CHAPTER II

REVIEW OF RELATED LITERATURE

This literature review consists of theoretical as well as empirical studies conducted on dietary supplementation and athletic performance. A brief account of use of dietary supplementation among athletes, and the intake of vitamins and minerals in specific to endurance and exhaustive exercises are provided. Specific studies relating to the Vitamin E supplementation on physiological indices, blood parameters, immune parameters and exercise performance are illustrated which provides a background for the present study.

2.1 Studies related to vitamin and mineral supplementations

Yahya (2011) studied to determine the effect of eight weeks zinc supplementation on the erythrocyte and leukocyte counts and other hematological parameters in male kick boxers. Twenty-four subjects were included in the study. They were equally divided into three groups as follows: Group EZ, training and receiving 2.5 mg/kg zinc supplement per day; Group SZ, receiving the zinc supplement but no training and Group E, who exercised but received no supplement. Erythrocyte, platelet and leukocyte counts, hematocrit, hemoglobin and the mean corpuscular volume (MCV) were determined in blood samples taken from each participant at rest and exhaustion. The erythrocyte count of Group EZ was significantly higher than in the E and SZ groups, p < 0.001. The number of leukocytes was higher in the two groups that trained. The hemoglobin and hematocrit levels were
increased in the EZ group (p < 0.05). The platelet number increased with exhaustion in the E and EZ groups (p < 0.001). The MCV values were lower in group EZ as compared to the other two groups. The E and EZ subjects had higher neutrophil counts (p < 0.05). These results suggest that the combined effects of exercise and zinc supplementation have a positive effect in the hematological parameters of athletes, which may result in better performance and increased endurance.

Gauche et al (2010) in their double-blind study investigated the effects of vitamin and mineral complex supplementation on the neuromuscular function of the knee-extensor muscles after a prolonged trail running race. Twenty-two well-trained endurance runners took either placebo (Pl group) or vitamins and minerals (Vm group) for 21 d before the race and for 2 d after the race. Maximal voluntary contractions (MVC) and surface EMG activity of the vastus lateralis (VL) muscle were recorded before (pre) and 1 h (post), 24 h (post 24) and 48 h (post 48) after the race. Central activation ratio (CAR), neural (M-wave), and contractile (muscular twitch) properties of the quadriceps muscles were analyzed using electrical stimulation techniques. The knee-extensor MVC was significantly (P < 0.01) reduced after exercise for both groups (Vm: 36.5 +/- 3.0 %; Pl: 36.9 +/- 2.1%), but MVC recovery was greater for Vm than Pl after 48 h (11%, P < 0.05). The reduced MVC after exercise was associated with a significant reduction in maximal EMG normalized to the M-wave in VL muscle and in CAR for both groups. Characteristics of the muscular twitch were not significantly altered for either groups, whereas M-wave duration increased significantly (P < 0.05) after exercise.
The reduction of MVC immediately after the race appeared to result from peripheral mechanisms such as a failure in muscle membrane excitation and, to a lesser extent, from reduced central activation. The cause of the depressed MVC 24 h after the race seemed to be located within the muscle itself. A dietary supplementation of a vitamin and mineral complex does not attenuate the loss of contractile function immediately after the running exercise, and it may accelerate the recovery of maximal force capacity.

Knez and Peake (2010) assessed the vitamin and mineral intake of ultra marathon athletes. Ultraendurance exercise training places large energy demands on athletes and causes a high turnover of vitamins through sweat losses, metabolism, and the musculoskeletal repair process. Ultra endurance athletes may not consume sufficient quantities or quality of food in their diet to meet these needs. Consequently, they may use oral vitamin and mineral supplements to maintain their health and performance. The authors assessed the vitamin and mineral intake of ultra endurance athletes in their regular diet, in addition to oral vitamin and mineral supplements. Thirty-seven ultra endurance triathletes (24 men and 13 women) completed a 7-day nutrition diary including a questionnaire to determine nutrition adequacy and supplement intake. Compared with dietary reference intakes for the general population, both male and female triathletes met or exceeded all except for vitamin D. In addition, female athletes consumed slightly less than the recommended daily intake for folate and potassium; however, the difference was trivial. Over 60% of the athletes reported using vitamin supplements, of which vitamin C (97.5%), vitamin E (78.3%), and multivitamins (52.2%) were the most commonly used supplements. Almost half
(47.8%) the athletes who used supplements did so to prevent or reduce cold symptoms. Only 1 athlete used supplements on formal medical advice. Vitamin C and E supplementation was common in ultraendurance triathletes, despite no evidence of dietary deficiency in these 2 vitamins.

Armin (2008) studied to investigate the influence of intake of vitamins and minerals before an ultra-endurance triathlon and its effect on race performance in a descriptive field study. Participants of the “Triple Iron Triathlon Germany 2006“ in Lensahn, Schleswig-Holstein, Germany, were contacted by a newsletter six weeks before the race by the organizer and received a questionnaire to fill in their intake of vitamins and minerals. Questionnaires were self-administered and not administered by trained personnel. During this race the athletes had to cover 11.4 km swimming, 540 km cycling and 126.6 km running within 58 hours. The athletes were divided into two categories: successful finishers with intake of vitamins and minerals and successful finishers without intake prior to the race. Race performance (total running time in h) of athletes with intake and athletes without intake of these substances was compared. In the four-week period prior to the race, nine athletes (53 %) ingested vitamins and eight athletes (47 %) minerals. Athletes with intake of vitamins (44.7 ± 7.0 h versus 50.4 ± 4.4h; p>0.05) and minerals (45.3 ± 7.2 versus 49.3 ± 5.4 h, p>0.05) finished the race not faster than athletes without intake of vitamins and minerals. In the “Triple Iron Triathlon Germany 2006“ in Lensahn, Germany, no influence on race performance was observed concerning the regular intake of vitamins and minerals in the last four weeks before the race.
Knetchtle et al (2008) investigated the effect of pre-race intake of vitamins and minerals, in the form of supplementation, before a multi-stage ultra-endurance run and their effect on race performance. At the Deutschlandlauf 2006 in Germany, where athletes had to run across Germany from the north (Kap Arkona - Rügen) to the south (Lörrach) over 1,200 km within 17 consecutive stages, twenty male ultra runners (46.2 ± 9.6 years, 71.8 ± 5.2 kg, 179 ± 6 cm, BMI 22.5 ± 1.9 kg/m²) completed a questionnaire about their intake of vitamin and mineral supplements in the four weeks before the race. Race performance of athletes with- and athletes without regular intake of these supplements were compared. In the four weeks before the run, nine runners (45%) ingested vitamin- and twelve athletes (60%) mineral supplements. Athletes with an intake of vitamins (152.8 ± 14.1 h versus 160.6 ± 14.6 h, \( p > 0.05 \)) and minerals (151.6 ± 14.5 h versus 165.3 ± 10.8 h, \( p > 0.05 \)) finished the race no faster than athletes without an intake of vitamins and minerals. We concluded that in the Deutschlandlauf 2006 of over 1,200 km within 17 consecutive stages, athletes with a regular intake of vitamin and mineral supplements in the four weeks before the race finished the competition no faster than athletes without an intake of vitamins and minerals.

Fry et al (2006) studied to determine if supplementation with a liquid multi-vitamin/mineral would improve anaerobic exercise performance. Fourteen resistance-trained men performed a 30-second cycle sprint and one set of squat exercise on 2 separate days before and following 8 weeks of supplementation with either a liquid multi-vitamin/ mineral or a placebo. Heart rate, perceived exertion, blood lactate, peak and mean power, and rate of fatigue were determined for all tests. No differences were
noted for any variable (P > 0.05). When controlling for pre-supplementation values, however, a decreased rate of fatigue was noted for both exercise tests following the multi-vitamin/mineral supplementation. These data suggest that in resistance trained men consuming a nutritionally sound diet, supplementation with a liquid multi-vitamin/mineral does not favorably impact most anaerobic exercise performances. Such supplementation, however, may result in a minor decreased rate of fatigue. It appears that, in terms of improved short duration anaerobic exercise performance, supplemental micronutrients may not be efficient ergogenic agents for well-trained individuals consuming an adequate diet.

The aim of this study by Schroder et al (2002) was to determine the type, frequency and amount of dietary supplement consumption among a group of professional basketball players. The type, amount and specific timing of supplement use were recorded by 55 professional basketball players from seven different teams of the First Spanish Basketball League. Most participants (58%) consumed dietary supplements. Multivitamins and vitamins were the most frequently used supplements among the athletes (50.9%), followed by sport drinks (21.8%), miscellaneous supplements (21.8%), amino acids (14.5%), proteins (12.7%) and carbohydrates (12.7%). The average daily dietary supplement was one capsule of multivitamins, one capsule of antioxidant vitamins, 0.2± 1.0 g vitamin C, 10.3 g protein, 1.9 g amino acids, 16.2 g carbohydrates and 377 ml of a commercial sport drink. Although the proportion of participants who consumed dietary supplements before, during and immediately after exercise was 25.4%, 16.3% and 7.3% respectively, only a few consumed a potentially ergogenic supplement at these times. It would appear unlikely
that the type or amount of dietary supplements consumed had a beneficial effect on the physical performance of these professional basketball players, with the possible exception of antioxidant vitamins and the commercial sport drinks.

Finstad et al (2001) studied to determine the effects of magnesium (Mg\textsuperscript{2+}) supplementation on performance and recovery in physically active women using the sensitive and recently advanced measure of ionic Mg\textsuperscript{2+} (iMg). Participants (\(N = 121\)) were screened for [iMg] in plasma, with 44 (36.4\%) exhibiting [iMg] below the normal range of 0.53–0.67 mmol·L\textsuperscript{-1} (4). Thirty-two subjects representing a broad range of [iMg] (0.54 ± 0.04 mmol·L\textsuperscript{-1}) completed the main 14-wk study. At baseline, participants submitted to a resting blood pressure measurement, and they completed both an anaerobic treadmill test and an incremental (aerobic) treadmill test. For the latter, values for workload, oxygen uptake, and heart rate were obtained at both anaerobic threshold and maximal effort. Blood samples for iMg, total serum Mg\textsuperscript{2+} (TMg), erythrocyte Mg\textsuperscript{2+} (EMg), Ca\textsuperscript{2+}, K\textsuperscript{+}, Na\textsuperscript{+}, hemoglobin, hematocrit, lactate, and glucose were also collected pre test, and 4, 10, 30 min, and 24 h post test. Subjects received 212 mg·d\textsuperscript{-1} Mg oxide or placebo in a double-blind fashion and were re-tested after 4 wk. After a 6-wk washout period, the testing was repeated with a treatment crossover. Results indicated that Ionic Mg\textsuperscript{2+} increased with Mg\textsuperscript{2+} treatment versus placebo (\(P , 0.05\)); however, performance and recovery indices were not significantly affected. Four weeks of 212 mg·d\textsuperscript{-1} Mg oxide supplementation improves resting [iMg] levels but not performance or recovery in physically active women.

