ZITA MEDICAL MANAGEMENT

www.hsmc.gr/en/pharmakeftiki-journal/

ΦΑΡΜΑΚΕΥΤΙΚΗ, 36, II, 2024 | 67-76 ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

PHARMAKEFTIKI, 36, II, 2024 | 67-76 RESEARCH ARTICLE

CoQ10 Improved Liver Function and Redox Status in Pollution-exposed Workers

Zeina A. Al-Thanoon, Marwan M. Merkhan*

College of Pharmacy, University of Mosul, Mosul, Iraq

KEYWORDS:
Co-enzyme Q10, Pollution, Oxidative stress, Liver enzyme.

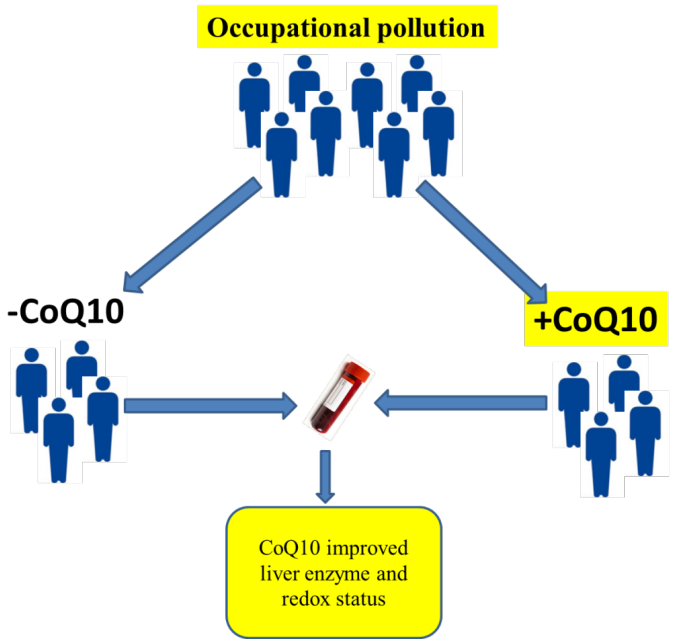
ARTICLE INFO:
Received" October 23, 2023
Revised:March 18, 2024
Accepted: April2. 2024
Available on line: June 18, 2024

*** CORRESPONDING AUTHOR:**
Marwan M. Merkhan
email: marwanmerkhan@uomosul.edu.iq
Tel.: +9647508662343

ABSTRACT

Chronic exposure to workplace pollution has been increasingly reported as a potential hazard for the induction of diseases or involved in the pathogenesis of already present conditions. The aim of the present randomized, double-blind, controlled, clinical trial was to investigate the protective role of CoQ10 in improving liver function and redox status of occupationally exposed workers. To do so, blood samples were collected from 132 participants working in a polluted environment for a period of longer than 1 year, with most of them working for a period between 5-10 years. They were then divided into a control group (n=60) receiving placebo therapy and an intervention group receiving CoQ10 (200mg/day) therapy for 2 months Blood samples were withdrawn and the serum was then analysed for total antioxidant capacity (TAOC), malondialdehyde (MDA), glutathione-peroxidase enzyme (GSH-Px), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), albumin, and bilirubin. Results: CoQ10 has significantly ($P<0.05$) increased TAOC and GSH-Px alongside significantly ($P<0.05$) reducing MDA. Liver function test has shown no changes regarding ALT, ALP, and albumin, with a significant reduction of bilirubin and AST. Moreover, weight-related indices (body weight, BMI, waist and hip circumferences) have shown non-significant changes after CoQ10 therapy. Systolic blood pressure significantly reduced in treated group compared to control group. Conclusion: CoQ10 could be advised as a supplement to protect against the hazard of exposure to pollution.

Graphical Abstract



Introduction

Pollution exposure has increasingly become an important risk factor for public concern resulting in increased morbidity or mortality due to its impact on exaggerating the condition of already sick people or inducing new diseases on its own; These hazards doubled in workers close to the source of pollution[1]. These include, but are not limited to, workers in various jobs like metal processing, car repair, mining, coal burning and dealing with petroleum have increased risk of heavy metals exposure or even heavy metals linked adverse effects and intoxication[2]. This pollution is then represented as a causative agent inducing pathophysiological changes in terms of proinflammatory remarks and redox imbalances[3,4].

One of the major health concerns nowadays is heavy metal-induced cellular toxicity. The usage of heavy metals in various industrial fields can produce environmental contamination and result in severe hazards to health. The primary cellular response to heavy metal toxicity is oxidative stress induction, which can be defined as an imbalance in the redox system. The increase in oxidative stress and free radical generation are associated with the damage to macromolecular and activation of specific cell survival/ death pathways[5,6].

