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Study the Effect of Selenium Supplementations on the Liver, Kidney and Thyroid Gland Activities in Male Rats

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ABSTRACT

The liver, kidney, and thyroid glands are main vital in biochemical and physiological activities in animals and humans. In this study, we examined the effects of adding selenium supplementation on the improvement activity of many glands such as the liver, kidney, and thyroid after cadmium chloride administration (induced toxicity) in male rabbits. This study included 16 male rabbits divided into four groups, the 1st group (CON) was control and administration normal fed and drinking water, the 2nd group (NC) was negative control group that administration of 1ml of cadmium chloride (100ppm) with normal fed, the 3rd group (S1) was administration of 1ml of sodium selenite, and 4th group (S2) was administration of 5ml of selenium and all groups continuous for same style up to 8th week of experiment. Antioxidant and oxidative stress status was investigated by measuring the levels of T-AOC and MDA. The liver was assessed by estimation of ALT, AST, TP, and TB while kidney was assessed by calculation of blood CRI and UR and the thyroid gland assessed by measurement of serum T3 and T4. The levels of selenoprotein (SeP) mg/l were assessed by HPLC for standard and S2 group. The results of present study shows highly statistical differences between four group when compare the mean±SD of the levels of ALT,AST,TP,TB,CRI,UR,T3, and T4 (p-value <0.005). In conclusion, this study showing highly ability of selenium supplementation to lowering the levels of the markers of liver, kidney, and thyroid gland and work as protective factor from toxicity induced by cadmium in male rabbits.

KEYWORDS: Liver, Kidney, Thyroid gland, Selenium**,** Cadmium.

ARTICLE DETAILS

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INTRODUCTION

The liver is a critical organ in the human body that is responsible for an array of functions that help support metabolism, immunity, digestion, detoxification, vitamin storage among other functions. It comprises around 2% of an adult's body weight (1). The liver is a unique organ due to its dual blood supply from the portal vein (approximately 75%) and the hepatic artery (approximately 25%) (2). The functional unit of the liver is the lobule. Each lobule is hexagonal and a portal triad (portal vein, hepatic artery, bile duct) sits at each corner of the hexagon (3). The foundation of the lobule is composed of hepatocytes, which have physiologically distinct apical and basolateral membranes (4). The kidney is composed of two regions: the cortex and medulla. The cortex is composed of renal corpuscles, convoluted tubules, straight tubules, collecting tubules, collecting ducts, and vasculature. Medullary rays, comprised of straight tubules and collecting ducts, extend into the cortex from the medulla. The medulla also contains the vasa recta, a network of capillaries integral to the countercurrent exchange system (16). Pyramids are conical structures formed by the collecting of tubules in the medulla, oriented with the base towards the cortex and apices towards the hilum. The papillae at the apices of the pyramids extend into minor calyces and drain via the collecting ducts at their tips, the area cribrosa. A collecting duct and the group of nephrons that it drains is referred to as a lobule (17). The thyroid is an endocrine gland. Its location is in the inferior, anterior neck, and it is responsible for the formation and secretion of the thyroid hormones as well as iodine homeostasis within the human body. The thyroid produces approximately 90% inactive

thyroid hormone, or thyroxine (T4), and 10% active thyroid hormone, or triiodothyronine (T3). Inactive thyroid hormone is converted peripherally to either activated thyroid hormone or an alternative inactive thyroid hormone (23). The aim of this work to Investigation the effects of adding of selenium supplementation in normal daily drinking water of male rabbits on functions of liver, kidney, and thyroid gland.

MATERIALS AND METHODS

Materials:

This study was conducted at the period December 2022-March, 2023 in the physiology department of veterinary medicine of AL-Qasim Green University. Selenium was purchased from BIOCHEM/ China as sodium selenite and other chemicals and kits provided by the biochemistry laboratory of our department.

Animal and Experimental Design:

Healthy 16 male rabbits weighed 1.5- 2 kg, purchased from the animal market in Babylon province and were used for this study. The animals were randomly divided into four groups of four animals in each after an acclimatization period of two weeks. They were fed with standard diet, had free access to water, housed under standard conditions of humidity and controlled temperature (25˚C). The protocol was approved by the Institutional Animal Ethics Committee of Al-Qasim Green University and dose was 0.5 ml/ kg body weight) for all.