Kim and Keen (1999) surveyed 1,355 adolescent boys and girls attending athletic high schools in Korea for their usage patterns of vitamin/mineral supplements.
The usage rate of the vitamin/mineral supplements was 35.8%. The most favored supplements were vitamin C, multivitamins, and calcium. The reasons most cited for taking supplements were "to recover from fatigue," and "to maintain health." Vitamin and mineral intakes occurred over a wide range; mean intake values were typically higher than the Korean RDA. Vitamins B1, B12 and C were consumed in very high amounts at 29.7, 17.9 and 11.1 times the Korean RDA, respectively. When the intakes of nutrients from supplements and diet were combined, it was observed that the intakes of niacin, folic acid, vitamin C, and iron exceeded levels that have been proposed as upper safe limits. The above data underscore the need to provide sound nutritional education to athletic adolescents and their coaches with respect to the use of vitamin/mineral supplements and the links between adequate diet, good health, and physical performance.

Three studies conducted in Indonesia are reported by Soewondo (1995). Soewondo investigated the relation of iron deficiency and cognitive function and impact of iron supplementation on verbal intelligence, attention and concept learning among iron deficient children without anemia and iron deficient anemic children. Half of 176 children, aged 3-6 years, received elemental Fe for 8 weeks and the other half received placebo. There were significant changes from pre to post intervention evaluations in ferritin, transferrin saturation, free erythrocyte protoporphyrin, and hemoglobin in the iron deficient anemic children. Pre and post treatment psychological test data showed that iron deficiency anemia produced alterations in cognitive processes related to visual attention and concept acquisition. These alterations can be reversed with iron treatment. Idjradinata assessed the impact of iron
supplementation on iron deficient infant's mental and psychomotor development. Hundred and twenty six subjects aged 12 to 18 month were randomly assigned to either iron treatment or placebo intervention. After 4 months of iron supplementation, the hemoglobin, ferritin and transferrin saturation changed significantly in the iron deficient infants. A developmental delay was observed in the iron deficient anemic infants before intervention and the conditions were reversed after 4 months of iron treatment. Soemiarti examined the effectiveness of a training course given to mothers of children aged 12 to 24 months on the rearing environment and consequently to the child's development. The subjects were 69 mothers of 20-35 years old. The training lasted for 21 days by giving mothers training using the program "Ibu Maju Anak Bermutu". The rearing environment improved, also the child's mental and psychomotor development.

Telford et al., (1992) studied the effect of vitamin and mineral supplementation over 7 to 8 months of training and competition in 82 athletes from four sports: basketball, gymnastics, rowing, and swimming. Matched subgroups were formed and a double-blind design used, with subgroups being given either the supplementation or a placebo. All athletes were monitored to ensure that the recommended daily intakes (RDI) of vitamins and minerals were provided by diet alone. Sport-specific and some common tests of strength as well as aerobic and anaerobic fitness were performed. Coaches' assessment of improvement was also obtained. The only significant effect of supplementation was observed in the female basketball players, in which the supplementation was associated with increased body weight, skinfold sum, and jumping ability. A significant increase in skinfold sum was also demonstrated over the
whole group as a result of supplementation. In general, however, this study provided little evidence of any effect of supplementation to athletic performance for athletes consuming the dietary RDIs.

Haymes (1991) reports that vitamin and mineral supplements are frequently used by competitive and recreational athletes. Dietary deficiencies of most vitamins are not very common among athletes except in those who restrict their food intake in order to maintain body weight. Vitamins most likely to be deficient in the diet are folate, B6, B12, and E. Biochemical evidence of vitamin deficiencies in some athletes have been reported for thiamine, riboflavin, and B6. When the diet is deficient, vitamin supplements may improve performance but are not likely to be effective if the dietary intake is adequate. Some female athletes' diets are low in calcium, iron, and zinc. Low calcium intake may reduce peak bone mass in young women. Iron deficiency may impair performance and needs to be corrected with an iron supplement. Zinc supplements that exceed the RDA interfere with the absorption of copper and lower HDL-cholesterol.

Cai and Yan (1990) conducted a study on iron-deficiency anemia (IDA) in adolescence among 478 teen-age students in Shanghai. The study indicated that the intake of nutrients among the students was generally insufficient. The lack of protein, calcium, Vitamin A, Vitamin B1, and Vitamin B2 was more serious. The morbidities of IDA among male and female students were 15.8 and 32.6%, respectively, higher in the female group (P less than 0.01). The iron-deficiency sufferers among male and female students were 46.8 and 61.8%, respectively, also higher in the female group (P less than 0.01). The causes of IDA were analyzed by the method of stepwise
review. In a study of the effect of IDA on intelligence and physical development in adolescents, we found that there was no significant effect of IDA on intelligence quotient (IQ) and school performance. However, the speed and endurance capabilities of students of both sexes were correlated directly with hemoglobin level. In female students, the speed capability was correlated directly with the serum ferritin content. On the basis of these findings, a special 3-month school lunch program was initiated. The results indicate that a comprehensive, rational, and balanced diet is beneficial to hemoglobin, free erythrocyte porphyrin, and serum ferritin contents and improves adolescent development.

Williams (1989) reports on vitamin supplementation and athletic performance. Vitamins serve primarily as regulators of metabolic functions, many of which are critical to exercise performance. Depending upon the nature of their sport, e.g., strength, speed, power, endurance, or fine motor control, athletes may use mega doses of various vitamins in attempts to increase specific metabolic processes important to improved performance. Surveys have indicated that most elite athletes do take vitamin supplements, often in dosages greater than 50-100 times the United States Recommended Dietary Allowances. The theoretical basis underlying the use of each vitamin depends upon its specific metabolic function in relation to sport. Vitamin A functions to maintain night vision; thiamin, riboflavin, niacin, and pantothenic acid are all involved in muscle cell energy metabolism; niacin may also block free fatty acid release; pyridoxine is involved in the synthesis of hemoglobin and other oxygen transfer protein; folic acid and vitamin B12 are integrally involved in red blood cell (RBC) development; vitamins C and E are antioxidants, possibly preventing the
destruction of the red blood cell membrane during exercise; vitamin D may be involved in muscle cell energetics through its influence on calcium. These are but a few of the possible metabolic functions of vitamins which have been suggested to have ergogenic applications to sport. Research has shown that a vitamin deficiency impairs physical performance. If this deficiency is corrected, performance usually improves. In general, vitamin supplementation to an athlete on a well-balanced diet has not been shown to improve performance. However, additional research with certain vitamins appears to be warranted, such as with the vitamin B complex and fine motor control, and with vitamin E and endurance at high altitudes. Moreover, research with megadose supplementation may also be necessary.

Weight, Myburgh, and Noakes (1988) investigated the effect of vitamin and mineral supplementation on running performance of trained athletes. They used a 9-mo, placebo-controlled crossover study design to determine whether a multivitamin and mineral supplement influenced the athletic performance of 30 competitive male athletes. At 0, 3, 6, and 9 mo the runners performed a progressive treadmill test to volitional exhaustion for measurement of maximal oxygen consumption, peak running speed, blood lactate turn point, and peak post-exercise blood lactate level. Running time in a 15 km time trial was also measured. None of these variables was influenced by 3 mo of active supplementation. The authors conclude that 3 mo of multivitamin and mineral supplementation was without any measurable ergogenic effect.

Lukaski (1989) reports on vitamin and mineral status and its effects on physical performance. Public health recommendations encourage the selection of a balanced diet and increasing physical activity to foster health and well-being. Whereas
the adverse effects of restricted intakes of protein, fat, and carbohydrate on physical performance are well known, there is limited information about the impact of low intakes of vitamins and minerals on the exercise capacity and performance of humans. Physically active people generally consume amounts of vitamins and minerals consistent with the recommendations for the general public. However, when intakes are less than recommendations, some noticeable functional impairments occur. Acute or short-term marginal deficiencies, identified by blood biochemical measures of vitamin B status, had no impacts on performance measures. Severe deprivation of folate and vitamin B12 result in anemia and reduce endurance work performance. Evidence of vitamin A and E deficiencies in athletic individuals is lacking apparently because body storage is appreciable. In contrast to vitamins, marginal mineral deficiencies impair performance. Iron deficiency, with or without anemia, impairs muscle function and limits work capacity. Magnesium deprivation increases oxygen requirements to complete submaximal exercise and reduces endurance performance. Use of vitamin and mineral supplements does not improve measures of performance in people consuming adequate diets. Young girls and individuals participating in activities with weight classifications or aesthetic components are prone to nutrient deficiencies because they restrict food intake and specific micronutrient-rich foods. This information will be useful to professionals who counsel physically active people and scientific groups who make dietary recommendations to improve health and optimize genetic potential.
2.2 Studies related to Vitamin C supplementation

Bohlooli, Rahmani-Ni, Babaei, and Nakhostin-Roohi (2012) studied to evaluate the effect of moderate dose vitamin C supplementation on exercise-induced lipid peroxidation, muscle damage and inflammation. Sixteen healthy untrained male individuals participated in a 30-min exercise at 75% VO2max. Subjects were randomly assigned to one of two groups: 1) placebo (P) and 2) vitamin C (VC: 500 mg vitamin C). Blood samples were obtained prior to supplementation (baseline), 2 h after supplementation (immediately pre-exercise), immediately, 2 and 24 h after exercise. Plasma levels of vitamin C, total antioxidant capacity (TAC), creatine kinase (CK), malondialdehyde (MDA), total leukocytes, neutrophils, lymphocytes, interleukin-6 (IL-6), and CRP were measured. With supplementation, plasma vitamin C concentration increased significantly only in the VC group (P<0.05). TAC decreased significantly just in P group, 2 and 24 h after exercise (P<0.05). Although MDA levels were similar between groups at the baseline, only in the P group it increased significantly after exercise (P<0.05). CK increased immediately and 2 h after exercise in both groups and 24 h after exercise just in placebo group compared with pre-exercise (P<0.05). Markers of inflammation (total leukocytes, neutrophils, CRP and IL-6) increased significantly in response to the exercise in both groups (P<0.05). In conclusion, it seems that vitamin C acute moderate dose supplementation affects exercise-induced lipid peroxidation and muscle damage, but not inflammatory markers.

Gomez-Cabrera (2005) designed a study to find out the effect of vitamin C on training efficiency in rats and in humans. The human study was double-blind and
randomized. Fourteen men (27–36 y old) were trained for 8 wk. Five of the men were supplemented daily with an oral dose of 1 g vitamin C. In the animal study, 24 male Wistar rats were exercised under 2 different protocols for 3 and 6 wk. Twelve of the rats were treated with a daily dose of vitamin C (0.24 mg/cm² body surface area). The administration of vitamin C significantly ($P < 0.014$) hampered endurance capacity. The adverse effects of vitamin C may result from its capacity to reduce the exercise-induced expression of key transcription factors involved in mitochondrial biogenesis. These factors are peroxisome proliferator–activated receptor coactivator, nuclear respiratory factor, and mitochondrial transcription factor A. Vitamin C also prevented the exercise-induced expression of cytochrome C (a marker of mitochondrial content) and of the antioxidant enzymes superoxide dismutase and glutathione peroxidase. Vitamin C supplementation decreases training efficiency because it prevents some cellular adaptations to exercise.

