Vitamin E and Curcumin Intervention on Lipid-Peroxidation and Antioxidant Defense System

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Abstract: The generation of free radical species may represent the negative aspect of exercise. There are a lot of data which have been shown an association between exercise and the increased free radical formation. Living cellular damage may lead human towards hasty aging and variant cancers. It is widely agreed that with increasing consumption of fruits and vegetables, decreased intake of unsaturated fat and moderate exercise will enhance fitness and improved cardiovascular health of the population in most of the developed and near-developed countries. Vitamin E and Curcumin have been known as a strong Antioxidant for prevent of the lipid peroxidation and improve the antioxidant defense system. Curcumin is a phenolic compound presented as a strong anti-oxidative, anti-inflammatory and anti-septic property, widely used in Indian medicine and culinary traditions. Recent investigation has shown that curcumin prevents lipid peroxidation and DNA strand breakage. This review have been shown the effect of the curcumin and vitamin E supplement on the lippid peroxidation and antioxidant defense system specify during the exercise. [Journal of American Science 2010;6(3):52-62]. (ISSN: 1545-1003).

Keywords: Vitamin E, Curcumin, Exercise, Antioxidant, Lipid-Proxidation, Free radical

1. Introduction: It is widely agreed that with increasing consumption of fruits and vegetables, decreased intake of unsaturated fat and moderate exercise, will enhance fitness and improved cardiovascular health of the population in most of the developed and near-developed countries(Lloyd et al., 1998). Fruits, vegetables and grains are rich of antioxidant because they contain ascorbate, tocopherols, tocotrienols, flavonoids, other phenols and carotenoids (Stangeland, Remberg, & Lye, 2008). An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. Oxidation is a chemical reaction that transfer electron from a substance to an oxidizing agent. Oxidation reaction can produce free radicals. Antioxidant terminates the chain of the reaction by removing free radicals and inhibits other oxidation reaction by oxidizing themselves. The balance between free radicals formation and antioxidant activity is called oxidative stress. When the oxidative stress is unbalanced in favor for free radicals, such as acute and chronic exercises, damage occurs to many cellular membranes such as the hearth and skeletal muscles (Jenkinson, Franklin, Wahle, & Duthie, 1999).

2. Methodology. The current studies has been focused on Curcumin intervention as an herbal antioxidant on lipid-peroxidation during the exercise. PubMed and SPORT Discus databases were searched from 1982 to 2009 using the terms Curcumin, Vitamin E, Curcumin and Exercise, Vitamin E and Exercise and Lipid Peroxidation. Related studies were located by reviewing the reference lists of the articles identified through the computer database search. There are many studies of the effects of Curcumin supplementation in lipid Peroxidation among human and animal subject. Some limitation in muscle sampling among the human people was the cause to do research in antioxidant among rats and other animal that are closely respond similar with human.

Free radicals and antioxidant enzymes have been implicated as important factors in fitness and for the battle of some diseases such as diverse cancer, diabetes and cardiovascular diseases in recent century. It has been demonstrated that antioxidant enzymes can prevent living cells' membrane from damage and lipid proxidation where free radicals may cause damage to the cellular agent. Researchers

showed that the increase of free radicals is the result of the increased oxygen utilization. Physical exercise associated with oxidative damage is dependent on the type and intensity of exercises. However, some investigations have demonstrated that by endurance training improved the antioxidant defense system as well as oxidative capacity in the skeletal muscles (Powers, Ji, & Leeuwenburgh, 1999; Terblanche, 1999). Metabolic rates as a result of exercise may increase oxygen consumption (VO_2 max) up to 20 times over steady state. Evidences have shown that aerobic exercise generated reactive oxygen species such as superoxide radical (O_2^-), hydroxyl radical (^-OH), perhydroxyl radical ($HO2^-$) and Conjugated peroxyl radical which are capable of damaging living cellular and caused inflammation(Alessio & Goldfarb, 1988; Liu et al., 2000). The benefits of using supplementary antioxidant to prevent reactive oxygen species (ROS) appear in large investigations. Curcumin is a phenolic compound present as a strong anti-oxidative, anti-inflammatory and anti-septic property, widely used in Indian medicine and culinary traditions. Recent investigation has shown that curcumin prevents lipid peroxidation and DNA strand breakage(James S. Wright, 2002). The presumption of whether the combined effect from both the exercise and curcumin would yield more antioxidant activity or free radicals damage and muscle lipid peroxidation remain controversial. The only research which has tested antioxidant and exercise have provided contradictory conclusion. In the research, they used vitamin E as an antioxidant supplement(Viitala, Newhouse, LaVoie, & Gottardo, 2004).

