JABS Journal of Applied Biological Sciences 5 (2): 81-84, 2011
ISSN: 1307-1130, E-ISSN: 2146-0108, www.nobel.gen.tr

Does Lycopene Decrease the Inflammation in Airway Epithelial Cells?

Ahmad SAEDISOMEOLIA[1] Ali Malekshahi MOGHADAM[2]

[1]Department of Nutrition and Biochemistry, School of Public Health, Tehran University of Medical Sciences, Tehran, IRAN

[2]Faculty of Veterinary Medicine, University of Tehran, Tehran, IRAN

*Corresponding Author
e-mail: a_saedi@tums.ac.ir

Received: April 05, 2011
Accepted: April 17, 2011

Abstract

The significance of airway inflammation in asthma has been completely understood. Oxidative stress also appears to play an important role in the pathophysiology of asthma. Lycopene as a potent antioxidant and anti-inflammatory agent is considered to inhibit airway inflammation in the asthmatics. The aim of current article is to review the latest evidences regarding the implication of lycopene in airway inflammation. For this purpose, published Papers in U.S. National Library of Medicine – National Institutes of Health (Pubmed) were reviewed. Evidences showed that lycopene can protect cells from inflammation via its redox-based property on suppression of nuclear factor-kappa B (NF-κB), which is a key nucleic factor that facilitates the production of inflammatory biomarkers. Therefore, it has been suggested that consuming fresh vegetables and fruits (especially tomato) as the sources of lycopene can help asthmatics to decrease airway inflammation.

Keywords: Antioxidant; Asthma; Inflammation; Lycopene; Nuclear factor- kappa B

INTRODUCTION

As antioxidants are reported to decrease the inflammation in the human body, it is aimed to review the latest evidences about the effects of lycopene on the inflammation in airway epithelial cells, especially in some inflammatory situations such as asthma. On the other hand, correlation among asthma, inflammation and oxidative stress was studied.

Inflammation is considerably increased in asthma

However, asthma is characterized by variable and reversible obstruction of airflow; it is considered as a chronic inflammatory disease [1]. It has been shown that even in the newly diagnosed asthmatics; there is an increased inflammation in the airways, which has been defined as increased number of inflammatory cells such as eosinophils, mast cells and macrophages [2]. Inflammation is a complex process, which initiated by tissue damage. Regardless of the type of tissue damage, multiple substances are released by the injured tissues causing dramatic secondary changes, which worsen the disease [3]. A wide range of mediators and immune cells are involved in the pathophysiology of asthma [4]. Many studies have confirmed an increased number of inflammatory cells including eosinophils, mast cells, T lymphocytes (T cells), neutrophils and macrophages in the bronchoalveolar lavage (BAL) of asthmatics [5]. The role of these cells in chronic airway inflammation is well known, specifically their ability to produce inflammatory biomarkers, which may affect the airways [2, 6]. However, the precise mechanism by which inflammatory cells and their mediators cause airway hyperresponsiveness in asthma remains unclear. Figure 1 shows the pathways of innate and acquired immunity, which are involved in the pathophysiology of asthma. The key role of neutrophils has recently been understood in the eosinophilic asthma [5]. Eosinophils are one of the inflammatory cells, which found in the epithelial and submucosal layers. It has been reported that 50% of asthmatic patients are attributed to the eosinophilic airway inflammation [5]. Activated eosinophils produce cytokines, which result in further production of cytokines by epithelial cells [6]. It has been shown that mast cells are increased in the bronchoalveolar lavage of asthmatics and they associate with severity of asthma [2]. It has also been reported that mast cells are immunoreactive to the some inflammatory biomarkers such as Interleukin (IL)-3, Interleukin (IL)-4, Interleukin (IL)-5, Interleukin (IL)-6 and Granulocyte-macrophage colony-stimulating factor (GM-CSF) [7]. It has recently been found that increased mast cells are located within airway smooth muscles [7]. Furthermore, it has been proposed that airway inflammation can be induced by exposure to the reactive oxygen species (ROS). On the other hand, ROS can be produced by epithelial cells, macrophages and/or neutrophils during inflammatory periods [8].