Ozaslan, et al (2004) studied the effects of vitamin C supplementation on the leucocyte counts and exercise performance of mice. Mice were divided into 4 groups; 1 control and 3 experimental. We supplemented the diet of the mice from each experimental group with different doses of ascorbic acid (4mg, 8.8 mg, and 13 mg/day; C4, C9, C13, respectively) by intra-peritoneal injection. Physiological serum was given to the control group (CON) via the same procedure. Exercise performance was based on swim time to fatigue. Blood samples were taken and evaluated at day 7, 14, 21, and 28. At the end of day 28, tissue samples were taken from different organs for pathological examination. The lymphocyte percentage was $40.2 \pm 6$ % for CON on day 28. For all C groups, the range of the lymphocyte percentage was 47.5 %– 57.1
% (p < 0.001). Swim time was 1.6 ± 0.3 min at day 28 for CON. This value was increased to 4.6-8.8 min for the C groups (p < 0.001). No pathological differences in organs (skeleton muscle, stomach, spleen, kidney, liver, heart, skin, brain) were determined between the control and experimental groups. In conclusion, it was found that vitamin C supplementation increased the lymphocyte level in blood and improved swim time to fatigue.

2.3 Studies related to Vitamin E supplementation

Cobley and Marrin (2012) studied to determine the direction of change in performance variables at fixed blood lactate concentrations following vitamin E (VE) supplementation. In a paired-matched design twelve (male: N.=8; female: N.=4) trained runners were allocated to a VE (N.=6; 268 mg·d⁻¹) or placebo (N.=6; glucose: 30 mg·d⁻¹) group for 35 days. Participants completed a discontinuous incremental exercise test, pre and post supplementation, to determine peak oxygen uptake (VO2peak) running velocity and percentage of peak oxygen uptake (%(VO2peak)) at the lactate threshold (TLAC) and the onset of blood lactate accumulation (OBLA). Participants maintained a standardised training regime throughout the supplementation period. VE supplementation failed to significantly enhance velocity at TLAC (P=0.91) and OBLA (P=0.22) compared to a placebo treatment. Analogously, VE did not significantly enhance % (VO2peak) at TLAC (P=0.85) and OBLA (P=0.71) compared to a placebo treatment. Whilst VE supplementation did not enhance performance; it did not impair performance compared to a placebo. Training significantly enhanced velocity at TLAC (P=0.00) and OBLA (P=0.05). No training-induced improvements in %VO2peak at TLAC (P=0.06) and OBLA (P=0.40) were observed. Daily VE
supplementation for 35 days does not enhance or impair physiological performance at fixed blood lactate concentrations. Long-term VE supplementation for the purposes of performance enhancement is not recommended.

Theodorou et al (2012) aimed to investigate the effects of vitamin C and vitamin E supplementation on muscle performance, blood and muscle redox status biomarkers, and hemolysis in trained and untrained men after acute and chronic exercise. A specific type of exercise was applied (eccentric) to produce long-lasting and extensive changes in redox status biomarkers and to examine more easily the potential effects of antioxidant supplementation. In a double-blinded fashion, men received either a daily oral supplement of vitamin C and vitamin E ($n = 14$) or placebo ($n = 14$) for 11 wk (started 4 wk before the pre-training exercise testing and continued until the post-training exercise testing). After baseline testing, the subjects performed an eccentric exercise session 2 times/wk for 4 wk. Before and after the chronic eccentric exercise, the subjects underwent one session of acute eccentric exercise, physiologic measurements were performed, and blood samples and muscle biopsy samples (from 4 men) were collected. The results failed to support any effect of antioxidant supplementation. Eccentric exercise similarly modified muscle damage and performance, blood redox status biomarkers, and hemolysis in both the supplemented and non-supplemented groups. This occurred despite the fact that eccentric exercise induced marked changes in muscle damage and performance and in redox status after exercise. The complete lack of any effect on the physiologic and biochemical outcome measures used raises questions about the validity of using oral
antioxidant supplementation as a redox modulator of muscle and redox status in healthy humans.

Nikolaidis et al (2012) reports on whether vitamin C and vitamin E supplementation impair favourable adaptations to regular exercise. The detrimental outcomes associated with unregulated and excessive production of free radicals remains a physiological concern that has implications to health, medicine and performance. Available evidence suggests that physiological adaptations to exercise training can enhance the body’s ability to quench free radicals and circumstantial evidence exists to suggest that key vitamins and nutrients may provide additional support to mitigate the untoward effects associated with increased free radical production. However, controversy has risen regarding the potential outcomes associated with vitamins C and E, two popular antioxidant nutrients. Recent evidence has been put forth suggesting that exogenous administration of these antioxidants may be harmful to performance making interpretations regarding the efficacy of antioxidants challenging. The available studies that employed both animal and human models provided conflicting outcomes regarding the efficacy of vitamin C and E supplementation, at least partly due to methodological differences in assessing oxidative stress and training adaptations. Based on the contradictory evidence regarding the effects of higher intakes of vitamin C and/or E on exercise performance and redox homeostasis, a permanent intake of non-physiological dosages of vitamin C and/or E cannot be recommended to healthy, exercising individuals.

Chatterji, Maitra, and Amit (2011) investigated to determine the effects of Vitamin E supplementation on cardio-respiratory responses during endurance exercise
in different phases of menstrual cycle in female athletes. Twenty five unmarried adult female athletes (21–25 years) were recruited in this placebo-control double-blind randomized experimental trial. Their average duration of menstrual cycle was 28–32 days. Vit-E was supplemented at a dose of 400mg.day for 7 days. The pre-exercise heart rate and peak heart rate were significantly higher in the flow phase than the follicular and luteal phases during pre and post-supplemental trials. The post supplementation values of maximum oxygen uptake (VO2max), O2 pulse, maximum pulmonary ventilation and endurance capacity were significantly (P<0.001) higher than the pre-supplementation values in all the phases of menstrual cycle. As far as the comparison of these parameters between the different phases of menstrual cycle is concerned, all these parameters were significantly different in the flow phase than their corresponding values in the follicular and luteal phases. From the present investigation it is concluded that Vit-E supplementation at a dose of 400 mg.day-1 for 7 days significantly improved the VO2max, maximum voluntary ventilation, O2 pulse and endurance capacity in female athletes during different phases of menstrual cycle. Therefore, such supplementation may be recommended to improve the endurance performance of female athletes.

Kyparos (2011) investigated the potential protective role of vitamin E treatment against eccentric exercise-induced muscle injury by examining morphological and functional alterations in rat soleus muscle after downhill running as well as muscle injury markers in the blood. Sixty adult male Wistar rats were randomly assigned to vitamin E-treated or placebo-treated groups studied at rest, immediately post-exercise or 48 h post-exercise (n = 10 per group). Vitamin E was
administered by daily intraperitoneal injections of 100 mg/kg body mass of DL-a-tocopheryl acetate for five consecutive days prior to exercise, resulting in the doubling of its plasma concentration. Downhill running resulted in significant (P<0.05) changes in all injury markers for the placebo-treated rats at 0 and 48 h post-exercise. However, significantly smaller soleus muscle single-twitch tension (Pt) and unfused (40 Hz) tetanic force, and greater plasma creatine kinase (CK) and lactate dehydrogenase (LD) activities compared with the control were found only immediately post-exercise for the vitamin E-treated rats (P<0.05). Maximal tetanic force (Po) did not decline significantly compared to sedentary controls at neither time points measured. The vitamin E-treated rats had significantly (P<0.05) higher soleus muscle Pt immediately post-exercise than the placebo-treated rats as well as lower plasma CK and LD activity 48 h post-exercise. However, there was no difference in Po decline between groups at either time points measured. Vitamin E-treated rats had less pronounced morphological alterations in muscle in the immediate and 48-h post-exercise period. In conclusion, the effect of short-term vitamin E supplementation against eccentric exercise-induced muscle injury did not appear to be physiologically significant, because vitamin E failed to prevent the decline in the functional measure of Po compared to the placebo conditions.

Gomes, Allgrove; Florida-James, and Stone, (2011) studied the effect of vitamin C and E supplementation on lung injury and performance of runners were analyzed. Using a randomized, double-blinded, crossover design, nine runners participated in two experimental trials: a 2-week Vitamin trial (vitamin C = 500 mg/day + vitamin E = 100 IU/day) and a 2-week Placebo trial. At the end of
each supplementation period the runners performed an 8-km time-trial run in a hot (31°C), humid (70% rh), and ozone-polluted (0.10 ppm O₃) environmental chamber. Nasal lavage and blood samples were collected pre-, post-, and 6-h post-exercise to assess antioxidant status and CC16 as lung injury marker. Higher plasma (pre- and post-exercise) and nasal lavage (post-exercise) antioxidant concentration were found for the Vitamin trial. Nevertheless, this did not result in performance differences (Vitamin trial: 31:05 min; Placebo trial: 31:54 min; \( P = 0.075 \)) even though significant positive correlations were found between antioxidant concentration and improvement in time to complete the run. CC16 was higher post-exercise in the Placebo trial \( (P < 0.01) \) in both plasma and nasal lavage. These findings suggest that antioxidant supplementation might help to decrease the lung injury response of runners when exercising in adverse conditions, but has little effect on performance.

Yfanti et al (2010) investigated the effects of combined vitamin C and E supplementation to healthy individuals on different measures of exercise performance after endurance training. Using a double-blinded placebo-controlled design, moderately trained young men received either oral supplementation with vitamins C and E (n=11) or placebo (n=10) before and during 12 weeks of supervised, strenuous bicycle exercise training of a frequency of 5 days/week. Muscle biopsies were obtained before and after training. After the training period, maximal oxygen consumption, maximal power output, and workload at lactate threshold all increased markedly \( (P < .01) \) in both groups. Also, glycogen concentration, citrate synthase (CS), and β-hydroxyacyl-CoA dehydrogenase (β-HAD) activity in muscle were significantly higher in response to training \( (P < .01) \) in both groups. However, there
were no differences between the two groups with regard to any of the physiological and metabolic variables measured. The study results suggest that administration of vitamins C and E to individuals with no prior vitamin deficiencies has no effect on physical adaptations to strenuous endurance training.