Heavy metal exposure can produce oxidative stress and this in turn, is linked to many pathological conditions such as increased risk of neoplasm, premature cardiovascular disease, infertility, diabetes, renal failure, neurological disorders or even developmental disorders. In recent years, enter-relation among heavy metal toxicity, oxidative stress initiation and activation of specific signaling pathways become important areas for research to show the role of heavy metal in many pathophysiological conditions. The role of heavy metals in oxidative stress induction and activation of many signaling pathways is not fully understood, however, important and well-related signaling pathways involved[7]

Co-enzyme Q10 (CoQ10) is a co-factor in enzyme complexes that participate in oxidative phosphorylation in the mitochondrial production of adenosine triphosphate. In addition, CoQ10 serves as an antioxidant or free radical scavenger. Ubiquinol, a reduced

form of CoQ10, is potent lipophilic antioxidant and can regenerate and recycle other antioxidants in the body. Numerous other functions of CoQ10 have been described, such as cell signaling, membrane stabilization and gene expression[8].

In the present study, we aimed to determine the impact of supplementation of CoQ10 on improving liver function tests including liver enzymes (alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, and bilirubin. Moreover, the impact of CoQ10 was also assessed on redox parameters via measuring total antioxidant capacity (TAOC), malondialdehyde (MDA), and glutathione peroxidase (GSH-Px) in individuals at high risk at their workplaces for occupational pollution.

Materials and Methods

Study Settings and Design: This study is designed as a randomized, double-blind, placebo-controlled 2-month clinical trial. Participants work in an industrial career (car repairing, gas station, local generators, and painting) for at least 1 year. The study protocol is approved by the Ethics Committee for Medical Research of Mosul University as well as the Research Ethical Committee of Nineveh Health Directorate. Consent form signed by participants to participate in this study. Exclusion criteria include females and males who are under 18 and over 75 years old, participants who are alcoholics. If a person has less than the one-year duration of working in the industrial field has been excluded. Males who are intermittently exposed to industrial pollution were excluded. Patients with chronic diseases, such as diabetic patients, patients with renal failure gastrointestinal diseases, stroke, and neurological disorders were excluded.

Inclusion criteria: participants were males, aged between 18–75 years, working in different industrial fields that are exposed to industrial pollution of heavy metals. These subjects include workers in car-repairing, gas stations, local generators, and painting.

The number of participants as cases were 72, while the number of participants as control was 60, age groups were (18 -75 years), and they were randomly divided into two groups. The case group was given CoQ10 (NATROL® company /USA) at the dose of 200mg per day for two months. Blood pressure, body weight, hip circumference, or waist circumference were recorded initially and after therapy.

Blood was withdrawn from patients and serum was separated and frozen at -20°C for further analysis. The serum samples were analysed for total bilirubin, albumin, liver enzymes (ALT, AST, and ALP), TAOC, MDA, and GSH-Px. TAOC was measured by colorimetric method using the TAOC assay kit supplied by (Elabscience®, USA). GSH-Px was measured by colorimetric method using the GSH-Px assay kit supplied by (Elabscience®, USA). MDA, were measured by the ELISA method using the MDA ELISA kit supplied by (Elabscience®, USA). ALP was measured by colorimetric method using the alkaline phosphatase assay kit supplied by (Giesse Diagnostic®, Italy). ALT was measured by colorimetric method using the ALT Assay kit supplied by Linear chemicals (Spain). AST was measured by colorimetric method using the AST assay kit supplied by Biolab (France). Albumin was measured by colorimetric method using an albumin assay kit supplied by Biolab (France). Bilirubin was measured by colorimetric method using the bilirubin assay kit supplied by Biolab (France).

Results

The duration of occupation exposure of the participants in the study is tabulated in Table 1. The participants were most often exposed to causative agents for a period between 5-10 years.

The results express no significant change in body weight, BMI, hip circumference, or waist circumference after two months of therapy. Systolic, but not diastolic, blood pressure in participants group exposed to pollution were significantly ($p<0.05$) reduced when they were given CoQ10. The age of all participants ranged between (18-75) years with the average for the control group (35±5) and CoQ10 treated group (42±8) years (Table 2).

The change in TAOC in the CoQ10 receiving group indicate a significant increase in TAOC level with a p-value of 0.001; while for the placebo group, the p-value was 0.177. Glutathione peroxidase also dis-

played a significant change in the CoQ10 treated group compared to the placebo group with a p-value of 0.001 and 0.446, respectively. MDA increase in oxidative stress condition. In the current study, we can detect a decrease of MDA value in the group that received CoQ10 while changes in the control group were insignificant; the calculated p value was 0.001 for the CoQ10 group verses 0.438 for the placebo group (Figure 1).