- G1 (4 rabbits, control group: CON): Rabbits received subcutaneously normal fed and 1ml/kg body saline solution in drinking water subcutaneously up to 8 weeks.
- G2 (4 rabbits, negative control group: NC): Rabbits received subcutaneously 1ml/kg (100 PPM) body weight/day of cadmium chloride (induced toxicity) in drinking water for one week with normal fed up to 8 weeks.
- G3 (4 rabbits, selenium administration group: S1): Rabbits received subcutaneously cadmium chloride (100 PPM) (1ml/kg body weight/day) for one week (induced toxicity) and then 1ml/kg body weight/day Se solution in drinking water with normal fed up to 8 weeks.
- G4 (4 rabbits, selenium administration group: S2): Rabbits received subcutaneously cadmium chloride (100 PPM) (5ml/kg body weight/day) for one week (induced toxicity) and then 5ml/kg body weight/day Se solution up to 8 weeks.

Measurement of T-AOC and MDA

Trolox is used to standardize T-AOC, with all other antioxidants being measured in Trolox equivalents. Measurement of the combined nonenzymatic antioxidant capacity of biological fluids and other samples provides an indication of the overall capability to counteract reactive oxygen species (ROS), resist oxidative damage and combat oxidative stress-related diseases. T-AOC standard curve was done by standard solution of 0, 1, 2, 4, 8 U/ml for serial dilution of 0, 0.15, 0.26. 0.299, 0.322 as absorbance (570 nm) showing in figure 1.

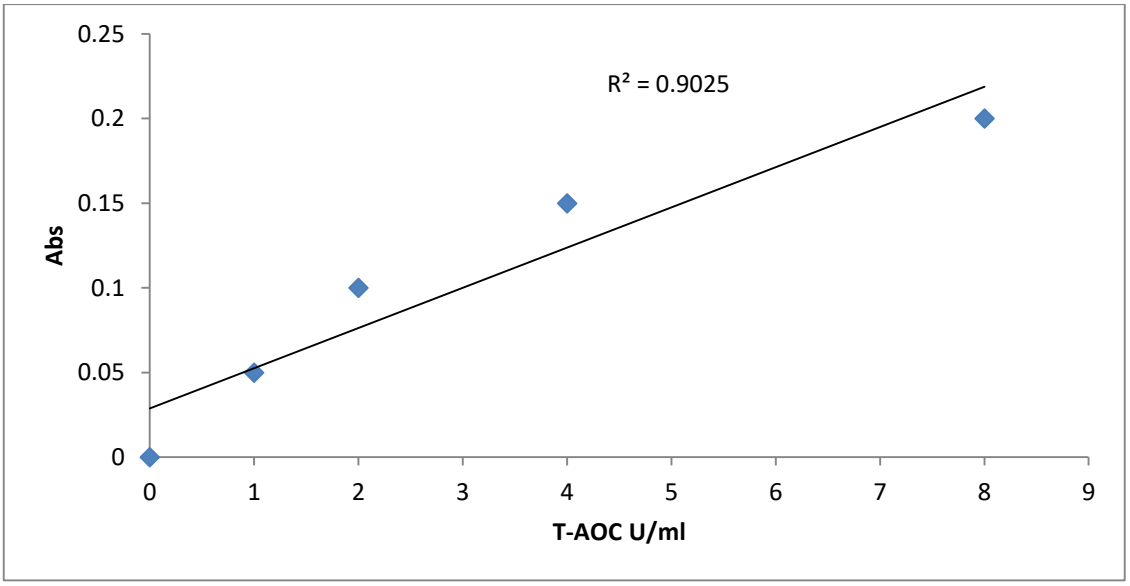

Fig.1: T-AOC standard curve

The method of determination of MDA is based on the colorimetric reaction with thiobarbituric acid (TBA) at 90-100˚C and pH 2-3 for 15 minutes to form pink color product, which can be measured by spectrophotometer at a wavelength of 532 nm.

Measurement of SeP:

This was performed by HPLC depending on the following conditions:

- Stationary Phase: C18 column, 5µm, 4.6 ×150mm
- Mobile phase: water: acetonitrile (20:80)(pH 4.7 ammonium acetate solution)
- Flow Rate: 1 mL/min

- Detection Type: UV at λ= 377 nm

Measurement of AST and ALT

The levels of ALT and AST activities in serum of rats were determined calorimetrically by using Biolabo diagnostic kits (France) according to manufacture protocol. The absorbance of the assay (A) was read against blank at 540 nm after 5 min. U/ml were used to expressed of activity the ALT and AST with comparing to specific standard curves.

