ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 12, pp.63112-63116, December, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ROLE OF VITAMIN E AS THERAPEUTIC AGENT TO COPE UP WITH LIVER FUNCTIONS IN CHROMIUM TREATED LABORATORY CHICKS

***Dharmendra Kumar, Vandita Kandpal and Sonu Khanka**

Department of Zoology, S. V. Govt. P. G. College Lohaghat, (Champawat) Uttarakhand, India

ARTICLE INFO

Article History:
Received 20th September, 2017
Received in revised form
17th October, 2017
Accepted 14th November, 2017
Published online 31st December, 2017

Key words:
Chromium,
Vitamin E,
Detoxification,
Biotransformation,
SGOT,
SGPT,
ALP.

ABSTRACT

Importance of exogenous application of vitamin E in the acceleration of Cr elemination in the liver function have been discussed in the present investigation. Developing chicks (100±20 gm body weight, 2-3 weeks old) were used as experimental animals. Present investigation revealed that deposition of Cr in all tissues affect the proper function of liver. Liver specific function defence offered by protective influence of vitamin E may be channelized through different mechanism. Vitamin E not only restricted the detoxification but also improved the liver functions. High concentration of Cr was determined in Cr treated chicks. Selective prefrences for chromium was shown by vitamin E for maintaining optimal serum glutamic oxaloacetate transaminase – SGOT (AST), serum glutamic pyruvic transaminase – SGPT (ALT) and alkaline phosphatase (ALP) activity. Vitamin E appreciably improve the detoxication ability of liver. SGOT, SGPT and ALP were significantly increased in chicks treated with chromium compared to normal control group. Chicks treated with vitamin E along with Cr, shows significant decrease in SGOT, SGPT and ALP activity compared to Cr treated chicks where it was high. Hence, elevation in SGOT, SGPT and ALP could be due to biotransformation of heavy metals in liver leading to hepatic injury. This injury may be decreased by the supplimentation of vitamin E in laboratory chicks.

Citation: Dharmendra Kumar, Vandita Kandpal and Sonu Khanka, 2017. "Role of Vitamin E as therapeutic agent to cope up with liver functions in chromium treated laboratory chicks", *International Journal of Current Research*, 9, (12), 63112-63116.

INTRODUCTION

Chromium is a naturally occurring element found in rocks, animals, plans, soil, volcanic dust and gases. It occurs in various oxidative states from Cr (II) to Cr (VI). A significant amount of chromium enters into the environment form chrome plating, textile dyes and paint industries. Hexavalent chromium is the most dangerous form of chromium used in chrome plating and causes cancer and mutagenesis (Gomez and Callao, 2006). Anthropogenic activities like tannery effuents, smelting, electroplating, metallurgy, industrial and agricultural practices have increased Cr level beyond the assimilation capacity of biota in the ecosystem (Vlizlo *et al*., 2014) which ultimately bioaccumulate in different organisms i.e. fish and poultry. Therefore, it has become the most toxic substance in marine and terrestrial ecosystems (Costa, 2003; Iftikhar *et al*., 2015; Bouaziz *et al*., 2015). Cr(VI) is more toxic and carcinogenic than chromium(III) (Bianchi *et al*., 1983; Tsuda *et al*., 1977; De Flora *et al*., 1989), because in contrast to Cr(III), Cr(VI) activity enters cells by the sulfate transport system (De Flora *et al*., 1989; Costa *et al*., 1984; Jennette, 1979). However, once inside the cells, Cr(VI) is readily reduced to Cr(III) (De Flora *et al*., 1989; Costa *et al*., 1984; Jennette, 1979). Therefore, the cellular metabolism of Cr(VI) may play a role in the induction of chromate toxicity and carcinogenicity. Cr(VI) compounds have been shown to produce DNA single strand breaks and DNA-protein crosslinks (De Flora *et al*., 1989; De Flora *et al*., 1990; Sugiyama *et al*., 1986; Sugiyama *et al*., 1988; Fornace *et al*., 1981; Tsapoakos *et al*., 1983; Cupo *et al*., 1985), and to selectively inhibit the activity of glutathion reductase (Koutras *et al*., 1964; Koutras *et al*., 1965; De Flora *et al*., 1984). Free radical injury produced by Cr(VI) is responsible for many pathological conditions. Free radicals can exist independently and they bear one or two unpaired electrons in valance shell. They are highly reactive to cell organelles e.g. polyunsaturated fatty acids, proteins and nuclear acids (Sanchez-Mendoza *et al*., 2015). Metals like Cr are very reactive and induce oxidative damage by generating reactive oxygen species (ROS) (Zhang *et al*., 2014). It interfers with metabolic process and biological reactions i.e. change in enzyme activity, membrane fluidity, ion transport and protein synthesis (Javed, 2015). Cr(VI) once entered in a cell is converted into its lower oxidation state i.e. Cr(III), which is a reactive intermediate of Cr(VI) responsible for the generation of ROS (Shati *et al*., 2014). However, the benificial aspects of Cr with its effect in different doses and antioxidant combinations to explore and promote its optimum utilization in poultry nutrition and

