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Effect of arsenic trioxide along with tannic acid, di-sodium hydrogen phosphate, alum and effects of sand-charcoal-iron-filter bed filtrated water along with alum on body weight and liver functions in rabbit

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Abstract: The Effect of Arsenic trioxide alone and in combination with tannic acid, di-sodium hydrogen phosphate (DSHP), alum and effects of sand-charcoal-iron-filter (SCIF) bed filtrated water along with alum on body weight and liver functions in rabbit were carried out on a total of one month old thirty apparently healthy adult Newzealand white rabbits . The rabbits were randomly divided in to six (6) equal groups (A,B,C,D,E & F,) at the ratio of three males and two females in each group, rats of group A was kept as control without giving any treatment, rabbits of group B received arsenic trioxide@100ppm, group C received arsenic trioxide @ 100ppm plus tannic acid @100ppm, group D received arsenic trioxide @ 100ppm plus di-sodium hydrogen phosphate(DSHP)@100ppm, group E received arsenic trioxide @100ppm plus alum @100ppm orally daily for 60 days in all cases and group F received alum@100ppm in SCIF-bed filtrated water orally daily for 60 days. The result showed that body weight gain of control group (A) per week per rabbit was found to increase but in treated group B (arsenic trioxide@100ppm orally daily) the mean body weight were decreased gradually and significant ($P<0.05$) decrease in body weight was observed at 40 days of feeding and at day 60 it was highly significant ($P<0.01$). Rabbits of group C, D and E were apparently normal and mild body weight reductions were observed which was statistically insignificant. No body weight loss was observed in rabbits of group F. A most significantly ($P< 0.01$) increased SGOT and SGPT values were observed in Group B on day 60 but significant increase ($P< 0.05$) were observed in day 30. From the study it was concluded that treatment with arsenic trioxide at low doses has adverse effects on body growth and liver functions in experimental animals.
Keywords: Arsenic trioxide, tannic acid, DSHP, alum, SCIF-bed, body weight gain, liver function test, rabbit

INTRODUCTION

Arsenic (As) is "The Silent killer" for Bangladesh at present. In world water day 1998 arsenic marked as the king of poisons. This poison created a major health concern affecting millions of people around the world, including Bangladesh. The arsenic disaster of Bangladesh has been called the most terrible environmental catastrophe of the twenty first century. WHO described the condition as "the largest mass poisoning of a population in history" [1]. About 85 million people are at risk of drinking arsenic contaminated water and foodstuffs [2, 3]. Together with the poor socioeconomic and nutritional status of the population, the chronic exposure to arsenic in drinking water is causing widespread health hazards in both man and animals in Bangladesh. Drinking water normally contains inorganic arsenic as arsenate (As (V)) and arsenite (As (III)). Inorganic arsenic is more dangerous than many other toxic substances. Arsenic remains one of the most important carcinogens and diabetogenics in human [4, 5, 6, 7]. Nowadays it is, after lead considered the most common toxic heavy metal affecting domestic animals [8, 9, 10]. Ingested inorganic arsenic is readily absorbed through the gastrointestinal tract and distributed in various tissues through blood circulation [11]. This arsenic eventually causes growth retardation, blood cells distortion and elevation of various serum enzymes like lactate dehydrogenase (LDH), alkaline phosphatase (ALP), serum glutamic pyruvic transaminase (SGPT) etc. in human and rodents. Chronic arsenic exposure is accompanied by its accumulation in liver, kidney, heart, lung, gastrointestinal tract and spleen [12, 13, 14, 15]. Hepatic damage has been reported as the most common complication of chronic arsenic exposures [16, 17, 18]. Although the toxic effects of arsenic are known for long time, the mechanism of its toxicity is still poorly understood. One of the known functions of arsenic is its high reactivity to sulfhydryl groups of proteins/enzymes. Binding of arsenic to proteins or

cross-linking of proteins involving sulfhydryl group may activate potential intracellular signaling pathways that ultimately lead to arsenic-mediated adverse effects [19, 20, 21]. To understand the arsenic-mediated health hazards in human experiments with human subjects is almost impossible for various legal reasons. Suitable animal model experiments, however, can help in this regard. These findings in Rabbit model might be useful for better understanding of the toxic effects of arsenic in order to develop effective remediation process against arsenic mediated effects on human health. The aim of the present study is to show the effect of arsenic alone and in combination with tannic acid, di-sodium hydrogen phosphate (DSHP) and alum on body growth & some biochemical parameters related to liver functions in rabbit.