Oxidative stress is increased in the airway epithelial cells during asthma

Studies suggest that acute exacerbations of asthma are associated with increased oxidative stress [9]. In asthma; ROS are produced by the inflammatory cells such as neutrophils and eosinophils, when they are stimulated by triggers like allergens, viruses and air pollution [10]. Moreover, it has been reported that in asthma, oxidative stress is overwhelmed antioxidants [11]. Reactive oxygen species increase epithelial shedding, contraction of smooth muscle cells, functional impairment of beta-adrenoceptors, pulmonary vasoconstriction and the vascular permeability in the airway structures [12]. ROS may

also result in some pathological changes such as hardening of the airways, bronchial hyperreactivity and inflammation [12]. Catalase and glutathione peroxidise (GSH-Px) activities are decreased in asthma [13]. Indicators of free radical activity are also increased in the asthmatic children and adults. Therefore, there is an evidence for imbalance oxidants and antioxidants equilibrium in the patients with chronic and acute asthma [11].

Antioxidants may decrease inflammation

The nutritional status plays an important role in the susceptibility of body to the inflammation [14]. There are many findings about effects of antioxidants on nuclear factor- kappa B. This factor can increase the expression of selected cytokines and chemokines including IL-6 and Interleukin (IL)-8 and eventually promotes inflammation in the body [15]. As noted above, some of the antioxidants have an influential effect on NF-κB. Lycopene [15], vitamin C [16] and vitamin E [16] are shown to decrease the inflammation via their probable redox-based effect on NF-κB. On the other hand, studies have shown that inflammation considerably affects the level of some nutrients in blood serum [17]. During inflammation, the concentrations of vitamin A, vitamin E and carotenoids are decreased [17]. It has also been reported that the concentrations of serum α-carotene, β-carotene and lycopene are in the lowest phase in inflammatory situations [18]. In one study, it has been suggested that dietary supplementation with lycopene may be an effective approach to reduce the oxidative stress and improve the inflammatory status of colitis [19]. It has also been found that circulating levels of antioxidant nutrients have an inverse correlation with IL-6 and C - reactive protein (CRP) concentrations [18, 19]. It was previously reported by corresponding author that lycopene decreases release of IL-6 and Interferon gamma-induced protein 10 kDa (IP-10) (IP-10, is increased in viral infections), in cultured airway epithelial cells [20]. Probably, this effect of nutrients on inflammation is not exclusively restricted to the antioxidants, as the authors reported that docosahexaenoic acid (DHA), which is an omega-3 fatty acid, can decrease the release of some inflammatory biomarkers [21].

Lycopene; a potent antioxidant

The antioxidant activity of carotenoids can be ranked as follows: lycopene > α-carotene > β-cryptoxanthin > zeaxanthin = β-carotene > lutein [22]. Therefore, lycopene is the most powerful antioxidant among carotenoids [22]. Lycopene is a key antioxidant in tomatoes and tomato products [23].Studies have reported that higher plasma lycopene concentrations are associated with increased activities of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase and have also decreased lipid peroxidation biomarkers such as malondialdehyde (MDA) [24]. It has been shown that lycopene via its redox- based property, prevents cutaneous damage and nephrotoxicity due to gentamicin [23]. Some studies have shown that consumption of processed tomato products enhances plasma lycopene concentrations in association with reduced lipoprotein sensitivity to oxidative damage [25]. It has been proposed that other components in tomato have a synergistic effect with lycopene [26]. Corresponding author previously reported that lycopene usage is increased while cultured airway epithelial cells faced to lipid peroxidation [27]. Lycopene scavenges peroxyl radicals via special processes including "electron transfer", "allylic hydrogen abstraction" and "addition" [28]. Following equations show these mechanisms:

