Comparative Study of the Biochemical Behavior of some Highly Toxic Minerals on Selenosis in Rats

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Research

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Abstract

Objective: An investigation of the potential influences of As, Hg, Tl and Pb on Se metabolism, which can suggest new drugs to cope the poisonousness of Se.

Methods: Chronic cases were carried out with the nursing of rats with a purified diet of water-soluble vitamin mix, fat-soluble vitamin mix, saccharides, oil, and salts. One week after the basic diet, the rats taken Se have received diets containing 10 ppm of the element as sodium selenite or selenate added in the salts.

Result: As, Hg, and Tl were repressed the volatilized Se excreted from the lungs. As has assisted the biliary excretion of Se and inhibited the chronic selenosis. Tl has increased the retention of Se in the liver and kidney, but, had no chronic effect on the amount of Se deposited in all the studied tissues. Similarly, Hg has increased the retention of Se but in the spleen and carcass of rats indicating to the high Se concentration in blood. Hg and Tl have inhibited the Se in urine.

Conclusion: No effects of the doses rich in As, Hg, and Tl on the Se excretion in fecal. Even though, we suggest As as a possible medication to chronic selenosis.

Introduction

Recently, many countries have posed several legislations [1] and slated very specific strategies [2] in pharmaceutical industry that serve health challenge [3]. However, these created new modifying rules and regulations should control the added ingredients to the drugs including minerals and radioactive materials but in innocuous quantities [1, 2]. These supplemented constituents to the pharmaceutical products should be analyzed in reliable analytical procedures [4] which must satisfy the international pharmacological standards [2].

Among such trials, Hamid et al. [5] has stimulated much research concerning the metabolism of toxic elements as selenium. However, this element is mostly existed in biological medium as selenite (SeO_3^{-2}) and selenate (SeO_4^{-2}).

Selenite is called as gypsum flower, desert rose, satin spar, and satin spar are four assortments of mineral crystals of gypsum. Those four kinds of gypsum can be assembled together and termed selenite [6]. The selenite anion is a Se oxoanion of a formula SeO_3^{-2} . A selenite is a compound of this ion. Under weak acidic conditions, hydrogenselenite ion, HSeO_3^{-} , is formed; however, in higher acid cases, selenous acid H_2SeO_3 , occurs. It is more required in minute quantities for the proper growth, development, and physiology of an organism [7]. SeO_3^{-2} exacerbates hepatic insulin resistance in mouse model of type II diabetes through oxidative stress-mediated JNK pathway [8]. In A549 cancer cells, the discerning increment of SOD1 content is accompanied with SeO_3^{-2} generation of superoxide radical anions and this boosts apoptosis and Se-Cu linkage [7].

Selenate is a sturdy dibasic acid with molecular formula (H_2SeO_4), so it is an acid form of inorganic salts of dihydrogen selenium tetraoxide. It is toxic by dust ingestion, inhalation or skin contact. Selenate is naturally occurring or synthetic substances that inhibit or retard oxidation reactions. They counteract the damaging effects of oxidation in animal tissues [6].

By hand, several metabolic interrelationships among minerals and Se are instituted [9, 10]. As represses Se toxicity [11, 12] and diminishes Se retention in mice' livers [13]. This advantageous trait of As is owing to the augmented clearance of Se from liver into bile [14].

Cd inhibits Se detoxification and forms volatile methylated Se compounds, so results in increasing Se retained in liver [15–17]. However, Cd in rats which causes testis injury can be protected by Se [17–19].

Novel studies show that Se can protect against Hg and Tl toxification [20–23]. The aim of the current study was to compare the influences of As, Hg, Tl, and Pb on Se metabolism. It was concluded that As, Hg, and Tl all repressed the pulmonary excreted amount of Se volatilized compounds, but that As alone was capable to improve the excretion of Se in bile. As was also the only cooperating tested element that reduced the chronic Se poisoning effects.

Methods

Acute studies. Nursling male of Holtzman rats (in small bowels, one contained significantly lower concentrations of adenosine – 3',5'- cyclic monophosphate than all the others) (Photo 1) was nourished a stock diet [23] for 2–3 weeks and their pulmonary excretions of exhausted Se compounds were assessed.