The ALT activity measurement indicates that there is a significant reduction in its activity in the CoQ10 receiving group after two months of management with a p-value of 0.005, while in placebo receiving group reduction is insignificant with the p-value equal to 0.316. The reduction in the activity of AST is noted in both the placebo and CoQ10 groups, but the p-values indicate that the change is significant in the CoQ10 group while it occurs by chance in the placebo group. The activity of ALP is reduced to a minor extent in both groups and p values indicate that there is no significant effect of CoQ10 on the activity of alkaline phosphatase after two months. The result shows no significant change in the concentration of serum albumin after two months of CoQ10 administration. The last measured parameter of liver function tests is total bilirubin concentration. The result showed a reduction in total bilirubin concentration from 0.486 to 0.372 mg/dl with p p-value equal to 0.003 (Figure 2).

Discussion

The present study conducted on pollutant exposed workers and the outcomes revealed that CoQ10 has positively modulated the blood pressure, redox parameters, and liver enzymes in participants who have been working in area of exposure to heavy metals for long term. The weight indices were not changed after two months of CoQ10 use.

The weight assessment of the patients was based on four basic parameters which include weight, hip circumference, waist circumference, and BMI. The outcome has ultimately shown no significant change of body weight indices in the group that received CoQ10 versus placebo group. Many studies were conducted to assess the effect of CoQ10 and weight and their outcomes were in line with the findings of this study[9,10]. A Muhtaroğlu study succeeded in finding a negative correlation between CoQ10 level and BMI. Besides, it is mentioned that endogenous CoQ10 synthesis might not compensate great demand for lipophilic antioxidants in obese individuals explaining the negative role of CoQ10 on body weight indices[11]. Conversely, body weight indices improved by CoQ10[12-14], and this change has been linked to leptin level modulation, since administration of CoQ10 results in reduced leptin levels. Leptin can stimulate lipolysis and inhibit lipogenesis by affecting the activity of the enzymes in the pathways for the synthesis and breakdown of fatty acids, although an increased level of leptin may be associated with leptin resistance and increased weight[12,13]. The effect of the administration of CoQ10 on BMI at longer duration and higher doses needs further studies.

The results of the current study regarding blood pressure agrees with many researches and meta-analysis data[15,16]. There is a reduction in systolic, but not diastolic blood pressure, to a significant extent. This reduction in blood pressure values showed a slightly lower improvement compared to the conducted result of the meta-analysis study with a decrease of about 8 units for systolic and 5 units for diastolic blood pressure when the result of blood pressure lowering ranges for systolic blood from 10 to 21 mm Hg and for diastolic from 7 to 16 mm Hg in meta-analysis study. The participants in meta-analysis were hypertensive individuals, while in the current study, the participants range from normotensive to prehypertensive[16]. This could be explained in the context of oxidative stress invoke vasoconstriction and CoQ10 is a potent lipid-soluble antioxidant with the ability to offset this vasoconstriction and thus lower blood pressure[16]. Additionally, CoQ10 encourage vasodilation via a direct effect on the vascular smooth muscle and endothelium. The studies of hypertensive patients treated with co-enzyme Q10 showed decrease peripheral resistance with lowering of blood pressure and unaffected cardiac output. It should be noted that in normal animals or humans, co-enzyme Q10 has no vasodilating or hypotensive effect. This indicates that the hypotensive effect of co-enzyme Q10

Table 1. Period of exposure to causative agents at workplace.

Time of exposure	Placebo	CoQ10
Occupation exposure	n (%)	n (%)
<5 Years	24 (40)	30 (42)
5 to 10 years	27(45)	24(33)
>10 Years	9(15)	18(25)

Table 2. The impact of CoQ10 on body weight-related indices and blood pressure.

Parameters	-CoQ10 Baseline	-CoQ10 At the end	+CoQ10 Baseline	+CoQ10 At the end
Age (Years)	35±5		42±8	
BMI (kg/m^2)	27.38±4.69	27.52±4.75	29.11±4.68	28.81±4.51
Weight(kg)	82.25±18.4	82.47±18.7	84.9±14.1	83.7±13.5
Waist circumference (cm)	92.25±16.4	92.5±16.4	96.9±11	95±9.95
Hip circumference (cm)	100.8±9.07	100.7±8.96	102.3±7.2	101.7±7.34
SBP (mmHg)	130±12	132±12	135±12	127±6*
DBP (mmHg)	81±7	80±8	85±7	79±7
Data expressed as mean±SD, *significant differences as compared to other groups at p value p<0.05, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure				

is specific to the state of exaggerated oxidative stress condition that occurs in hypertensive patients. Co-enzyme Q10 has been shown to target the expression of many genes, particularly those involved in signaling and metabolism and this may have a role in blood pressure reduction[16].

The TAOC reduces due to exposure to occupational pollution, which is mainly due to heavy metals exposure, thereby increases oxidative stress and results in the exhausting of TAOC within the body. The number of epidemiological studies regarding TAOC and air pollution remains limited. One study in India reported increased reactive oxygen species (ROS) generation after exposure to environmental pollution and this resulted in a depletion in TAOC[17]. Another study among elderly people who lived in Mexico City, showed low TAOC level because of high air pollution exposure[18].