$$\text{Lycopene} + \text{ROO}^{\bullet} \rightarrow \text{Lycopene}^{\bullet+} + \text{ROO}^{-} \quad \text{(Electron transfer)}$$

$$\text{Lycopene} + \text{ROO}^{\bullet} \rightarrow \text{Lycopene}^{\bullet} + \text{ROOH} \quad \text{(Allylic hydrogen abstraction)}$$

$$\text{Lycopene} + \text{ROO}^{\bullet} \rightarrow \text{ROO Lycopene}^{\bullet} \quad \text{(Addition)}$$

Lycopene and inflammation

Lycopene as an anti-inflammatory agent [19] reduces inflammatory biomarkers *in vivo* [29] and *in vitro* [15]. The authors previously reported that lycopene decreases the production of two inflammatory biomarkers (IL-6 and IP-10), which may attribute to its redox-based activity [20]. As mentioned before, studies have shown that lycopene supplementation may reduce oxidative stress and improve inflammatory status in colitis [19]. It has also been reported that lycopene diminishes inflammatory signals in the lateral prostate lobes [30] and inhibits the expression of inflammatory agents in hyperhomocysteinemic rats [31]. The mechanism by which carotenoids decrease the inflammation is related to their redox-based action on suppression of NF-κB. NF-κB has an essential role in expression of many inflammatory biomarkers [32]. It has been found that β-carotene can inhibit NF-κB activity in the exposed cells [15]. Furthermore, it has been shown that lycopene can suppress NF-κB via decreased nuclear translocation of p65 subunit in lipopolysaccharide (LPS)-stimulated dendritic cells [15].

Applicable dietary approaches to decrease airway inflammation

Circulating levels of lycopene are in the lowest phase in asthmatics compared to healthy people [22]. As noted above, lycopene can reduce production of inflammatory biomarkers by cells via its antioxidant activity. Redox-based effect of antioxidants on suppression of NF-κB establishes an important link between antioxidants and inflammation [22]. Many studies showed the beneficial effect of antioxidant rich foods such as fruits and vegetables on prevalence rate of asthma. For example, in one study has been shown that there is a negative association between the intake of fresh fruits and asthma in adults [33]. It has been found that consumption of fresh fruits and vegetables in childhood may decrease the risk of asthma in adults [34]. Therefore, it seems that consuming a balanced diet can diminish inflammation and oxidative stress in airway cells of asthmatics. It is clear that this approach is not a substitute for patient's medication, which is prescribed by physician. Actually, scientists and researchers need to investigate more about the effects of different foods on inflammatory situations.

CONCLUSION

As inflammation is increased in asthma, consumption of potent dietary anti-inflammatory antioxidants such as lycopene is suggested in this disorder.

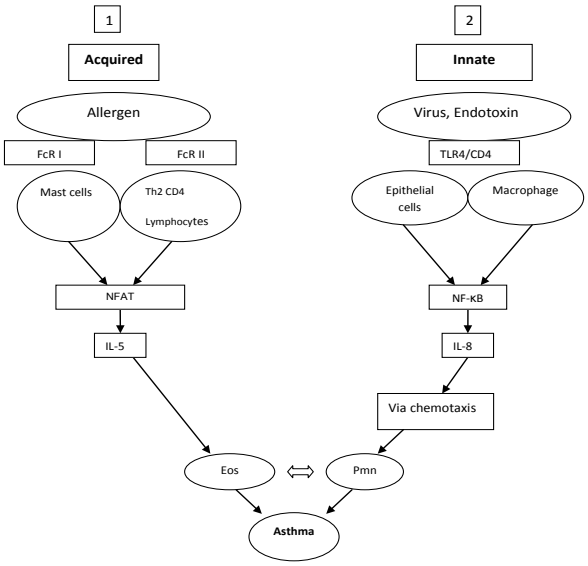

Fig 1. Pathways of innate and acquired immunity (the first pathway describes eosinophilic asthma and the second pathway shows neutrophilic asthma)

