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# Impact of Low-Intensity Exercise on Liver Enzymes and Antioxidants Systems of the Body

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## ABSTRACT

***Background:*** *Liver is the most important organ performing more than 500 functions in the body. In addition, the human cell has a natural antioxidants system which maintains the production of antioxidants and reactive oxygen species (ROS) during the metabolic process of the cell.* ***Objective:*** *This particular research study is basically conducted for the purpose to assess the impact of low-intensity exercise on liver enzymes and antioxidants systems of the body.* ***Methods and materials:*** *Total 40 subjects (20 from low-intensity exercise as an experimental group and 20 subjects as a control group) were included as the participants of the study. For assessment of liver functions and redox state of the body, 5 ml blood was collected from all subjects. Liver functions tests (LFTs) were performed for the assessment of liver enzymes and ferric reducing assay protocols (FRAP) was performed for the assessment of the redox state of the body. The data obtained about liver functions and redox state were processed through statistical package for social sciences (SPSS) version 23 and thus different statistical tools i.e. mean, standard deviation and T-score were used for the analysis of data.* ***Results:*** *Data analysis reveals that; no significant effect was found on liver enzymes as well as on antioxidants system of the body.* ***Conclusion:*** *On the basis of findings the researcher concluded that low-intensity exercise has no significant effects on liver enzymes. In addition, it was also concluded that low-intensity exercise helps in the improvement of blood life quality by reducing various health problems related to oxidative damages of cells and muscles fatigue.*

**Keywords:** Low-intensity exercise, Liver, Enzymes, Antioxidants, ROS, FRAP

## INTRODUCTION

During the process of metabolism free radicals, reactive oxygen and nitrogen varieties are produced by the cells. As a natural process, the antioxidants system comprised of catalase, superoxide dismutase, glutathione peroxidase, and many non-enzymatic antioxidants, consisting of vitamins A, E and C, glutathione, ubiquinone, and flavonoids that take away the free radicals [1]. The author further stated that aerobic exercise as the chief offender of enhanced oxidative stress.

In the biological arrangement of the body, cells respond to moderate oxidative stress by producing their antioxidant impedance and other protective methods [2]. The capabilities of antioxidants in tissues are well unified to suit the rates of oxygen intake and radical formation. Oxidation occurs in numerous ways, for instance, in the formation of energy by the cells using glucose, in the process of immunization when bacteria is to be diminished and to make inflammation and to detoxify harmful waste, pesticides, and cigarette smoke. To add more, oxidation also makes a person free from physical and/or emotional stress [3].

The process of cellular respiration renders us reactive oxygen species (ROS). The ROS regulates gesturing and homeostasis. During unstable reactive oxygen species and antioxidants, aerobic stress is formed. The physical exercises also affect the antioxidants and reactive oxygen species (ROS) and result in oxidative stress [3]. Exercises lead to oxygen consumption and the hectic process eat cells which have been demonstrated by the augmentation of sarcolemma disruption [4].

Yet this attitude of exercise does not stand for the entire situation. However, it is true that excessive exercise lowers oxidative stress and consequently, cellular proteins, lipids, and nucleic acids are transformed into the glutathione system [5]. Exercise also affects the pro and anti-inflammatory cytokine formation [6]. Protein which is a basic component of the cell can be affected due to the overuse or during the continuous performance of exercise and similarly when proteins level in the cell is affected then it can cause oxidative stress [7].

**Free Radicals**

The metabolic system ensures the production of free radicals [8]. Free radicals are a molecule or parts of molecules that have one or more odd number of electrons in the outer cloud layer". They are thought to be having a very short half-life and its own specific advanced level of reactivity. Destructive private property of free radicals is due to their naive inclination to achieve electronic stability. In this way, while finding an opportunity to react with its first neighboring stable molecule picking an electron and emerges a new free radical. The affected molecules become unbalanced itself and enter into reaction with other molecules it gets near to, which caused a disturbance in the components of cells. Free radicals are generated during the process of oxidative phosphorylation in mitochondria [9].