The animals were shot subcutaneously in one hind flank with the appropriate test element in physiological saline and then 10 min later in the opposite hind flank with 2 mg Se per kg as sodium selenite (Na_2SeO_3) containing approximately 1 microcurie (μCi) of $\text{H}_2^{75}\text{SeO}_3$ (Preliminary observation: a formation of dimethylselenide (CH_3Se) and dimethyldiselenide ($(\text{CH}_3)_2\text{Se}_2$) in the breath of the rats). For capturing the exhausted Se, the animals were left 12 hours in all-glass metabolism cages furnished with sintered-glass scrubbers containing 8N HNO_3 . The rats were sacrificed, and the tissues were isolated for direct measurement of radioactivity in a well-type scintillation counter (Perkin Elmer Tri-Carb). Data are expressed as percentage of the dose of labeled selenium injected.

In newborn Holtzman male rats nursed a routine diet, Se excretion from the bile has been investigated. The bile ducts have been cannulated as described in many works [24–26]. In one flank, about 0.5 μCi of radioactive Se in physiological saline was subcutaneously injected, and the participating element was given in the opposite flank.

Dose and timing schedules are registered in Tables I-3. Where required, radioselenate was made by a repetitive digestion of radioselenite with conc. HNO_3 [27, 28]. Bile was collected for 1 hour and the radioactivity was detected in a well-type scintillation counter. Data are expressed as percentage of the dose of labeled selenium injected.

Chronic studies. Neonatal masculine Holtzman rats were nourished a purified diet which included the following components in g/kg: sucrose ($C_{12}H_{22}O_{11}$), 710; casein ($C_{38}H_{57}N_9O_9$), 200; corn oil (calories, total fat were 122 and 21%, respectively) 50; salts [29], 35; water-soluble vitamin mix, 2; fat-soluble vitamin mix, 2; and choline chloride ($(CH_3)_3NCH_2CH_2OH$)]Cl, 1. The water-soluble vitamin mix contained, in mg/g: myo-inositol ($C_6H_{12}O_6$), 100; nicotinic acid (vitamin B3 (VB3), $C_6H_5NO_2$), 11; calcium pantothenate (Ca salt of water-soluble VB5, $C_{18}H_{32}CaN_2O_{10}$), 6; riboflavin (VB2, $C_{17}H_{20}N_4O_6$), 2; pyridoxine. HCl (4-methanol form of VB6, $C_8H_{12}ClNO_3$), 1; thiamine. HCl (VB1, $C_{12}H_{18}Cl_2N_4OS$), 1; folic acid (VB9, $C_{19}H_{19}N_7O_6$), 0.1; *d*-biotin (VB7, $C_{19}H_{19}N_7O_6$), 0.1; VB12, 0.005; sucrose ($C_{12}H_{22}O_{11}$), 878.8. The fat-soluble vitamin mixture supplied, per kg of diet, 3000 IU of crystalline VA, 2000 IU of VD3, 90 mg of dl- α -tocopherol ($C_{31}H_{52}O_3$), and 150 μ g of menadione ($C_6H_4(CO)_2C_2H(CH_3)$). The rats were distributed into sets of analogous mean weights and launched their investigational diets after one week on basal food regime.

The rats fed selenium received diets containing 10 ppm of the element as Na_2SeO_3 or Na_2SeO_4 added in the salts. So that, the tested elements were participated by means of their soluble salts at a level of 10 ppm in the potable water to examine their impacts on Se metabolism and toxification. The weights were logged twice each 7-days. The living rats were sacrificed and checked for gross pathological lesions. Samples of tissues were frozen and saved for selenium analysis by calorimetry [30–33].