Roshen and Najaafabadi (2009) studied the effect of short term vitamin E supplementation on some indexes of athletic performances and relaxation lipid peroxidation after an exhaustive train session at the sea level. 16 healthy male students (age = 21.3 ± 1.2 years, weight = 66.94 ± 6.5 kg, BMI = 21.95 ± 2.5, and VO$_2$ max = 37.91 ± 4 ml/kg/min.) were selected and randomly divided into two Vitamin E (9 subjects) and placebo (10 subjects) groups. Vitamin E group used one capsule of 400IU alpha tocopheryl acetate and placebo group used 0.4 gr of amylum each day for 14 days. Blood samples were drawn in completely similar conditions and in two phase, ie before and after supplementation each of which were performed before and immediately after the exhaustive test on the ergometer cycle (it started with 25 watt workload and 50 round/min severity for 3 minutes and then until exhaustion. 25 watt were added to it each 2 minutes). To calculate the amount of malondialdehyde (MDA), Thiobarbituric (TBARS) was used. Data were analysed using repeated measure ANOVA and independent and dependent t test. P = 0.05. Results showed an insignificant increase of exhaustive time and a significant increase in VO$_2$ max in the supplement group, while changes of these two indexes were not significant between the two groups. Moreover, exhaustive activity in both groups resulted in significant increase in lipid per-oxidation index (MDA) which significantly decreased after taking vitamin supplementation in both rest and after training states. On the other hand lipid
per-oxidations of rest and post-training condition significantly changed in both groups after supplementation. Based on the findings, it can be stated that short term vitamin E supplementation may lead to an increase in some indexes of athletic performance through a decrease in lipid per-oxidation.

Chatterjee, Maitra, and Amit (2009) recruited thirty six female athletes (Athletes=18, Sedentary=18) in the study to evaluate the effects of Vitamin E supplementation (at a dose of 400mg per day for 7 days) on platelet aggregation and endurance capacity. Platelet aggregation was and endurance capacity was measured by Optical absorbance technique and exercising on bicycle ergometer, respectively. The post-supplemental values of endurance capacity (min) in sedentary females were higher than the pre-supplemental values in different phases of menstrual cycle. Female athletes also exhibited significantly higher values of post-supplemental endurance capacity than the pre-supplemental values in follicular phase, luteal phase and flow phase of menstrual cycle. Vit-E also significantly decreased the platelet aggregation in all the phases of menstrual cycle in both the groups especially during the follicular phase. From the present investigation it can be concluded that Vitamin E significantly inhibited the platelet aggregation and improved the endurance capacity in all the phases of menstrual cycle in female athletes as well as in sedentary female subjects. Accordingly the study establishes the beneficial effects of Vitamin E supplementation on endurance performance of the athletes.

Gupta, Gupta and Singh (2009) studied the effect of vitamin supplementation (composed of 400 IU of vitamin E and 500 mg ascorbic acid for 2 months) on oxidative and enzymatic exercise stress markers during endurance training activity in
50 trained elite Indian cyclists attending national camp at Sports Authority of India, Netaji Subash National Institute of Sports (SAI-NSNIS), Patiala, India. Serum concentrations of ascorbic acid, alpha tocopherol, malondialdehyde (MDA), superoxide dismutase (SOD) and catalase were measured before supplementation and after completion of 2 months of antioxidant supplementation. Antioxidant supplementation led to significant increase in serum alpha-tocopherol and ascorbic acid from pre-supplementation to post-supplementation stage. Serum MDA concentration and SOD activity decreased significantly after 2 months of antioxidant treatment. There was increase in serum catalase activity after supplementation compared to before supplementation. The results of the present study suggest that antioxidant supplementation may strengthen the antioxidant defense system, thus reducing the oxidative stress produced after endurance training in elite Indian cyclists.

Jourkesh; Ostojic and Azarbeyjani (2007) studied the effects of vitamin E and vitamin C supplementation on the bio-energetic index, 36 male physical education students were selected non randomly and assigned to a different supplementation protocol. The average age, weight, height, and fat percentage were 22.48 +/- 1.84 years, 64.93 +/- 7.84 kg, 175.4 +/- 5.66 cm, and 10.94 +/- 5.29%, respectively. The period of supplementation lasted 3 weeks. The subjects from group 1 consumed a daily dose of 400 mg of vitamin E, subjects from group 2 ingested 1000 mg of vitamin C, subjects from group 3 ingested 400 mg of vitamin E along with 1000 mg of vitamin C, and subjects from group 4 (control group) consumed a placebo. The tests applied were the running anaerobic sprint test (RAST) and the Cooper 12-min run test. The results indicate that there were no significant differences between groups during the
study in anaerobic power assessed by RAST. The authors found a significant
difference between group's, however, in aerobic power ($p < 0.05$). It was concluded
that daily consumption of vitamin E, vitamin C, and a combination of vitamin E and
vitamin C for a period of 3 week significantly improved aerobic power

Dyslipidemia and oxidative stress are thought to be important mechanisms in
pathogenesis of disease in hemodialysis patients. The study by Mortzzavimoghaddam,
Zarban, Asghar and Rezvani (2007) was designed to investigate the efficacy of oral
vitamin E supplementation on lipid profile and oxidative stress in hemodialysis
patients. The study group consisted of 26 uremic patients (10 women and 16 men), 16-
68 years of age undergoing maintenance hemodialysis three times a week
(12 hours/week), lasting a range of 6-108 months, at Vali-e-Asre Hospital in Birjand
(Iran). Total Antioxidant Capacity (TAC), lipid peroxidation, cholesterol, triglyceride,
high-density lipoprotein and low-density lipoprotein levels were determined before
and after oral vitamin E supplementation, 400 mg/d for 90 days.

Zoppi (2006) investigated to determine the effects of these supplemental
antioxidant vitamins on markers of oxidative stress, muscle damage and performance
of elite soccer players. Ten male young soccer players were divided into two groups.
Supplementation group ($n = 5$) received vitamins C and E supplementation daily
during the pre-competitive season (S group), while the placebo group (PL group, $n =
5$) received a pill containing maltodextrin. Both groups performed the same training
load during the three-month pre-season training period. Erythrocyte antioxidant
enzymes glutathione reductase, catalase and plasma carbonyl derivatives did not show
any significant variation among the experimental groups. Similarly, fitness level
markers did not differ among the experimental groups. However, S group demonstrated lower lipid peroxidation and muscle damage levels (p < 0.05) compared to PL group at the final phase of pre-competitive season. In conclusion, the data demonstrated that vitamin C and E supplementation in soccer players may reduce lipid peroxidation and muscle damage during high intensity efforts, but did not enhance performance.

Keong, Singh and Singh (2006) investigated the effects of tocotrienol-rich palm vitamin E supplementation on exercise induced lipid peroxidation and endurance performance in the heat. In a double blind, cross-over study, eighteen healthy, male recreational athletes completed two endurance running trials, until exhaustion, on a motorized treadmill at 70% VO2max on two separate occasions following a 6-week supplementation regimen of either tocotrienol-rich palm vitamin E (E) or placebo (P). Both trials were conducted in the heat (31 oC, 70% relative humidity). During the trials, rectal temperature (Trec), ratings of perceived exertion (RPE) and oxygen uptake (VO2) were recorded. Blood samples were collected for the determination of plasma volume changes (PVC), malondialdehyde (MDA), creatine kinase (CK), total antioxidant status (TAS) and vitamin E. After the supplementation regimen, serum alpha-tocopherol increased ~33% but serum concentrations of tocotrienols were negligible. No significant differences were evident in mean Trec, RPE, VO2 or in the time to exhaustion between the E-supplemented and the placebo-supplemented groups. Similarly, mean PVC, CK and TAS were also not different between the two groups. Resting plasma mean MDA concentration in the E-supplemented group was significantly lower than that in the placebo-supplemented group. At exhaustion,
plasma mean MDA was higher than the resting values in both groups. Although tocotrienol-rich palm vitamin E supplementation decreased lipid peroxidation at rest and, to some extent, during exercise in the heat, as evident from the lower MDA levels, it however did not enhance endurance running performance or prevent exercise-induced muscle damage or influenced body core temperature or plasma volume changes during exercise in the heat.

Gaeini, Rahnama, and Hamedinia, (2006) studied to determine the effect following exercise to exhaustion of vitamin E supplementation on oxidative stress in athletic students. Twenty male students voluntarily participated in the study and were randomly assigned (double blind) to either a vitamin E (daily dose of 450 mg of α-tocopherol for a period of 8 weeks) or a placebo group (took capsules containing 450 mg of lactose for 8 weeks). Before and after 8 weeks blood samples were collected at rest and after exercise to exhaustion. Oxidative stress markers were malondialdehyde (MDA), carbonylated proteins (CP) and creatine kinase (CK). Also, the effect of vitamin E on ergometer cycling time, as an example of endurance performance, was evaluated. ANOVA and independent t-tests indicated that vitamin E supplementation did not significantly change (P > 0.05) MDA, CP and CK values at rest, after exercise to exhaustion, and cycling time, but plasma volume after exercise to exhaustion significantly decreased (P < 0.05). Although vitamin E supplementation had no effect on exercise performance or capacity in athletic students, further investigation is required using larger numbers of subjects and measures of vitamin E before unequivocal conclusion can be stated.
Traber (2006) investigated the relationship of vitamin E metabolism and oxidation in exercising human subjects. During endurance exercise, oxygen consumption by the skeletal muscle can increase 100–200 times. Previous research by the same author found that during an ultra marathon race (50 km, forest trail through hilly terrain) compared with a day of rest, vitamin E disappeared faster (as measured using 2H-labelled α-tocopherol) and lipid peroxidation increased. Therefore, we hypothesized that prior supplementation with antioxidants (vitamins E and C) would decrease oxidative stress during distance running and, therefore, decrease lipid peroxidation and inflammation, decrease DNA damage, decrease muscle damage and/or improve recovery. To test these hypotheses, we carried out a randomized, double-blind study in runners (n 11 females, 11 males) who were participants in an annual ultra marathon race. We found that supplementation with both vitamins E and C only prevented increases in lipid peroxidation, but had no apparent effect on DNA damage, inflammation or muscle damage. These results suggest that the mechanism of oxidative damage is operating independently of the inflammatory and muscle damage responses.

The relationship between omega-3 fatty acids and surrogate circulating markers of cardiovascular disease (CVD) risk, especially in healthy individuals remains to be determined. Ghiasvand (2006) investigated the effects of Eicosapentaenoic acid (EPA) supplementation, with or without vitamin E, on serum lipid profile, C-reactive protein (CRP), blood pressure (BP) and total antioxidant capacity in a sample of male athletes. This randomized double blind placebo-controlled clinical trial was conducted on 34 apparently healthy, well-trained male
Review of Related Literature

basketball players, aged 17-35 years. Venous blood samples were obtained between 5:00 and 6:00 p.m., after exercising for 2 hours, at the baseline and after intervention. Participants received 2 g EPA and/or 400 IU vitamin E and/or placebo depending on their groups. For 6 weeks, eight subjects received an EPA supplement with vitamin E (group 1), nine subjects received an EPA supplement with vitamin E placebo (group 2), nine subjects received an EPA supplement placebo and vitamin E (group 3), and eight subjects received an EPA supplement placebo and vitamin E placebo (group 4).