FcR: Fc receptor, Th: T-helper cell, CD4: Cluster of differentiation 4, NFAT: Nuclear factor of activated T-cells, IL: Interleukin, Eos: Eosinophils, Pmn: Polymorphonuclear, TLR: Toll - like receptor, NF- κB: Nuclear factor- kappa B

REFERENCES

[1] Cullinan P, Taylor AN. 2003. Asthma: environmental and occupational factors. Br Med Bull. 68:227-242.

[2] Barnes PJ, Chung KF, Page CP. 1998. Inflammatory mediators of asthma: an update. Pharmacol Rev. 50(4):515-596.

[3] Guyton A, Hall J. 2000. Textbook of Medical Physiology. 10th ed. W. B. Saunders Company.

[4] Macdowell AL, Peters SP. 2007. Neutrophils in asthma. Curr Allergy Asthma Rep. 7(6):464-468.

[5] Douwes J, Gibson P, Pekkanen J, Pearce N. 2002. Non-eosinophilic asthma: importance and possible mechanisms. Thorax. 57(7):643-648.

[6] Chung KF, Barnes PJ.1999. Cytokines in asthma. Thorax. 54(9):825-857.

[7] Forsythe P, Ennis M.1999. Adenosine, mast cells and asthma. Inflamm Res.48(6):301-307.

[8] Wright DT, Cohn LA, Li H, Fischer B, Li CM , Adler KB. 1994. Interactions of oxygen radicals with airway epithelium. Environ Health Perspect. 102 (Suppl 10):85-90.

[9] Nadeem A, Raj HG, Chhabra SK. 2005. Increased oxidative stress in acute exacerbations of asthma. J Asthma. 42(1):45-50.

[10] Wood LG, Gibson PG, Garg ML. 2003. Biomarkers of lipid peroxidation, airway inflammation and asthma. Eur Respir J. 21(1):177-186.

[11] Rahman I, Morrison D, Donaldson K, MacNee W. 1996. Systemic oxidative stress in asthma, COPD, and smokers. Am J Respir Crit Care Med. 154(4 Pt 1):1055-1060.

[12] Godard P, Damon M, Cluzel M, et al. 1987. Oxygen free radicals and bronchial asthma. Allerg Immunol (Paris). 19(8 Suppl):15-18.

[13] Novak Z, Nemeth I, Gyurkovits K, Varga SI, Matkovics B.1991. Examination of the role of oxygen free radicals in bronchial asthma in childhood. Clinica Chimica Acta. 201:247-252.

[14] Beck MA, Handy J, Levander OA. 2000. The role of oxidative stress in viral infections. Ann N Y Acad Sci. 917:906-912.

[15] Kim GY, Kim JH, Ahn SC, et al. 2004. Lycopene suppresses the lipopolysaccharide-induced phenotypic and functional maturation of murine dendritic cells through inhibition of mitogen-activated protein kinases and nuclear factor-kappaB. Immunology. 113(2):203-211.

[16] Cindrova-Davies T, Spasic-Boskovic O, Jauniaux E, Charnock-Jones DS, BurtonGJ. 2007. Nuclear factor-kappa B, p38, and stress-activated protein kinase mitogen-activated protein kinase signalling pathways regulate proinflammatory cytokines and apoptosis in human placental explants in response to oxidative stress: effects of antioxidant vitamins. Am J Pathol. 170(5):1511-1520.

[17] Stephensen CB, Gildengorin G. 2000. Serum retinol, the acute phase response, and the apparent misclassification of vitamin A status in the third National Health and Nutrition Examination Survey. Am J Clin Nutr. 72(5):1170-1178.

[18] Boosalis MG, Snowdon DA, et al. 1996. Acute phase response and plasma carotenoid concentrations in older women: findings from the nun study. Nutrition. 12(7-8): 475-8.

