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Review Article

Lycopene Promotes Bone Metabolism

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ABSTRACT

Lycopene is antioxidants and natural substance which found in large quantities in reddish color fruits, especially in tomatoes. Consuming lycopene, which is abundant in tomato plants and its products that made from tomatoes, reduce the risk and development of diseases like heart and cancer disease in several recent studies, in addition, lycopene levels in the blood and tissues are reversely related to these chronic diseases, however, studies and researches on the effects of lycopene on bones are rare. Lycopene can prevent loss of bone, especially, there are many drugs used to treat osteoporosis, but this treatment causes harmful side effects. This review outlines the currently available studies on lycopene sources, structure and absorption. This review aims to summarize and investigation the effectiveness of lycopene on bone metabolism that include formation and resorption of bone through its effect on osteoblast cell, and Bone Mineral Density (BMD). Bone turnover signs in women after menopause were reviewed and hypotheses explores that its supplementation with lycopene would increase antioxidant capacity and decreasing oxidative stress parameters.

Keywords: Lycopene, Bone metabolism, Osteoblast cells, Osteoprosis.

INTRODUCTION

Lycopene is one of the major antioxidants and it is one of natural pigments known as carotenoids (Takashi, 2020). Lycopene is naturally occurs in red fruits and vegetables and some algae and fungi. The main origins of lycopene are in tomato as well as tomato based products. In the human diet, the presence and concentration of lycopene in tomatoes has been processed is often greater than in fresh tomatoes because the processed tomato is often involves concentrations via water loss (Bohm *et al.,* 2004). Many studies showed that lycopene in processed tomato products that treated by heat are more bioavailable than lycopene that occurs in fresh tomatoes. Ketchup contains 167.07 μ**g**/g whereas tomato, red, ripe raw (fresh) contains 25.73 μ**g**/g that shown in (Table 1) (Tonucci *et al.*,1995). Lycopene,which has the chemical formula $C_{40}H_{56}$, is a polyunsaturated hydrocarbon. Lycopene has a high potential as an antioxidant activity that can remove reactive oxygen species (Srinivasan *et al.*,2007). Lycopene from a major group of pigments called carotenoids; however, the lycopene has not the activity of provitamin A. The importance of this , that the body does not have the ability to transform lycopene into vitamin A. β-carotene and lycopene possess nearly identical structure; the main difference is that the β-ionone ring. This difference gave lycopene the ability to get rid of single oxygen as well as prevents damage to cellular structures and molecules in the body due to its distinct structure, which consists of eleven double bonds conjugated, in addition to that it does not contain circular groups Fig. (1) (Merve *et al.,* 2017). This one seemingly small difference results in lycopene possessing significantly stronger antioxidant capabilities (Tilman *et al.,* 2010). The useful properties of lycopene originate from the antioxidant properties primarily. The bioavailability of lycopene, its distribution in the human body, metabolism and excretion, and all its biological activities need to accumulate, and this needs research and necessary studies. (Gurpreet *et al.,* 2017).

Table 1: Lycopene content of foods rich in lycopene, shown in μg/g and per average serving size (Tonucci *et al.*, 1995)

Food	Average amount of lycopene	
	By weight (μg/g)	**Per average serving size (mg/serving)**
Grapefruit, pink/red, raw	14.19	3.26
Ketchup	167.07	2.51[b]
Pasta sauce	126.55	31.64
Papaya, raw	36.50	5.11
Pink guava, raw	54.00	8.91
Pizza sauce	127.10	7.75[a]
Rosehip	240.50	4.81[b]
Salsa	105.13	6.52[a]
Tomato, canned (puree)	217.54	54.39
Tomato, canned, stewed	40.88	10.42
Tomato juice	90.37	21.96
Tomato, paste	287.64	4.71[b]
Tomato, red, ripe raw	25.73	4.63
Tomato soup	53.45	13.04
Vegetable juice	96.60	23.38
Watermelon, raw	45.32	6.89

Serving sizes were calculated based on weight per 1 cup measure, unless indicated by [a] for ¼ cup or [b] for 1 tablespoon.