Significant decreases were documented in the serum levels of total cholesterol (TC), triglycerides (TG), LDL-C and CRP in group1 (p<0.01), in TC, TG, LDL-C, CRP, and BP in group 2 (p<0.01), and significant increase in total antioxidant capacity in group 3 (P<0.05). No significant difference was found in LDL between groups 1 and 4 (P<0.05), and in total antioxidant capacity between groups 2 and 3 (p<0.001) and groups 3 and 4 (p<0.001), and in CRP level between groups 2 and 3 (P<0.05). There were no significant differences in TC, TG, HDL-C and BP between the groups after 6 weeks of intervention. Six weeks of EPA + vitamin E supplementation improved the lipid profile and reduced the CRP level, whereas six weeks of EPA supplementation without vitamin E improved the lipid profile, but increased CRP and BP. Six weeks of vitamin E supplementation alone increased total plasma antioxidant capacity.

Aquilo (2004) studied to find out the effects of antioxidant supplementation (vitamins E and C, and beta-carotene) on the basal iron status of athletes prior to and following their training and competition season (3 months). Eighteen amateur trained
male athletes were randomly distributed in 2 groups: placebo (lactose) and antioxidant supplemented (vitamin E, 500 mg/d; vitamin C, 1 g/d; and beta-carotene, 30 mg/d). The study was double blind. Hematological parameters, dietary intake, physical activity intensity, antioxidant status (GSH/GSSG ratio), and basal iron status (serum iron, transferrin, ferritin, and iron saturation index) were determined before and after the intervention trials. Exercise decreased antioxidant defenses in the placebo group but not in the antioxidant-supplemented group. No changes were found in the number of erythrocytes, hematocrit, or hemoglobin concentration, or in values of serum iron parameters, after taking the antioxidant cocktail for 3 months, in spite of the exercise completed. The placebo group showed a high oxidative stress index, and decreases in serum iron (24%) and iron saturation index (28%), which can neither be attributed to aspects of the athletes' usual diet, nor to hemo-concentration. Antioxidant supplementation prevents the decrease of serum iron and the iron saturation index, and a link between iron metabolism and oxidative stress may also be suggested.

Williams (2004) tested the development of oxidative stress and the effects of antioxidant supplementation in an 80-km ride. A pre-competition survey revealed that no competitor would participate without vitamin E supplementation; therefore, 46 horses were paired for past performances and randomly assigned to two groups of 23 each for 3 wk of supplementation before the ride. One group (E) was orally supplemented with 5,000 IU of vitamin E per day; the other group (E+C) received that dose of vitamin E plus 7 g/d of vitamin C. Blood samples, temperature, and heart rate were taken the day before the race, at 21 and 56 km during the ride, at completion, and after 20 min of recovery. Plasma was assayed for lipid hydroperoxides, alpha-
tocol, total ascorbate, albumin, creatine kinase (CK), and aspartate aminotransferase (AST). Total glutathione and glutathione peroxidase activity were determined in red blood cells and white blood cells. Thirty-four horses completed the race, 12 horses (six in E and six in E+C) did not finish for reasons including lameness, metabolic problems, and rider option. Plasma ascorbate was higher (P = 0.045) in the E+C group than in the E group. Other than ascorbate, neither antioxidant status nor CK and AST activities were affected by supplementation with E+C vs. E. Red blood cell glutathione peroxidase, white blood cell total glutathione, lipid hydroperoxides, CK, and AST increased, and red blood cell total glutathione and white blood cell glutathione peroxidase activity decreased with distance (P < 0.001). Positive correlations were found for plasma lipid hydroperoxides on CK (r = 0.25; P = 0.001) and AST (r = 0.33; P < 0.001). These results establish an association between muscle leakage and a cumulative index of oxidative stress.

Nieman et al (2004) studied to measure the influence of vitamin E ingestion on oxidative stress and immune changes in response to the Triathlon World Championship in Kona, Hawaii. Thirty-eight triathletes received vitamin E (Vit-E) (800 IU·d⁻¹ -tocopherol) or placebo (Pla) capsules in randomized, double-blind fashion for 2 months before the race event. Blood, urine, and saliva samples were collected the day before the race, 5–10 min post race, and 1.5 h post race. The results indicated that race times did not differ between Vit E (N = 19, 721 ± 24 min) and Pla groups (N = 17, 719 ± 27 min, P = 0.959), and both groups maintained an intensity of 80% maximum heart rate during the bike and run portions. Plasma -tocopherol was approximately 75% higher in the VitE versus Pla group prerace (24.1 ± 1.1 and 13.8 ±
Plasma F2-isoprostanes increased 181% versus 97% postrace in the VitE versus Pla groups (P < 0.044). IL-6 was 89% higher (166 ± 28 and 88 ± 13 pg·mL⁻¹, respectively, P = 0.016), IL-1ra was 107% higher (4848 ± 1203 and 2341 ± 790 pg·mL⁻¹, respectively, P = 0.057), and IL-8 was 41% higher postrace in the VitE versus Pla groups (26.0 ± 3.6 and 18.4 ± 2.4 pg·mL⁻¹, respectively, P = 0.094). The study concluded that that vitamin E (800 IU·d⁻¹ for 2 months) compared with placebo ingestion before a competitive triathlon race event promotes lipid peroxidation and inflammation during exercise.

Zimmermann (2003) reports that supplements of vitamins C and E have shown promise in reducing exercise-related symptoms (delayed muscle soreness) and biochemical indices of oxidative stress in both trained and untrained individuals. However, these antioxidant supplements appear to have no beneficial effect on performance and more research is needed to prove their long-term use is safe and effective. A prudent recommendation for athletes is to consume a diet rich in antioxidants. For female athletes, vegetarian athletes, and distance runners, daily consumption of foods rich in bio-available iron together with periodic monitoring of iron status will minimize risk of iron deficiency. Iron supplementation is clearly indicated for cases of iron-deficiency anemia and may be beneficial in cases of low serum ferritin without anemia. The effect of magnesium (Mg) supplementation on exercise performance is equivocal. Overall, studies suggest Mg supplementation does not affect performance when serum Mg is within the range of normal values, but may improve performance when marginal or clinical Mg deficiency is present.
Jessup, Home and Yarandi (2003) examined the effects of exercise and vitamin E supplementation on oxidative stress in older adults, 59 participants, age 76.3 ± 4.2 years, were randomly assigned to 1 of 4 groups: an exercise group taking placebos (EGP) or vitamin E (EGE) or a sedentary group taking placebos (SGP) or vitamin E (SGE). Measures included weight, VO₂ max, blood pressure (BP), and serum concentrations of vitamin E and lipid hydroperoxide (LOOH). At the end of the 16-week trial, the EGP and EGE had significant increases in VO₂ max and significant decreases in resting BP, weight, and LOOH concentrations ($P < 0.05$). The SGE had significant decreases in LOOH and BP ($P < 0.05$). There were no significant changes in the SGP ($P > 0.05$). The results suggest that endurance exercise in combination with vitamin E reduces oxidative stress, improves aerobic fitness, and reduces BP and weight in older adults. Even sedentary participants who take vitamin E may reduce oxidative stress and lower BP.

Avery et al (2003) examined the effects of vitamin E (VE) supplementation (1200 IU/day) on recovery responses to repeated bouts of resistance exercise. Non–resistance trained men were assigned to supplement with VE (n 5 9) or placebo (PL; n 5 9) for 3 weeks and then perform 3 resistance exercise sessions separated by 3 days of recovery (EX-1, EX-2, and EX-3). Performance was assessed at EX-1, EX-2, and EX-3. Fasting morning blood samples and perceived muscle soreness were obtained before EX-1 and for 10 consecutive days. Muscle soreness peaked after EX-1 and gradually returned to baseline values by day 6. Lower and upper body maximal strength and explosive power were significantly ($p < 0.05$) decreased at EX-2 and EX-3 (10%). Plasma malondialdehyde (MDA) was significantly elevated on days 7 and 8.
There were no significant differences between VE and PL in muscle soreness, performance measures, or plasma MDA. Creatine kinase (CK) area under the curve from day 1 to day 10 was significantly greater for VE because of a nearly 2-fold greater increase in CK after EX-1 in VE, compared with PL (404 ± 146 and 214 ± 179 U/L, respectively). VE supplementation was not effective at attenuating putative markers of membrane damage, oxidative stress, and performance decrements after repeated bouts of whole-body concentric/eccentric resistance exercise.

Takanami, Iwane, Kawai, and Shimomitsu, (2000) reports on the benefits of Vitamin E supplementation on endurance exercise. It has been widely noted that vitamin E shows numerous beneficial effects through and beyond its antioxidative properties; consequently, vitamin E is expected to prevent degenerative diseases. In the field of sports medicine, many studies dealing with vitamin E have been conducted originally from the point of view of its effects on physical performance. Although some earlier studies indicated that vitamin E supplementation could improve physical performance, defects in the study design or statistical analysis were pointed out at a later time. The majority of subsequent well controlled studies have reported no significant effect on physical performance from vitamin E supplementation. Recent studies suggest that endurance exercise may promote free radical generation in the body, and vitamin E may play an important role in preventing the free radical damage associated with endurance exercise. Although there is evidence of free radical involvement in exercise-induced muscle injury, vitamin E supplementation might not be expected to prevent muscle damage caused by exercise in humans without a vitamin E deficiency. Since it is still unclear whether exercise induces lipid
peroxidation in the human body, the beneficial effect of vitamin E supplementation on
exercise-induced lipid peroxidation has not yet been established. However, it is
proposed that as a result of exercise vitamin E may be mobilised from store tissues and
redistributed in the body to prevent oxidative damage. The authors report that they are
convinced that vitamin E contributes to preventing exercise-induced lipid
peroxidation. It has also been indicated that strenuous endurance exercise may
enhance the production of oxidised low density lipoprotein (LDL), which plays a key
role in the initiation and progression of atherosclerosis. It is also suggested that this
enhanced production of oxidised LDL could be reduced if a higher vitamin E status is
maintained. Supplementation with 100 to 200mg of vitamin E daily can be
recommended for all endurance athletes to prevent exercise-induced oxidative damage
and to reap the full health benefits of exercise.