Measurement of TP and TB

Serum TP and TB were performed calorimetrically using Biolabo diagnostic Kits (France) according to the method illustrated in kit. Albumin level was calculated using the following equation: TP and TB levels in mg/dl = concentration of standard TP or TB × Abs A/Abs S.

Measurement of CRI and UR

Serum CRI and UR was determined calorimetrically using Biolabo diagnostic Kit (France), according to manufacture protocol.

Measurement of Cd

In the nuclear retention spectrometry (AAS) strategies, the examples are disintegrated into free, unbiased molecules and enlightened by a light source that discharges the nuclear range of the component under investigation. The absorbance gives a quantitative proportion of the centralization of the component. Inductively coupled plasma nuclear outflow spectrometry (ICP-AES) and inductively coupled plasma mass spectrometry (ICP-MS) are multi-component methods. Planning of standard bend of minor components by expansion of 10 µl of (20, 40, 60, 80, and 100) ppb of Cd answer for the graphite container of graphite heater nuclear ingestion instrument. Convergences of serum minor components in patients and control were estimated by a similar instrument reliance on the accompanying standard curve, as shows in figure 2.

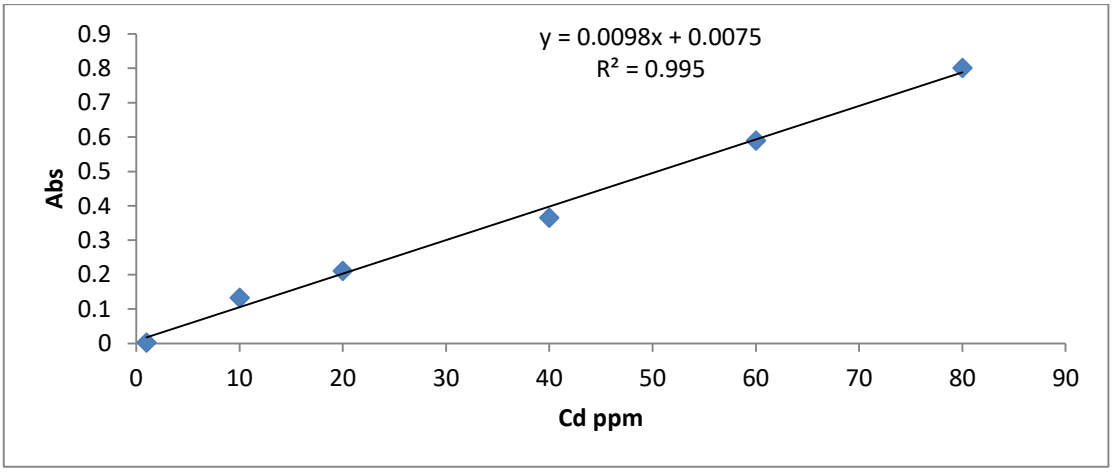

Fig.2:Standard curves of Cd (ppm) done by AAS

STATISTICAL ANALYSIS

The statistical analysis of this prospective study performed with the statistical package for social sciences (SPSS) 20.0 and Microsoft Excel 2013. Independent sample t-test used for comparison between two groups while, ANOVA used for comparison among more than 2 groups. Categorical data were described as count and percentage. Chi-square test used to estimate the association between variables. The lower level of accepted statistically significant difference is bellow or equal to 0.05.

RESULTS

Liver assessment

Table 1, showing the levels of ALT, AST, TP, and TB as liver assessment:

Table 1: ALT, AST, TP, and TB as liver assessment

Parameters	CON mean±SD	NC mean±SD	S1 mean±SD	S2 mean±SD	P-Value
ALT (IU/L)	37.1 ±2.0	137.1 ±4.2	57.1 ±2.0	48.0 ±3.1	0.001
AST (IU/L)	40.5 ±1.3	124.6 ±2.5	97.5 ±4.3	44.3 ±2.4	0.001
TP (mg/dl)	79.4 ±2.3	122.3 ±5.1	111.2 ±4.7	87.2 ±3.7	0.001
TB (mg/dl)	0.79 ±0.032	2.79 ±0.012	1.23±0.012	0.99±0.101	0.001

Figure 3, showing the statistically significant differences between study groups in ALT, AST, TP, and TB. The in vitro dissolution tests were performed to analyze the selenium administration groups S1 and S2.