Free radicals may result in the destruction of cells and their elements. The body does possess a large number of antioxidant resistivity both for internal and external purposes. These internal and external performance immune the cellular process from free radical persuaded harm [10]. Following is a categorized process of free radicals.

- Antioxidant enzymes
- Chain breaking antioxidants
- Transition metal binding proteins

**Reactive Oxygen and Nitrogen Species (RONS)**

Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are the 2 coinages used for free radicals and non-free radicals' concluded from oxygen and nitrogen. These species can be created by the release or gain of a single electron. Moreover, superoxide ($O_2^{-\bullet}$) and nitric oxide ($NO^{\bullet}$) are the 2 principal oxygen and nitrogen derived free radical species charged within reactive oxygen and nitrogen species (RONS) [11]. The system of electron transport chain is one of the principal industry of superoxide ($O2^{-\bullet}$) in the process of cellular respiration through oxidation. A large number of free radicals resulting into *in vitro* or originate from reactive oxygen species (superoxide ($O2^{-\bullet}$), hydroxyl ($OH^{\bullet}$), alkoxyl ($RO^{\bullet}$), peroxyl ($ROO^{\bullet}$) and hydroperoxyl (ROOH•) or reactive nitrogen species (nitric oxide, nitrogen dioxide, peroxynitrite oxidized) [12].

**Physical Activity and Oxidative Stress**

Consistent bodily exercise reinforces the immune system and makes one capable of avoiding cardiovascular diseases. To promote health and avoiding cardiovascular diseases, 30 minutes per day of moderate-intensity physical activity, including brisk walking are suggested [13]. Bodily exercises have helpful properties such as keeping the level of cholesterol, healthy muscles, bones and joints and its aids in regulating the body weight [14].

However, active bodily exercise does not incite the same result as long term exercise training. Regular physical exercise helps the body to get an adjustment and to escape from the harmful effects of oxidative stress [15]. Energetic or acute bodily exercise can cause oxidative stress and resulting injury to cellular proteins, lipids, and nucleic acids as well as changes to the glutathione system. It is also obvious that regular exercise permits the antioxidant scheme to control the making of reactive oxygen and nitrogen species [16].

Research indication shows that severe aerobic physical exercise or training causes oxidative stress chiefly when its intensity and length is more than the approach of the body [17]. Severe muscular exercise results in an augmented production of free radicals and other forms of reactive oxygen species such as superoxide and hydrogen peroxide.

The antioxidant system is used to defend the organism from the injurious effects of free radicals. This system contains antioxidant enzymes (catalase, glutathione peroxidase, superoxide dismutase) and non-enzymatic antioxidants (vitamin E, vitamin A, vitamin C, glutathione and uric acid). The no uniformity between free radical production and antioxidant resistance leads to an oxidative stress state.

The high amount of exercise results in an increased amount of reactive and nitrogen species and in this way, the amount of ROS increases and RNS may cause imbalance among RONS and antioxidants. The resulting oxidative injury due to oxidation of lipids, proteins, and DNA, is that the bodily exercise no longer helps the body but costs it, increasing the body vulnerability to exhaustion and often to injury and disease [18].

Bodily exercise may become a source of unstable reactive oxygen species and antioxidants in the body and thus, this disorder is considered very dangerous due to its negative effect on overall practical abilities of the body [19]. To achieve success in sports or to carry the sports activities in successful manners one would need to be free from all kind of psychological as well as physiological stressors. Because any kind of stress either they are physiological or psychological adversely influence body performance. High-intensity exercise induces oxidative stress which affects the performance of a person. Oxidative stress accurses, when free radicals attack the cells similarly it affects the performance such as; accelerated gaining, muscles pain, anti-inflammatory medications and overuse injuries [19].

An imbalance may be created by frequent preformation of exercise in reactive oxygen species and antioxidants thus may result in oxidative stress [20]. This intern results in various chronic diseases [21]. Muscular exhaustion is very closely related to oxidative stress [22]. The author further specified that oxidative stress may cause muscles injury and dysfunction of the immune system. Muscular exercise tempted oxidative stress by generating the reactive species (ROS) and nitrogen species (RONS) due to metabolic and mechanical stresses during skeletal muscle contractions [23].