2.1 Free Radicals and Oxidative Stress: Any chemical species which has an unpaired electron or an odd number of electrons may be labeled as free radicals. Free radicals are the very high reactive molecular that seek to combine with other molecular to react and make their way to unpaired electron molecules (McBride & Kraemer, 1999). The term free radical has been around for over 40 years. However, this term may have many meanings according to the variety of specific researches. In general free radical is an atom or group of atoms with an unpaired electron in the outer orbits. Some of the free radicals such as melanin are not chemically reactive, but this is not true for most of the biological-relevant oxygen free radicals. The unpaired electron is usually extremely exchangeable, which is the chemical and physical reason for the reactivity of radical species(Urban Wiklund, 2009). The level of the free radicals' reactivity depends on their life span or the survival of the radical species. Some radicals exist only for a fraction of seconds before they participated in a chemical reaction. Some radicals which have obtained an extremely low energy level, are therefore referred to as the stable radicals(Sawyer, 1988). Normally millions of free radicals are continually created in our physiology to carry on the metabolic activity of the body. They are essential to life, we need them, and they fight infections. Our cells boost up these free radicals to kill the germs when we are infected with *bacteria, fungus, and parasites*. Oxygen is known to be a free radical; it is highly unstable. Oxygen is a life saver but if one is to be given 100% oxygen, it is highly toxic. Why does oxygen become toxic? It is a molecule which consists of two atoms of oxygen, and when they are combined, they balance out each other. But if it is unstable, and if the two atoms are separated, they became two free radicals. But free radicals are not limited only of oxygen. Any molecules, any atoms in the body can become a free radical, and when it does, it will try to balance itself by picking up an electron from a neighboring molecule which in turn will become a free radical and this vicious cycle will continue until it is checked and controlled. If it is not controlled, damage will occur in different parts of the body(Sharma, 1993). There are many environmental and biochemical factors which hinder the production of free radicals such as metabolism, pollution, radiation, cigarette smoke and herbicides. However, free radicals can be produced by several mechanisms. Dissolution of the cells, hemolytic fission and electron transfer in the mitochondria are the few most important ways to produce free radicals (Cheeseman & Slater, 1993). It has been nearly 50 years since Denham Harman suggested that free radicals produced during aerobic respiration caused cumulative oxygen damage, resulting in aging and death. Oxygen is an essential molecule for all aerobic forms. Hence, Oxygen is indispensable for all cells for chemistry energy production (ATP). It is often transformed into a highly reactive form: reactive oxygen species (ROS), which is very toxic for all cells and can damage the molecular membrane(Haddad, 2002), (Figure 1).

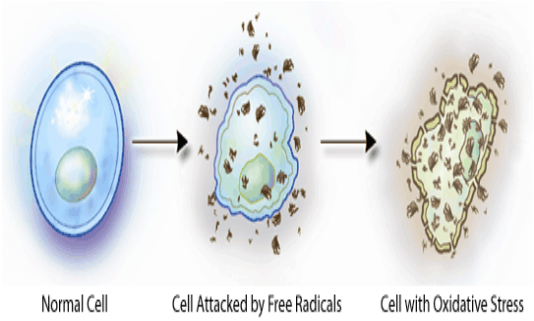

Figure 1. Free Radicals And Oxidative Stress

In chemistry, radicals (often referred to as free radicals) are atoms, molecules or ions with unpaired electrons on otherwise open shell configuration. These unpaired electrons are usually highly reactive, whereby radicals are likely to take part in chemical reactions (Figure 1).