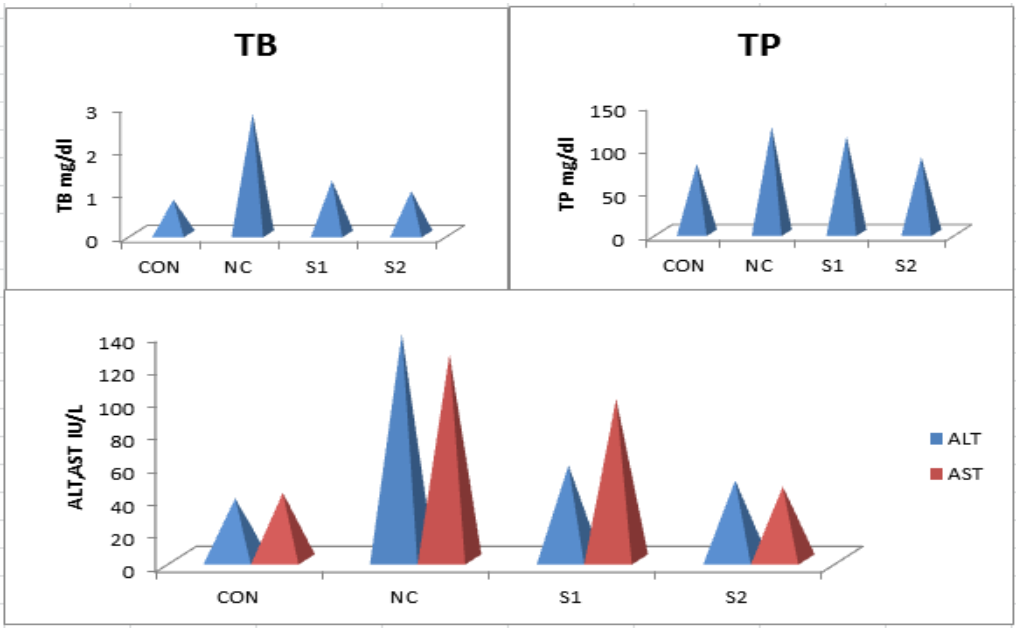

Fig.3: ALT, AST, TP, and TB levels in study groups as liver recovery

Kidney assessment

Table 2, showing levels of CRI and UR (mg/dl) as kidney assessment:

Table 2: CRI and UR (mg/dl) as kidney assessment

Parameters	CON mean±SD	NS mean±SD	S1 mean±SD	S2 mean±SD	P-Value
CRI	2.475±0.07	3.245±0.08	3.145±0.09	2.7±0.03	0.0000
UR	29.49 ± 1.9	35.49 ± 1.8	33.06 ± 1.7	31.86 ± 0.8	0.0000

Figure 4, showing the significant differences in levels of CRI and UR levels between study groups CON, NS, S1, and S2.