Serafini, (2000) reports on dietary vitamin E and T cell-mediated function in
the elderly. One of the most dramatic and consequence-bearing age-related
phenomena is the decline of the immune function with old age. Age-related T cell-
mediated immunity dysfunction has been implicated in the etiology of many of the
chronic degenerative diseases of the elderly, including arthritis, cancer, autoimmune
diseases and increased susceptibility to infectious diseases. T cells from aged
individuals are impaired in their response to mitogens and in their cytokine
production. In recent years, several studies have emphasized the importance of
intra-cellular anti-oxidant levels for preserving the immune function. Recent progress
in understanding the mechanisms of action of anti-oxidants on cellular metabolism,
have shown that anti-oxidants may modulate signal transduction and gene expression
Review of Related Literature

in immune cells. Vitamin E is widely recognized as a major lipid-soluble chain-breaking anti-oxidant in the biological membrane, where it scavenges free radicals, inhibiting the initiation and chain propagation of lipid peroxidation and protecting cellular structures against oxidative stress damage. Experimental studies have provided evidences for a role of vitamin E in protecting the immune system of elderly subjects. This article reviews the studies concerning the effect of both vitamin E deficiency and supplementation on T cell-mediated immune function in aging.

Evans (2000) reviews regarding vitamin E and vitamin C and exercise. Exercise increases the generation of oxygen free radicals and lipid peroxidation. Strenuous exercise in a person who is unconditioned or unaccustomed to exercise will induce oxidative damage and result in muscle injury. However, aerobic exercise training strengthens the antioxidant defense system by increasing superoxide dismutase. Vitamin C and, especially, vitamin E are shown to decrease the exercise-induced increase in the rate of lipid peroxidation. No ergogenic effects of either vitamin C or E have been shown. Vitamin E was shown to significantly increase circulating neutrophils in older, but not younger, subjects performing eccentric exercise that causes an increase in skeletal muscle damage. In addition to its effect in augmenting the neutrophil response to eccentric exercise, vitamin E causes a greater increase in circulating creatine kinase activity, perhaps indicating increased skeletal muscle repair. Increased vitamin E intake has been associated with enhanced glucose tolerance and insulin action as well as improved lipoprotein status. Future research should examine the combined effects of exercise training and vitamins E and C on these health-related outcomes.
Buchman (1999) sought to determine if pre-race vitamin E supplementation would prevent intestinal ischemia/reperfusion injury in humans. Forty subjects who planned to complete the 1996 Houston-Tennaco Marathon were randomized to receive vitamin E (1000 IU daily) or placebo (soya lecithin) for 2 wk before the race in a double-blinded trial. Inclusion criteria included no use of non-steroidal anti-inflammatory drugs (NSAIDs) within 24 d of the race or vitamin or mineral supplements containing vitamins C or E or selenium within 30 d of the race. Subjects were studied 2 wk before the race and immediately following the race. Blood was obtained for serum vitamin E and total lipid and salicylate concentrations. A solution of lactulose (5 g) and mannitol (2 g) was consumed and urine was collected for 6 h. Aliquots were assayed for lactulose and mannitol concentration. Stool samples were tested for occult blood and following the race subjects rated their nausea, abdominal pain, and cramping on a 1–5 scale. Twenty-six subjects (24 male, 2 female) completed the marathon. Finish times ranged between 2 h 43 min and 5 h 28 min. All subjects had heme-negative stool pre-race and four developed heme-positive stool post-race, with no difference between vitamin E and placebo groups (Fisher’s exact = 0.63). All had non-detectable salicylate concentrations pre- and pos-race. Serum vitamin E concentration increased in both groups (1.56 ± 0.27 to 3.46 ± 1.25 mg/dL, $P = 0.02$ in the vitamin E group and 1.45 ± 0.40 to 1.66 ± 0.48 mg/dL in the placebo group, $P = 0.02$). However, the serum vitamin E: total lipid ratio increased significantly in the vitamin E-supplemented group (0.0022 ± 0.0002 to 0.0051 ± 0.0015, $P= 0.02$), but not in the placebo group ($P = 0.25$). Overall, the urinary lactulose :mannitol ratio increased from 0.03 ± 0.02 to 0.06 ± 0.08 postrace ($P = 0.06$) without difference
between vitamin E or placebo groups. Intestinal permeability increased significantly more in those who developed occult bleeding. More subjects in the placebo group developed abdominal cramping (Fisher’s exact = 0.04) and abdominal pain (Fisher’s exact = 0.06), although there was no difference in severity between groups. There was no difference in the incidence of nausea and no diarrhea was reported by any subject. Intestinal permeability tends to increase and occult gastro-intestinal bleeding occurs during endurance running, suggesting the occurrence of intestinal ischemia/reperfusion injury. Pre race supplementation with the antioxidant vitamin E had no effect on performance, intestinal injury, occult bleeding, or the severity of post race gastrointestinal complaints. Vitamin E supplementation was associated with a decreased incidence of these complaints but had no effect on their severity.

The oxidative effects were investigated of exhausting exercise in smokers, and the possible protective role of 400 mg á day1 vitamin E (Vit E) supplementation over a period of 28 days by Surmen-gur et al (1999). The subjects exercised to exhaustion including concentric-eccentric contractions following maximal cycling. The haematocrit and haemoglobin, leucocyte (WBC), plasma lactic acid (La) and malondialdehyde (MDA), erythrocyte superoxide dismutase (SOD) and glutathione peroxidase (GPx), serum Vitamin E and ceruloplasmin (CER) concentrations were measured pre and post exercise. Supplementation increased Vit E concentrations 28% and 31% in the controls and the smokers, respectively. Cigarette smoking and/or Vit E supplementation did not influence plasma lipid peroxidation or the antioxidant status at rest. Exercise caused significant haemoconcentration in all groups. When the post-exercise concentrations were adjusted for haemoconcentration, a significant elevation
in La concentrations due to exercise was observed in all groups. Similarly, there were significant elevations in the adjusted WBC counts in all groups except the Vit E supplemented controls. The MDA concentrations on the other hand, when adjusted for haemoconcentration, did not exhibit any difference due to exercise. Exercise did not affect the GPx and CER activities either, while causing a SOD activity loss in all groups except the Vit E supplemented non-smokers. Serum Vit E concentrations diminished significantly in all groups after exercise. Post-exercise plasma MDA and blood antioxidant concentrations were not altered by smoking. The results would suggest that plasma volume changes should always be taken into account when assessing post-exercise plasma concentrations and that smoking and exercise do not have an additional collective effect on plasma lipid peroxidation and the dose of Vit E administered was insufficient to maintain the serum concentrations after exercise.

Vitamin E supplementation caused a significant decrease in ThioBarbituric Acid Reactive Substances (TBARS) level as a marker for lipid peroxidation (2.97±0.52 vs. 2.55±0.44, P<0.001) and a significant increase in plasma TAC (1252±348 vs. 1398±372, P<0.01). Although there was a decrease in the level of lipid profile, there were no statistically significant differences in the means of cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein before and after vitamin E supplementation among patients. The study results indicated that oral vitamin E supplementation might be able to modify oxidative stress by an increase in TAC, and a decrease in lipid peroxidation; that could be considered as a preventive strategy in hemodialysis patients.
Gohil et al (1986) investigated the effects of dietary antioxidant vitamins E and C on exercise endurance capacity and mitochondrial oxidation in rats. The endurance capacity of both vitamin E-deficient and vitamin C-supplemented, E-deficient rats was significantly (P less than 0.05) lower (38.1 and 33.6%, respectively) than control animals. Compared with the normal and vitamin E-deficient rats, there was a significant (P less than 0.05) increase in the concentration of vitamin C in blood and liver of the vitamin E-deficient, C-supplemented animals. Hence dietary vitamin C supplementation does not prevent the inhibition of exercise endurance capacity or increased hemolysis seen in vitamin E deficiency. The mitochondrial activities for the oxidation of palmitoyl carnitine and alpha-ketoglutarate were significantly (P less than 0.05) decreased by a single bout of exercise in brown adipose tissue but not in muscle, heart, or liver from vitamin C-supplemented, E-deficient groups of rats when compared with the activities in the tissue from the same group of rats killed at rest. Similar results were also seen in brown adipose tissue from vitamin E-deficient rats. The results suggest a tissue-specific role for vitamins E and C in substrate oxidation and show that the poor endurance capacity of vitamin E-deficient rats cannot be attributed to any changes in the mitochondrial activity in skeletal or cardiac muscles. It is also concluded that vitamin C supplementation, at least at the dose employed in the present study, cannot counteract the detrimental effects associated with vitamin E deficiency.

2.4 Studies related to other supplementation

Pryor; Craig; Stuart; and Swensen (2012) examined the effect of betaine supplementation on cycling sprint performance. Sixteen recreationally active subjects
Review of Related Literature

(7 females and 9 males) completed three sprint tests, each consisting of four 12 sec efforts against a resistance equal to 5.5% of body weight; efforts were separated by 2.5 min of cycling at zero resistance. Test one established baseline; test two and three were preceded by seven days of daily consumption of 591 ml of a carbohydrate-electrolyte beverage as a placebo or a carbohydrate-electrolyte beverage containing 0.42% betaine (approximately 2.5 grams of betaine a day); half the beverage was consumed in the morning and the other half in the afternoon. We used a double blind random order cross-over design; there was a 3 wk washout between trials two and three. Average and maximum peak and mean power were analyzed with one-way repeated measures ANOVA and, where indicated, a Student Newman-Keuls. Compared to baseline, betaine ingestion increased average peak power (6.4%; p < 0.001), maximum peak power (5.7%; p < 0.001), average mean power (5.4%; p = 0.004), and maximum mean power (4.4%; p = 0.004) for all subjects combined. Compared to placebo, betaine ingestion significantly increased average peak power (3.4%; p = 0.026), maximum peak power max (3.8%; p = 0.007), average mean power (3.3%; p = 0.034), and maximum mean power (3.5%; p = 0.011) for all subjects combined. There were no differences between the placebo and baseline trials. One week of betaine ingestion improved cycling sprint power in recreationally active males and females.

Powers, Nelson and Larson-Meyer (2011) reports on whether athletes should be supplemented with antioxidants and vitamins. The idea that dietary supplements can improve athletic performance is popular among athletes. The use of antioxidant supplements is widespread among endurance athletes because of evidence that free
radicals contribute to muscle fatigue during prolonged exercise. Furthermore, interest in vitamin D supplementation is increasing in response to studies indicating that vitamin D deficiency exists in athletic populations. This review explores the rationale for supplementation with both antioxidants and vitamin D and discusses the evidence to support and deny the benefits of these dietary supplements. The issue of whether athletes should use antioxidant supplements remains highly controversial. Nonetheless, at present there is limited scientific evidence to recommend antioxidant supplements to athletes or other physically active individuals. Therefore, athletes should consult with their health care professional and/or nutritionist when considering antioxidant supplementation. The issue of whether athletes should supplement with vitamin D is also controversial. While arguments for and against vitamin D supplementation exist, additional research is required to determine whether vitamin D supplementation is beneficial to athletes. Nevertheless, based upon the growing evidence that many athletic populations are vitamin D deficient or insufficient, it is recommended that athletes monitor their serum vitamin D concentration and consult with their health care professional and/or nutritionist to determine if they would derive health benefits from vitamin D supplementation.