Corresponding author:* **Dharmendra Kumar,
Department of Zoology, S. V. Govt. P. G. College Lohaghat, (Champawat) Uttarakhand, India.

production. The hexavalent form of Cr has toxic effects on birds as it promotes the early aging process, reduces hatching ability and effects liver also (Asmatullah *et al*., 1999). It also causes malformation or fetal death and leads to neural deformities. It has damaging effects on DNA and leads to mutation. It affects the function of gastrointestinal microflora on chronic exposure to high doses (Upreti *et al*., 2004). It has the lethal effects on embryo and causes the defects in the development process leading to early chick mortality. It has the negative effect on chick growth and development (Asmatullah *et al*., 1999). Toxicity can be developed when there wiil be the excess amount of trace mineral added in the feed of the poultry that may lead to decrease the production parameters such as egg production and defective embryo development along with toxicities (Miles, 2000).

Natural antioxidant vitamin E, ascorbic acid, riboflavin, cytochrome P-450 reductase, glutathione reductase etc. are free radical scavenger and quickly convert the highly toxic form of Cr (VI) to Cr (III) in the tissues which does not readily leave the cell (ATSDR, 1999). The metal is slowly released through kidney and bile (Yamaguchi *et al*., 1983). However, during its stay, Cr (III) forms stable complexes with legands of protein, DNA and GSH and causes all kind of metabolic, genetical, immunological, developmental and carcinogenic changes (ATSDR, 1999; Singh *et al*., 1998), therefore, a quick removal of the metal from the body is necessary. Poultry cannot synthesize vitamin E, thus, vitamin E requirements must be met from dietary sources (Sahin *et al*., 2002) in case of increased demand in stress. Vitamin E is a biological chain-breaking antioxidant that protects cells and tissue from lipoperoxidative damage induced by free radicals (McDowel,l 1989). Vitamin E has chromanol ring in its structure which donates hydrogen to free radicals thus making them unreactive (Kumari *et al*., 2013). It is a lipid soluble antioxidant and biologically crucial for reducing heavy metal toxicity. In poultry feed, it is used to prevent different stress related diseases occurring due to intensive rearing (Murakami *et al*., 2007; Mashkoor *et al*., 2013). In literature, there is scanty information available regarding the use of vitamin E as ameliorative agent in Cr intoxicated birds and since vitamin E and selenium (Se) have protective effects against kidney toxicity (Arreola-Mendozoa *et al*., 2006) and liver damage (Soudani *et al*., 2011), therefore, the following study was designed to determine the Cr induced toxicity and its amelioration with vitamin E. So it will be highly useful for scientists, researchers, veterinary professionals, poultry industry, pharmaceutical industry to enrich their knowledge in promoting Cr and its antioxidant combination usage.