$$H_2O_2 + Fe^{2+} \rightarrow \cdot OH + OH^- + Fe^{3+}$$

Figure 2. Free Radicals Formation Mechanisms

The most important free radicals in our bodies are the radical derivatives of oxygen better known as reactive oxygen species (Cheeseman & Slater, 1993). These include oxygen in its triplet state ($3O_2$) or singlet state ($^1O_2$), superoxide anion ($O_2^{\cdot\square}$), hydroxyl radical (·OH), nitric oxide (NO·), peroxynitrite (ONOO□), hypochlorous acid (HOCl), hydrogen peroxide (H_2O_2) alkoxyl radical (LO·), and the peroxyl radical ($LO\cdot_2$). Another than that, there is the carbon-centered free radical ($CCl_3\cdot$) which arises from the attack of an oxidizing radical at an organic molecule. Hydrogen centered radical is a result from an attack of the H atom (H·). Another form is the sulfur-centered radical produced from the oxidation of glutathione which resulted in the thiyl radical (R-S·). A nitrogen-centered radical also exists for example the phenyl diazine radical. Under normal condition (at rest), the antioxidant defense system within the body can easily handle free radicals that are produced. During times of increased oxygen flux (i.e. exercise), free radicals production may ultimately exceed removal resulted in lipid peroxidation. Free radicals have been implicated to play a role in the etiology of cardiovascular disease, cancer, Alzheimer's disease, and Parkinson's disease. Although it is worthy of a discussion, these conditions are not the focus of the current literature reviews(Valko et al., 2007).

Table 1 . Bilogicaliy Significant Free radical

Reactive Oxygen Species	
$O_2\cdot^-$	Superoxide radical
·OH	Hydroxyl radical
ROO·	Peroxyl radical
H_2O_2	Hydrogen peroxide
$^1O_2$	Single oxygen
NO·	Nitric oxide
$ONOO^-$	Peroxynitrite
HOCl	Hypochlorous acid

2.2 Lipid-Proxidation: Free radicals may attack many components of a cell such as the polyunsaturated fatty acid (PUFA), deoxyribonucleic acid (DNA) and proteins. The damage of the lipid membrane is called lipid peroxidation. Lipid peroxidation is a process related to free radicals whereby in this process, free radicals got hold of electrons from the lipid such as the cellular membrane. This process often affects the polyunsaturated fatty acid (figure 2), because they contain multiple double bands in between which lie the methylene-CH_2 groups that contain the reactive oxygen. In the cellular membrane, the oxidative stress is the by-product of the free radicals oxygen (Viitala, Newhouse, LaVoie, & Gottardo, 2004). Lipid peroxidation is the most popular biomarker of the oxidative stress. There are three steps in lipid peroxidation as in the following:

a) First step is the initiation: the initiation is the step where the fatty acid radical is produced. In this step, a reactive oxygen species or (ROS) such as OH° is combined with a hydrogen atom to make water and a fatty acid radical.

b) Second step of the lipid peroxidation is called the propagation. In this step, the fatty acid radical which is the by-product of the first step, is a set of very unstable molecules where it reacts readily with oxygen to create the peroxyl-fatty acid radical.

c) Radical Reaction stops when two radicals react and produce a non-radical species. This happens when the concentration of radical species is high enough to enable two radicals to react together and produce a non-radical species.

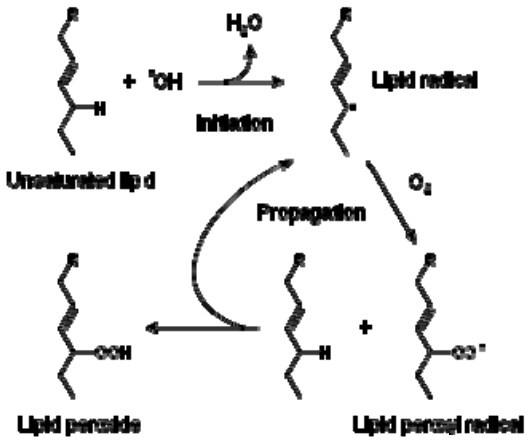

Figure 3. Mechanism of Lipid-Peroxidation

Malonaldehyde (MDA), thiobarbituric acid reactive substance (TBARS), lipid hydroperoxides (LH), and 4-hydroxyalkenals (4-HNE) are the example of lipid peroxidation by-products which have been used as biomarker of lipid peroxidation level. Many investigations have shown that MDA, TBARS, LH and 4-HNE are directly linked to increase the rates of lipid peroxidation(Jenkins, Kendall, Axelsen, Augustin, & Vuksan, 2000).