Konrad et al (2011) tested the acute anti-inflammatory influence of a quercetin-based supplement consumed by endurance athletes 15-min prior to an intense 2-h run. In this randomized, crossover study, 20 long distance runners (N=11 males, N=9 females, age 38.4±2.1 y, VO2max 52.6±2.0) completed two 2-h treadmill runs at 70% VO2max (3 weeks apart) that incorporated a closing 15-min time trial. In double-blinded fashion, subjects ingested either four Q-chews or placebo chews (PL)
15 min prior to the treadmill runs. The four Q-chews provided 1000 mg quercetin, 120 mg epigallocatechin 3-gallate (EGCG), 400 mg isoquercetin, 400 mg eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), 1000 mg vitamin C, and 40 mg niacinamide. Subjects provided blood samples 30 min before, immediately following and 1-h post-exercise, and were analyzed for plasma quercetin concentration, total blood leukocytes (WBC), and nine inflammatory cytokines (IL-6, TNFα, GM-CSF, IFNγ, IL-1β, IL-2, IL-8, IL-10, IL-12p70) using an electrochemiluminescence based solid-phase sandwich immunoassay (Meso Scale Discovery, Gaithersburg, MD, USA). Plasma quercetin was elevated from 80.0±26.0 μg/L (pre-exercise) to 6,337±414 (post-exercise) and 4,324±310 μg/L (1-h post-exercise) after ingestion of Q-chews compared to no change in PL (interaction effect, P<0.001). No difference was measured between Q-chew and PL conditions in the distance run during the 15-min time trial (3.08±0.11 and 3.13±0.11 km, respectively, P=0.370). Exercise caused significant increases in WBCs, GM-CSF, IL-10, IL-1β, IL-2, IL-6, IL-8, and TNFα, but no differences in the pattern of change were measured between Q-chew and PL trials.

Acute ingestion of Q-chews 15 minute before heavy exertion caused a strong increase in plasma quercetin levels but did not counter post-exercise inflammation relative to placebo. These data are in contrast to the anti-inflammatory effect measured with this same quercetin-based supplement when consumed for two weeks prior to a 3-day period of intensified exercise. Taken together, these data imply that a prolonged Q-chew supplementation period is needed before anti-inflammatory effects can be achieved.
β-Alanine (βA) has been shown to improve performance during cycling. The study by Jordan, Lukaszuk, Misic; and Josephine (2010) was the first to examine the effects of βA supplementation on the onset of blood lactate accumulation (OBLA) during incremental treadmill running. Seventeen recreationally-active men (mean ± SE 24.9 ± 4.7 yrs, 180.6 ± 8.9 cm, 79.25 ± 9.0 kg) participated in this randomized, double-blind, placebo-controlled pre/post test 2-treatment experimental design. Subjects participated in two incremental treadmill tests before and after 28 days of supplementation with either βA (6.0 g·d⁻¹)(βA, n = 8) or an equivalent dose of Maltodextrin as the Placebo (PL, n = 9). Heart rate, percent heart rate maximum (%HRmax), %VO₂max@OBLA (4.0 mmol.L⁻¹ blood lactate concentration) and VO₂max (L.min⁻¹) were determined for each treadmill test. Friedman test was used to determine within group differences; and Mann-Whitney was used to determine between group differences for pre and post values (p < 0.05). The βA group experienced a significant rightward shift in HR@OBLA beats.min⁻¹ (p < 0.01) pre/post (161.6 ± 19.2 to 173.6 ± 9.9) but remained unchanged in the PL group (166.8 ± 15.8 to 169.6 ± 16.1). The %HRmax@OBLA increased (p < 0.05) pre/post in the βA group (83.0% ± 9.7 to 88.6% ± 3.7) versus no change in the PL group (86.3 ± % 4.8 to 87.9% ± 7.2). The %VO₂max@OBLA increased (p < 0.05) in the βA group pre/post (69.1 ± 11.0 to 75.6 ± 10.7) but remained unchanged in the PL group (73.3 ± 7.3 to 74.3 ± 7.3). VO₂max (L.min⁻¹) decreased (p < 0.01) in the βA group pre/post (4.57 ± 0.8 to 4.31 ± 0.8) versus no change in the PL group (4.04 ± 0.7 to 4.18 ± 0.8). Body mass kg increased (p < 0.05) in the βA group pre/post (77.9 ± 9.0 to 78.3 ± 9.3) while the PL group was unchanged (80.6 ± 9.1 to 80.4 ± 9.0). A supplementation for 28 days enhanced sub-
maximal endurance performance by delaying OBLA. However, βA supplemented individuals had a reduced aerobic capacity as evidenced by the decrease in VO$_{2\text{max}}$ values post supplementation.

Carr et al (2008) examined the effects of 6 mgxkg ($-1$) caffeine ingestion in team-sport players ($N.=10$) on repeated-sprint running performance (5 sets of 6 x 20 m) and reaction times, 60 min after caffeine or placebo ingestion. Best single sprint and total set sprint times, blood lactate and simple and choice reaction times (RT) were measured. Total sprint times across sets 1, 3 and 5 (departure every 25 s) were significantly faster after caffeine (85.49+/−5.55 s) than placebo (86.98+/−5.78 s) ($P<0.05$). Similarly, total sprint times across sets 2 and 4 (departure every 60 s), were significantly faster after caffeine (55.99+/−3.64 s) than placebo (56.77+/−3.74 s) ($P<0.05$). Significantly higher blood lactates were recorded in caffeine compared to placebo after set 3 (13.1+/−1.2 vs 10.3+/−1.4 mmolL(−1)) ($P<0.05$) and set 5 (13.1+/−1.3 vs 10.3+/−1.6 mmolL(−1)) ($P<0.01$). There were no significant effects on simple or choice RT, although effect sizes suggested improved post-exercise times after caffeine. Caffeine ingestion 60 min prior to exercise can enhance repeated sprint running performance and is not detrimental to reaction times.

Unt, Kairane, Vaher and Zilmer (2008) evaluated the changes in glutathione redox ratio (GSSG·GSH−1) in red blood cells (RBCs) and whole blood in well-trained men following a ski marathon. 16 male subjects (27.0 ± 4.7 yrs, 1.81 ± 0.06 m, 77.6 ± 9.6 kg, VO$_2$max 66.2 ± 5.7 ml·kg−1·min−1) were examined before the competition (pre-COMP), after the competition (post-COMP) and during an 18-hour recovery period (RECOV). There was a slight decrease in reduced glutathione (GSH) in blood
and in RBCs in post-COMP. During RECOV, the GSH level in blood was reduced, the GSH level in RBCs was significantly elevated (a statistically significant difference as compared to the pre-COMP level). The post-COMP GSSG-GSH-1 in full blood did not increase significantly, but its increase was statistically significant during the 18-hour recovery period. During the post-COMP and RECOV, the GSSG-GSH-1 in RBCs slightly decreased in comparison with the pre-COMP. Vitamin C concentration in serum increased in post-COMP (49% vs. pre-COMP) and decreased to the baseline level during RECOV. In conclusion, our data show that acute exercise slightly increases the GSSG-GSH-1 in whole blood, while GSSG-GSH-1 in RBCs significantly decreases. Thus, exercise-related changes in the non-enzymatic components of the glutathione system (GSSG and GSH) in whole blood and RBCs are not identical.

Aguilo et al (2005) demonstrated the occurrence of oxidative stress during exhaustive exercise and to determine the antioxidant response. Eight voluntary male subjects participated in this study. The exercise was a cycling mountain stage (171 km) and the cyclists took a mean FS.E.M. time of 270F12 min to complete it. Blood samples were taken before the cycling stage, immediately after the stage, 3 h after finishing the stage and on the morning of the following day. The study determined the activities of erythrocyte antioxidant enzymes, blood levels of oxidised glutathione, plasma levels of antioxidant vitamins and carotenoids, and the serum lipid and cholesterol profile. The mountain cycling stage induced significant increases in catalase and glutathione reductase activities. Significant decreases in glutathione peroxidase activity, both determined with hydrogen peroxide and with cumene
hydroperoxide as substrates, were observed. Blood oxidised glutathione and serum uric acid rose after the stage. Plasma vitamin E increased after the stage but dropped to below basal values after 3 h of recovery. Triglycerides and VLDL-cholesterol increased significantly after the stage and remained high 3 h after the cycling stage. The mountain cycling stage induced oxidative stress, as was evidenced by the increases in blood GSSG and in serum urate concentrations and by the pattern of change of erythrocyte antioxidant enzyme activities. A specific utilisation of α-tocopherol against oxidative stress during recovery was evidenced

Maragritis et al (2003) in their controlled-training, double-blind study (supplemented, n = 7; placebo, n = 9) investigated whether taper training (TT) and antioxidant supplementation, i.e., 150 _g of selenium, 2000 IU of retinol, 120 mg of ascorbic acid and 30 IU of _-tocopherol, modulates antioxidant potential, redox status and oxidative damage occurrence both at rest and in response to exercise. Two weeks of TT followed four weeks of overloaded training. Dietary intakes were recorded. Before and after TT, triathletes did a duathlon consisting of 5-km run, 20-km bike and 5-km run. Biological studies were conducted at rest and after exercise. Whatever the nutritional status, TT induced a decrease in resting blood reduced glutathione (GSH) concentration (\( p < 0.001 \)), erythrocyte superoxide dismutase (SOD) activity (\( p < 0.0001 \)) and plasma total antioxidant status (TAS) (\( p < 0.05 \)). Only in the supplemented group (Su) with TT, did plasma glutathione peroxidase (GSH-Px) activity decrease (\( p < 0.05 \)) and CD4_ cell concentration increase (\( p < 0.05 \)). However, antioxidant supplementation increased plasma TAS increase in response to exercise and TT (\( p < 0.05 \)). After exercise, TT also induced a lower decrease in blood reduced
and oxidized (GSSG) glutathione ($p < 0.01$) in both groups, but TT had no effect on lipoperoxidation as estimated by plasma thiobarbituric reactive substances or on muscular damage occurrence estimated by plasma creatine kinase isoenzyme MB mass. During TT, antioxidant supplementation at nutritional doses reinforces antioxidant status response to exercise, with an effect on exercise-induced oxidative stress, and no effect on oxidative damage.