MATERIALS AND METHODS

The experiment was carried on Domestic chicks-Croiler Chabro (*Gallus gallus domesticus*). Newly hatched chicks were purchased from the Uttarakhand Village Poultry Project (State Govt. Poultry Farm), Bin, Pithoragarh (Uttarakhand). Selected all chicks were maintained and acclimalized according to the laboratory conditions. The animals were housed in battery cages under laboratory conditions at existing room temperature and relative humidity. They were fed on commercial food (Starter, Grower and Finisher) purchased from the local market and tap water *ad libitum*. Healthy male and female chicks (approximately 2-3 weeks old, body weight 100±20 gm) were used in present study.

The selected chicks were divided into three groups (A, B and C) randomly, each containing at least 6 chicks. Chicks of group A were administered with sublethal dose of potassium dichromate ($K_2Cr_2O_7$) (5 mg/100 gm body weight) by gavage on each alternate day for 30 days. Chicks of group B were treated with potassium dichromate ($K_2Cr_2O_7$) as chicks of group A but also administered with vitamin-E (intramuscularly) (0.5 IU/100 gm body weight) on each alternate day for 30 days. Chicks of Group C were administered with saline only to serve as purely control. Blood samples were collected from the wing vein using 3ml disposable syringe than directly transferred into a labeled test tube without anticoagulant. Serum was prepared by centrifugation and stored at 0ºC for further analysis. The serum ALT, AST and ALP enzymatic activity were determined using commercial kits.

Statistical analysis

All serum SGOT, SGPT and ALP values were expressed as mean ± SE. Parameters of all treatments were compared using Student's "t" test. Data were subjected to one way ANOVA for calculating the significance difference between the treatment. The level of significance were reported at $p<0.05$.

RESULTS

Enzymes markers of liver functions viz. serum glutamic oxaloacetate transaminase - SGOT (AST), serum glutamic pyruvic transaminase - SGPT (AST) and alkaline phosphatase (ALP) offer reliable information on status of liver function. Present results reveals that activity of SGOT and SGPT significantly increased in chromium treated chicks. While, the chicks supplemented with antioxidant i.e. vitamin E shows improvement in liver functions. It means vitamin E reduce the accumulation of chromium in liver by different channalized mannar. Vitamin E restore the liver functions nearest to control level. Similarly, results on alkaline phosphatase shows that enzyme leakage increased in the serum after chromium treatment. Vitamin E succeeded in inhibiting the secretion of enzyme level and control upto the level of normal value. Hence, it protects the liver by oxidative stress by breaking different chain reactions (Table 1).