Results

Acute studies

30% of the dosage was exhaled as Se volatilized shape in 12 hours of injecting the control animals with 2 mg Se/kg as SeO_3^{-2} and saline (Table 1). The quantity of the volatilized Se was diminished to 5.4% of dosage when the rats were administered 4 mg As/kg as arsenite (AsO_2^{-}). Even the animals needed higher dosages, but we registered a pulmonary Se excretion inhibition when Hg or TI was administered. High dosages of Pb (48 mg/kg) did not show any effect on the Se circulation or volatilization. However, the noticeable reduction of the Se volatilized shape during As and Hg treatment was followed with high levels of Se in the kidney and carcass. Treatment with TI had retained higher amounts of Se in the kidney and liver. Possibly due to the Se increasing concentrations in the gastrointestinal innards, high quantities of Se in the carcass were enrolled when As has been taken [34]. In addition, probably due to the extremely high concentration of Se in blood, the retention of this element in carcass has been noticed during Hg intake. This is not just the interesting notice with Hg administration in rats, nevertheless, we also observed a large amount of Se retained in spleen.

Table 1

Effect of AsO_2^- and the collaborated chemical elements on SeO_3^{2-} metabolism by rats.

Chemical form and dosage of test elements ^b (mg/kg)	Proportion of the dose of selenium (%) ^a							
	Volatile compounds	Liver	Kidney	Carcass ^c	Spleen	Blood, ml	Feces	Urine
None	30.6 ± 3.72	11.3 ± 0.02	1.90 ± 0.11	20.2 ± 1.07	0.20 ± 0.05	0.80 ± 0.16	1.10 ± 0.54	14.7 ± 2.38
NaAsO_2 -4	5.40 ± 0.74	8.65 ± 0.01	5.02 ± 0.29	42.8 ± 1.70	0.10 ± 0.05	0.40 ± 0.02	0.40 ± 0.32	16.0 ± 0.97
HgCl_2 -12	8.70 ± 2.11	15.8 ± 0.84	4.23 ± 0.27	37.4 ± 0.60	1.80 ± 0.11	1.70 ± 0.20	0.50 ± 0.20	7.80 ± 1.60
TIAc -12	5.90 ± 1.27	37.5 ± 6.20	9.83 ± 0.52	17.9 ± 1.20	0.30 ± 0.00	0.42 ± 0.00	0.90 ± 0.21	6.33 ± 0.50
$\text{Pb}(\text{Ac})_2$ -48	32.6 ± 2.40	13.7 ± 2.65	2.17 ± 0.36	21.3 ± 1.40	0.34 ± 0.10	1.15 ± 0.40	0.92 ± 0.50	13.9 ± 0.60
^a Distribution of radioactivity 12 hours after subcutaneous injection of 2 mg of Se per kilogram body weight containing approximately 1 μCi ^{75}Se as $\text{H}_2^{75}\text{SeO}_3$; mean of four animals $\pm$ standard error; weight range of animals 119–189 g. ^b Before injecting with Se by 10 min, the rat has been injected with saline solution or the test element subcutaneously. ^c Includes gastrointestinal contents.								

No treatment of the groups in any of these short-interim testing was affected Se fecal excretion, but the depressing properties of Tl and Hg on Se in urine were recorded. Similar to the Experiment A presented in Table 2, in another study [24], As has promoted Se bile excretion. Animals receiving only selenium excreted about 1% of the dose in the bile in 1 hour whereas animals receiving both arsenic and selenium excreted over 20% of the dose of selenium in the same time interval. Under similar tentative conditions, trials of using Hg, Tl, or Pb were failed to initiate Se excretion from the bile.

Table 2
Effect of AsO_2^- and heavy metals (i.e. Hg, Tl, Pb) on Se excretion in bile.

Chemical form and dosage (mg element/kg)		Proportion of the dose of selenium (%) ^d	
Selenium	Test element	Bile	Liver
Experiment A ^e			
Na_2SeO_3 -0.5	None	1.18 ± 0.20	28.6 ± 1.01
Na_2SeO_3 -0.5	NaAsO_2 -1	21.2 ± 4.47	10.6 ± 1.73
Na_2SeO_3 -0.5	HgCl_2 -1	1.50 ± 0.32	28.8 ± 1.51
Na_2SeO_3 -0.5	TlAc-1	0.90 ± 0.25	29.3 ± 2.96
Na_2SeO_3 -0.5	$\text{Pb}(\text{Ac})_2$ -1	1.08 ± 0.11	28.9 ± 0.74
Na_2SeO_4 -0.5	None	0.90 ± 0.13	22.0 ± 2.57
Na_2SeO_4 -0.5	NaAsO_2 -1	3.90 ± 3.69	8.10 ± 1.32
Na_2SeO_4 -0.5	TlAc-1	0.90 ± 0.21	19.7 ± 2.08
Experiment B ^f			
Na_2SeO_3 -2.4	None	0.34 ± 0.00	15.0 ± 0.50
Na_2SeO_3 -2.4	HgCl_2 -4	0.35 ± 0.00	15.6 ± 0.80
Experiment C ^g			
Na_2SeO_3 -4.2	None	0.17 ± 0.00	10.2 ± 0.60
Na_2SeO_3 -4.2	TlAc-30	0.19 ± 0.01	27.4 ± 0.70
Na_2SeO_4 -4.2	None	0.33 ± 0.00	10.3 ± 0.30
Na_2SeO_4 -4.2	TlAc-30	0.23 ± 0.50	16.5 ± 1.80