2.3 Antioxidant Properties of Curcumin. An antioxidant molecule can prevent the oxidation of other molecules. Oxidation is a chemical reaction that transfers an electron from a molecule to an oxidizing agent. Oxidation reaction can produce free radicals which caused cellulars to damage. Antioxidants terminate this chain reaction by removing the free radical species and inhibit other oxidation reactions by oxidized themselves(Jenkins, Kendall, Axelsen, Augustin, & Vuksan, 2000). There are two major antioxidant defense systems to protect our bodies against the reactive oxygen species and cellular damage, which are the enzymatic and non-enzymatic antioxidants. The non-enzymatic system includes the glutathione, uric acid, vitamin C, and vitamin E. Antioxidant enzymes are also produced by our bodies which include catalase, superoxide dismutase, and glutathione perixidase (Szymonik-Lesiuk et al., 2003). These two type of antioxidant systems are working together to ameliorate any harmful effects of oxidant in the cell. Both of the enzymatic and non-enzymatic antioxidants detoxify ROS in the intracellular and extracellular environments(Jenkins, Kendall, Axelsen, Augustin, & Vuksan, 2000). To provide maximum intracellular protection, these scavenger agents are strategically located in the cells.

2.4 Curcumin: is a yellow agent from curcuma longa(figure2-7 to 2-10). It is a major component of trumic and is commonly used as spice and food coloring component in some countries especially in India and the Middle East area. Three decades of researches show that curcumin is a component with anti-inflammatory, antitumor and antioxidant properties. The first chemical characterization of curcumin was obtained in 1910, with the molecular formula of $C_{21}H_{20}O_6$. The antioxidant mechanism of curcumin has recently been the focus of free-radical chemists and biologists. Curcumin is the main biologically active phytochemical(of chemical reactions resulting from the influence of light or radiation) compound of Turmeric(Fahey & Talalay, 1999). More than one billion people consume curcumin regularly in their daily diet. Curcumin has long been used in some Eastern medicine and also used for protection against cancer and cardiovascular disease nowadays.(Menon & Sudheer, 2007)

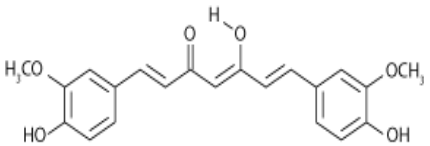

Figure 4. Curcumin Molecule Structure

Curcumin keeps the heart healthy by preventing a plaque build-up in the arteries, which can lead to atherosclerosis. In one study, participants who take 500 milligrams of curcumin each day significantly have their cholesterol levels reduced in simply 10 days. Preliminary research indicates that curcumin may also help lower blood pressure and prevent blood clots (Martin -2003).

Figure 5. Turmeric Rhizome

Numerous research teams provide evidence that curcumin contributes to the inhibition of tumour formation and is promoted as the inhibition of cancer. This compound is also known to decrease and block the progression of tumours. Azuine et al. described curcumin as inhibit tumor.

Most of the antioxidants have either a phenolic functional group or a B-diketone group. Curcumin is a unique antioxidant which has a variety of functional groups including the carbon-carbon double bond, B-diketon group and phenyl rings that contain varying amounts of hydroxyl and methoxy substituents (James S. Wright, 2002). Recently, many studies on the health benefits associated with curcumin have been reported. In the present study, an attempt has been made to test individual curcuminoids, such as curcumin, bisdemethoxycurcumin and demethoxycurcumin, for their antioxidant activities with the in vitro model systems. Water and fat-soluble extracts of turmeric and its curcumin components exhibit strong antioxidant activities, compared to vitamins C and E. A study has showed curcumin to be eight times more powerful than vitamin E in the case of preventing lipid peroxidation(Majeed, 1999).