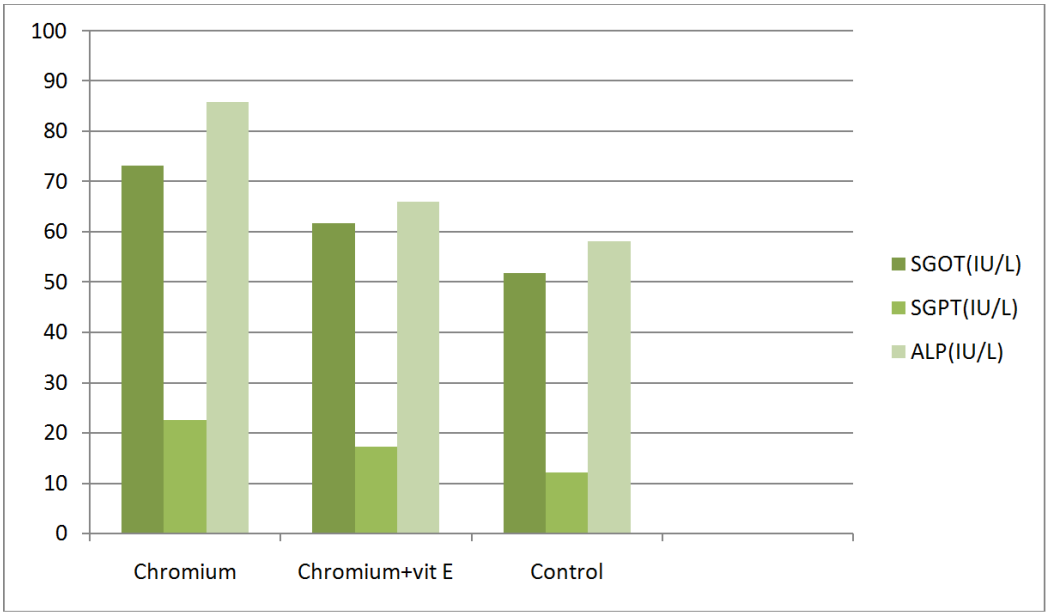
DISCUSSION

Cr(VI) compounds have been shown to manifest toxic and carcinogenic effects in humans (Morris *et al*., 1988; Anttila, 1990). Protection against metal toxicity has been a centre of attraction for industrial hygienists, public health officials, toxicologists and pharmacologists. For considerable longer period specific chelating agents were used to reduce the body burden of heavy metals. However, they were not preferred due to their own adverse effects. Since the discovery of the fact that oxidative damage is one of the mechanism responsible for their toxicity, the use of antioxidants was considered to be a suitable alternative. Antioxidants restricted the uptake and distribution of chromium in liver and other organs also. Efflux of enzymes in blood has been treated as a sensitive index of hepatotoxicity. Amongst them serum glutamic oxaloacetate transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) possess significance diagnostic value. SGOT and SGPT have been extensively studied during acute or chronic intoxication of the liver (Rees and Sinha, 1960; Griffiths *et al*., 1961).

Table 1. Effect of vitamin E on SGOT, SGPT and ALP in chromium fed chicks

Group	Treatment	SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	Level of Significance
A	Chromium	73.18 ± 3.99	22.49 ± 2.65	85.76 ± 5.73	**
B	Chromium + Vitamin E	61.78 ± 2.42	17.30 ± 0.89	66.0 ± 13.91	**
C	Control	51.83 ± 5.77	12.15 ± 1.66	58.04 ± 4.88	**

Results are expressed as mean ± SE, ** indicates significant at $p < 0.05$



Influence of Vitamin E on liver enzymes in chromium fed chicks

In present study, SGOT, SGPT and ALP were significantly ($p \leq 0.05$) increased in Cr treated chicks compared to control group. Previous study noted an elevation in the level of SGOT and SGPT i.e. in fish (Shaheen and Akhtar, 2012) and rats (Kim *et al*., 2004; Mehany *et al*., 2013). Cr toxicity cause elevation of serum hepatic enzymes due to leakage of these enzymes or increase in their production. Maximum leakage of these enzymes occurred in chicks treated with chromium. Co-treatment with antioxidant i.e. vitamin E influenced the hepatotoxicity of chromium and reduced it up to the control level. Hence, protective effects of vitamin E against chromium toxicity has been observed in chicks. The antioxidant effect of vitamin E is well documented in the literature, and this effect may be due in part to efficient radical scavenging (Dean and Cheeseman, 1987; Lieber *et al*., 1986; Ames, 1983). Thus the protective mechanism of vitamin E in preventing DNA breaks produced by chromate might be due to its scavenging of paramagnetic chromium (V) during reduction of Cr(VI) in cells. In respect to DNA breaks, Cr(VI) reacts with hydrogen peroxide to form Cr(V), leading to the generation of hydroxyl radicals, which caused DNA breaks *in vitro* (Kawanishi *et al*., 1986).

Similarly, alkaline phosphatase (ALP) was also included in this study. Alkaline phosphatase has a dimeric structure in serum and exist in same form when released from liver plasma membrane by phospholipase and proteases enzymes (Hartmann, 1989). The enzyme anchored to the plasma membrane by a glycosylphosphatidylinositol structure and when solublized from membrane with non-ionic detergent triton X-100 or with butanol treatment at higher pH, the hydrophobic phosphatidylinositol remains covalently attached to C-terminal amino acid residue of the enzyme (Hawrylok and Stinson, 1988). Present results showed that enzyme leakage increased in the serum after chromium treatment. Co-treatment with antioxidants diminished SGOT, SGPT and ALP activity nearest to control level. Therefore, vitamin E is an important antioxidant to protect the organs from harmful effects of heavy metals.