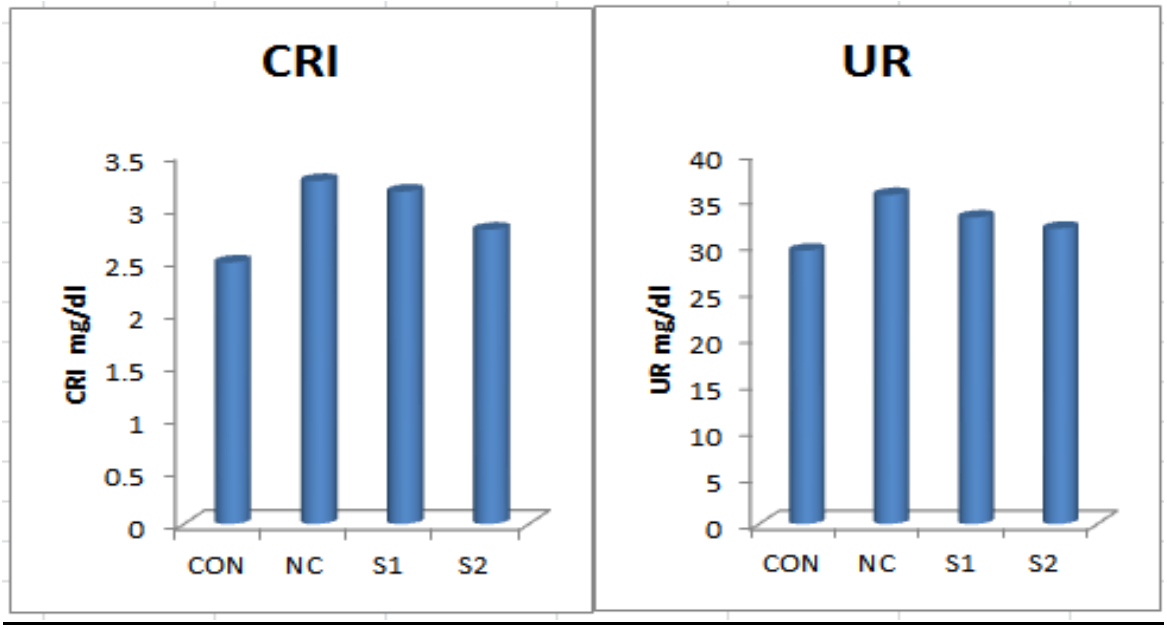

Fig.4: CRI and UR levels in study groups as kidney recovery

Thyroid assessment

Figure 5, showing the significant differences in levels of T3 and T4 levels between study groups CON, NS, S1, and S2.

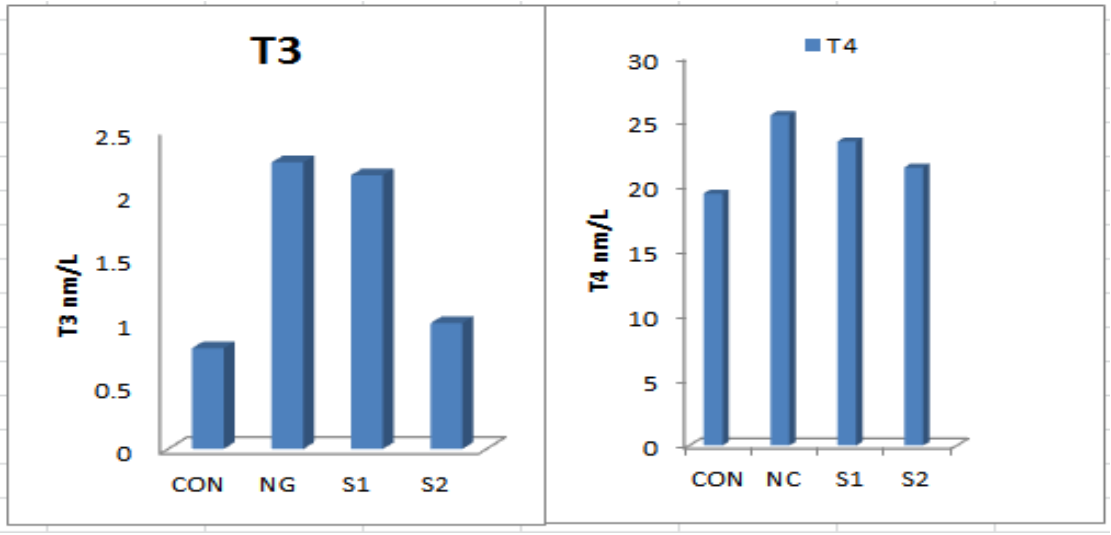

Fig.5: T3 and T4 (nm/l) levels in study groups as thyroid recovery

Figure 6, shows the weekly concentration of cadmium (ppm) in the serum of rabbits in CON, NC, S1, and S2 groups from the start to the final time of the experiment.