MATERIALS AND METHODS

MATERIALS

Experimental Animals

One month old thirty apparently healthy adult Newzealand white rabbits (Oryctolagus cuniculus) weighing between 250-450 g were purchased from a local private farm of Muktagacha, Mymensingh, Bangladesh and brought to the Experimental Pharmacology and Toxicology laboratory at Bangladesh Agricultural University (BAU) for the present study. After two weeks of acclimatization animals were segregated on the basis of their age and body weight without significant differences. They were housed throughout the entire period of study in well ventilated animal house at a room temperature of 23 $\pm 1^0$C and were supplied with standard ration formulated by ICDDRB, Dhaka and supplied fresh water ad libitum.

SCIF –bed filtered water

Sand-Charcoal-Iron-Filter (SCIF) bed was developed and used as arsenic purifying system. The artificially as contaminated water was passed sequentially four times through SCIF bed. The filtrated water was collected and examined by using Merck Arsen test kit and was used in the study.

Experimental chemicals

The alum, tannic acid, activated charcoal (Merck KGa, Darmstadt, Germany), wood charcoal (kat koila), sand were collected from local source and the Arsenic trioxide (AS_2O_3,MW 197.84g/mol; product No. 37274, Loba chemic pvt. ltd, Mumbai, India), di-sodium hydrogen phosphate (Merck, India), iron oxide (BDH Lab., poole, England) were collected from Dhaka for this study.

Experimental design

The Rabbits were randomly divided in to 6 equal groups (A,B,C,D,E & F) at the ratio of three males and two females in each group, rats of group A was kept as control without giving any treatment, rabbits of group B received arsenic trioxide@100ppm, group C received arsenic trioxide@100ppm plus tannic acid@100ppm, group D received arsenic trioxide@100ppm plus di-sodium hydrogen phosphate@100ppm, group E received arsenic trioxide@100ppm plus alum @100ppm and group F received alum @100ppm in SCIF-bed filtrated water orally daily for 60 days in each cases. Prior to segregation, initial body weight of each rabbit was recorded and kept group wise in cages. After treatment all the rabbit were kept under close observation for a whole period of study and all the parameters (body weight gain or loss, some biochemical parameters related to liver functions) were recorded before and during treatment at specific time intervals.

Reagents for Liver function test

For determination of SGOT

1. Buffer substrate: (i) Tris buffer (84mmol/L P^H7.5) (ii) L-aspartate (260nmol/L)
2. Enzyme/ co-enzyme/α-oxoglutarate: (i) α-oxoglutarate (12 mmol/L) (ii) LD ≥1.2 U/ml (iii) NADH 0.18 mmol/L (iv) MDH ≥ 420U/L

For determination of SGPT

1. Buffer substrate: (i) Tris buffer (100mmol/L P^H7.5) (ii) L-alanine (0.6 mol/L)
2. Enzyme/ co-enzyme/α-oxoglutarate: (i) α-oxoglutarate (15 mmol/L) (ii) LD ≥1.2 U/ml (iii) NADH 0.18 mmol/L

METHODS

Measurement of body weight

The body weight of each rabbit was measured just before starting of treatment and body weight gain or loss was recorded in each 10 days interval up to sacrificing of the animals.

Procedures for the collection of blood sample for serum separation

Blood was collected just before treatment i.e. day 0 and during treatment on day 20, 40 and day 60 directly from marginal ear vein of rabbit. Immediately after collection blood was transferred to sterile tube containing anticoagulant (4% sodium citrate solution) at a ratio of 1:10 and used for determination of some biochemical parameters.