^d Distribution of radioactivity 1 hour after subcutaneous injection of stated dose of selenium containing approximately 0.5 μCi ^{75}Se as $\text{H}_2^{75}\text{SeO}_3$ or $\text{H}_2^{75}\text{SeO}_4$; weight range of animals 344–403 g; mean of three or four animals $\pm$ standard error.

^e Se injection followed by 10 min the saline or the specified test element injection subcutaneously.

^f Se injection after 1 hour of injection subcutaneously with the saline or the specified dose of Hg.

^g Se injection after 2 hrs of injection subcutaneously with the saline or the specified dose of Tl.

Yet, As may possess diverse impacts on Se metabolism depending on the time interval between injections, valance state, and dose of the elements [35, 36]. Similar reports to the current experiments had demonstrated an antagonism effect of Se against Tl and Hg [35–38]. Even though, according to the Experiments B & C in Table 2 and under the prespecified conditions, Tl and Hg have not exhibited any effect on Se excretion from the bile. Likewise, that was also right once Tl was experienced along with Se introduction as selenate (SeO_4^{-2}) in lieu of SeO_3^{-2} .

Chronic studies

Conferring to Experiment A in Table 3, As was the one tested element that shielded rats against chronic selenosis [39] as ruled by 3-unlike measures: reduced liver damage, reduced Se retention in diverse tissues, and high mass gains. Under parallel conditions, compared to the rats which did not fed Se, these animals that received Se + As have exercised no substantial growth-promoting effect even they showed growing mass gain (the mass gain of control and As treated animals was 235 ± 9.80 and 249 ± 15.5 g, respectively, $P > 0.3$). This cluster of rats which supplemented Se + As exhibited quite pretty normal on gross checkup, even just a few showed a little grainy appearance. However, an extreme plain form of liver injury was observed uniform with seleniferous control. Hg administration to the animals has associated with mass gain in analogy to the As set, however, they conveyed ascites fluid. Besides, the survival was lowermost archived in this set and the liver damage has been largely dominant in the control set who acknowledged Se alone. Thallium did not improve weight gains although in this group there was a slightly favorable effect against liver damage due to selenium. Giving the results of Experiment B that presented in Table 3 and in equivalent to the previous tests, Tl and Se provided as SeO_4^{-2} in lieu of SeO_3^{-2} , has shaped parallel outcomes. As component critically depressed the quantity of Se reserved in the tissues of animal nourished enduring contents of Se, despite the rats possibly assimilated extra meal comprising this element, as evinced by their larger mass gains. Hg was virtually not active as As, in spite of, the first element leaned to decline to a certain degree the Se retained in liver and kidney. Tl did not demonstrate any effect on the precipitated Se content in the tissues of the animal administered Se as SeO_3^{-2} . Moreover, the latter testing element (Tl) was fairly diminished the quantity of the Se compounds retained in livers of SeO_4^{-2} -fed rats. However, more notably, Tl resulted an increase in the content of Se observed in kidney.

Table 3
Effect of AsO_2^- and heavy metals in chronic selenosis.