There are many studies suggest that there is an increase in the level of MDA is due to an increase generation of free radicals due to exposure to various pollutants this in turn results in lipid peroxidation and damage to cell membranes which act as easy targets for free radicals since it contains a large proportion of unsaturated fatty acid[19,20-22]. The rise in MDA is an indication of the occurrence of oxidative stress among workers exposed to different industrial pollutants. This increase in the concentration of MDA is due to the increased generation of free radicals during exposure to different types of industrial pollutants (heavy elements) such as cadmium and lead and their accumulation in the body, which in turn leads to an increase in lipid peroxidation, which results in oxidative damage in the cell membrane. Cell membrane is the main target of free radicals since it contains mul-

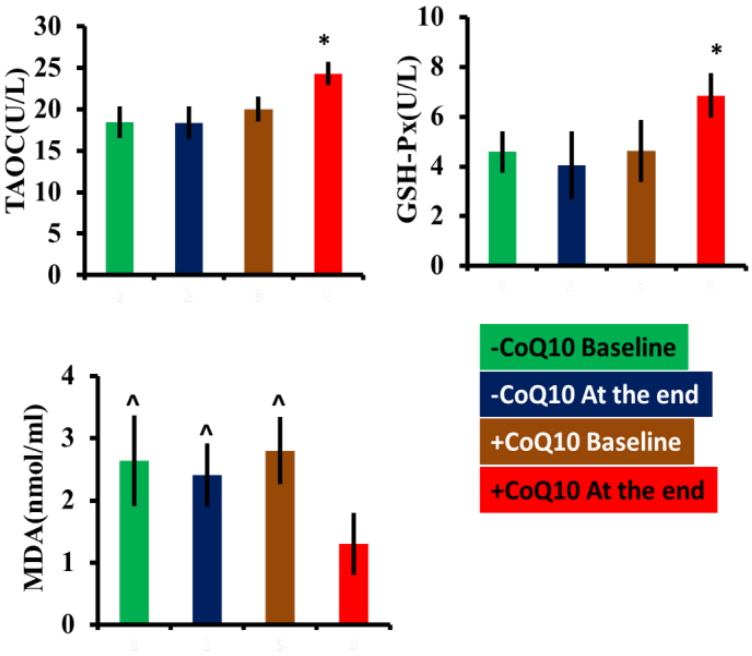


Figure 1. *Redox parameters improved by CoQ10 therapy. Data expressed as mean±SD. *^P<0.05. * as compared to all other groups, ^ as compared to the CoQ10 treated group at the end of two months of therapy. TAOC=total antioxidant capacity, GSH-Px=glutathione-peroxidase, MDA=malondialdehyde, CoQ10=Coenzyme Q10 or Ubiquinone.*

tiple polyunsaturated fatty acids and is rich in double bonds, and this leads to increased MDA concentration which is one of the main final products of lipid peroxidation[20,23]. Heavy elements act as catalysts for ROS production and this leads to lipid peroxidation, in addition to the depleting of antioxidants[24,25]. The extent of change in MDA concentrations varies and can be correlated with periods of exposure. This study is consistent with the findings of those who have mentioned that exposure to industrial pollutants leads to a significant increase in MDA concentration, and this is directly proportional to the increase in periods of annual exposure[20,26].

The activity of GSH-Px can also change in population exposure to occupational pollution. The association between GSH-Px activity and pollution exposure has been inconsistent across epidemiological studies. Some studies have found that lower GSH-Px activity in pollution conditions[26,27], while others have found that GSH-Px activity is higher in pollution conditions[28]. It is suspected that individuals' long-term exposure to pollution might have decreased antioxidant enzyme activity due to long-term oxidative stress. This suggestion was supported by previous experimental and human studies[26,29,30] .

In the line of the present study, CoQ10 has been reported to exert antioxidant effects against ROS-environmental contaminants. For instance, CoQ10 has reduced oxidative stress in Inuit people due to their diet-rich with prooxidants[31]. Environmental contamination with chemicals (Bisphenol A- or Arsenic- or Lead Acetate-Induced Oxidative stress) have been tackled by CoQ10 and restored infertility[32-34]. Moreover, anticancer induced oxidative tissue damages have been dampened by CoQ10[35].