Biochemical study related to liver functions

Two widely used biochemical test such as SGOT and SGPT were determined by UV method using IFCC used Humalyzer 2000, Human type Germany

Determination of SGOT & SGPT

0.1 ml of serum was mixed with 1.0 ml kit solution 2 enzyme/coenzyme/α-oxoglutarate AL 1205 including buffer substrate with L-aspartate for SGOT and buffer substrate with L-alanine for SGPT determination. The wave length was set at 340nm Hg, 1 cm light path cuvette was used and analysis was done at 37^0C. After mixing the cuvette was placed in the

Humalyzer 2000. Initial absorbance was read after 1 minute. The final record was made at 1, 2, 3 minutes after initial reading. Absorbance was recorded each time (0.11 and 0.16 at 340nm/Hg 340nm). First two values for the first 2 minutes were used for the calculation.

Calculation: SGOT concentration: 1746 x absorbance U/1
Calculation: SGPT concentration: 1746 x absorbance U//1

Statistical Analysis

Collected data were statistically analyzed by the computer using statistical package programme MSTAT-C developed by [22]. A one way ANOVA was made by F variance test.

RESULTS AND DISCUSSIONS

Effect on body weight

The mean body weight of rabbits of group F (+9.15%) significantly increased as like control group (group-A) (+6.79%) which was statistically significant (P<0.01). In group B significant decreased of body weight was observed on 60 days of arsenic trioxide feeding which was statistically highly significant (P<0.01). The body weight of group C, D and E was slightly increased on 60 days of arsenic trioxide feeding in combination with tannic acid, DHSP and alum respectively but were statistically not significant (Table-1). The mean body weight of group B were decreased gradually and significant (P<0.05) decrease in body weight was observed at 40 days of feeding and at day 60 it was highly significant (P<0.01) .The similar result on body weight was observed by many other workers [23, 24]. Rabbits of group C,D and E were apparently normal and mild body weight reduction were observed at the last part of the experiment which was statistically insignificant, this might be due to the interaction of arsenic oxide with other chemicals like tannic acid, DSHP and alum used in those groups respectively. No loss of body weight in rabbits of group F were observed during the whole experiment period might be due to supplied SCIF bed filtrated water with alum which indicates the successful use of SCIF bed to filtrate arsenic contaminated water as arsenic purifying system. The results of this study was in agreement with the findings of a research conducted by [25] on mice, ducklings and broiler chicken in Pakistan.

Table-1: Effect of Arsenic trioxide along with tannic acid, DSHP, alum and effects of SCIF-bed filtrated water along with alum respectively on body weight (gm) in rabbits

	Chemicals with dose & route	**Pre treatment**	**During treatment**						
		Day 0	**Day 10**	**Day 20**	**Day 30**	**Day 40**	**Day 50**	**Day 60**	**% increased/ decreased**
A	Control(untreated)	1620± 1.7029	1630± 1.7029	1650± 1.7029	1670± 1.7029	1695±2.5 298	1720± 3.5214	1730± 3.5355	+6.79
B	Arsenicosis control group AS_2O_3@100ppm orally	1650± 1.7029	1660± 3.7947	1663± 1.0000	1600± 1.7029a	1550± 3.2275a	1520± 2.0412*a	1480± 5.7735**b	- 10.30
C	AS_2O_3@100ppm +Tannic acid @100ppm orally	1350± 3.5355	1358± 3.4059	1367± 3.2249	1373± 3.3823	1376± 3.4059	1368± 3.2249	1360± 3.5355	+0.75
D	AS_2O_3@100ppm +DSHP @100ppm orally	1715± 3.5355	1719 ±3.405 9	1725± 3.5355	1730± 3./5355	1726± 3.6878	1722± 3.8601	1720± 3.5355	+0.29
E	AS_2O_3@100ppm +Alum @100ppm orally	1430± 1.7029	1435± 3.2619	1441± 1.3638	1444± 1.4142	1446± 1.5811	1445± 3.5355	1440± 3.5355	+0.69
F	SCIF –bed filtrated water + Alum @100ppm orally	1420 ±1.7029	1423± 2.4083	1428± 3.4059	1433± 1.1402	1439± 3.5355	1445± 1.8439	1550± 1.7029	+9.15

Values above represent the mean ± SE of 5 rabbits
a= Mean+ SE of four rabbits
b= Mean+ SE of two rabbits
* Indicates significant values
** Indicates highly significant values
+ indicates % increased – indicates % decreased.