2.5 Vitamin E is referred to a related compound (tocopherols) which have hydroxylated aromatic rings and isoprenoid side chain. The hydrophilic molecule is the major lipid soluble antioxidant in the membranes of living cells and it protects cells against lipid peroxidation by acting directly with a variety of oxygen reactive radicals, containing single oxygen, lipid peroxidation products and supperoxide radicals to form relatively harmlessly with tocopherol radical to regenerate reduced tocopherol (Rumsey, Wang, & Levine, 1999).

2.6 effects of training on the antioxidant defense system

As the number of studies which investigate the impact of exercise on oxidative stress increased, researchers speculate that regular exercise training induced an adaptive response in the antioxidant defense system. Consequently, this enhances the protection against reactive oxygen species (ROS) and decrease the accumulation of oxidative damage in living cells. Exercise volume is related to the blood antioxidants and antioxidant enzymes. Some of the other investigations show that specific evidence of exercise induces oxidative stress due to the lack of mitochondrial to generate free radicals. This is because these reactive oxygen species are very short-lived and also difficult to measure directly(Di Meo & Venditti, 2001). Reactive oxygen species (ROS) can be generated through different pathways and from different forms of exercise and training. The balance between the production of reactive oxygen species and the capacity of the antioxidant defense system determines the extent of oxidative stress within the system. Jackson (1994) suggested that the title of exercise is an umbrella term. Since there are different forms of exercise, oxidative stress induced by exercise must be considered based on the type of exercise performed.

During aerobic exercise, there is an increased need for the production of adenosine three phosphate (ATP) in the muscle cells. This production occurs through the reduction of molecular oxygen in the mitochondria. With the increased aerobic metabolism, this provides an increase in the electron flux among the mitochondrial electron transport chain. The increased oxygen metabolism will increase the formation of oxygen radical through the mitochondrial respiratory chain. In addition, if the exercise has a high mechanical impact, there may be destruction of erythrocytes, which could release iron into the circulation. Myoglobin may also be released into the circulation if there is any damage to the skeletal muscle. The production of Hydroxyl radical can be stimulated by these free iron ions by catalyzing the “Fenton reaction” ((Halliwell & Gutteridge, 1985)).

In studies which deal with vitamin C supplement in humans, the doses have varied considerably. Alessio et al. (1997) used acute (1 and 7 days) (1.0 g/day) vitamin C supplement and did not observe a reduction in oxidative stress induced by exercise. Conversely, a higher dose of (3.0 g/day) vitamin C supplement for two weeks was shown to be able to reduce plasma protein carbonyls(Bryer & Goldfarb, 2006). Goldfarb and Patrick (2005) reported that both 500 mg and 1 gm of vitamin C that were given two weeks prior to exercise could attenuate the oxidative stress induced by exercise as indicated by the reduction of protein carbonyls. The results showed reduction was dependent on the doses given. Interestingly, there were no changes with the glutathione status during the exercise or the treatment. Muscle soreness and oxidative stress had both been reported to be reduced with high 27doses of vitamin C supplement following an eccentric exercise (Kaminski et al., 1992; Bryer and Goldfarb, 2006). It seems that higher doses of vitamin C supplement create beneficial effects when dealing with oxidative stress induced by exercise. The role of vitamin C supplement has not been studied in myocardium where oxidative stress is induced by exercise.

There are a lot of interests in the effects of antioxidant supplement both in terms of promoting performance and also preventing tissues damage, which occur during exercise, particularly for those who undertake irregular and strenuous activity.

The states of Cellular proxidant are defined as the increased concentrations of active oxygen, organic peroxides, and radicals. A proxidant state may be induced by environmental factors, such as by chemicals and irradiation, as well as physiological

factors, for example, under the condition of physical exercise. The effects of Proxidant from the various factors of biological systems are most commonly estimated by the degree of consequent lipid peroxidation. However, it is not clear whether the products of lipid peroxidation is a cause or a consequence of diseases(Esterbauer, Gebicki, Puhl, & J-Rgens, 1992).