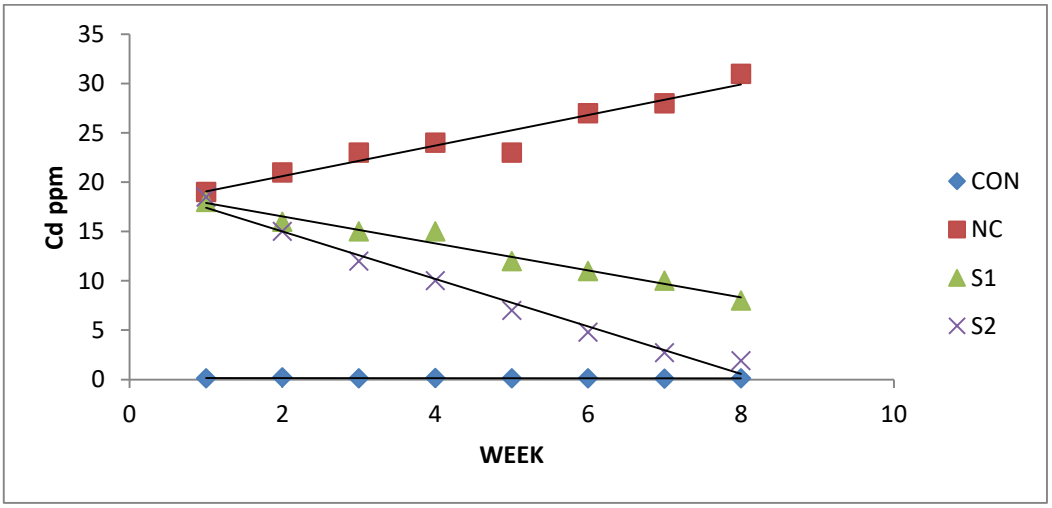

Fig.6: Weekly concentration of cadmium (ppm) in study groups

Figure 7, showing the significant levels (p-value < 0.05) between study groups in T-AOC and MDA as antioxidant and oxidative stress markers.

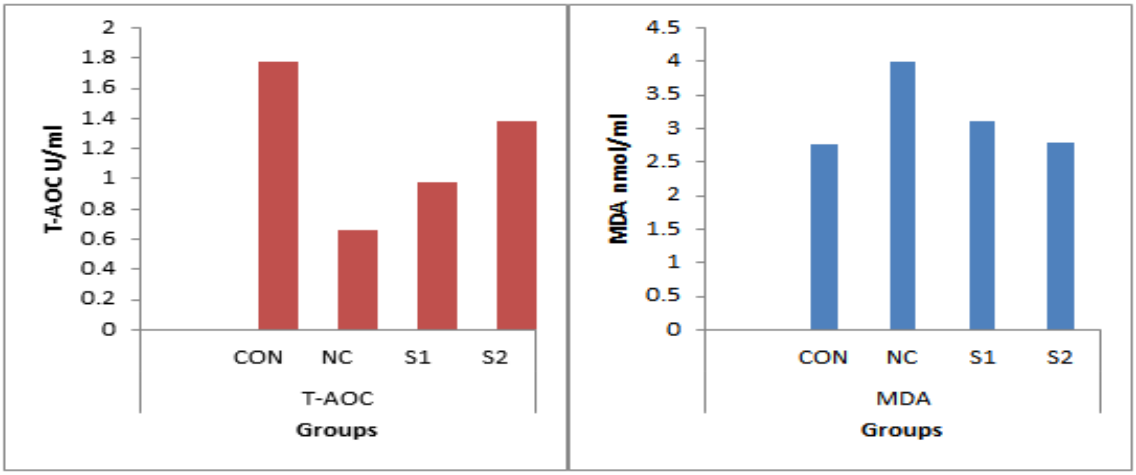

Fig.7: T-AOC and MDA levels in study groups as antioxidant/oxidative stress markers

Figure 8, showing the significant levels of SeP (mg/l) (p-value < 0.05) between study groups (S2 and standard).