Effect on Biochemical parameters related to liver functions

Effect on SGOT/ AST and SGPT/ ALT

Table-2 represents the results of the effects of arsenic trioxide along with tannic acid, DSHP, alum and effects of SCIF bed filtrated water along with alum respectively on SGOT and SGPT in rabbit. The activities of SGOT and SGPT were elevated in all treated groups than control. But in group B, the elevation of SGOT and SGPT were higher at day 30($P< 0.05$) and much higher at day 60 which were statistically significant ($P<0.01$). The findings of the present study were in agreement with the findings observed by [26] in cattle at West Bengal, India, by [27] in sheep in Iran, by [28] in Swiss Albino Mice. The activities of two enzyme namely serum glutamate pyruvate transaminase (SGPT) recently called as alanine transaminase (ALT) and serum glutamate oxaloacetates transaminase (SGOT) recently called aspartate transaminase (AST) have been widely used to assess the liver function. ALT was a cytoplasmic enzyme while AST was found in both cytoplasm and mitochondria. SGPT or ALT was found to increase in acute hepatitis (viral or toxic), jaundice, and liver cirrhosis. SGOT or AST was found to increase in myocardial infarction and different liver disorders. Activities of both SGOT and SGPT were significantly higher in arsenic treated mice indicated liver dysfunction. Arsenic was known to produce disturbance in liver function [29]. SGOT and SGPT were found as reliable determinants of liver parenchymal injury [30]. The increment of the activities of SGOT and SGPT in plasma might be mainly due to the leakage of these enzymes from the liver cytosol into the blood stream [31], which gave an indication on the hepatotoxic effect of arsenic. The effects of arsenic on liver were found to depend completely on the nature of the arsenicals. Sodium arsenate was found to cause liver fibrosis in goat [32, 33], in rat [34, 35, 36, 37], liver necrosis in Duckling [38, 39, 40]. Sodium arsenite caused hepatocyte degeneration in mice [41]. Histopathological studies also revealed liver and spleen damage in arsenic induced toxicity [41]. These findings supported the results of the present study. Necrosis of hepatocytes and cytoplasmic blebbing in mice due to arsenic toxicity observed by [42] which was similar to the findings reported by [43, 44] in rat. Findings of Histopathological studies was also supported the findings of the present study. In the present study the values of SGOT and SGPT were significantly increased in all treated groups than in control group. In group B the elevation of SGOT and SGPT were much higher than other treated groups i.e. group C, D, E and F. But in other treated groups elevation of SGOT and SGPT were not statistically significant. This might be due to interaction of arsenic trioxide with others such as tannic acid DSHP, alum used in those group and use of SCIF bed filtrated water.

Table-2: Effect of Arsenic trioxide along with tannic acid, DSHP, alum and effects of SCIF-bed filtrated water along with alum respectively on SGOT/AST and SGPT/ALT (U/L at 37^0C) in rabbits