There are many studies indicating that the CoQ10 has a protective effect on the liver either by direct antioxidant effect or by its anti-inflammatory effect[9,36]. The results of this study confirmed that CoQ10 has a beneficial effect on liver enzymes and it is associated with the reduction in both the activities of ALT and AST. The result in the placebo group showed no difference between the measurement of both ALT and AST. This may be in part because the

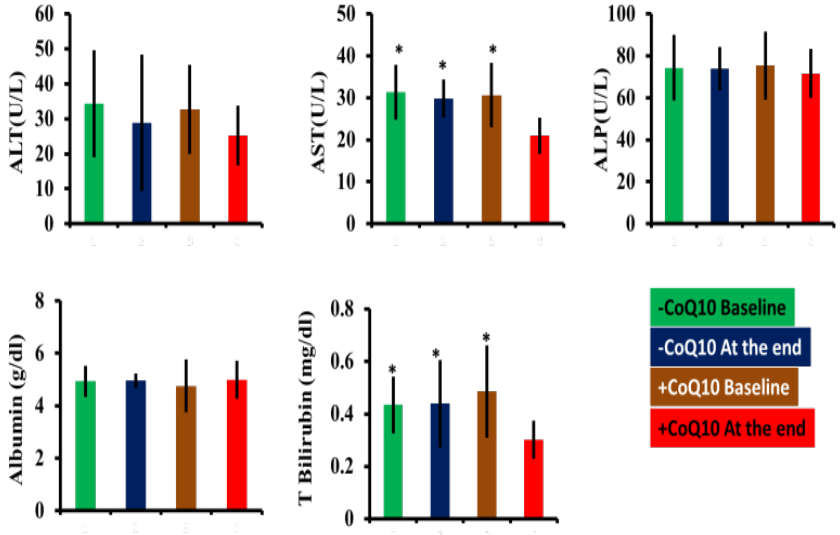


Figure 2. *Liver function parameters improved by CoQ10 therapy. Data expressed as mean±SD. *P<0.05. * as compared to the CoQ10 treated group at the end of two months of therapy. ALT=alanine aminotrasferase, AST=aspartate aminotrasferase, ALP= alkaline phosphatase CoQ10=Coenzyme Q10 or Ubiquinone.*

liver's transferase enzymes are elevated related to oxidative stress and in the CoQ10 receiving group there is a reduction in the generation of free radicals and subsequent oxidative stress occurrence[9]. As a result, damage to liver cells is minimized and the death of hepatocytes is reduced so the amount of released transferase will be reduced[9]. The results of the current study agree with the results of[37,38]. Also, many animal studies show the same protective effect of CoQ10 on the liver, it showed that CoQ10 usage was associated with a decrease in both improvement in the level of ALT and AST[39,40].

Many studies are conducted to assess the effect of occupational pollution on liver enzymes which showed varying results between insignificant increase to significant increase that may be in part due to different experimental settings with different impacts and different exposure periods[41]. Alkaline phosphatase activity changes with pollution also range from significant reduction in their activity to insignificant changes. The reduction of their activity may result in part due to the replacement of magnesium co-factor in this enzyme by lead[42]. The effect of CoQ10 on the level of alkaline phosphatase showed no significant results and the results in both CoQ10 treated group and placebo group are parallel. This indicates that the administration of CoQ10 has shown no improvement in ALP activity. The results agree with the studies reported no significant change in ALP activity[43,44]. Decreased activity of ALP may result in part from the replacement of lead for magnesium and zinc[42]. Others expect that the cause of reduced alkaline phosphatase activity in pollution conditions results in part from the low level of zinc or magnesium[45]. In a related issue, the result of animal studies showed an increase in the activity of alkaline phosphatase by administration of CoQ10 and that has a beneficial effect in many species. Supplementation with CoQ10 may increase mitochondrial $Mg2^{+}$ and enhance alkaline phosphate activity in some species[42,46].

Exposure to occupational pollution may result in a decreased ability of the liver to synthesize albumin and this may have appeared as a reduction in its level or might be due to pollution induced oxidative stress leading to kidney damage which may result in leaks of albumin out of the body via excretion[19]. The results of the current study showed no significant change in serum albumin concentration in either CoQ10 or placebo-receiving groups. The results of some studies indicate a significant change in the serum albumin perhaps due to higher doses used and longer periods this may be due to that the majority of these studies

are performed in animal models or persons with obvious liver or kidney impairment with previously altered albumin levels[42,47].

The level of total bilirubin shows a significant reduction in the CoQ10-treated group compared to the placebo group. This indicates that CoQ10 has a protective effect on the liver. In addition, it may improve red blood cell survival and one result of this is reduced total bilirubin. This effect may in part be due to the potent antioxidant and anti-inflammatory effect of CoQ10[48]. There are various studies performed to illustrate the effect of the administration of CoQ10 with total bilirubin concentration and the result of this study agrees with the results of many studies[40,49]. On the other hand, no significant change in total bilirubin is seen in another study[49] and that may be in part due to lower dose or duration of management, also since the concentration of total bilirubin is not affected to a significant extent in participants so no significant change is detected. Another liver function test parameter that shows change due to occupational pollution is total bilirubin. Many studies indicate that exposure to occupational pollution may be associated with increased bilirubin levels both by direct damage to the liver which may result in reduced efficacy of the liver to extract bilirubin and also by increasing breakdown of red blood cells due to oxidative stress [19,50].