[19] Reifen R, Nur T, Matas Z, Halpern Z. 2001. Lycopene supplementation attenuates the inflammatory status of colitis in a rat model. Int J Vitam Nutr Res.71(6):347-351.

[20] Saedisomeolia A, Wood LG, Garg ML, Gibson PG, Wark PA. 2009. Lycopene enrichment of cultured airway epithelial cells decreases the inflammation induced by rhinovirus infection and lipopolysaccharide. J Nutr Biochem. 20(8):577-85.

[21] Saedisomeolia A, Wood LG, Garg ML, Gibson PG, Wark PA. 2009. Anti-inflammatory effects of long-chain n-3 PUFA in rhinovirus-infected cultured airway epithelial cells. Br J Nutr. 101(4): 533-540.

[22] Stahl W, Junghans A, de Boer B, Driomina ES, Briviba K, Sies H. 1998. Carotenoid mixtures protect multi lamellar liposomes against oxidative damage: synergistic effects of lycopene and lutein. FEBS Lett. 427(2):305-308.

[23] Tyssandier V, Feillet-Coudray C, Caris-Veyrat C, et al. 2004. Effect of tomato product consumption on the plasma status of antioxidant micro constituents and on the plasma total antioxidant capacity in healthy subjects. J Am Coll Nutr. 23(2):148-156.

[24] Pan H, Shi G, ChenW, Wang D. 2003. Effect of lycopene on the function of antioxidative enzyme system in rats. Wei Sheng Yan Jiu. 32(5):441-442.

[25] Hadley C, Clinton S, Schwartz J. 2003. The consumption of processed tomato products enhances plasma lycopene concentrations in association with reduced lipoprotein sensitivity to oxidative damage. Journal of Nutrition. 133(3):727-732.

[26] Stacewicz-Sapuntzakis M, Bowen P. 2005. Role of lycopene and tomato products in prostate health. Biochim Biophys Acta. 1740(2):202-205.

[27] Saedisomeolia A, Wood LG, Garg ML, Gibson PG, Wark PA. 2008. Supplementation of long chain n-3 polyunsaturated fatty acids increases the utilization of lycopene in cultured airway epithelial cells. Journal of Food Lipids. 15(4):421-432.

[28] Polyakov NE, Leshina TV, Konovalova TA, Kispert, LD. 2001. Carotenoids as scavengers of free radicals in a Fenton reaction: antioxidants or pro-oxidants? Free Radic Biol Med. 31(3):398-404.

[29] Jacob K, Periago MJ, Bohm V, Berruezo GR. 2007. Influence of lycopene and vitamin C from tomato juice on biomarkers of oxidative stress and inflammation. Br J Nutr. 99(1):137-46.

[30] Herzog A, Siler U, Spitzer V, et al. 2005. Lycopene reduced gene expression of steroid targets and inflammatory markers in normal rat prostate. Faseb J. 19(2):272-274.

[31] Liu X, Qu D, He F, Lu Q, Wang J, Cai D. 2007. Effect of lycopene on the vascular endothelial function and expression of inflammatory agents in hyperhomocysteinemic rats. Asia Pac J Clin Nutr. 16 (Suppl 1):244-248.

[32] Blackwell TS, Christman JW. 1997.The role of nuclear factor-kappa B in cytokine gene regulation. Am J Respir Cell Mol Biol.17(1):3-9.

[33] Butland BK, Strachan DP, Anderson HR. 1999. Fresh fruit intake and asthma symptoms in young British adults: confounding or effect modification by smoking? Eur Respir J. 13(4):744-750.

[34] Nja F, Nystad W, Lodrup Carlsen KC, Hetlevik O, Carlsen KH. 2005. Effects of early intake of fruit or vegetables in relation to later asthma and allergic sensitization in school-age children. Acta Paediatr. 94(2):147-154.