2.7 Mechanisms and the peroxide-removing antioxidant system.

To assess the peroxidation process, the products of lipid peroxidation will be analyzed. Thus, conjugated dienes arises as an early event of reactions to lipid peroxidation. Several end products of lipid peroxidation(Uotila, Tuimala, Aarnio, Pyykko, & Ahotupa, 1993), such as aldehydes, react readily with thiobarbituric acid (TBA) and is defined as thiobarbituric acid reactive material (TBARM). Fluorescent chromolipids are inactive compounds formed by the reactions of aldehydes with free amino groups .Reactive oxygen species (ROS) are of biological molecules such as lipids, proteins and DNA. Antioxidant molecules prevent and/or inhibit these harmful reactions(Erel, 2004).

In 1978, Dillard et al. were the first to demonstrate that physical exercise could lead to an increase of lipid peroxidation. They observed a 1.8-fold increase in the exhaled pentane level, a possible by-product of oxidative lipid damage, after 60 minutes of cycling at 25–75% of $\dot{V}O_2max$. Since then, increased bodies of evidence have been accumulated to support the hypothesis that physical exercise has the potential to increase the production of free radicals which lead to oxidative stress. To measure the production of free radicals directly is difficult, primarily because of the short life-span of this species. The use of free radicals' spin traps could increase this life-span and there have been recent studies demonstrated that the blood removed from an individual who does exercise has an enhanced ability to trap free radicals when assayed by *ex vivo(Powers et al., 1994)*.

They reported that Long Evans male rats, who do exercise, have increased lipid peroxidation, as measured by the used of TBARS. Since then, studies have been carried out on humans to evaluate whether exercise increases oxidative stress. While many studies supported Davies' findings, at the same time many refuted of them also(Bor, ضZdemir, & TüRkan, 2003; Davies, Quintanilha, Brooks, & Packer, 1982).

The generation of Reactive radical oxygen species (ROS) increases with the aerobic endurance stress. The major source of ROS is thought to be the mitochondria of active muscles, but free radicals are also produced by red blood cells or during inflammatory response. When the antioxidant system is not adapted to excessive production of ROS, oxidative stress initiates. ROS are potent to induce various cellular damage affecting lipids, proteins and nucleic acids. The imbalance between oxidants and antioxidants will affect the normal function of immune cells. In order to prevent exercise-induced oxidative stress, the organism is well equipped with antioxidant defense systems including enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GSH-Px), and non-enzymatic substances such as reduced glutathione (GSH) and vitamins A, C, E, and selenium that act in synergy. Vitamin E is considered the most important lipid-soluble exogenous antioxidant in humans. Vitamiserves as an antioxidant directly by scavenging aqueous peroxyl radicals and indirectly by regenerating reduced vitamin E(Bonithon-Kopp et al., 1997).

Packer (1991) suggested that there was an increased requirement for vitamin E during endurance training. There may be a number of sources of this oxidative stress, including the production of mitochondrial superoxide, ischaemia-reperfusion mechanisms and auto-oxidation of catecholamines. Severe or prolonged exercise could overwhelm antioxidant defences, which included vitamins E and C and thiol antioxidants where both were interlinked in an antioxidant network, as well as the antioxidant enzymes (Packer, 1997).

The Emory's researchers found that people who had participated in an aerobic exercise program for a year actually had greater rate of LDL oxidation than a similar group who did not exercise (Shern-Brewer, Santanam, Wetzstein, White-Welkley, & Parthasarathy, 1998).

In an investigation by Afzalpour et al. (2008), they examined the effect of moderate and vigorous aerobic exercise with the serum oxidized low density lipoprotein (ox-LDL) levels and total antioxidant capacity (TAC) in trained and untrained health subjects. In this investigation, they found out that serum ox-LDL and TAC were not affected by exercising, and concluded that there was a positive correlation between VO2max and total antioxidant capacity (TAC) whereas there was a negative correlation between TAC and LDL-C as well as TC. Afzalpour (2008) suggested that physical training could improve the antioxidant defense systems(Afzalpour et al., 2008).