Conclusion

The toxic effects of Cr and its amelioration with vitamin E on liver function were profiled in this study. In present study, chromium appears as a strong toxicity inducer and it alter all the functions of liver. However, administration of Vitamin E ameliorate Cr-induced toxicity efficiently. Vitamin E is a principle chain breaking antioxidant *in vivo* and have protective effect.

REFERENCES

Ames, B. N. 1983. Dietary carcinogens and anticarcinogens; oxygen radicals and degenerative diseases. *Science* 221: 1256-1264.

Anttila, S. 1990. Metal Ions in Biology and Medicine. *Jhon Libbey Eurotext, Paris.* pp:315-319.

Arreola-Mendoza, L., Reyes, J. L., Melendez, E., Martin, D., Namorado, M. C., Sanchez, E., *et al*., 2006. Alpha-tocopherol protects against the renal damage caused by potassium dichromate. *Toxicology,* 218: 237-46.

Asmatullah, A., Asma, A., Latif A., Shakoori, A. R. 1999. Effect of hexavalent Cr on laying capacity, hatchablity of eggs, thickness of egg shell and post hatching development in *Gallus domesticus*. *Asian-Aust. J. Anim. Sci.* 6: 944-950.

ASTDR: 1999. Toxicological profile for chromium (update). U. S. Department of Health and Human Service, Public Health Services.

Bianchi, V., Celotti, L., Lanfranchi, G., Majone F., Marin, G., Montaldi, A., Sponza, G., Tamino, G., Venier, P.,

Zantedeschi, A., and Levis, A. G. 1983. Genetic effects of chromium compounds. *Mutat. Res*. 117:279-300.

Bouaziz, H., Rafrafi M.., Ben Salah, G., Marrekchi, R., Boudawara, O., Kammoun, H., Jamoussi, K., Boudawara, T. and Zeghal, N., Najiba, 2015. Nitrate provoked kidney toxicity and DNA impairment in adult rats: Alleviation by *Hyparrhenia hirta. Pak. Vet. J.,* 35: 397-402.

Costa, M., 2003. Potential hazards of hexavalent chromium in our drinking water. *Toxicol. Appl. Pharmacol.,* 188: 1-5.

Costa, M., Kraker, A. J., and Patierno, S. R. 1984. Toxicity and carcinogenicity of essential and non-essential metals. *Prog. Clin. Biochem*. 1: 49.

Cupo, D. Y., and Wetterhahn, K. E. 1985. Modification of chromium(VI)-induced DNA damage by glutathione and cytochrome P-450 in chicken embryo hepatocytes. *Proc. Natl. Acad. Sci. U. S.* 82: 6755-6759.

De Flora S., Bagnasco, M., Serra, D., and Zanacchi, P. 1990. Genotoxicity of chromium compounds. A Review. *Mutat. Res.* 238: 99-172.

De Flora, S., and Wetterhahn, K. E. 1989. Mechanisms of chromium metabolism and genotoxicity. *Life Chem. Rep*. 7: 169-244.

De Flora, S., Bennicelli, C., Zanacchi, P., Camoirano, A., Morelli, A., and De Flora, A. 1984. *In vitro* effects of N-acetylcysteine on the mutagenicity of direct acting compounds and procarcinogens. Carcinogenesis 5: 505-510.

Dean, R. T. and Cheeseman, K. H. 1987. Vitamin E protects protein against free radical damage in lipid environment. *Biochem. Biophys. Res. Commun*. 148: 1277-1282.

Forance, A. J., Seres, D. S., Lechner, J. F., and Harris, C. C. 1981. DNA-protein cross linking by chromium salts. *Chem.-Biol. Interact*. 36: 345-354.

Gomez, V. and Callo, M. P., 2006. Chromium determination and speciation since 2000. *Trends Analyt. Chem.,* 25: 1006-1015.

Griffiths, D. B., Rees, K. R. and Sinha, K. P. 1961. Blood and bile composition in experimental Cirrhosis. *J. Pathol. Bacteriol.* 82: 109-115.

