
6. Karleen M Nicholson, Neil G Anderson, The protein Kinase B /Akt Signalling Pathway In Human Malignancy. *Cellular Signalling* May 2002; 14(5): 381-395.
7. Dorien W.Voskuil, Alina Vrieling, Laura j.Van't Veer, et.al, Insulin Like Growth Factor System In Cancer Prevention:Potential Of Dietary Intervention Strategies. *Cancer epidemiology Biomarkers &prev* 2005; 14: 195-203.
8. Xunxian Liu, Jeffrey D. Allen , Julia T. Arnold et.al , Lycopene inhibits IGF-I signal transduction and growth in normal prostate epithelial cells by decreasing DHT-modulated IGF-I production in co-cultured reactive stromal cells. *Carcinogenesis* 2008; 29(4): 816-823
9. Vamsidhar MD*; Govindan, Ramaswamy MD* et.al, Insulin-Like Growth Factor and Lung Cancer. *Journal of Thoracic Oncology*: Sep 2006 ; 1(7): 607-610
10. Walfisch S, Walfisch Y, Kirilov E et.al, Tomato lycopene extract supplementation decreases insulin-like growth factor-I levels in colon cancer patients. *Eur J Cancer Prev* . Aug 2007; 16(4): 298-303
11. Andrew L Harris. Emerging Issues Of Connexin Channels:Biophysics Fills The gap. *Quarterly Reviews Of Biophysics* 2001; 34: 325-472.
12. <http://www.lef.org/protocols/prtel-138a.shtml>.
13. Craig W Hadley, Elizabeth C. Miller, Steven J. Schwartz et.al, Tomatoes, Lycopene And prostate Cancer:Progress And Promise. *Exp Biol Med* Nov 2002; 227(10): 869-880
14. Di Mascio p, Kaiser, Sies H .”Lycopene as the most efficient biological carotenoid singlet oxygen quencher. *Arch Biochem Biophys* Nov 1989; 274(2): 532-8.
15. <http://www.everydayhealth.com/prostate-cancer/tomatoes-and-lycopene.aspx>
16. Basu A, Imrhan V. “Tomatoes versus lycopene in oxidative stress and carcinogenesis: conclusions from clinical trials”. *Eur J Clin Nutr* 61 (3): 295–303. doi:10.1038/sj.ejcn.1602510. PMID 16929242.
17. www.raysahelian.com/lycopene.html.