To Our Readers

The current issue (26) of the Update Series consists of two manuscripts and a case study.

The first article is a review article which updates our existing knowledge regarding lycopene, an important pigment synthesized by some plants and microorganisms and its documented role in health promotion and disease prevention in human beings.

The second article on “fenugreek” attempts to review the studies conducted in human beings and experimental animals. It describes in detail some studies carried out on fenugreek in a leading institute of Nutrition in the country.

The thought provoking case study draws the reader’s attention to the practical problems encountered during breast feeding in early infancy and emphasizes that correct advice regarding feeding should be followed up with regular monitoring. The case has been described from the viewpoint of the dietitian who had been consulted for advice regarding feeding.

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The Role of Lycopene in Human Health Promotion and Disease Prevention

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INTRODUCTION

In addition to the genetic factor, there is a strong association between life style factors including diet and the risk of chronic diseases. International dietary guidelines recommend increased consumption of fruits and vegetables, rich in antioxidants, to prevent such diseases. Lycopene, a potent carotenoid antioxidant naturally present in some fruits and vegetables, is the focus of recent research as a strategic chemopreventive agent against degenerative diseases. The chemistry, bioavailability and its role in human health is addressed in this review.

CHEMISTRY AND BIOAVAILABILITY OF LYCOPENE

Lycopene is a natural pigment synthesized by some plants and microorganisms but not by animals and humans. Tomatoes and processed tomato products constitute the major sources of lycopene accounting for up to 85% of the total dietary lycopene 1. It is a highly unsaturated, straight-chained hydrocarbon containing a total of 13 double bonds of which 11 are conjugated 2. It is one of the most potent antioxidant.
In nature it is present predominantly in its all-trans iso-meric form. Upon thermal processing of raw tomatoes part of the all-trans lycopene is converted to its cis-configuration. Although the biological significance of lycopene isomerization is not yet fully understood, it is thought that cis-isomerization improves the absorption of lycopene 3. Recent studies have shown the absorption of lycopene to be significantly higher from processed tomato products compared to raw tomatoes.

Absorption of lycopene is mediated through the chylomicrons. Due to their lipophilic nature, lycopene, like the other carotenoids, is found to concentrate in the LDL and VLDL fractions of the serum 4. Recent studies have shown that lycopene is metabolized in the body. Two different metabolites of lycopene have so far been reported in the literature 5.

**LYCOPENE AND HUMAN HEALTH**

Epidemiological, experimental and human intervention studies all provide strong support to the role of lycopene in the prevention of several human diseases.

**Cancer:** Tissue culture studies utilizing different cancer cell lines, animal studies and epidemiological studies provide the main supporting evidence for the role of lycopene in cancer prevention 6. An inverse relationship between the consumption of tomatoes and tomato products and the incidence of prostate cancer was reported in 1995 7. In this study, a consumption frequency of 10 or more servings of tomato products per week, showed a 35% reduction in the risk of prostate cancer. In 1997 La Vecchia reported that the Mediterranean diet, rich in tomatoes and tomato products was responsible for the lower incidence of cancer in that region 8. In other studies serum and tissue levels of lycopene were shown to be inversely associated with the risk of breast cancer 9 and prostate cancer 7,10. In a recently published meta-analysis paper of epidemiological studies including dietary intake estimations of tomatoes and lycopene and the circulatory levels of lycopene in relation to the risk of cancer showed that out of a total of 72 studies reviewed, 57 showed an inverse association, and 35 of these inverse associations were found to be statistically significant 11.

Very little information is available about the status of lycopene and other anti-oxidants as well as oxidative stress biomarkers in cancer patients. In one study 12,13, significantly lower levels of serum and tissue lycopene but not other antioxidants were observed in patients with prostate cancer compared to their age matched controls. Protein oxidation in the cancer patients was found to be significantly higher. An inverse relationship was also observed between serum lycopene and prostate specific antigen (PSA) levels. In another study 14, consuming tomato sauce containing 30 mg lycopene per day for 3 weeks by patients with localized prostate adenocarcinoma resulted in significant increases in the serum and prostate lycopene levels and a reduction of serum PSA levels and DNA oxidation. In a recent study 15, when patients with diagnosed prostate cancer were given 15 mg of lycopene daily for three weeks prior to surgery, they showed higher levels of plasma lycopene and lower plasma PSA levels compared to the controls. Tumor volume was also found to be smaller in the treated group and the surgical stage of the tumors delayed. These observations suggest that lycopene may also play a role in the treatment of cancers.

