



# The Effects of Curcumin on Plasma Levels Cytokines, on Endurance-Trained Athletes

Omid Salehian\*, Golrokh Mohammadi, Naser Amiri

Department of Physical Education and Sport Sciences, Islamic Azad University, Iran.

\*Corresponding Author

**Abstract:** *The purpose of this study was to determinate the effects of natural curcumin supplementation on Levels of plasma cytokines during 8 weeks of long-term intensity treadmill training in endurance-trained athletes. 20 male endurance-trained athletes (age 20 years, weight 75 kg) participated in this study. The participants were randomly assigned to exercise supplement (E+S, n=8), and exercise (E, n=8) groups. All subjects participated in 8 weeks of long-term intensive treadmill training. Venous blood samples were collected immediately after exercise (T1), 1 hour after exercise (T2), 24 hours after exercise (T3). In the E group 8 weeks of training increased the seminal, IL-6, tumor necrosis factor (TNF)- immediately after exercise (T1), 1 h after exercise (T2), 24 hours after exercise (T3) ( $P < 0.05$ ) and but E+S group showed decrease significantly in levels of TNF and IL6 and increased significantly in IL10 immediately after exercise (T1), 1 h after exercise (T2), 24 hours after exercise (T3)  $p < 0.05$ . It may be possible that intake curcumin supplementation lead to decrease inflammatory cytokine such as IL6 and TNF and increase anti inflammatory cytokine such as IL10.*

**Keywords:** *Curcumin Supplementation, Inflammatory and Anti Inflammatory Cytokine, Long-Term Intensive Treadmill Training*

## INTRODUCTION

Inflammation is a response of the innate immune system, and is the reaction of the body to various stresses including cellular damage or infection caused by physical and/or chemical agents. The inflammatory response includes release of various soluble molecules called cytokines and chemokines, which mediate interactions between cells, thus affecting processes such as immunity and protein synthesis. (Wise, 2002; Hughes et al., 2004) As these inflammatory markers accumulate, they facilitate the infiltration and activation of Neutrophils, Macrophages, and lymphocytes which are needed to destroy and remove pathogens and damaged tissue. These molecules typically appear within an hour following tissue damage with Neutrophils appearing on the scene first. Innate immunity provides the body with a very rapid first line of defense (Calder et al., 2002). Myriad studies have linked exercise to a change in cytokine levels. Plasma concentrations of TNF- $\alpha$ , IL-1S, IL10, IL-6, IL-8, and IFN  $\gamma$  - have been shown to increase in response to exercise in humans (Hiscock et al., 2003). Several factors including type, intensity and duration of physical work have been shown to influence this effect (Helge et al., 2003). Strenuous exercise has been shown to increase inflammation as noted by dramatic increases in cytokines such as interleukin (IL-6) and IL-1 receptor agonist (IL-ra) (Nieman et al., 2003). A significant increase in plasma IL6 and IL10 was observed immediately post-exercise. The mechanism for the effect of exercise on inflammation is unclear and has been suggested to be the result of various triggers such as hypoglycemia, low muscle glycogen, muscle damage, oxidative stress (OS), or stimulation of immune cells

(Nieman et al., 2003), Over 5,000 flavonoids have been identified and are commonly found in varying amounts in fruits, vegetables, herbs, spices, teas, dark chocolate, red wine, and curcumin. In vitro studies consistently show reductions in inflammatory and inflammation responsive cytokines in cultures of immune cells after treatment with flavonoids. (Boots et al., 2008)

Decreases in the levels of TNF- $\alpha$ , IL-1, IL-6, and nitric oxide (NO) are regularly reported (Kaneko et al., 2008). Increases in the level of the anti-inflammatory cytokine IL-8 have also been shown, but do not follow a dose-response curve (Okoko & Oruambo, 2009). One food source that may have ergogenic properties for sports such as running is curcumin. As a natural product, the composition of curcumin is highly variable. The major components of curcumin are sugars, of which the monosaccharide's fructose and glucose together make up around 70% of the total product. The remaining 30% consists of disaccharides such as sucrose, and water (Nieman, 2006). Various forms of curcumin are also sources of antioxidants and have been shown to increase serum antioxidant capacity in humans after just one serving (Schramm et al., 2003) showed that total plasma phenolics and plasma antioxidant capacity were increased within 1 h after ingestion of curcumin. Research into the effect of curcumin supplementation on immune system factor in athletics, is extremely limited. So we investigate the effect of curcumin intake on immune system factors in elite runners.

### Materials and Methods

20 male endurance-trained athletes (age 20 years, weight 75 kg) were recruited into study after obtaining an informed consent. Subjects divided randomly in two E groups and E+S group. E performed exercise protocol without curcumin and E+S group performed exercise with curcumin.