Gr.	**Chemicals with dose & route**	**Pretreatment**		**During treatment**			
		Day 0		**Day 30**		**Day 60**	
		SGOT/AST	SGPT/ALT	SGOT/AST	SGPT/ALT	SGOT/AST	SGPT/ALT
A	Control(untreated)	72.31 ±0.7071	65.71± 0.7071	72.38± 0.7071	66.35 ±0.7071	72.43± 0.7071	67.07± 0.7071
B	Arsenicosis control group AS_2O_3@100ppm orally	70.91± 0.7071	69.18 ±0.8602	93.91± 1.414*a	92.95± 2.121*a	129.0± 1.5811**b	126.0 1.0000**b
C	AS_2O_3@100ppm +Tannic acid @100ppm orally	70.06± 0.7071	68.01 ±0.8602	80.21± 0.7071	73.31± 0.7071	83.45± 0.7071	79.19± 1.0677
D	AS_2O_3@100ppm +DSHP @100ppm orally	70.17± 0.7071	68.19± 0.8602	82.13± 0.7071	76.25± 0.7071	86.67± 0.7071	81.31 ±0.7071
E	AS_2O_3@100ppm +Alum @100ppm orally	71.07± 0.7071	68.23± 0.8602	78.03± 0.7071	72.23 ±2.025	82.98± 0.7071	77.19 ±0.7071
F	SCIF –bed filtrated water + Alum @100ppm orally	71.98 ±0.7071	67.31± 0.8602	75.10± 0.7071	70.07± 1.3038	76.43± 0.7071	74.12± 0.7071

Values above represent the mean ± SE of 5 rabbits

a= Mean+ SE of four rabbits

b= Mean+ SE of two rabbits

* Indicates significant values

** Indicates highly significant values

CONCLUSION:

Treatment with arsenic oxide at low doses has harmful effects on experimental animals including disturbances of liver functions. Therefore, intake of alum treated SCIF bed filtered water might be helpful to reduce the body burden of arsenic toxicities.