**Cardiovascular Disease (CVD):** Oxidation of the circulating low-density lipo-protein (LDL) to oxidized LDL is thought to play a key role in the pathogenesis of CVD 16,17. Several epidemiological and prospective studies as well as in vitro, animal and human intervention studies have all shown that consumption of antioxidant vitamins such as vitamin E and b-carotene may reduce the risk of CVD 2,15,17. To date only a few such studies have been performed with lycopene. The evidence in support of the role of lycopene in the prevention of CVD comes primarily from epidemiological observations 18. Mediterranean regions with high intakes of tomato and tomato products have the lowest rates of CHD 19. Several studies have shown inverse association between blood levels of lycopene and the risk of CVD 18, 20-22. The strongest population-based evidence for the role of lycopene in CVD comes from a multicentre, case-control study (EUEAMIC) that evaluated the relationship between adipose tissue antioxidant status and acute myocardial infarction 23. In this study a total of 662 cases and 717 controls from 10 European counties were recruited. Needle aspiration biopsy samples of the adipose tissue taken shortly after infarction were used to measure a and b-carotenes, lycopene and a-tocopherol levels. After adjusting for other variables, only lycopene, and not the other antioxidants, were found to be protective against CVD. A more detailed analysis of the data from the Malaga region of the study showed significant inverse relationship between the risk of myocardial infarction and the adipose tissue lycopene levels 24.
Only a few human dietary intervention clinical trials studying the relationship between lycopene intake and CVD risk have so far been reported in the literature. In a small dietary supplementation study when 6 healthy human subjects consumd 60 mg/day of lycopene for a period of 3 months, a significant 14% reduction in their plasma LDL cholesterol levels was observed. In a randomized, cross-over dietary intervention study, 19 healthy human subjects, consumed 20 – 150 mg lycopene per day from tomato juice, tomato sauce and lycopene capsules for a period of one week. A significant increase in serum lycopene levels and lower levels of lipid, protein and DNA oxidation were observed. With the increase in serum lycopene levels, a significant reduction in LDL oxidation was also observed in this study.

**Osteoporosis:** There is evidence to suggest that oxidative stress caused by reactive oxygen species (ROS) is associated with the pathogenesis of osteoporosis. Epidemiological evidence suggests that certain antioxidants including vita-min C, E and b-carotene may reduce the risk of osteoporosis. However, there is a lack of reported studies in the literature evaluating the role of lycopene in osteoporosis. Recently, two in vitro tissue culture studies have been reported that investigated the effect of lycopene on bone resorbing osteoclasts. Lycopene was shown to inhibit osteoclastic mineral resorption, formation of tartrate resistant acid phosphatase positive (TRAP)+ multinucleated osteoclasts and the production of ROS by osteoclasts. Studies on the effect of lycopene in the bone forming osteoblasts are also limited to two reported studies. Kim et al showed that lycopene stimulated the proliferation of the osteoblast-like cell line, SaOS-2 cells. These findings are the first report on the effect of lycopene on human osteoblasts. A clinical study is currently being carried out to study the role of lycopene in postmenopausal women who are at risk of osteoporosis. In this study, the status of antioxidants and biomarkers of oxidative stress in postmenopausal women will be measured and correlated to the risk of osteoporosis. A dietary intervention study will then be undertaken to evaluate the role of lycopene in improving bone health and formulating guidelines for the intake of lycopene.

Although there is epidemiological evidence in support of the beneficial effects of tomatoes, the predominant source of lycopene, the direct role of lycopene has not yet been explored in the prevention of osteoporosis in the Mediterranean population. The effect of lycopene in osteoblasts and osteoclasts have been reported may provide evidence that lycopene may indeed be important for the prevention and management of osteoporosis.

**Hypertension, Male Infertility and Neurodegenerative diseases:** Increasingly, lifestyle and diet are being recognized as major risk factors associated with these diseases. In a recent study, lycopene supplementation of grade one-hyper-tensive patients for a period of eight weeks showed reduction of up to 10mmHg in the systolic blood pressure. This observation is considered to be significant in the dietary management of hypertension in view of the concentration of lycopene used and the relatively short period of treatment.

Oxidative stress has been suggested as an important contributory factor in male infertility. Significant levels of ROS are detectable in the semen of up to 25% of infertile men. To date, a small number of studies have evaluated the role of antioxidant vitamins such as vitamins C and E in male infertility. In general, these studies suggest a beneficial role of antioxidant therapy in the treatment of male-factor infertility. A limited number of studies are reported on the role of lycopene in male infertility. In one study, men with antibody-mediated infertility were found to have lower semen lycopene levels than fertile controls. In another recent study, 39 infertile male volunteers between the ages of 21-50 years consumed a daily dose of 8 mg lycopene in capsule form. After a 12-month follow up, it was reported that lycopene treatment resulted in significant increases in serum lycopene concentration, sperm motility index, sperm morphology and functional sperm concentration. The partners of 18 out of the 50 subjects had successful pregnancies, accounting for 36% success rate. Other studies are now in progress and their results will further advance our knowledge of the beneficial role of lycopene in male infertility.

Brain and the nervous system are particularly vulnerable to the free radical damage since the membrane lipids in brain contain high levels of polyunsaturated fatty acid side chains, which are prone to free radical attack. Brain also consumes large quantities of total oxygen for its relatively small weight, which contributes further to the formation of ROS. Several antioxidant vitamins and phytonutrient antioxidants have been studied for their role in various neurodegenerative diseases. Few studies have been reported in the literature showing lower levels of lycopene in patients with Parkinson’s Disease, vascular de-mentia and microangiopathy. In one study, a direct relationship was reported between high blood lycopene levels and a positive influence on the functional capacity of the elderly such as the ability to perform self-care tasks.
CONCLUSION

Oxidative stress plays an important role in the development of several chronic diseases. Antioxidants provide effective preventive strategy against the damaging effects of ROS. Lycopene, being the most potent natural antioxidant, has received considerable interest recently for its role in human health. The evidence so far in favor of the beneficial effects of lycopene is based primarily on epidemiological observations. In vitro cell culture and animal studies also support the role of lycopene in the prevention of human diseases. Human clinical intervention studies are now being reported increasingly in the scientific literature. Results from these studies will undoubtedly help further our understanding of the role of lycopene in disease prevention and its mechanisms of action. Based on the evidence to date, it would be prudent to include sources of lycopene such as tomatoes and tomato products as a regular part of a healthy diet.

REFERENCES