Conclusion

The environmental pollutant exposure at workplace potentially modulates redox balances and liver damage. CoQ10 dampens this potential deleterious impact via reducing lipid peroxidation and maintaining higher antioxidant levels alongside reduced liver enzyme and liver parameters against damage induced by environmental pollutant. A recommendation should be directed toward indicating these supplements in high-risk group individuals heavily exposed to workplace pollution. □

REFERENCES

1. Gu J., Shi Y., Zhu Y., Chen N., Wang H., Zhang Z., Chen T. Ambient air pollution and cause-specific risk of hospital admission in China: a nationwide time-series study. *PLoS Medicine*, 17(8), 1-26, 2020.
2. Wang C., Zhu G., Zhang L., Chen K. Particulate matter pollution and hospital outpatient visits for endocrine, digestive, urological, and dermatological diseases in Nanjing, China. *Environ. Pollut*. 261, 1-24, 2020.
3. Risom L., Møller P., Loft S. Oxidative stress-induced DNA damage by particulate air pollution. *Mutat. Res.* 592(1-2), 119-137, 2005.
4. Farhat Z., Browne R.W., Bonner M.R., Tian L., Deng F., Swanson M., Mu L. How do glutathione antioxidant enzymes and total antioxidant status respond to air pollution exposure? *Environ. Int.*112, 287-293, 2018.
5. Rehman K., Fatima F., Waheed I., Akash, M.S.H. Prevalence of exposure of heavy metals and their impact on health consequences. *J. Cell Biochem*. 119(1), 157-184, 2018.
6. Ommati M.M., Heidari R. Betaine, heavy metal protection, oxidative stress, and the liver. *Toxicology* 387-395, 2021.
7. Paithankar J.G., Saini S., Dwivedi S., Sharma A., Chowdhuri D.K. Heavy metal associated health hazards: An interplay of oxidative stress and signal transduction. *Chemosphere* 262, 1-15, 2021.
8. Wang Y., Hekimi S. Understanding ubiquinone. *Trends Cell Biol*. 26(5), 367-378, 2016.
9. Farsi F., Mohammadshahi M., Alavinejad P., Rezazadeh A., Zarei M., Engali K.A. Functions of coenzyme Q10 supplementation on liver enzymes, markers of systemic inflammation, and adipokines in patients affected by nonalcoholic fatty liver disease: a double-blind, placebo-controlled, randomized clinical trial. *J. Am. Coll. Nutr.* 35(4), 346-353, 2016.
10. Gholami M., Rezvanfar M.R., Delavar M., Abdollahi M., Khosrowbeygi A. Effects of coenzyme Q10 supplementation on serum values of gamma-glutamyl transferase, pseudocholinesterase, bilirubin, ferritin, and high-sensitivity C-reactive protein in women with type 2 diabetes. *Exp. Clin. Endocrinol.* Diabetes 127(05), 311-319, 2019.
11. Muhtaroğlu S., Koçak S.Ö., Çetin İ., Barlak Keti D., Kendirci M. Investigation of ischemia modified albu-

min and coenzyme Q10 levels in obese children with metabolic syndrome. *Turk. J. Biochem.* 41(6), 443-449, 2016.