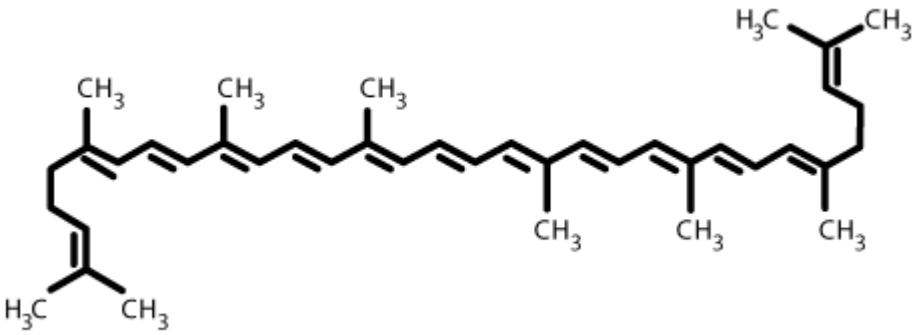

Fig. 1: structure of lycopene

The rate of absorption of carotenoids is low lie between ten to thirty percent of this amount, and the largest proportion of carotenoids is eliminated from the body through feces. The decrease in the rate of absorption of lycopene and the increase in the rate of excretion outside the body are partly due to the fact that it binds closely with large molecules and forms protein complexes in foods, and the separation of carotenoids from these complexes occurs when exposed to heat (Conrad and Gan, 2007). Lycopene is more lipophilic, because the lycopene is non-polar compound carried only by low density lipoprotein (LDL). The deeply position of lycopene in LDL molecules responsible for it is taken up by the tissue (Carroll *et al.*,2000). Because lycopene is lipophilic, it tends to accumulate in the tissues of the body and is more concentrated in the liver, prostate, adrenal glands and testes organs, and its concentration is approximately 80% in the adrenal gland and testes which is higher than in the liver tissues. The general mechanisms of carotenoids, believed to influence the prevention of the development of chronic diseases and oxidative damage in biological systems, including damage to cell membranes and structures such as DNA and proteins, as well as lipids (Tapiero *et al.,* 2004). The damage results from exposure to free radicals, and these molecules contain a single electron in the farther shell of the atom (Ismail, 2021; Rana, 2022). The action of lycopene through its oxidative capacity in reducing oxidative damage and bone turnover indicators (Lobo *et al.,* 2010). Carotenoids play a major role in regulating and influencing bone metabolism (Xiang-Dong, 2012). Carotenoids are often referred to by their oxidative properties by ridding the body of reactive oxygen species (Andrew and Gordon, 2018). Some European studies have shown, that carotenoids intake enhance bone mineral density and prevents the risk of osteoporosis (Jiuhong *et al.,* 2017). Lycopene is one of the most important and highest antioxidant compounds and has the ability to protect tissues and cells by eliminating free radicals (Jalil and Habib, 2015). Dietary lycopene as well as its supplements can be of benefit in preventing the development of a number of chronic diseases such as heart diseases and cancer, as well as lycopene has positive effects on neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease as well as the effects of carotenoids on immune cells such as its effect on T and B lymphocytes cells, as well as through its effect on natural killer cells and macrophages (Erica *et al.,* 2010; Singh and Goyal, 2008). Despite of all this, there is a lack of laboratory and clinical studies on the influence of lycopene and lycopene-rich foods that affect and prevent bone loss (Przybylska, 2020). Because of most previous studies and researches concentrated on the role of calcium and proteins only ,and there importance on bone health. Recent studies confirmed the importance of vegetables and fruits on bone health (Susan *et al.,* 2000).

1. Lycopene promotes osteoblast cells

Osteoblasts are the cells responsible for the formation of new bone, which derives from the bone marrow, which forms new bone called "osteoid"; this new bone consists of collagen and some proteins and is responsible for the deposition of minerals and calcium (Rinaldo *et al.,* 2015; Zorab and Salih, 2021). In 2003, a study explored the effect of lycopene, which is abundant in tomato and its product, on the proliferation and differentiation of osteoblasts and these cells responsible for bone formation (Linda *et al.*, 2003). In respect to influence of lycopene on osteoblast cells; in 2018, a laboratory study showed the effect of antioxidant lycopene on human-like osteoblast cells by Gene Expressions of Type 1 collagen (COL- 1) and Real Time Cells Analysis (RTCA) system, Growth Differentiation Factor- 5 (GDF- 5) and Osteocalcin hormone. Depending on the dose of lycopene which was given in this research, the human like osteoblast cells were proliferated when compared with the control group (Bengi *et al.,* 2018).

2. Lycopene promotes mineral bone density (BMD)

Measure of Bone Mineral Density (BMD) is typically performed by dual X ray absorptiometry (DXA), which provides a static, complete measure of the skeletal status. Bone Mineral Density is measured in different locations of the skeleton such as the spine, hip and wrist. Central DXA of the hip and spine provides the best predictive evidence for fracture risk (Glen and Ignac, 2007; Muhamad *et al.,* 2021). In 2003, a study showed that lycopene improved bone mineral density, showing a relationship and positive results between eating vegetables and fruits and bone health. This study showed the positive relationship between retinol and carotenoids. The research was conducted on 68 men and 137 women, when one group of Australian population was consumed vegetables and fruits containing phytonutrient. The intake of lycopene led to an improvement in the total bone mass of the body, as well as an improvement in the lumbar spine for men, as well as lycopene, lutein and zeaxanthin ingested in premenopausal women, while there is an improvement and a positive relationship between taking β-carotene and bone mass in the lumbar spine in postmenopausal women and hence this study suggests the positive relationship between the consumption and intake of fruits and vegetables through dietary carotene and bone health through anti-oxidation mechanisms (Naiyana *et al.,* 2003). In another study published in 2014, its study showed the important influences of lycopene as an antioxidant in reducing oxidative stress in growing female rats. The contained of lycopene in the diet that received to female rats (1.5 months old) in study was 0, 50 and 100 ppm. The results showed that taking of lycopene led to an increase in the bone mass of the body, lumbar spine and proximal tibial metaphysis in the 100 ppm group, and an increase in the activity of bone-alkaline phosphatase in the 100 ppm group more than in the 0 ppm group. The conclude from this study that taking lycopene helps and facilitates the process of bone formation and reduces and prevents bone resorption, which subsequently leads to an increase in BMD in growing female rats (Yuki *et al.,* 2014).