Exercise causes oxidative stress. Numerous research studies related to aerobic exercises such as running and cycling found that aerobic activities need more oxygen consumption ($VO_2$) which culminates in an increase in both free radical production and activity. However, this phenomenon is not evident at exercising of low intensity (<50% $VO_2$ max) likewise in such case the antioxidant capacity is not exceeded and damages induced by free radicals did not take place. The making of free radicals and oxidative stress is advanced if a more rigorous physical activity is performed [20].

The principal cause of the production of radicals and other reactive oxygen species (ROS) is muscular exercise. Research indication shows that an intensified exercise leads the body towards protein oxidation which causes muscles fatigue. Muscles cells comprise of a complex endogenous cellular resistance (enzymatic and non-enzymatic antioxidants) to eliminate reactive oxygen species and to decrease the muscles injuries [24]. Muscular exercise ignites the oxidative stress and so the muscles remain unable to perform the activity because of fatigue. To lessen fatigue and do the exercise, the body needs to utilize antioxidants supplementations [24].

Exercise is supposed to be the leading cause of bringing increment in the formation of reactive oxygen species (ROS) possibly causing mutations, tissue, and immune system damage. A stress protein shows one of the common protective mechanisms which enable the cells and the organism to overcome stress [25,26]. The author further added that relationship in stress protein, reactive oxygen species (ROS) and physical activity is still needed to be discovered.

## MATERIALS AND METHODS

The below procedures were adopted by the researcher for reaching certain findings and conclusion.

### Chemical and Reagents

Analytical grade chemicals such as ferric chloride, 2, 4, 6-tripyridyl- s-triazine (tptz), standard antioxidant "trolox" (Merck, Germany) dimethylsulfoxide (DMSO), methanol, L-ascorbic acid (Sigma Aldrich, Germany) were used for the experimental setup of the study.

### Participants of the Study

According to Dayan, et al., and Clark, et al., low-intensity exercise is that which gets you to about 40-50% of your Maximum heart rate (MHR). It includes routine jogging and walking. Based on this justification low intensity exercise performers were recruited from Department of Sports Sciences and Physical education, Gomal University, Kp, Pakistan by the application of international physical activity questionnaire (IPAQ).

**Sample and Sample Size**

Total 2 different groups of subjects were voluntarily included in the study. One group comprised of 20 subjects of low-intensity exercise performers (EXG) who were recruited from the Department of Sports Science and Physical Education Gomal University and thus the second group comprised of 20 subjects, performing no activities (CONT) was recruited from various departments of Gomal University, KP, Pakistan. Study objectives were explained to the participants and those who consented and fulfill the inclusion criteria were included in the study. During the selection process of the subjects all those subjects were included in the study that represents the exercise-trained cohort, and age and sex-matched sedentary control.

**Exclusion Criteria**

Subjects were excluded from the study by adopting the following exclusion criteria:

- Subject with complete sedation
- Subject taking any kind of medication for long term
- A subject having a chronic disease
- The subject refused written consent of participation
- Subject aged more than 30 years

**Blood Sample Collection**

Blood samples (5 ml) were collected from all subjects by vein puncture and immediately transferred in heparinized tubes and centrifuged to separate plasma for determination of ALT, AST, and ALP. Each tube was marked with a subject distinguishing proof code. For the assessment of redox body state (antioxidants system), serum was excreted from each blood sample.

**Procedures for Excretion of Serum from the Blood**

- The collected blood was kept in a freezer at 200°C
- The blood samples were centrifuged at 15000 rpm for 20 minutes at room temperature
- Serum or plasma was separated from the whole blood within 6 hours after sampling
- The serum or plasma was then transferred to sterile polypropylene tubes

**Ethical Approval of the Study Protocols**

Regarding the protocols of this research study, ethical approval was sought out from the ethical and research board of Gomal University. Permission was taken from the Department of Sports Sciences and Physical Education, Gomal University. Written informed consent was taken from the respondents before participating in the process of this research project. Privacy of participants was safeguarded at all times. Withdrawal policy was also ensured during the filling of the consent form.