REFERENCES

1. WHO; Arsenic and Arsenic Compounds. 2nd edn. Environmental Health Criteria 224.Geneva, World Health Organization 2001.
2. Hossain MF; Arsenic contamination in Bangladesh - An overview. Agril. Eco. & Environ. 2006; 113(1-4): 1-16.
3. Wahidur R; Arsenic Exposure in Bangladesh: The Reproductive and Developmental Health Effects in Humans. Philadelphia Annual Meeting held on 22–25 October, 2006; 67-3.
4. Eisler R; Arsenic Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review. U.S. Fish and Wildlife Service Patuxent, Wildlife Research Center Laurel, MD 20708. Contaminant Hazard Reviews. 1988; Report No. 12.
5. Biswas U, Sarkar S, Bhowmik MK, Samanta AK, Biswas S; Chronic toxicity of arsenic in goats: Clinico biochemical changes, pathomorphology and tissue residues. Small Rumin. Res., 2000; 38(3): 229–235.
6. Mukherjee S, Das D, Darbar S, Mukherjee M, Das AS, Mitra C; Arsenic trioxide generates oxidative stress and islet cell toxicity in rabbit. Curr Sci., 2004; 86 (6): 854–857.
7. Rana T, Bera AK, Das S, Bhattacharya D, Bandyopadhyay S, Pan D, Kumar DS; Effect of chronic intake of arsenic-contaminated water on blood oxidative stress indices in cattle in an arsenic-affected zone. Ecotoxicol Environ Saf., 2010; 73(6): 1327–1332
8. Selby LA, Case AA, Osweiler GD, Hayes HM, Jr. ; Epidemiology and toxicology of arsenic poisoning in domestic animals. Environ. Health Perspect, 1977; 19: 183–189.
9. Doyle JJ, Spaulding JE; Toxic and essential trace elements in meat—A review. J. Anim. Sci., 1978; 47(2): 398–419.
10. Bazargani TT, Ashrafihelan JA, Salar-amoli J; Arsenic poisoning in a dairy herd in Isfahan. Iran Vet. J., 2007; 3(1): 77–83.
11. McKinney JD; Metabolism and disposition of inorganic arsenic in laboratory animals and humans. Environ. Geochem. Health.1992; 14: 43-48.
12. Khan MMH, Aklimunnessa K, Ahsan N, Kabir M, Mori M; Case-control study of arsenicosis in some arsenic contaminated villages of Bangladesh. Sap. Med. J., 2006; 75: 51-61.
13. Benramdane L, Accominotti M, Fanton L, Malicier D, Vallon JJ; Arsenic speciation in human organs following fatal arsenic trioxide poisoning-a case report. Clin. Chem. 1999; 45: 301-306.
14. Kitchin K.T, Kirk T; Recent advances in arsenic carcinogenesis: Modes of action, animal model sys-tems, and methylated arsenic metabolites. Toxicol. Appl. Pharmacol., 2001; 172:249-261.
15. Rahman A, Vahter M, Ekström EC, Rahman M, Mustafa G, Wahed AH, *et al.;* Association of arsenic exposure during pregnancy with fetal loss and infant death: a cohort study in Bangladesh. Am.J. Epidemiol., 2007; 165: 1389-1396.
16. Islam K, Haque A, Karim R, Fajol A, Hossain E, Salam KA *et al.;* Dose response relationship between arsenic exposure and the serum enzymes for liver function tests in the individuals exposed to arsenic: a cross sectional study in Bangladesh. Environ. Health. 2011; 10**:** 64.
17. Clarkson TW; Inorganic and organometal pesticides. In W. J. Hayes, Jr. and E. R. Laws, Jr. 43 (Eds.), Handbook of Pesticide Toxicology. Academic press, San Diego, 1991; 545-552.
18. Santra A, Maiti A, Das S, Lahiri S, Charkaborty SK, Mazumder DNG; Hepatic damage caused by chronic arsenic toxicity in experimental animals. J Toxicol. Clin. Toxicol, 2010; 38: 395-405.
19. Akhand AA, Du J, Liu W, Hossain K, Miyata T, Nagase F *et al.;* Redox-linked cell surface-oriented signaling for T-cell death. Antioxid Redox Signal, 2002; 4**:** 445-454.
20. Hossain K, Akhand AA, Kato M, Du J, Takeda K, Wu J, *et al.;* Arsenite induces apoptosis of murine T lymphocytes through membrane raft-linked signaling for activation of c- Jun amino-terminal kinase. J. Immunol., 2000; 165: 4290-4297.
21. Hossain K, Akhand AA, Kawamoto Y, Du J, Takeda K, Wu J, *et al.;* Caspase activation is accelerated by the inhibition of arsenite induced, membrane raft-dependant Akt activation. Free Radic. Biol. Med., 2003; 34**:** 598-606.
22. Russel D; MSTAT Director. Crop and Soil Science Department, Michigan State University, USA, 1996.
23. Byron WR,Bierbower GW, Brouwer JB, Hansen WH; Pathologic changes in rats and dogs from two-year feeding of sodium arsenite or sodium arsenate. Toxicol. Applied Pharmacol, 1967; 10(1): 132-147.
24. Confer AW, Ward BC, Hines FA; Arsenilic acid toxicity in Rabbits. Lab. Anim. Sci., 1980; 30(2): 234-236.
25. Khan A, Hussain HI, Khan MZ, Abbas RZ; Toxicopathological aspects of Arsenuic in