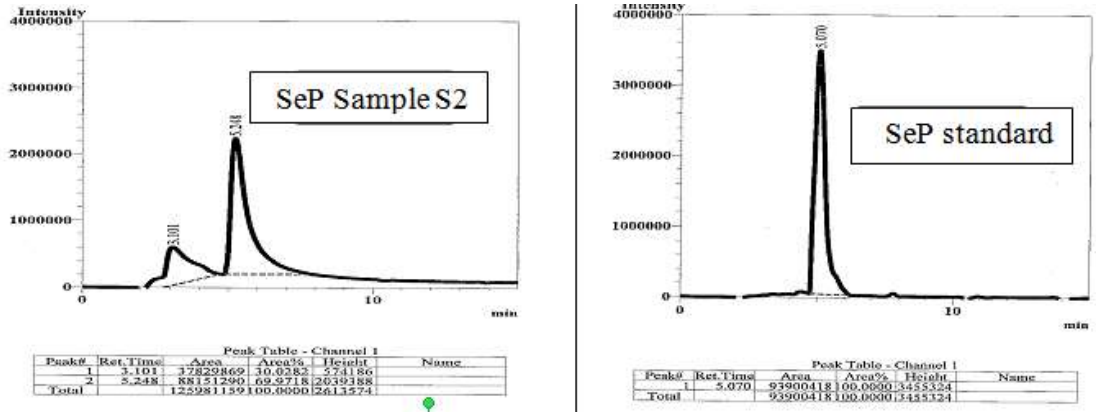

Fig.8: levels of SeP in S2 group compare to standard

DISCUSSION

Selenium is an essential trace element required for various biological processes. Selenium present in selenoproteins affects various enzymes (peroxidases, phosphatases, and transcriptase) that maintain different biochemical pathways in the body, thus preventing several conditions like oxidative stress and tumor formation (8). Cadmium is modern toxic metals (discovered in 1817) . The results of current study revaluated the action of selenium supplementation on improvement the activity of liver enzyme such as ALT and AST. The results shows statistical significant differences between levels of these enzymes (IU/L) between four groups CONT, NC, S1, S2 that listed in table 1, 37.1 ±2.0 137.1 ±4.2,57.1 ±2.0, 48.0 ±3.1 and 40.5 ±1.3 124.6 ±2.597.5 ±4.3, 44.3 ±2.4, respectively (p-value <0.05). Also TP and TB results supported the above our finding. Selenium supplementation can reduce pro-inflammatory cytokines and the expression of inflammation-related proteins in the liver, such as TLR4, NF-κB, JNK, and p38, as well as up-regulating heme oxygenase-1 (HO-1) to reduce the inflammatory response. Al-Dossari et al. found that the selenium treatment (0.1 mg/kg/d) mitigated lipopolysaccharide (LPS)/Diclofenac (DCL)-induced injury in the liver through suppressing the LPS-induced TLR4 signaling pathway and boosted antioxidant defenses to reduce oxidative stress in rats (10). Studies have long found that the plasma levels of selenium in patients with cirrhosis were lower than physical plasma concentrations and that they decrease in proportion to the severity of the cirrhotic condition (11). In rats with carbon tetrachloride (CCl4)/ethanol-induced cirrhosis, the co-treatment of selenium and vitamin E significantly decreases the amount of hepatic fibrosis (12). A meta-analysis shows the increased concentration of serum selenium could be related to a lower risk of hepatocellular carcinoma (13). On the other hand, the results of suggested the effect of selenium supplementation on improvement the activity of kidney markers such as CRI and UR. The results shows statistical significant differences between levels of these markers that 2.475±0.07, 3.245±0.08, 3.145±0.09, 2.7±0.03 and 29.49 ± 1.9, 35.49 ± 1.8, 33.06 ± 1.7, 31.86 ± 0.8, respectively (p-value <0.05). In this study, the biochemical and physiological examination showed that administration of Se decreased renal injury following Cd administration. The results from the recent studies suggest that Se can help to protect tissues against oxidative damage. In this study, it was found that Se has antioxidant protective effects on the kidney tissue and it prevents apoptosis. These results were in agreement with our biochemical and histological observations. CRN and UR are indicators of the kidney structure and when the kidney structure becomes damaged, the levels of these enzymes increased (14). These results agree with several studies have shown that antioxidants may reduce BUN serum levels and CRN (15). In fact, it has been shown that Se is reduced associated with the renal disease development process (16). The results of this study suggested the effect of selenium supplementation on improvement the activity of thyroid gland markers T3 and T4. The results shows statistical significant differences (p-value <0.05) between levels of these markers in four study groups, 0.79±0.02, 2.245±0.08, 2.145±0.09, and 0.987±0.03 for T3 and for T4 results were that 19.44 ± 1.5, 25.49 ± 1.3, 23.46 ± 1.4, and 21.46 ± 0.4 in CON, NC, S1, S2 groups, respectively. Selenocysteine is an essential component of several enzymes. There are four selenium-dependent glutathione peroxidases known in humans (17). Studies of selenium and thyroid hormone metabolism have been conducted in rats. Unfortunately, studies in rats cannot be extrapolated to humans because circulating T3 is produced mainly by deiodination of T4 in liver in humans (18). Most studies of selenium and thyroid hormone have used sodium selenite as the source of dietary selenium. However, selenite is an insignificant source of selenium in human diets (except for some selenium supplements) and possesses potent pharmacologic activities unrelated to the nutritional requirement for selenium, including prooxidant (19). The results of this study suggest that dietary selenium modulated thyroid hormone metabolism and serum T3 and T4 concentrations, which led to changes in

induced cadmium toxicity in thyroid and this may be correct the kidney, and liver markers.