Subjects in the E + S group received 50 g of curcumin dissolved in 200 ml tap water for 8 weeks. Both of groups performed treadmill exercise protocol for 1 hour with 80%  $v_{o2max}$  3 days per week for 8 weeks. They were also instructed to consume a diet as similar as possible in each sampling day. Levels of plasma cytokines measurement Venous blood samples were collected immediately after exercise (T1), 1 hour after exercise (T2), 24 hours after exercise (T3)

Venous blood was drawn at each time point using tubes containing no anticoagulant or the anticoagulants ethylenediamine tetra acetic acid or heparin. Blood collected in a serum separation tube, stood for 15 min and was centrifuged at 2500 g for 15 min. All serum and plasma samples were then stored at -80°C until analysis. Plasma IL-6, TNF, and serum IL10 were measured in duplicate using high sensitivity ELISA procedures (R & D Systems, Minneapolis, MN)

### Result

E group showed increased significantly in levels of TNF and IL6 and decreased significantly in IL10 immediately after exercise (T1), 1 h after exercise (T2), 24 h after exercise (T3)  $p < 0.05$ , but E+S group showed decrease significantly in levels of TNF and IL6 and increased significantly in IL10 immediately after exercise (T1), 1 h after exercise (T2), 24 hours after exercise (T3)  $p < 0.05$ . (Table 1-3)

**Table 1:** TNF plasma in groups

Group/time	T1	T2	T3
E	8.2	11.05	12.6
E+S	7.01	7.09	8.11
sig	0.005*	0.007*	0.004*

**Table 2:** IL6 plasma in groups

Group/time	T1	T2	T3
E	9.05	12.05	13.07
E+S	6.2	8.3	7.01
sig	0.008*	0.001*	0.002*

**Table 3:** IL10 plasma in groups

Group/time	T1	T2	T3
E	9.01	9.07	9.13
E+S	12.4	13.05	14.09
sig	0.001*	0.000*	0.001*

## Conclusion

Results of the present study indicated that mean values for seminal IL-6, and TNF- $\alpha$  in the E group increased significantly after 8 weeks of intensive treadmill training compared with E+S group. Increase in the levels of plasma IL-6, IL-8, and TNF- $\alpha$  in response to intense and prolonged exercise programs have been reported previously (Yu-yawn et al., 2008; Nieman et al., 2001). Previous studies indicate that prolog and training with high intensity to initiate an inflammatory response in whole body and subsequently in cyclists' seminal plasma, and thereby increase the levels of seminal cytokines IL-1B, IL-6, IL-8, and TNF-, Our finding demonstrate that the curcumin supplementation lead to significantly decreased the levels of IL-6 and TNF Immediately, 1 hour and 24h after exercise in the E + S group. The beneficial effect of curcumin on immune responses during different types of exercise programs has also been studied (Chepulis, 2007). There are less reports to show the effects of curcumin supplementation on immunological response of human. also our result showed that intake curcumin supplementation cause to increase il1 ra that it is anti inflammatory cytokine. Curcumin is types of falvonoid compounds that act as antioxidants; and has also been reported to increases serum antioxidant capacity in humans. Curcumin has modulatory effects on immune system of human. Finding showed that doing exercise with high intensity or long duration lead to increase free radical and decrease antioxidant defense (Earnest et al., 2004).

There seems little doubt that relationships between exercise, immune function inflammation, and cytokines exist. Plasma concentrations of TNF-  $\alpha$ , IL-1S, IL10, IL-6, IL-8 ,and IFN-  $\gamma$  can increase in response to exercise in humans (Moldoveanu et al., 2000; Helge et al., 2003). Several factors including type, intensity and duration of physical work have been shown to influence this effect (Kimura et al., 2001). Exercise-induced increases in inflammatory cytokines can result in vitro studies consistently show reductions in inflammatory cytokines in cultures of immune cells after treatment with quercetin, a flavonoid found in a variety edible plants including numerous berries, onions, apples, tea leaves, broccoli and curcumin. Decreases in the levels of TNF-? IL-1, IL-6, and nitric oxide (NO) are regularly reported (Okoko & Oruambo, 2009). Increases in the level of the anti-inflammatory cytokine IL-8 have also been shown Several factors including type, intensity, and duration of physical work have been shown to influence the effect of exercise on cytokine levels in humans (Moldoveanu et al., 2000). The same discrepancy can be found in studies measuring concentrations of IL-1, with some studies showing increases and others showing no change (Ostrowski et al., 1999). In a review paper, Pedersen et al. postulated that these differences are likely due, at least in part, to intensity, type, and duration of the exercise. In the case of IL-6, previously studies demonstrated that eccentric-type exercise was much more likely to cause a detectable IL-6 increase than was concentric exercise, and a recent review offered convincing evidence that IL-6 levels do not rise significantly unless aerobic exercise, such as bicycling or running, is performed for at least 30 – 60 minutes (Pedersen & Febbraio, 2008).