Demant and Rhodes (1999) reports on the effect of creatine supplementation on exercise performance. While creatine has been known to man since 1835, when a French scientist reported finding this constituent of meat, its presence in athletics as a performance enhancer is relatively new. Amid claims of increased power and strength, decreased performance time and increased muscle mass, creatine is being hailed as a true ergogenic aid. Creatinine is synthesised from the amino acids glycine, arginine and methionine in the kidneys, liver and pancreas, and is predominantly found in skeletal muscle, where it exists in 2 forms. Approximately 40% is in the free creatine form (Cr$_{\text{free}}$), while the remaining 60% is in the phosphorylated form, creatine phosphate (CP). The daily turnover rate of approximately 2 g per day is equally met via exogenous intake and endogenous synthesis. Although creatine concentration (Cr) is greater in fast twitch muscle fibers, slow twitch fibers have a greater re-synthesis capability due to their increased aerobic capacity. There appears to be no significant difference between males and females in Cr, and training does not appear to effect Cr. The 4 roles in which creatine is involved during performance are temporal energy buffering, spatial energy buffering, proton buffering and glycolysis regulation. Creatine supplementation of 20 g per day for at least 3 days has resulted in significant
increases in total Cr for some individuals but not others, suggesting that there are 'responders' and 'non responders'. These increases in total concentration among responders is greatest in individuals who have the lowest initial total Cr, such as vegetarians. Increased concentrations of both Crfree and CP are believed to aid performance by providing more short term energy, as well as increase the rate of re-synthesis during rest intervals. Creatine supplementation does not appear to aid endurance and incremental type exercises, and may even be detrimental. Studies investigating the effects of creatine supplementation on short term, high intensity exercises have reported equivocal results, with approximately equal numbers reporting significant and non significant results. The only side effect associated with creatine supplementation appears to be a small increase in body mass, which is due to either water retention or increased protein synthesis.

Fortes (1998) investigated to determine if either supplemental vitamin A, zinc, or both increases cell-mediated immune response in an older population. A double-blind, randomized, controlled trial of supplementation with vitamin A and zinc. The health and nutritional status of 178 residents were evaluated. One hundred thirty-six residents agreed to participate in the trial and were randomized into four treatment groups, and 118 of these residents completed the trial. The four treatments consisted of: (1) Vitamin A (800 micrograms retinol palmitate); (2) Zinc (25 mg as zinc sulfate); (3) Vitamin A and Zinc (800 micrograms retinol palmitate and 25 mg as zinc sulfate); (4) Placebo capsules containing starch. Immune tests-counts of leucocytes, lymphocytes, T-cell subsets, and lymphocyte proliferative response to mitogens-were measured before and after supplementation. Zinc increased the number of CD4 + DR
+ T-cells (P = .016) and cytotoxic T-lymphocytes (P = .005). Subjects treated with vitamin A experienced a reduction in the number of CD3 + T-cells (P = .012) and CD4 + T-cells (P = .012). These data indicate that zinc supplementation improved cell-mediated immune response, whereas vitamin A had a deleterious effect in this older population. Further research is needed to clarify the clinical significance of these findings.

2.5 Studies related to Immune function

Maggini et al (2007) emphasizes that adequate intakes of micronutrients are required for the immune system to function efficiently. Micronutrient deficiency suppresses immunity by affecting innate, T cell mediated and adaptive antibody responses, leading to dysregulation of the balanced host response. This situation increases susceptibility to infections, with increased morbidity and mortality. In turn, infections aggravate micronutrient deficiencies by reducing nutrient intake, increasing losses, and interfering with utilization by altering metabolic pathways. Insufficient intake of micronutrients occurs in people with eating disorders, in smokers (active and passive), in individuals with chronic alcohol abuse, in certain diseases, during pregnancy and lactation, and in the elderly. This paper summarizes the roles of selected vitamins and trace elements in immune function. Micronutrients contribute to the body’s natural defenses on three levels by supporting physical barriers (skin/mucosa), cellular immunity and antibody production. Vitamins A, C, E and the trace element zinc assist in enhancing the skin barrier function. The vitamins A, B6, B12, C, D, E and folic acid and the trace elements iron, zinc, copper and selenium work in synergy to support the protective activities of the immune cells. Finally, all
these micronutrients, with the exception of vitamin C and iron, are essential for antibody production. Overall, inadequate intake and status of these vitamins and trace elements may lead to suppressed immunity, which predisposes to infections and aggravates malnutrition. Therefore, supplementation with these selected micronutrients can support the body’s natural defense system by enhancing all three levels of immunity.

Nieman and Bishop (2006) narrate on nutritional strategies to counter stress to immune system among athletes. Although epidemiological data indicate that athletes are at increased risk of upper respiratory tract infection (URTI) during periods of heavy training and the 1-2 week period following endurance race events, there is very limited information on the responses to football training and match play. For several hours subsequent to heavy exertion, components of both the innate (e.g., natural killer cell activity and neutrophil oxidative burst activity) and adaptive (e.g., T and B cell function) immune system exhibit suppressed function. Although such responses to football play and training do not appear to be as pronounced, variations in immune cell numbers and function are reported in professional football players over the course of a season. Attempts have been made through nutritional means (e.g., glutamine, vitamins C and E, and carbohydrate supplementation) to attenuate immune changes following intensive exercise and thus lower URTI risk. Carbohydrate supplementation during heavy exercise has emerged as a partial countermeasure and attenuates increases in blood neutrophil counts, stress hormones, and inflammatory cytokines, but has little effect on decrements in salivary IgA output or natural killer cell function. Animal research indicates that other nutritional components such as beta-glucan, quercetin,
and curcumin warrant human investigations to determine if they are effective countermeasures to exercise-induced immune dysfunction.

Gleeson and Bishop (2000) mentions regarding modification of immune responses to exercise by carbohydrate, glutamine and anti-oxidant supplements Immune-suppression in athletes involved in heavy training is undoubtedly multifactorial in origin. Training and competitive surroundings may increase the athlete’s exposure to pathogens and provide optimal conditions for pathogen transmission. Heavy prolonged exertion is associated with numerous hormonal and biochemical changes, many of which potentially have detrimental effects on immune function. Furthermore, improper nutrition can compound the negative influence of heavy exertion on immune-competence. An athlete exercising in a carbohydrate-depleted state experiences larger increases in circulating stress hormones and a greater perturbation of several immune function indices. The poor nutritional status of some athletes may predispose them to immune-suppression. For example, dietary deficiencies of protein and specific micronutrients have long been associated with immune dysfunction. Although it is impossible to counter the effects of all of the factors that contribute to exercise-induced immune-suppression, it has been shown to be possible to minimize the effects of many factors. Athletes can help themselves by eating a well-balanced diet that includes adequate protein and carbohydrate, sufficient to meet their energy requirements. This will ensure a more than adequate intake of trace elements without the need for special supplements. Consuming carbohydrate (but not glutamine or other amino acids) during exercise attenuates rises in stress hormones, such as cortical, and appears to limit the degree of exercise-induced
immune-suppression, at least for non-fatiguing bouts of exercise. Evidence that high
doses of anti-oxidant vitamins can prevent exercise-induced immune-suppression is
also lacking.

Spiller et al (1998) studied to determine whether a multiple vitamin and
mineral supplement can impact immune-competence in healthy, older individuals. One
year, randomized, double-blind, placebo-controlled trial. 39 healthy men and women
between the ages of 60 and 80 years. Subjects were randomly assigned to receive
either a complete vitamin and mineral supplement, or a placebo consisting of calcium
and vitamin D only. The subjects were asked to maintain their normal dietary,
exercise, and lifestyle habits. Illness reports were completed and evaluated every time
illness occurred and subjects were seen quarterly to review compliance, physical
activity, diet, medications and general health reports. Blood samples were drawn at the
end of one year, and selected vitamin, mineral, and immune parameters were
measured. Compared to placebo, those taking the supplement experienced a
significant 65% fewer days of infection-related illness over the study period compared
to placebo (p <0.01). Serum levels of folate and zinc were negatively correlated with
days of illness (p <0.05), suggesting a salutary effect of the supplement on immune
function. In addition, the percent of lymphocytes as well as levels of helper T-cells
and suppressor cytotoxic T-cells all were positively correlated with days of illness
(p<0.005; p<0.06). The dietary composition of both groups remained unchanged.

These results confirm that adding a multiple vitamin and mineral supplement
to the typical diets of healthy older individuals may lesson infection related illness and
enhance immune function. These findings are in agreement with previous research
Review of Related Literature

(Chandra et al. JAMA 1992; 340:1124), and suggest that the addition of a multiple vitamin and mineral supplement to the typical diets of healthy older individuals may help maintain normal immune function.

The study by Hopkins (2003) evaluated inflammation, immune function and iron status in athletes completing a 50K ultra-marathon. Twenty-two well-trained distance runners, 11 males and 11 females, were randomized in a double blind manner into--1) those who consumed 300 mg vitamin E and 1000 mg vitamin C (500 mg twice daily) or 2) placebos--for six weeks before and one week following a 50K ultra-marathon race. Blood samples were obtained on 13 separate occasions throughout the study: before supplementation, during supplementation, the day before the race, pre-race, mid-race, immediately post-race, 2 hours following the race, and daily for six days following the race. Each subject recorded immune function in an activity log and incidence of illness was tabulated as number of days ill. Ferritin was measured by enzyme immunoassay. Hemoglobin, hematocrit, and total-iron binding capacity (TIBC) and serum total iron were analyzed by standard procedures. Plasma concentrations of ascorbic acid and α-tocopherol increased significantly in supplemented subjects (p<0.0001). Although the ultramarathon race elicited an inflammatory response, antioxidant supplementation did not alter the responses of IL-6 and TNF-α, which both increased from pre-race to mid-race, post- and post-2 h (Scheffe post-hoc analysis, p<0.0001) and returned to pre-race concentrations by 1 day after the race. Male supplemented subjects had lower IL-1β concentrations compared to females consuming the supplement or to males consuming the placebo (ANCOVA, gender/time/treatment interaction; p<0.01) at mid-race (p<0.05 females,
p<0.005 males), post 1 and 2 days (all p<0.002). Males had significantly higher ferritin levels than the female subjects (ANOVA, p<0.0001); supplementation resulted in lower ferritin concentrations at post-5 days (p<0.02, ANCOVA treatment time interaction, p<0.005). Supplementation did not reduce the days illness among those consuming antioxidants compared to those consuming the placebos. Ferritin not only increases during inflammation, it also is a measure of iron stores. Females had significantly lower levels of iron than the male subjects for each of the iron parameters measured (hemoglobin and hematocrit both p<0.0001, ferritin p<0.001, TIBC p<0.02) excluding serum total iron. The ferritin concentrations measured in the women were indicative of depleted iron stores (<12 μg/l), and antioxidant supplementation increased hematocrit levels in the female subjects (p<0.05). This investigation indicates that female distance runners need to be aware of an increased susceptibility to iron depletion compared to their male counterparts. Antioxidant supplementation improved hematocrit levels (p<0.05) among female runners and may improve iron status among females with depleted stores. Although other investigations have suggested that antioxidant vitamins decrease exercise induced inflammation, no profound benefit of supplementation was found in this investigation though a response similar to the acute phase response was elicited by the ultramarathon race. Improvements in IL-i and ferritin in response to antioxidant supplementation may indicate that the supplementation was beneficial, but more research is needed to draw definitive conclusions.