Rafael et al. (2007) investigated the effects of aerobic exercise training on the activities and mRNA level of catalase (CAT), glutathione peroxidase (GPX), Cu-Zn soperoxide dismutase and

manganese superoxide dismutase (Mn-SOD), the TBARS contents and the activities of xanthine oxidase (XO), in the soleus muscle of young and aged rats. In this investigation, it was shown that the activity and mRNA level of antioxidant enzyme had markedly increased in the soleus muscle along with aging. An increase of all antioxidant activities except for the Cu-ZN superoxide dismutase were found in the young rats with induced exercise training. In this group, Xanthine oxidase (XO) also did not change. TBARS which is the by-product of lipid peroxidation had increased in the soleus muscle of young rats involved with the training. The activity level of catalas (CAT), glothation peroxide (GPX) and Cu- Zn superoxide dismutase did not change on the soleus muscle of aged rats with exercise training while activities of Mn-SOD and XO increased (40%) and (27%) respectively. TBARS in aged rats with training had increased by (80%). This investigation showed that lipid peroxidation level increased with training in both aged and young rats by exercise training(Lambertucci, Levada-Pires, Rossoni, Curi, & Pithon-Curi, 2007).

The influence of vitamin C as a parameter for the blood oxidative stress in basketball players in response to maximal exercise was investigated by Cholewa et al. (2007). This investigation showed that there were significant effects of vitamin E supplement in the serum of vitamin C concentration and that there was no effect as in the 21 days of vitamin C intake at the blood antioxidant system as well as the MDA (Lipid peroxidation products) and VO_2max as an aerobic capacity. This investigation also showed that exercise did not change the SOD enzymes, GPx, CAT, GR and GSH activities but changes could be seen in vitamin C and MDA concentration. The final of this research showed that vitamin C has no effect at the blood antioxidant statues and VO_2max in basketball players. (Cholewa, Poprzecki, Zajac, & Waskiewicz, 2008)

Mustafa Gul (2003) and his colleagues investigated the effects of endurance training and acute exhaustive exercise of the antioxidant defense mechanism in rats' hearts. In this investigation they used the male rats with 8-weeks of treadmill training. The Malondialdehyde level in the heart tissues was not affected by acute exhaustive exercise for both trained and untrained rats. In both acute exercise and trained groups, the activities of the glutathione reductase and glutathione peroxidase enzymes decreased while the activity of catalase was not affected. Additionally in this investigation, the activities of the total and non-enzymatic superoxide scavenger were not affected. The activity of Superoxide dismutase decreased with acute exercise in untrained rats. The result of this investigation showed that a rat's heart has sufficient capacity of antioxidant enzyme to cope with exercise-induced oxidative stress and adaptive changes in antioxidant enzymes due to the limited endurance exercise (Williams et al., 2007).

Alessio and Goldfarb (1988) had examined lipid peroxidation and scavenger enzymes during exercise: adaptive response to training. In this study, it was shown that the training program which contained the endurance exercise caused a 64% increase of oxidative capacity in the leg muscle. With the sedentary exercise group, there was an increase during lipid peroxidation in the liver and white muscle. The endurance group of rats did not have any increase of the lipid peroxidation after exercise. In this investigation, it also showed that the activity of catalase (CAT) was higher in both red and white muscles after exercise for trained rats. Acute and chronic exercise was not affected by super oxide dismutase (SOD) in both acute and chronic group of rats. This investigation showed that endurance training could reduce lipid peroxidation indicated by malondialdehyde (MDA) in the rats(Alessio & Goldfarb, 1988).

Dietary intakes of polyunsaturated fatty acids and the indices of oxidative stress in human volunteers were investigated by Jenkinson et al. (1999). In this investigation, Jenkinson and his colleagues used human subjects in their investigation. A significant increase in the whole blood of oxidised glutathione where there was an index of oxidative stress had been found after consumption of high polyunsaturated fatty acids (PUFA) diet. The investigation also showed that TBARS as an index of lipid peroxidation was increased using the high PUFA and decreased by consuming the low PUFA diet. Superoxide dismutase and total cholestraol decreased after consumption of the low PUFA diet. In this investigation they suggested that the increase of vitamin E intake was required when PUFA diet increased(Jenkinson, Franklin, Wahle, & Duthie, 1999).