Birds and Mammals: A Review, Int. J. Agric. Biol. ,2014; 16: 1213- 1224.
26. Bertin Fr, Baseler LJ, Wilson CR, Kritchevsky JE, Taylor SD; Arsenic Toxicosis in Cattle: Meta-Analysis of 156 Cases. J Vet Intern Med., 2013; 27:977–981.
27. Rezazadeh F, Sheikhzadeh JR, Paktinat**;** A study on wool arsenic concentration and some blood parameters in sheep flocks grazing around tailing dams of gold mines in Takab, Iran. Res. Opin. Anim. Vet. Sci., 2014; 4(5): 233-236.
28. Yasmin S, Das J, Stuti M, Rani M, D'Souza D; Sub Chronic Toxicity of Arsenic Trioxide on Swiss Albino Mice. International journal of environmental sciences, 2001; 1(7); 20-24.
29. Fowler BA, Woods JS, Schiller CM., "Ultra structural and biochemical effects of prolonged oral arsenic exposure on liver mitochondria of rats". Environmental Health Perspectives, 1977; 19: 197204.
30. Moss DW, Henderson AR, Kachmar JFIn; "Fundamentals of Clinical Chemistry". 3rd Edn. (Ed: N.W. Tietz). W.B. Saurders, Philadelphia. 1987:346421
31. Navarro CM, Montilla PM, Martin A, Jimenez J, Utrilla PM; "Free radicals scavenger and antihepatotoxic activity of Rosmarinus". Plant Medicine, 2003; 59: 312–314.
32. Biswas U, Sarkar S, Bhowmik MK, Samanta AK; Biswas S; Chronic toxicity of arsenic in goats: clinicobioche mical changes, pathomorphology and tissue residues. Small Rumin. Res., 2000; 38: 229-235.
33. Roy S, Roy M, Pandey MK, Tiwari SP, Effect of tissue trace minerals status and histopathological changes in chronic arsenicosis goat. Vet. World, 2009; 2: 8-9.
34. Vodela JK, Renden JA, Lenz SD, Mcelhenney WH, Kemppainen BW; Drinking Water Contaminants (Arsenic, Cadmium, Lead, Benzene, and Trichloroethylene). 1. Interaction of Contaminants with Nutritional Status on General Performance and Immune Function in Broiler Chickens. J. Poult. Sci., 1997; 76: 1474–1492.
35. Jadhav SH, Sarkar SN, Patil RD, Tripathi HC; Effects of sub chronic exposure via drinking water contaminating metals: A Biochemical and histopathological study in male rats. Arch. Environ. Contam. Toxicol, 2007; 53: 666-677.
36. Singh N, Kumar D, Lal K, Raisuddin S, Sahu AP; Adverse health effects due to arsenic exposure: Modification by dietary supplementation of jaggery in mice. J. Toxicol. Appl. Pharmacol., 2010; 242: 247–255.
37. Ghatak S, Biswas A, Dhali GK, Chowdhury A, Boyer JL, Santra A; Oxidative stress and hepatic stellate cell activation are key events in arsenic induced liver fibrosis in mice. Toxicol. Appl. Pharmacol., 2011; 25: 59-69.
38. Camardese MB, Hoffman DJ, Lecaptain LJ, Pendleton GW; Effects of arsenate on growth and physiology in Mallard ducklings. Environ. Toxicol. Chem., 1990; 9: 785–795.
39. Whitworth MR, Pendleton GW, Hoffman DJ, Camardese MB; Effects of dietary boron and arsenic on the behavior of mallard ducklings. Environ. Toxicol. Chem., 1991; 10: 911–916.
40. Hoffman DJ, Sanderson CJ, LeCaptain LJ, Cromartie E, Pendleton GW; Interactive effects of arsenate, selenium, and dietary protein on survival, growth and physiology in mallard ducklings. Arch. Environ. Contam. Toxicol, 1992: 22: 55–62.
41. Wu J, Liu J, Waalkes MP, Cheng ML, Li L, Li CX,. Yang Q; High dietary fat xacerbates arsenic-induced liver fibrosis in mice. Exp. Biol. Med., (Maywood), 2008; 233: 377-384.
42. Ferzand R, Gadahi JA, Saleha S, Ali Q; Histological and Hematological disturbances caused by arsenic toxicity in Mice model, Pakistan Journal of Biological sciences, 2008; 11(11): 1405-1413.
43. Gyasi SF, Awuah ES, John A, Koffuor LGA, Osei OA; Clinical, Hematological and Histopathological Responses to Arsenic Toxicity in ICR Mice Using Arsenic Levels Synonymous to Buruli Ulcer Endemic Communities in the Amansie West District of Ghana., European Journal of Experimental Biology, 2012; 2 (3):683-689.
44. Hemalatha H, Reddy GA, Rani MU, Anandkumar A, Shivakumar P; Arsenic-induced histological alterations in various organs in rats. Int. J. LifeSc. Bt & Pharm. Res. 2013; 10(1):22-26.