3. Lycopene and osteoporosis

Osteoporosis is a common disease that affects millions of people around the world (Tümay *et al.,* 2017; Hamdoon *et al.,* 2020). Osteoporosis (OP) it's a systemic disease, characterized by decrease of minerals in bones, as well as a decrease in the fine structure of the bone, and this leads to bone fragility and fractures. Although, the current treatments used to treat osteoporosis are effective and achieve an improvement in bone mineral density and reduce fractures, but most patients don't take these therapy because of their side effects (Aasis *et al.,* 2010; Al-Hashemi *et al.,* 2013). Therefore, require to treat osteoporotic patients safely. New treatments are free from any adverse effects, several scientific evidence points to the use of plant food compounds that prevent bone loss or osteoporosis were documented, especially those demonstrated to the postmenopausal women (Prentice, 2004; Marcellus *et al.,* 2021; Rao and Rao, 2018; Rao and Ali, 2007). In 2009, a study was conducted to investigate the protective effect of lycopene intake

and total carotenoids and its effect on reducing and preventing fractures that occur in the hip bones. This study was conducted over 17 years of patients with osteoporosis in Framingham. The study concluded the protective role of various carotenoids on bone health in the elderly (Shivani *et al.*, 2009). In 2020, there was a study examined the influence of lycopene on osteoblast cells in addition the BMD and bone turnover markers in postmenopausal women showed the effect of lycopene on several important pathways and bone-specific markers, including Wnt/β-catenin, ERK 1/2, alkaline phosphatase, RUNX2, RANKL and COL1A of Saos-2 pathways. The results showed the effect of lycopene to prevent reduction of bone density in postmenopausal women (Russo *et al.*, 2020). Later, in 2020, the potential effect of lycopene to reduce and prevent loss of bone in postmenopausal women was included bone biology and pathophysiology of osteoporosis (Umani *et al.*, 2020).

CONCLUSIONS

The action of phytochemical constituents of lycopene and their roles as antioxidants in reducing oxidative stress and bone turnover, which reduce the risk of osteoporosis, especially in older women after menopause. Based on research and studies, the consumption of lycopene for women improves bone health, which includes improving osteoblast cells and Bone Mineral Density (BMD).

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اللايكوبين يعزز ايض العظام

الملخص

يعد اللايكوبين من مضادات الأكسدة وهو مركب طبيعي يوجد بكميات كبيرة في الثمار ذات اللون الأحمر وخاصة في الطماطم. ان استهلاك اللايكوبين المتواجد بكثرة في الطماطم والمنتجات المصنعة من الطماطم وجد بانها تقلل من خطورة وتطور الامراض المزمنة مثل امراض القلب والسرطان في العديد من الدراسات الحديثة، فضلا عن ارتباط مستويات اللايكوبين الموجودة في الدم والانسجة ارتباطا عكسيا بهذه الامراض المزمنة، و مع هذا فان الدراسات والابحاث حول تأثيرات اللايكوبين على العظام نادرة. يمكن أن يمنع تناول اللايكوبين فقدان العظام، خاصة ان هناك العديد من العلاجات المستخدمة لعلاج هشاشة العظام ومع ذلك تسبب هذه العلاجات اعراض جانبية ضارة. توضح هذه المراجعة الدراسات المتوفرة حاليًا حول مصادر اللايكوبين وتركيبه وامتصاصه، وكان هدفنا من هذه المراجعة تلخيص واستقصاء تأثيرات اللايكوبين على ايض العظام التي تشمل تكوين العظام وارتشافها من خلال تأثيره على خلايا بانيات العظام وايضا تأثيره على الكثافة المعدنية للعظام وعلامات تحول العظم عند النساء بعد سن اليأس واستكشاف الفرضيات، بأن مكملات اللايكوبين ستزيد من قدرة مضادات الأكسدة مع تقليل عوامل الإجهاد التأكسدي.

الكلمات الدالة: اللايكوبين، ايض العظام، خلايا بانيات العظم، هشاشة العظام.