CONCLUSION

This study showing highly ability of selenium supplementation to lowering the levels of the markers of liver, kidney, and thyroid gland and work as protective factor from toxicity induced by cadmium in male rabbits.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this manuscript was reported.

REFERENCES

I. Saxena R, Theise ND, Crawford JM. Microanatomy of the human liver-exploring the hidden interfaces. Hepatology. 1999 Dec;30(6):1339-46.

II. Si-Tayeb K, Lemaigre FP, Duncan SA. Organogenesis and development of the liver. Dev Cell. 2010 Feb 16;18(2):175-89.]

III. Almazroo OA, Miah MK, Venkataramanan R. Drug Metabolism in the Liver. Clin Liver Dis. 2017 Feb;21(1):1-20.

IV. O'Brien L, Hosick PA, John K, Stec DE, Hinds TD. Biliverdin reductase isozymes in metabolism. Trends Endocrinol Metab. 2015 Apr;26(4):212-20.

V. Zhang JL, Rusinek H, Chandarana H, Lee VS. Functional MRI of the kidneys. J Magn Reson Imaging. 2013 Feb;37(2):282-93.

VI. McMahon RS, Penfold D, Bashir K. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 25, 2022. Anatomy, Abdomen and Pelvis, Kidney Collecting Ducts.

VII. 23- Coste AH, Lofgren DH, Shermetaro C. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Sep 12, 2022. Branchial Cleft Cyst.

VIII. Kieliszek, M. Selenium−fascinating microelement, properties and sources in food. Molecules 2019, 24 (7), 1298−1311.

IX. Al-Dossari M.H., Fadda L.M., Attia H.A., Hasan I.H., Mahmoud A.M. Curcumin and Selenium Prevent Lipopolysaccharide/Diclofenac-Induced Liver Injury by Suppressing Inflammation and Oxidative Stress. Biol. Trace Elem. Res. 2020;196:173–183.

X. Nangliya V., Sharma A., Yadav D., Sunder S., Nijhawan S., Mishra S. Study of trace elements in liver cirrhosis patients and their role in prognosis of disease. Biol. Trace Elem. Res. 2015;165:35–40.

XI. Zhang M., Song G., Minuk G.Y. Effects of hepatic stimulator substance, herbal medicine, selenium/vitamin E, and ciprofloxacin on cirrhosis in the rat. Gastroenterology. 1996;110:1150–1155.

XII. ong Y., Dong F., Geng Y., Zhuang H., Ma Z., Zhou Z., Huang B., Sun Z., Hou B. Selenium concentration, dietary intake and risk of hepatocellular carcinoma—A systematic review with meta-analysis. Nutr. Hosp. 2019;36:1430–1437.

XIII. Vaidya VS, Ramirez V, Ichimura T, Bobadilla NA, Bonventre JV. Urinary kidney injury molecule-1: a sensitive quantitative biomarker for early detection of kidney tubular injury. Am J Physiol Renal Physiol. 2006;290:F517–29.

XIV. Hagiwara S, Koga H, Iwasaka H, Kudo K, Hasegawa A, Kusaka J. et al. ETS-GS, a New Antioxidant, Ameliorates Renal Ischemia-Reperfusion Injury in a Rodent Model. J Surg Res. 2011;171:226–33.

XV. Avlan D, Erdougan K, Cimen B, Dusmez Apa D, Cinel I, Aksoyek S. The protective effect of selenium on ipsilateral and contralateral testes in testicular reperfusion injury. Pediatr Surg Int. 2005;21:274–8.

XVI. Mills, G. C. (1959) The purification and properties of glutathione peroxidase of erythrocytes. J. Biol. Chem. 234:502–506.

XVII. Danforth, E., Jr & Burger, A. G. (1989) The impact of nutrition on thyroid hormone physiology and action. Annu. Rev. Nutr. 9:201–207.

XVIII. Shen, H. M., Yang, C. F. & Ong, C. N. (1999) Sodium selenite-induced oxidative stress and apoptosis in human hepatoma HepG(2) cells. Int. J. Cancer 81:820–828