**Ferric Reducing Antioxidant Power (FRAP) Assay for the Measurement of Oxidative Stress through Blood Sample**

The antioxidant capacity of the sample was estimated spectrophotometrically following the procedure of Benzie and Strain. The method is based on the reduction of $Fe^{3+}$ TPTZ complex (colorless complex) to $Fe^{2+}$-tripyridyltriazine (blue colored complex) formed by the action of electron donating antioxidants at low pH. This reaction is monitored by measuring the change in absorbance at 593 nm. The ferric reducing antioxidant power (FRAP) reagent was prepared by mixing 200 ml acetate buffer, 20 ml of 10 mM TPTZ, 20 ml of 20 mM ferric chloride (at 10:1:1). The concentration of ferric tripyridyltriazine (Fe-TPTZ) compound decreases and was converted to the ferrous form at acidic pH.

**Statistical Analysis**

The data obtained about liver functions and redox state were processed through statistical package for social sciences (SPSS) version 23 and thus different statistical tools i.e. mean, standard deviation and T-score for the analysis of data.

## RESULTS

There was a comparison of Control group N=20 (CG), Low-intensity exercise group, N-20 (EXG) regarding Body mass index (BMI), Alanine transferase (ALT), Alkaline phosphate (ALP), Aspartate (AST) and FRAP. Similarly, the data are articulated as mean, and standard deviation, T- score, and p-value. The data of both groups about; BMI shows that the mean of CG was 20.95 ± 1.79, mean of EXG was 22.35 ± 1.46, T-value of both CG and EXG was 2.709, the p-value was 0.010. Therefore significance difference is found in BMI of both groups CG and EXG (t 38=-2.709, $p<0.05$). The BMI of CG was less than the BMI of EXG. ALT shows that the mean of CG was 33.50 ± 2.11, mean of EXG was 40.60 ± 11.65, T-value of both CG and EXG was -2.680, the p-value was .011. (t 38=-2.680, $p<0.05$) Therefore significance difference was found in ALT of both groups CG and EXG. The ALT of CG was less than the ALT of EXG. ALP shows that the mean of CG was 40.60 ± 51.54, mean of EXG was 236.90 ± 50.96, T-value of both CG and EXG was 1.44, the p-value was 0.158 (t 38=1.44, $p>0.05$). Therefore no significant difference was found in ALP of both CG-I and EXG. The ALP of CG was high than the ALP of EXG. AST shows that mean of CG was 25.35 ± 4.81, mean of EXG was 27.60 ± 5.35, T-value of both CG and EXG was -1.40, the p-value was 0.170 (t 38=1.40, $p>0.05$). Therefore no significant difference was found in AST of both Groups CG and EXG. The AST of CG was less than the AST of EXG. FRAP shows that mean of CG was 138.59 ± 21.83, mean of EXG was 120.90 ± 13.45, T-value of both CG and EXG was 3.08, and the p-value was 0.004 (t 38=3.08, $p<0.05$). Therefore significance difference was found in FRAP value of both groups CG and EXG. The FRAP value of CG was high than the FRAP value of EXG (Table 1).

**Table 1 Mean difference between the BMI, ALT, ALP, AST, and FRAP of Control group (CG) and low-intensity exercise group (EXG)**

| Testing Variables | Category | N | Mean | SD | T | Sig. |
|---|---|---|---|---|---|---|
| Body Mass Index | Control group | 20 | 20.95 | 1.79106 | -2.709 | 0.010 |
| | LIE | 20 | 22.35 | 1.46089 | | |
| Alanine Transferase (IU/L) | Control group | 20 | 33.5 | 2.11511 | -2.680 | 0.011 |
| | LIE | 20 | 40.6 | 11.6592 | | |
| Alkaline Phosphate (IU/L) | Control group | 20 | 236.9 | 51.54548 | 1.441 | 0.158 |
| | LIE | 20 | 213.55 | 50.96074 | | |
| Aspartate (mg/dl) | Control group | 20 | 25.35 | 4.81527 | -1.400 | 0.170 |
| | LIE | 20 | 27.6 | 5.33509 | | |
| Ferric Reducing Antioxidant Power Assay (µmole/L) | Control group | 20 | 138.5925 | 21.83079 | 3.085 | 0.004 |
| | LIE | 20 | 120.901 | 13.45593 | | |