Salt in drinking water ^h	Weight gain (g)	Survival	Gross liver damage	Se content (µg/g wet weight)	
				Liver	Kidney
Experiment A ⁱ					
None	68.9 ± 8.91	9/10	Severe	7.64 ± 2.10	36.8 ± 2.76
NaAsO ₂	116 ± 16.3	8/10	Mild	2.72 ± 0.20	11.5 ± 2.30
HgCl ₂	105 ± 34.3	4/7	Severe	6.60 ± 0.90	24.3 ± 4.82
TIAC	70.0 ± 8.25	6/7	Moderately severe	7.48 ± 0.60	33.3 ± 6.50
Experiment B ^j					
None	75.0 ± 8.50	6/7	Severe	22.1 ± 5.80	42.5 ± 6.61
TIAC	72.0 ± 11.9	6/7	Moderately severe	14.3 ± 1.70	104.4 ± 5.30
^h Add at level of 10 ppm of the test element.					
ⁱ After 7 weeks on a diet containing 10 ppm Se as SeO ₃ ⁻² ; mean ± standard error.					
^j After 7 weeks on a diet containing 10 ppm Se as SeO ₄ ⁻² .					

Discussion

The current findings establish an exceptional aptitude of As to develop the excretion of Se bile and lessen Se toxification. The chronically selenized animals taken As showed a reduction in the Se retained in livers, makes it look as if appear that the valuable factor of As in chronic selenium poisoning is probably related to the increased Se excretion into the bile of As-handled rats. The later action of As performance on biliary Se is left over for further deep investigations to explain this important mechanism.

Ostensibly, Se pulmonary excretive reduction per se did not entail adequate conditions for enhancing Se excretion in bile, probably for a reason that As, TI, and Hg can impede the biosynthesis of Se volatile compounds. However, As is the sole among the other tested elements that has enthused the excretion of Se in bile. Likewise, the augmented quantity of Se in the bile of As-handled animals has not seemed to be associated to a wide-ranging infiltration of As on the active thiol functional groups of structural proteins or enzymes [40–43] attributing to the only fact that Pb, TI, and Hg all attack and strongly react with thiol groups (sulfhydryl, $-\text{SH}$) as well [44] and might be expected to mimic the effect of arsenic where this the lone factor involved.

The probability of constructing specific selenoarsenic conjugates as purifying agents excreted into the bile is being deliberated beforehand [11]. Nevertheless, the present biochemical fractionation investigations that propose an incidence of numerous diverse forms of biliary Se, lean towards rejecting this supposition.

Conclusion And Recommendations

Conclusion

The metabolism of Se is reliant on the valency state and the dose amount of the elements, in addition to the interval period among shoots. In addition, we refer clearly to the antagonism property including biliary excretion of Se against Hg and Tl. As compounds have successfully proved themselves as a medication of liver damage, which can be suggested as supplemented ingredients in releasing Se from various tissues.

Recommendations

More studies are needed to investigate the mechanism of the valuable arsenic performance in treating biliary selenium.

Declarations

Conflict of Interest

We have no conflicts of interest.

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Availability of data and materials

Data is available upon request.

Ethics approval and consent to participate

Concerning ethical issues, the proposed study was approved by the USEPA and ethics committee.

Consent for publication

Not applicable. This study does not contain any individual or personal data.

Competing interests

The author declares no competing interests.