In conclusion, we found that 8 weeks of long-term intensity treadmill training significantly increased a decrease anti inflammatory cytokines. Levels of plasma cytokines IL-6 and TNF Also we found that intake curcumin supplementation lead to decrease inflammatory cytokine such as IL6 and TNF and increase anti inflammatory cytokine such as IL10.Present study is the first research that show the beneficial effects of natural curcumin supplementation during long-term intensity treadmill training on inflammatory and anti inflammatory cytokines.

## References

1. Boots, A.W., G.R. Haenen, and A. Bast, Health effects of quercetin: from antioxidant to nutraceutical. *Eur J Pharmacol*, 2008. 585(2-3): p. 325-37.
2. Calder, P.C., C.J. Field, & H.S. Gill, Nutrition and immune function. 2002, New York, NY: CABI Publishing
3. Chepulis LM. The effects of curcumin compared with sucrose and a sugar-free diet on neutrophil phagocytosis and lymphocyte numbers after long-term feeding in rats. *J Complement Integrati Med*. 2007; 4: 1-8.
4. Earnest CP, Lancaster SL, Rasmussen CJ, Kerksick CM, Lucia A, Greenwood MC, Almada AL, Cowan PA, Kreider RB. Low vs. high glycemic index carbohydrate gel ingestion during simulated 64-km cycling time trial performance. *J Strength Condit Res*. 2004; 18: 466-472.
5. Helge, J., Stallknecht, B., Pedersen, B., Galbo, H., Kiens, B., Richter, E., 2003. The effect of graded exercise on IL-6 release and glucose uptake in human skeletal muscle. *Journal of Physiology* 546, 299-305.
6. Hiscock, N., Petersen, E., Krzykowski, K., Boza, J., Halkjaer-Kristensen, J., Pedersen, B., 2003. Glutamine supplementation further enhances exercise-induced plasma IL-6. *Journal of Applied Physiology* 95, 145-148.
7. Hughes, D.A., L.G. Darlington, & A. Bendich, Diet and human immune function. 2004, Totowa, NJ: Humana Press.
8. Kaneko, M., Takimoto, H., Sugiyama, T., Seki, Y., Kawaguchi, K., Kumazawa, Y., 2008. Suppressive effects of the flavonoids quercetin and luteolin on the accumulation of lipid rafts after signal transduction via receptors. *Immunopharmacology and Immunotoxicology* 30, 867-882.
9. Kimura, H., Suzui, M., Nagao, F., Matsumoto, K., 2001. Highly sensitive determination of plasma cytokines by time-resolved fluoroimmunoassay; Effect of bicycle exercise on plasma level of interleukin-1alpha (IL-1alpha), Tumor necrosis factor alpha (TNF-alpha), and Interferon Gamma (IFN gamma). *Analytical Sciences* 17, 593-597.
10. Moldoveanu, A., Shephard, R., Shek, P., 2000. Exercise elevates plasma levels but not gene expression of IL-1Beta, IL-6, and TNF-alpha in blood mononuclear cells. *Journal of Applied Physiology* 89, 1499-1504.
11. Nieman DC, Henson DA, Smith LL, Utter AC, Vinci DM, Davis JM, Kaminsky DE, Shute M. Cytokine changes after a marathon race. *J Appl Physiol*. 2001; 91: 89-114.
12. Nieman, D.C. Exercise Immunology: A 20-Year Perspective. in *Southeast American College of Sports Medicine Annual Meeting*. 2006.
13. Nieman, D.C., et al., Carbohydrate ingestion influences skeletal muscle cytokine mRNA and plasma cytokine levels after a 3-h run. *J Appl Physiol*, 2003. 94(5): p. 1917-25.
14. Okoko, T., Orumbo, I., 2009. Inhibitory activity of quercetin and its metabolite on lipopolysaccharide-induced activation of macrophage U937 cells. *Food and Chemical Toxicology* 47, 809-812.
15. Ostrowski, K., Rohde, T., Asp, S., Schjerling, P., Pedersen, B., 1999. Pro- and anti-inflammatory cytokine balance in strenuous exercise in humans. *Journal of Physiology* 515, 287-297.
16. Pedersen, B.K., Febbraio, M.A., 2008. Muscle as an endocrine organ: focus on muscle-derived IL-6. *Physiological Reviews* 88, 1379-1406.
17. Schramm, D.D., et al., Curcumin with high levels of antioxidants can provide protection to healthy human subjects. *J Agric Food Chem*, 2003. 51(6): p. 1732-5.
18. Wise, D.J.G.R.C., Immunology: a comprehensive review. 2002, Ames, IA: Iowa State University Press.
19. Yu-yawn C, Jasson C, Yu-jen C, Kung-tung C, Rong-sen Y, Jaung-geng L. Cycling and Tai Chi Chuan exercises exert greater immunomodulatory effect on surface antigen expression of human hepatitis B virus. *Chin Med J*. 2008; 121: 2172-2179.