12. Muhtaroğlu S., Koçak S.Ö., Çetin İ., Barlak Keti D., Kendirci M. Investigation of ischemia modified albumin and coenzyme Q10 levels in obese children with metabolic syndrome. *Turk. J. Biochem.* 41(6), 443-449, 2016.
13. Leibel R.L. The role of leptin in the control of body weight. *Nutr. Rev*. 60(suppl_10), S15-S19, 2002.
14. Fleisch A.F., Agarwal N., Roberts M.D., Han J.C., Theim K.R., Vexler A., Yanovski J. A. Influence of serum leptin on weight and body fat growth in children at high risk for adult obesity. *J. Clin. Endocrinol. Metab*. 92(3), 948-954, 2007.
15. Yang Y.K., Wang L.P., Chen L., Yao X.P., Yang K.Q., Gao L.G., Zhou X.L. Coenzyme Q10 treatment of cardiovascular disorders of ageing including heart failure, hypertension and endothelial dysfunction. *Clin. Chim. Acta* 450, 83-89, 2015.
16. Rosenfeldt F.L., Haas S.J., Krum H., Hadj A., Ng K., Leong J.Y., Watts G.F. Coenzyme Q10 in the treatment of hypertension: a meta-analysis of the clinical trials. *J. Hum. Hypertens.* 21(4), 297-306, 2007.
17. Mondal N.K., Mukherjee B., Das D., Ray M.R. Micronucleus formation, DNA damage and repair in premenopausal women chronically exposed to high level of indoor air pollution from biomass fuel use in rural India. *Mutat. Res. Genet. Toxicol. Environ. Mutagen.* 697(1-2), 47-54, 2010.
18. Sánchez-Rodríguez M.A., Retana-Ugalde R., Ruiz-Ramos M., Mendoza-Núñez V.M. Antioxidant capacity in relationship to serum lipid peroxides levels in healthy elderly of Mexico City. Acta Bioquím. *Clín. Latinoam.* 38, 193-198, 2004.
19. Liu J., Drane W., Liu X., Wu T. Examination of the relationships between environmental exposures to volatile organic compounds and biochemical liver tests: application of canonical correlation analysis. *Environ. Res.* 109(2), 193-199, 2009.
20. Jankeer M.H. The protective effect of Vitamin C and Vitamin E on some antioxidants and lipid peroxidation in blood and tissues of male albino rats treated with aluminum. *Int. J. Enh. Res. Sci. Tech. Engin.* 4(2), 34-44, 2015.
21. Patar A., Giri A., Boro F., Bhuyan K., Singha U., Giri S. Cadmium pollution and amphibians–Studies in tadpoles of Rana limnocharis. *Chemosphere* 144, 1043-1049, 2016.
22. Liu T., Zhang L., Joo D., Sun S.C. NF-κB signaling in inflammation. *Signal Transduct. Target Ther*. 2(1), 1-9, 2017.
23. Romieu I., Barraza-Villarreal A., Escamilla-Nuñez C., Almstrand A.C., Diaz-Sanchez D., Sly P.D., Olin A.C. Exhaled breath malondialdehyde as a marker of effect of exposure to air pollution in children with asthma. *J. Allergy Clin. Immunol.* 121(4), 903-909, 2008.
24. Flora S.J.S., Mittal M., Mehta A. Heavy metal induced oxidative stress and its possible reversal by chelation therapy. *Altern. Med. Rev.* 14(1), 87-88, 2009.
25. Engwa G.A., Ferdinand P.U., Nwalo F.N., Unachukwu M.N. Mechanism and health effects of heavy metal toxicity in humans. *Intechopen*. 10, 70-90, 2019.
26. Bentley A.R., Emrani P., Cassano P.A. Genetic variation and gene expression in antioxidant related enzymes and risk of COPD: a systematic review. *Thorax* 63(11), 956-961, 2008.
27. Yildiz L., Kayaoğlu N., Aksoy H. The changes of superoxide dismutase, catalase and glutathione peroxidase activities in erythrocytes of active and passive smokers. *Clin. Chem. Lab. Med.* 40(6):612-615, 2002.
28. Assi S.H., Al-Husain R.S. Study of Protective effect of Glutathione Peroxidase (GSH-Px), Vitamin E and Selenium on Iraqi children with Leukemia. *J. Biotechnol*. Res. 8(4), 15-21, 2014.
29. Metta S., Basalingappa D.R., Uppala S., Mitta G. Erythrocyte antioxidant defenses against cigarette smoking in ischemic heart disease. *J. Clin. Diagnostic Res.* 9(6), BC08, 2015.
30. Farhat Z., Browne R.W., Bonner M.R., Tian L., Deng F., Swanson M., Mu L. How do glutathione antioxidant enzymes and total antioxidant status respond to air pollution exposure? *Environ. Int.* 112, 287-293, 2018.
31. Bélanger M.C., Mirault M.É., Dewailly E., Berthiaume L., Julien P. Environmental contaminants and redox status of coenzyme Q10 and vitamin E in Inuit from Nunavik. *Metabolism* 57(7), 927-933, 2008.
32. Bradford B.R., Briand NE., Fassnacht N., Gervasio E.D., Nowakowski A.M., FitzGibbon T.C., Checchi P.M. Counteracting environmental chemicals with Coenzyme