Comparison of the low-intensity exercise group, N-20 (EXG) with nutritional supplementation (EXG-A) N-10 and non-nutritional supplementation (EXG-B) N-10 regarding Body mass index (BMI), Alanine transferase (ALT), Alkaline phosphate (ALP), Aspartate (AST) and FRAP. Similarly, the data are articulated as mean, and standard deviation, T-score and p-value. The data about BMI shows that mean of EXG-A was 22.40 ± 1.26, mean of EXG-B was 22.30 ± 1.70, T-value of both EXG (A and B) was 0.149, the p-value was 0.883 (t18=0.149, $p>0.05$). Therefore no significant difference was found in BMI of both EXG (A) and EXG (B). The BMI of EXG (A) was high than the BMI of EXG (B). ALT shows that mean of EXG (A) was 30.70 ± 1.33, mean of EXG (B) was 50.50 ± 8.20, T-value of both EXG (A and B) was -7.528, the p-value was 0.000 (t18=-7.528, $p<0.05$). Therefore significant difference was found in ALT of both EXG (A) and EXG (B). The ALT of EXG (A) was less than the ALT of EXG (B). ALP shows that mean of EXG (A) was 246.10 ± 33.60, mean of EXG (B) was 181.0 ± 44.7, T-value of both EXG (A and B) was 3.68, the p-value was 0.002 (t18=3.68, $p<0.05$). Therefore significant difference was found in ALP of both EXG (A) and EXG (B). The ALP of EXG (A) was high than the ALP of EXG (B). AST shows that mean of EXG (A) was 29.30 ± 2.40, mean of EXG (B) was 25.90 ± 6.90, T-value of both EXG (A and B) was 1.46, the p-value was 0.159 (t18= 1.46, $p>0.05$). Therefore no significant difference was found in AST of both EXG (A) and EXG (B). The AST of EXG (A) was high than the AST of EXG (B). FRAP shows that mean of EXG (A) was 115.25 ± 12.08, mean of EXG (B) was 126.55 ± 12.86, T-value of both EXG (A and B) was 2.02, the p-value was 0.058 (t18=2.02, $p>0.05$). Therefore no significant difference was found in FRAP of both EXG (A) and EXG (B). The FRAP of EXG (A) was less than the FRAP of EXG (B) (Table 2).

**Table 2 Mean difference in BMI, ALT, ALP, AST, and FRAP of low-intensity exercise group (EXG) with nutritional supplementation (EXG-A) and non-nutritional supplementation (EXG-B)**

| Testing Variable | Supplement | N | Mean | SD | t | Sig. |
|---|---|---|---|---|---|---|
| Body Mass Index | Use Supplement (LIE) | 10 | 22.400 | 1.26491 | 0.149 | 0.883 |
| | No Use Supplement (LIE) | 10 | 22.300 | 1.70294 | | |
| Alanine Transferase (IU/L) | Use Supplement (LIE) | 10 | 30.700 | 1.33749 | -7.528 | 0.000 |
| | No Use Supplement (LIE) | 10 | 50.500 | 8.20907 | | |
| Alkaline Phosphate (IU/L) | Use Supplement (LIE) | 10 | 246.100 | 33.60704 | 3.681 | 0.002 |
| | No Use Supplement (LIE) | 10 | 181.000 | 44.70645 | | |
| Aspartate (IU/L) | Use Supplement (LIE) | 10 | 29.300 | 2.40601 | 1.468 | 0.159 |
| | No Use Supplement (LIE) | 10 | 25.900 | 6.91938 | | |
| Ferric Reducing Antioxidant Power Assay (µmole/L) | Use Supplement (LIE) | 10 | 115.252 | 12.08049 | 2.025 | 0.058 |
| | No Use Supplement (LIE) | 10 | 126.550 | 12.86041 | | |