Hawrylak, K. and Stinson, R. A. 1988. The solubilization of tetrameric alkaline phosphatase from human liver and its conversion into various forms by phosphatidylinositol phospholipase C or proteolysis. *J. Biol. Chem.* 263: 14368-14373.

Hertmann, A. H., Bircher, J. and Creutzfeldt, W. 1989. Superiority of the Child–Pugh Classification to Quantitative Liver Function Tests for Assessing Prognosis of Liver Cirrhosis. *Scandinavian Journal of Gastroenterology*. 24: 269-276.

Iftikhar, A., Khaliq, T., Khan, J. A., Zia-ur-Rahman, Sajjid-ur-Rahman, Anwar, H.., Javed, I., Muzaffar, H. and Mahmood, A. 2015. Efficacy of vitamins, probiotics and protein supplementation on serum health biomarkers of molted male layer breeders. *Pak. Vet. J.,* 35: 519-521.

Javed, M., 2015. Chronic dual exposure (waterborne+dietary) effects of cadmium, zinc and copper on growth and their bioaccumulation in *Cirrhina mrigala. Pak. Vet. J.,* 35: 143-146.

Jennette, K., W. 1979. Chromate metabolism in liver microsomes. Biol. *Trace Elem. Res.* 1: 1-49.

Kawanishi, S., Inoue, S., and Sano, S. 1986. Mechanisms of DNA cleavage-induced by sodium chromate (VI) in the presence of hydrogen peroide. *J. Biol. Chem.* 261: 5952-5988.

Kim, H., Lee S. and Jang, B. 2004. Subchronic inhalation toxicity of soluble hexavalent chromium trioxide in rats. *Archiv. Toxicol.,* 78: 363-368.

Koutras, G. A., Hattori, J., Schneider, A. S., Ebaugh, F. G., Jr., and Valentine, W. N. 1964. Studies on chromate erythrocytes. Effect of sodium chromate on erythrocyte glutathione reductase. *J. Clin. Invest.* 43: 323-331.

Koutras, G. A., Schneider, A. S., Hattori, M. and Valentine, W. N. 1965. Studies on chromate erythrocytes. Mechanism of chromate inhibition of glutathione reductase. *Br. J. Haematol.* 2: 360-369.

Kumari, R. R., Kumar P. and Mondal T. K. 2013. Effect of vitamin E and selenium on haematological parameters in sub-acute toxicity of hexavalent chromium in broiler chick. *Nat. J. Physiol. Pharm. Pharmacol.,* 3: 158-161.

Lieber, D. C., Klings, D. S. and Read, D. J. 1986. Antioxidant protection of phospholipid bilayers by α-tocopherol status and lipid peroxidation of ascorbic acid and glutathione. *J. Biol. Chem.* 261: 12114-12119.

Mashkoor J., Khan A., Khan M. Z., Abbas R. Z. Saleemi M. K. and Mahmood F. 2013. Arsenic induced clinico-hemato-pathological alterations in broilers and its attenuation by vitamin E and selenium. *Pak. J. Agric Sci.,* 50: 131-138.

McDowell L. R. 1989. Vitamin A and E . Comparative Aspects to Human Nutrition:Vitamins in Animal Nutrition. London: *Academic Press; pp*. 93-131.

Mehany, H. A., Abo-youssef, A. M., Ahmad L. A., Arafa E. A. and Abd El-Latif, H. A. 2013. Protective effect of vitamin E and atorvastatin against potassium dichromate-induced nephrotoxicity in rats. *J. Basic. Appl. Sci.,* 2: 96-102.

Miles R. D. 2002. Trace minerals and avain embryo development. *Cien. Anim. Bras.* 2(1): 1-10.

Morris, B. W., Griffiths, H. and Kemp, G. J. 1988. Effect of glucose loading on concentrations of chromium in plasma and urine of healthy adults. *Clin. Chem.,* 34(6): 1114-1116.