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References

1. Aljerf L (2017) Syrian medical legislation impacts stories on pharmacy in the millennium. *Chronicles of Pharmaceutical Science* 1(5): 307-311.
2. Aljerf L, AlMasri N (2018) An assessment of the US and UN safety precautions for pesticides in milk by labeling medicine alarm strategy for all dairy animal products. *International Journal of Drug Safety and Discovery* 2(1): 009.
3. Aljerf L, AlHamwi B (2018) Carbon nanotubes - synthesis developmental engineering demands will overcome the health challenge of nanotoxicity and its acute mortality for humans. *Madridge Journal of Nanotechnology & Nanoscience* 3(2): 118-121.
4. Aljerf L, Beasley K, Smith B, Ganeshan N (2017) Glass chromatography application: TLC separation of benzoic esters in pharmaceutical products. *International Journal of Biochemistry Advances* 1(1): 1-8.
5. Hamid M, Abdulrahim Y, Liu D, Qian G, Khan A, Huang K (2018) The hepatoprotective effect of selenium-enriched yeast and gum Arabic combination on carbon tetrachloride-induced chronic liver injury in *J Food Sci* 83(2): 525-534.
6. Molnár Á, Feigl G, Trifán V, Ördög A, Szöllősi R, Erdei L, Kolbert Z (2018) The intensity of tyrosine nitration is associated with selenite and selenate toxicity in *Brassica juncea* L. *Ecotoxicol Environ Saf* 147: 93-101.
7. Nakazawa Y, Pauze M, Fukuyama K, Nagai N, Funakoshi-Tago M, Sugai T, Tamura H (2018) Effect of hesperetin derivatives on the development of selenite-induced cataracts in rats. *Mol Med Rep* 18(1): 1043-1050.
8. Zhou J, Xu G, Bai Z, Li K, Yan J, Li F, Ma S, Xu H, Huang K (2015) Selenite exacerbates hepatic insulin resistance in mouse model of type 2 diabetes through oxidative stress-mediated JNK pathway. *Toxicol Appl Pharmacol* 289(3): 409-418.
9. Aljerf L, AlMasri N (2018) A gateway to metal resistance: bacterial response to heavy metal toxicity in the biological environment. *Annals of Advances in Chemistry* 2(1): 32-
10. Aljerf L, AlMasri N (2018) Mercury toxicity: ecological features of organic phase of mercury in biota- Part I. *Archives of Organic and Inorganic Chemical Sciences* 3(3): 1-
11. Csanaky I, Gregus Z (2003) Effect of selenite on the disposition of arsenate and arsenite in rats. *Toxicol* 186(1-2): 33-50.

12. Issam S, Nawel N, Yassine C (2015) Selenium alleviates the arsenic toxicity in sunflower seedling. *J Adv Biol Biotechnol* 3(3): 101-109.
13. Suzuki Y, Hashiura Y, Matsumura K, Matsukawa T, Shinohara A, Furuta N (2010) Dynamic pathways of selenium metabolism and excretion in mice under different selenium nutritional statuses. *Metallomics* 2(2): 126-132.
14. Colombo C, Setchell KDR, Podda M (1991) Liver dysfunction in cystic fibrosis—beneficial effect of bile acid treatment. *Gastroenterol* 100(5): 1476-1477.
15. Jamall IS, Smith JC (1985) Effects of cadmium treatment on selenium-dependent and selenium independent glutathione peroxidase activities and lipid peroxidation in the kidney and liver of rats maintained on various levels of dietary Arch Toxicol 58(2): 102-105.
16. Száková J, Zídek V, Miholová D (2009) Influence of elevated content of cadmium and arsenic in diet containing feeding yeast on organisms of rats. *Czech J Anim Sci* 54(1): 1-9.
17. Rana SVS, Boora PR (1992) Antiperoxidative mechanisms offered by selenium against liver injury caused by cadmium and mercury in rat. *Bull Environ Contam Toxicol* 48(1).
18. Shiraishi K, Naito K, Yoshida KI (2000) Inhibition of calpain but not caspase protects the Testis against injury after experimental testicular torsion of rat. *Biol Reprod* 63(5): 1538-1548.
19. Şlencu BG (2018) Protective effects of selenium of hepatotoxicity caused by subacute experimental combined exposure to cadmium and lead in rats. *Farmacia* 66(5): 866-876.
20. Kramar R, Ulrich W, Hohenegger M (1989) Severe sublimate intoxication in the rat. *Exp Pathol* 36(2): 97-103.
21. Baiz N, Chastang J, Ibanez G, Annesi-Maesano I (2016) Prenatal exposure to selenium may protect against wheezing in children by the age of 3. *Immunity, Inflammation and Disease* 5(1): 37-44.
22. Tudor M (2018) Potential protective role of selenium in experimental subacute intoxication with ethephon in rats. *Farmacia* 66(3): 463-467.
23. Finley JW (1998) The absorption and tissue distribution of selenium from high-selenium Broccoli are different from selenium from sodium selenite, sodium selenate, and selenomethionine as determined in selenium-deficient J Agri Food Chem 46(9): 3702-3707.
24. Gregus Z, Gyurasics Á, Koszorus L (1998) Interactions between selenium and group Va-metalloids (arsenic, antimony and bismuth) in the biliary Environ Toxicol Pharmacol 5(2): 89-99.
25. Larsen GL (1998) Intermediary metabolism of pentachloronitrobenzene in the control and germfree rat and rat with cannulated bile Xenobiotica 28(10): 973-984.
26. Morisawa Y, Takikawa H (2009) Effect of bile acids on the biliary excretion of pravastatin in rats. *Hepatol Res* 39(6): 595-600.