## DISCUSSION

The finding of the present study reveals that mean and standard deviation (ALT) of CG was 33.50 ± 2.11, mean of EXG was 40.60 ± 11.65, T-value of both CG and EXG was -2.680, the p-value was 0.011 ($t38=-2.680$, $p<0.05$). Therefore a significant difference was found in ALT of both Groups CG and EXG. The ALT of CG was less than the ALT of EXG. The findings of studies conducted by George, et al., and Eckard, et al., testified that ALT was changed among the subjects as a result of low-intensity exercise. They further calculated the statistical difference in both the control group and the experimental group before and after exercise (SMD -0.40, 95% CI -0.75 ~-0.05, $p=0.03$). Findings of the study conducted by Eckard, et al., revealed that with or without nutritional supplementations (20 intervention groups) the level of ALT was not significantly altered in 10 groups and was significantly reduced (improved) in 5 groups and increased in 5 groups [27].

The study found out that mean and standard deviation (ALP) of CG was 40.60 ± 51.54, mean of EXG was 236.90 ± 50.96, T-value of both CG and EXG was 1.44, the p-value was 0.158 ($t38=1.44$, $p>0.05$). Therefore no significant difference was found in ALP of both CG-I and EXG. The ALP of CG was higher than the ALP of EXG. This emerging concept is supported by Statland, et al., and reported that ALP was almost unaltered during the 7-day period of exercise. Pettersson, et al., concluded that AST and ALT were pointedly increased for at least 7 days after the strenuous physical exercise. The findings of the study conducted by Sjogren, et al., indicated that strength training and very heavy manual labor are more likely to cause raised in ALT than aerobic exercise. ALT can be elevated in marathon runners and they have the potential to develop rhabdomyolysis in extreme [28-30].

Finding of the study indicates that mean and standard deviation of AST of CG was 25.35 ± 4.81, mean of EXG was 27.60 ± 5.35, T-value of both CG and EXG was -1.40, the p-value was 0.170 ($t38=1.40$, $p>0.05$). Therefore no significant difference was found in AST of both groups CG and EXG. The AST of CG was less than the AST of EXG. Bakowski, et al., reported that exercise has no effects on liver enzymes such as ALT, ALP, and AST. Although Fallon and colleagues found a significant increase in the level of liver enzymes after exercise. They also found that exercise improve the functional capacity of the liver if it is performed according to the nature and capacity of the body [31,32].

Findings show that mean and standard deviation FRAP of CG was 138.59 ± 21.83, mean of EXG was 120.90 ± 13.45, T-value of both CG and EXG was 3.08, and the p-value was 0.004 ($t38=3.08$, $p<0.05$). Therefore a significant difference was found in FRAP value of both groups CG and EXG. The FRAP value of CG was higher than the FRAP value of EXG. Previous studies by Turner, et al., and Berzosa, et al., indicated that low as well as moderate-intensity exercise causes an increase in oxidative stress in young healthy males if it is performed more according to the approach of the body [33,34].

Findings indicate that mean and standard deviation FRAP of EXG (A) was 115.25 ± 12.08, mean of EXG (B) was 126.55 ± 12.86, T-value of both EXG (A and B) was 2.02, the p-value was 0.058 ($t18=2.02$, $p>0.05$). Therefore no significant difference was found in FRAP of both EXG (A) and EXG (B). The FRAP of EXG (A) was less than the

FRAP of EXG (B). The findings of the study conducted by Dembinska-Kiec, et al., determine that diet with all its basics elements strengthen the antioxidants system of the body. Sin, et al., stated that different kind of micronutrients such as vitamins E and C help to maintain the balance in ROS and antioxidants. Therefore this findings also seemed inline of the present study finding [35,36].