Murakami, A. E., Sakamoto, M. I., Natali, M. R. M., Souza, L. M. G. and Franco, J. R. G. 2007. Supplementation of glutamine and vitamin E on the morphometry of the intestinal mucosa in broiler chickens. *Poult. Sci.,* 86: 488-495.

Rees, K. R. and Sinha, K. P. 1960. Blood enzymes in liver injury. J. *Pathol. Bacteriol.,* 80(2): 297-307.

Sahin, K., Sahin N. and Yaralioglu, S. 2002. Effects of vitamin C and vitamin E on lipid peroxidation, blood serum metabolites, and mineral concentrations of laying hens reared at high ambient temperature. *Biol. Trace Elem. Res.* 85(1): 35-45.

Sanchez-Mendozoa, B., Aguilar-Hernandez A., Lopez-Soto M. A., Barreras A., Estrada-Angulo A., Monge-Navarro F. J., Torrentera N. G., Zinn R. A. and Plascencia A. 2015. Effects of high-level chromium methionine supplementation in lambs fed a corn-based diet on the carcass characteristics and chemical composition of the longissumus muscle. *Turk. J. Vet. Anim. Sci.,* 39: 376-379.

Shaheen, T. and Akhtar T. 2012. Assesment of chromium toxicity in *Cyprinus carpio* through hematological and biochemical blood markers. *Turk. J. Zool.,* 36: 682-690.

Shati, A. A., 2014. Ameliorative effect of vitamin E on potassium dichromate-induced hepatotoxicity in rats. *J. King Saud. Uni-Sci.* 26: 181-189.

Singh, J., Carlisle, D. L., Pritchard, D. E. and Paterno, S. R. 1998. *Oncol. Rep.,* 5: 1307-1318.

Soudani, N., Amara, I. B., Sefi M., Boudawara Y. and Zeghal N. 2011. Effects of selenium on chromium (VI) induced

hepatotoxicity in adult rats. *Experimental and Toxicologic Pathology.* 63: 541-548.

Sugiyama, M., Costa, M., Nakagawa, Hidaka, T. and Ogura, R. 1988. Stimulation of polyadenosine diphosphoribose synthesis by DNA lesions induced by sodium chromate in Chinese hamster V-79 cells. *Cancer Res.* 48: 1100-1104.

Sugiyama, M., Patierno, S. R., Cantoni, O. and Costa, M. 1986. Characterization of DNA lesions induced by $CaCrO_4$ in synchronous and asynchronous cultured mammalian cells. *Mol. Phaemocol.* 29: 606-613.

Sugiyama, M., Wang, X. W. and Costa, M. 1986. Comparison of DNA lesions and cytotoxicity induced by calcium chromate in human, mouse and hamster cell lines. *Cancer Res.* 46:4547-4551.

Tsapoakos, J. J., Hampton, T. H. and Wetterhahn, K. E. 1983. Chromium (VI) induced DNA lesions and chromium distribution in rat kidney, liver and lung. *Cancer Res.* 43:5662-5667.

Tsuda, H. and Kato, K. 1977. Chromosomal aberrations and morphological transformation in hamster embryonic cells treated with potassium dichromate *in vitro*. *Mutat. Res.* 46: 87-94.

Upreti, R. K., Shrivastava R., Chaturvedi U. C. 2004. Gut microflora and toxic metals: Chromium as a model. *Indian J. Med. Res.* 119: 49-59.

Vlizlo, V., Iskra., R., Maksymovych, I., Lis M. W. and Niedziolka, J. W. 2014. Disturbance of antioxidant protection and natural resistance factors in rats with different availabilities of trivalent chromium. Turk. *J. Vet. Anim. Sci.* 38: 138-144.

Yamaguchi, S., Sano, K. and Shimojo, N. 1983. *Ind. Health.* 21: 25-34.

Zhang, W. Q., Liu, Y., Ge, M., Yao, C. Y., Xue J. D. and Zhang, Z. G. 2014. Resveratrol reduces oxidative stress and improves arsenic efflux in rats exposed to arsenic trioxide. *Pak. Vet. J.,* 34: 251-253.

****