Q10: an educational primer for use with "Antioxidant CoQ10 restores fertility by rescuing bisphenol A-induced oxidative DNA damage in the Caenorhabditis elegans Germline". *Genetics* 216(4), 879-890, 2020.
33. Silva S.V.E., Gallia M.C., Luz J.R.D.D., Rezende A.A.D., Bongiovanni G.A., Araujo-Silva G., Almeida M.D.G. Antioxidant effect of coenzyme Q10 in the prevention of oxidative stress in arsenic-treated CHO-K1 cells and possible participation of zinc as a pro-oxidant agent. *Nutrients* 14(16), 879–890, 2022.
34. El-Khadragy M., Al-Megrin W.A., AlSadhan N.A., Metwally D.M., El-Hennamy R.E., Salem F.E.H., Abdel Moneim A.E. Impact of coenzyme Q10 administration on lead acetate-induced testicular damage in rats. *Oxid. Med. Cell Longev.* 1-12, 2020.
35. Althanoon Z.A., Merkhan M.M. CoQ10 dampens the deleterious impact of doxorubicin-induced liver and spleen injury in white Albino rats. *Pharmacology* 27, 31-40, 2023.
36. Olivieri F., Lazzarini R., Babini L., Prattichizzo F., Rippo M.R., Tiano L., Procopio A.D. Anti-inflammatory effect of ubiquinol-10 on young and senescent endothelial cells via miR-146a modulation. *Free Radic. Biol. Med.* 63, 410-420, 2013.
37. Fouad A.A., Jresat I. Hepatoprotective effect of coenzyme Q10 in rats with acetaminophen toxicity. *Environ. Toxicol. Pharmacol.* 33(2), 158-167, 2012.
38. Jiménez-Santos M.A., Juárez-Rojop I.E., Tovilla-Zárate C.A., Espinosa-García M.T., Juárez-Oropeza M.A., Ramón-Frías T., Díaz-Zagoya J. C. Coenzyme Q10 supplementation improves metabolic parameters, liver function and mitochondrial respiration in rats with high doses of atorvastatin and a cholesterol-rich diet. *Lipids Health Dis.* 13(1), 1-10, 2014.
39. Cheignon C., Faller P., Testemale D., Hureau C., Collin F. Metal-catalyzed oxidation of Aβ and the resulting reorganization of Cu binding sites promote ROS production. *Metallomics* 8(10), 1081-1089, 2016.
40. Doynny, V. (2020). The effect of ubiquinone-10 on the biochemical parameters of the blood of intact mice. Scientific Collection «InterConf» : SCIENCE AND PRACTICE: IMPLEMENTATION TO MODERN SOCIETY December 26-28, 2020 https://ojs.ukrlogos.in-.ua/index.php/interconf/article/view/8006
41. Sahib A.A., Al-Qazzaz, M.A., Kareem S.K. Enzymatic Liver Changes among Workers Exposed to Vinylchloride. *Iraqi J. Med. Sci*. 10(1), 75-82 2012.
42. Sharma U., Pal D., Prasad R. Alkaline phosphatase: an overview. *Indian J. Clin. Biochem.* 29, 269-78, 2014.
43. Hernández-Ojeda J., Cardona-Muñoz E.G., Román-Pintos L.M., Troyo-Sanromán R., Ortiz-Lazareno P.C., Cárdenas-Meza M.A., Miranda-Díaz A.G. The effect of ubiquinone in diabetic polyneuropathy: a randomized double-blind placebo-controlled study. *J. Diabetes Complications* 26(4), 352-358, 2012.
44. Mabuchi H., Higashikata T., Kawashiri M., Katsuda S., Mizuno M., Nohara A., Kobayashi J. Reduction of serum ubiquinol-10 and ubiquinone-10 levels by atorvastatin in hypercholesterolemic patients. *J. Atheroscler. Thromb*. 12(2), 111-119, 2005.
45. Ray C.S., Singh B., Jena I., Behera S., Ray S. Low alkaline phosphatase (ALP) in adult population an indicator of zinc (Zn) and magnesium (Mg) deficiency. *Curr. Res. Nutr. Food Sci.* 5(3), 347-352, 2017.
46. Strachecka A., Olszewski K., Paleolog J., Borsuk G., Bajda M., Krauze M., .Chobotow J. Coenzyme Q10 treatments influence the lifespan and key biochemical resistance systems in the honeybee, Apis mellifera. *Arch Insect. Biochem. Physiol*. 86(3), 165-179, 2014.
47. Carrasco J., Anglada F.J., Campos J.P., Muntané J., Requena M. J., Padillo J. The protective role of coenzyme Q 10 in renal injury associated with extracorporeal shockwave lithotripsy: a randomised, placebo-controlled clinical trial. *BJU Int.* 113(6), 942-950, 2014.
48. Hao L., Sun Q., Zhong W., Zhang W., Sun X., Zhou Z. Mitochondria-targeted ubiquinone (MitoQ) enhances acetaldehyde clearance by reversing alcohol-induced posttranslational modification of aldehyde dehydrogenase 2: a molecular mechanism of protection against alcoholic liver disease. *Redox Biol.* 14, 626-636, 2018.
49. Hernández-Ojeda J., Cardona-Muñoz E.G., Román-Pintos L.M., Troyo-Sanromán R., Ortiz-Lazareno P.C., Cárdenas-Meza M.A., Miranda-Díaz A. G. The effect of ubiquinone in diabetic polyneuropathy: a randomized double-blind placebo-controlled study. *J Diabetes Complications,* 26(4), 352-358, 2012.
50. Ge X., Liu Z., Hou Q., Huang L., Zhou Y., Li D., Yang X. Plasma metals and serum bilirubin levels in workers from manganese-exposed workers healthy cohort. *Environ. Pollut.* 258, 1-15, 2020.