27. Awwad HK, El Sheraki AS, El Shetaiwi S, Helmi S (1973) Production of radiosulphate and radioselenate, and their reutilisation following injection of ^{35}S -cystine and ^{75}Se - Int J Appl Radiat Isot 24(2): 91-97.
28. Feist LJ, Parker DR (2001) Ecotypic variation in selenium accumulation among populations of *Stanleya* New Phytol 149(1): 61-69.
29. Ani I (2012) Biochemical effects of some traditional Nigerian diets in experimental diabetic rat Int J Biochem Res Rev 2(2): 70-77.
30. Stone WL, Dratz EA (1982) Selenium and non-selenium glutathione peroxidase activities in selected ocular and non-ocular rat Exp Eye Res 35(5): 405-412.
31. Dokoupilová A, Marounek M, Skřivanová V, Březina P (2008) Selenium content in tissues and meat quality in rabbits fed selenium Czech J Anim Sci 52(6): 165-169.
32. Zoidis E, Demiris N, Kominakis A, Pappas AC (2014) Meta-analysis of selenium accumulation and expression of antioxidant enzymes in chicken Animal 8(4): 542-554.
33. Pavlovic Z, Miletic I, Zekovic M, Nikolic M, Glibetic M (2018) Impact of selenium addition to animal feeds on human selenium status in Serbia. Nutrients 10(2): 225.
34. Kirchgessner M, Gabler S, Windisch W (1997) Homeostatic adjustments of selenium metabolism and tissue selenium to widely varying selenium supply in ^{75}Se labeled rats. J Anim Physiol Anim Nutr 78(1-5): 20-30.
35. Ishizaki M, Ueno S, Okazaki T, Suzuki T, Oyamada N (1988) Interaction of arsenic and selenium on the metabolism of these elements in hamsters. Appl Organomet Chem 2(4): 323-331.
36. Janasik B, Zawisza A, Malachowska B, Fendler W, Stanislawska M, Kuras R, Wasowicz W (2017) Relationship between arsenic and selenium in workers occupationally exposed to inorganic arsenic. J Trace Elem Med Biol 42: 76-80.
37. Staneviciene I, Bernotiene R, Sadauskiene I (2014) The comparison of the protective effect of zinc and selenite ions against cadmium induced changes of protein synthesis in mice organs. Trace Elem Electroly 31: 116-123.
38. Turgut B, Ergen I, İlhan N (2017) The protective effect of sesamol in the selenite-induced experimental cataract model. Turk J Ophthalmol 47: 309-314.
39. Kezhou W, Stowe HD, House AM, Chou K, Thiel T (1987) Comparison of cupric and sulfate ion effects on chronic selenosis in rats. J Anim Sci 64(5): 1467-1475.
40. Gregus Z (2000) Effects of arsenic-, platinum-, and gold-containing drugs on the disposition of exogenous selenium in rats. Toxicol Sci 57(1): 22-31.
41. Tanguy S, Besse S, Ducros V, de Leiris J, Boucher F (2003) Effect of increased dietary selenium intake on blood and cardiac selenium status during aging in rats. Nutr Res 23(2): 239-243.
42. Gailer J (2007) Arsenic–selenium and mercury–selenium bonds in biology. Coordin Chem Rev 251(1-2): 234-254.

43. Srivastava D, Subramanian R, Madamwar D, Flora S (2010) Protective effects of selenium, calcium, and magnesium against arsenic-induced oxidative stress in male rats. *Arh Hig Rada Toksikol* 61(2): 153-159.
44. Yang S, Liu Y (2015) Nuclear volume effects in equilibrium stable isotope fractionations of mercury, thallium and lead. *Sci Rep* 5(1): 12626.

Figures

Figure 1

Newborn Holtzman rat males.