## CONCLUSION

On the basis of findings, the researcher concluded that low-intensity exercise has no significant effects on liver enzymes. In addition, it was also concluded that low-intensity exercise helps in the improvement of blood life quality by reducing various health problems related to oxidative damages of cells and muscles fatigue.

## REFERENCES

[1] Urso, Maria L., and Priscilla M. Clarkson. "Oxidative stress, exercise, and antioxidant supplementation." *Toxicology,* Vol. 189, No. 1-2, 2003, pp. 41-54.

[2] Sen, Amartya. "Social exclusion: Concept, application, and scrutiny." 2000.

[3] Sabo, Arianna, et al. "Selective transcriptional regulation by Myc in cellular growth control and lymphomagenesis." *Nature*, Vol. 511 No. 7510, 2014, p. 488.

[4] Spaan, Willy, et al. "Coronavirus mRNA synthesis involves the fusion of non□contiguous sequences." *The EMBO Journal,* Vol. 2, No. 10, 1983, pp. 1839-44.

[5] Dellinger, R., Phillip, et al. "Surviving Sepsis Campaign: international guidelines for the management of severe sepsis and septic shock: 2008." *Intensive Care Medicine,* Vol. 34 No. 1, 2008, pp. 17-60.

[6] Druker, Brian J., et al. "Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia." *New England Journal of Medicine,* Vol. 355, No. 23, 2006, 2408-17.

[7] Wadley, Alex J., Jet JCS Veldhuijzen van Zanten, and Sarah Aldred. "The interactions of oxidative stress and inflammation with vascular dysfunction in aging: the vascular health triad." *Age*, Vol. 35 No. 3, 2013, pp. 705-18.

[8] Urso, Maria L., and Priscilla M. Clarkson. "Oxidative stress, exercise, and antioxidant supplementation." *Toxicology*, Vol. 189, No. 1-2, 2003, pp. 41-54.

[9] Villeneuve, Daniel L., et al. "Altered gene expression in the brain and ovaries of zebrafish (Danio rerio) exposed to the aromatase inhibitor fadrozole: microarray analysis and hypothesis generation." *Environmental Toxicology and Chemistry,* Vol. 28, No. 8, 2009, pp. 1767-82.

[10] Halliwell, Barry, and John M. C. Gutteridge. "[1] Role of free radicals and catalytic metal ions in human disease: an overview." Methods in Enzymology. *Academic Press*, Vol. 186, (1990), 1-85.

[11] Cooper, C. E., et al. "Exercise, free radicals, and oxidative stress." *Biochemical Society Transactions*, Vol. 30, 2000, pp. 280-85.

[12] den Hollander, Anneke I., et al. "Leber congenital amaurosis and retinitis pigmentosa with Coats-like exudative vasculopathy are associated with mutations in the crumbs homologue 1 (CRB1) gene." *The American Journal of Human Genetics*, Vol. 69, No.1, 2001, pp. 198-203.

[13] Hakim, A. A., et al. Effects of walking on mortality among non-smoking retired men. *New England Journal of Medicine*, Vol. 338, No. 2, 1998, pp. 94-99.

[14] Warburton, Darren E. R., Crystal Whitney Nicol, and Shannon S. D. Bredin. "Health benefits of physical activity: the evidence." *Canadian Medical Association Journal*, Vol. 174, No. 6, 2006, pp. 801-09.

[15] Oppmann, Birgit, et al. "Novel p19 protein engages IL-12p40 to form a cytokine, IL-23, with biological activities similar as well as distinct from IL-12." *Immunity*, Vol. 13, No. 5, 2000, pp. 715-25.

[16] Banerjee, Abhijit V., and Esther Duflo. "Inequality and growth: What can the data say?." *Journal of Economic Growth*, Vol. 8, No. 3, 2003, pp. 267-99.

[17] Alessio, Helaine M., et al. "Generation of reactive oxygen species after exhaustive aerobic and isometric exercise." *Medicine and Science in Sports and Exercise*, Vol. 32, No. 9, 2000, pp. 1576-81.