The effects of antioxidant vitamin supplement at the resistance of exercise which induced lipid peroxidation in trained and untrained participants were investigated by Viitala et al. (2004). At the end of this investigation, there was no any significant difference between placebo and vitamin E supplement in trained and untrained rats. All of the rats in this study had been selected equally in term of the blood's vitamin E level and the percentage of body fat (Viitala, Newhouse, LaVoie, & Gottardo, 2004).

Other than that, Wright (2002) investigated the prediction of antioxidant activity for curcumin and curcuminoids. Curcuminoids which included curcumin and other related molecules were strong

antioxidant with medical effects. The curcumin structure had multiple function groups including B-diketon. Carbon-carbon double bond and phenyl ring contained varying amount of hydroxyl and methoxy substituent. The site of the activity and reaction mechanism of the curcumin, responsible for the antioxidant effects were controversial(J. S. Wright, 2002).

The effects of dietary vitamin E, C and soybean oil supplement of the activities of antioxidant enzyme in the liver and muscles of rats were investigated by Shireen et al. (2008). In this study, they examined the effects of elevated levels of dietary vitamin E, C and the combination of vitamin E and vitamin C (E & C) combined with soybean oil of the activities of antioxidant enzymes important for the protection against lipid peroxidation in male rats. At the end of this research, it was showed that the combination of Vitamin C and vitamin E as well as separate daily supplement for 28 days increased catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR) activities in liver, pectoralis major and sartorius muscles. These enzymes increased significantly in rats fed with the diet which included vitamin C, E separately, and the combination of vitamin C and Vitamin E with the exception of superoxide dismutase (SOD), which showed no alteration. However this investigation showed that the combination of vitamin E and C enhanced the activities of antioxidant enzymes more significantly and also showed that the role of vitamin C and vitamin E and their combination to reduce the risk of chronic diseases and cells damage related to oxidative stress(Shireen, Pace, Mahboob, & Khan, 2008).

Davis and his colleagues investigated the effects of curcumin on inflammation and the recovery performance of running as in the downhill running of mice. At the end of this research, it was showed that Downhill running decreased both treadmill running time in term of fatigue (48h and 72h) and voluntary activity (24h) ($P<0.05$), where curcumin feedings offset these effects on the running performance. Downhill running was also associated with an increase of inflammatory cytokines (24h and 48h) and creatine kinase (24h) ($P<0.05$)that were blunted by curcumin feedings. These results supported the hypothesis that curcumin could reduce inflammation and offset some of the performance deficits associated with eccentric exercise-induced muscle damage (Davis et al., 2007).

Bryant et al. (2003) had investigated the effects of vitamin E and vitamin C supplement either individually or combined on the exercise-induced lipid peroxidation in trained cyclists. They used seven trained male cyclists who (at the age of 22.3 +/- 2 years) participated in four separate supplementary phases. The results of this investigation showed that the treatment of vitamin E alone was more effective than vitamin C. MDA level of pre-exercise in the plasma during the vitamin E trial and MDA level of pre-exercise with placebo was 2.94+/- 0.54 and 4.81+/-0.65 micromol per ml respectively. The plasma MDA level following the exercise in the vitamin group was lower than the placebo group. At the end of this research, it could be seen that 400IU/day of vitamin E reduced membrane damage more effectively than vitamin C but it did not enhance performance (Bryant, Ryder, Martino, Kim, & Craig, 2003).

3. Conclusion There are a lot of data which show that free radicals and reactive oxygen species increased cardiovascular risks and also increased damage done on the membrane of living cells. Curcumin and Vitamin E are as The strong antioxidant supplement which are decreases the lipid peroxidation and improves total antioxidant capacity in the human and animal body. Also have been shown that acute and chronic exercise training would increase the oxygen reactive concentration in the body. However for long term, regular endurance training improved the total antioxidant capacity. According to the last investigation, we can predicate that exercise will improve antioxidant defense system and increase lipid peroxidation in cells' membranes more significantly. This investigation will examine the affects of both supplementary curcumin and exercise on the antioxidant defence system and lipid peroxidation.

Acknowledgment
The authors are special appreciation extended to M.Mazandarani for her technical assistance.

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11/6/2009