[18] Bailey, Robert C., et al. "Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomized controlled trial." *The Lancet,* Vol. 369, No. 9562, 2007, pp. 643-56.

[19] Brito, Jerry, Houman B. Shadab, and Andrea Castillo O'Sullivan. "Bitcoin financial regulation: Securities, derivatives, prediction markets, and gambling." *Columbia Science and Technology Law Review*, 2014.

[20] De Wilde, A. N. N. I. K., et al. "On the fixation of needle biopsies of rat liver tissue as a model to study the fine structure of sinusoidal cells." *The Kupffer Cell Foundation*, 1982, pp. 85-92.

[21] Schwemmer, M., et al. "How urine analysis reflects oxidative stress-nitrotyrosine as a potential marker." *Clinica Chimica Acta,* Vol. 297, No. 1, 2000, pp. 207-16.

[22] Powers, Scott K., and Karyn Hamilton. "Antioxidants and exercise." *Clinics in Sports Medicine*, Vol. 18, No. 3, 1999, pp. 525-36.

[23] Bloomer, Richard J., et al. "Effects of acute aerobic and anaerobic exercise on blood markers of oxidative stress." *The Journal of Strength and Conditioning Research*, Vol. 19 No. 2, 2005, pp. 276-85.

[24] Powers, Scott K., et al. "Dietary antioxidants and exercise." *Journal of Sports Sciences*, Vol. 22, No. 1, 2004, pp. 81-94.

[25] Radovanović, Dragan S., and Goran Ž. Ranković. "Oxidative stress, stress proteins, and antioxidants in exercise." *Acta Medica Medianae*, Vol. 43 No. 4, 2004, pp. 45-47.

[26] George, Steven M. "Atomic layer deposition: an overview." *Chemical Reviews*, Vol. 110, No. 1, 2009, pp. 111-31.

[27] Meyer, C., et al. "The MLL recombinome of acute leukemias in 2013." *Leukemia,* Vol. 27, No. 11, 2013, p. 2165.

[28] Statland, B. E., Winkel, P., and Bokelund, H. Factors contributing to the intra-individual variation of serum constituents: 2. Effects of exercise and diet on the variation of serum constituents in healthy subjects. *Clinical Chemistry,* Vol. 19, No. 12, 1973, pp. 1380-83.

[29] Pettersson, Andreas, et al. "Age at surgery for undescended testis and risk of testicular cancer." New *England Journal of Medicine,* Vol. 356, No. 18, 2007, pp. 1835-41.

[30] Saxena, Richa, et al. "Genome-wide association analysis identifies loci for type 2 diabetes and triglyceride levels." *Science*, Vol. 316, No. 5829, 2007, 1331-36.

[31] Choueiri, Toni K., et al. "Efficacy of sunitinib and sorafenib in metastatic papillary and chromophobe renal cell carcinoma." *Journal of Clinical Oncology,* Vol. 26, No. 1, 2008, pp. 127-31.

[32] Alkire, M. T., R. J. Haier, and Fallon J. H.. "Toward a unified theory of narcosis: brain imaging evidence for a thalamocortical switch as the neurophysiologic basis of anesthetic-induced unconsciousness." *Consciousness and Cognition*, Vol. 9, No. 3, 2000. pp. 370-86.

[33] Roger, Véronique L., et al. "Heart disease and stroke statistics-2011 update: a report from the American Heart Association." *Circulation*, Vol. 123, No. 4, 2011, pp. e18-e209.

[34] Berzosa, C., et al. "Acute exercise increases plasma total antioxidant status and antioxidant enzyme activities in untrained men." *BioMed Research International*, 2011.

[35] Herrera Dutan, Edgar Vinicio, and Natali Estefanía Poveda Tapia. "Evaluation of the inhibitory activity of enzymes A and B glucosidase in fruits of the southern Ecuadorian highlands." *BS Thesis*, 2018.

[36] Vestbo, Jørgen, et al. "Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary." *American Journal of Respiratory and Critical Care Medicine*, Vol. 187, No. 4, 2013, pp. 347-65.