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Arsenic induced hepatotoxicity in Swiss albino mice

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Abstract : *An experiment was conducted to investigate the hepatotoxic effects of arsenic trioxide on the liver function of Swiss albino mice and also to detect the possible ameliorative effect of L-ascorbic acid and garlic juice on arsenic- induced hepatotoxicity. Our study revealed significant changes in the SGOT and SGPT levels in the treated groups of mice. However, the administered doses of ascorbic acid and garlic extract were not found to ameliorate the influence of arsenic. On the basis of these results, we conclude that arsenic trioxide could have direct toxic effects on the liver when it is consumed even in minimal quantity for a short period of time.*

Key words : *Arsenic trioxide, ascorbic acid, garlic extract, liver, SGOT, SGPT.*

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Introduction :

Arsenic is an odourless and tasteless semi-metal element which occurs naturally in the environment. Arsenic compounds are abundant in the earth's crust. Arsenic from weathered rocks and soil dissolves in ground water.The permissible limit of arsenic in water advised by WHO is 10 µg/l which is equivalent to 10 ppb. Recently, however, it has been reported that there is an increased risk of arsenic toxicity, even at the low and permissible dose of 10 ppb (Walker and Fosbury 2009). General adverse health effects associated with human exposure to arsenic include cardiovascular diseases, developmental abnormalities, neurologic and neuro - behavioral disorders, diabetes, hearing loss, fibrosis of the liver and lung, hematological disorders and Blackfoot disease (Abernathy et al., 1999).

While a number of studies have been conducted on the acute and chronic toxicity caused by moderate and high concentrations of arsenic on mice model, studies on the sub - chronic toxicity

of arsenic trioxide on liver function are lacking. Therefore, this study was undertaken to find out the short term effects of arsenic trioxide on the liver function of Swiss albino mice. Ascorbic acid predominantly works as a radical chain terminator (Combs and Gray, 1998), and the biological responses of garlic have been largely attributed to enhanced detoxification of foreign compound, hepato-protection and antioxidant effect etc. (Banerjee and Maulik, 2002). Therefore, possible protective role of ascorbic acid and garlic extract was also explored.

Materials and Methods :

Twenty healthy female inbred Swiss albino mice of the same age were selected. All animal treatments and protocols followed in this study received prior approval of the Institutional ethical committee and met the standard laid down by Government of India. After acclimatization to the laboratory conditions, mice were divided into 4 groups, each containing 5 mice. Mice of group A were given normal food and drinking water and treated as controls. Mice of group B were administered predetermined sublethal dose of arsenic trioxide (3mg/Kg body weight/day) .This dose is well within the range for the human lethal dose (1–4 mg/kg body wt) reported for arsenic (North et al 1997). Mice of group C were administered the same concentration of arsenic trioxide similar to group B and L-ascorbic acid (10 mg /Kg body weight). This dose of L-ascorbic acid is quantitatively equivalent to the human therapeutic dose (500 mg/day, Sahu and Das 1994) in terms of body weight. Mice of group D were administered the dose of arsenic trioxide in same concentration and manner similar to the mice of group B and C. Moreover they were administered with 100 mg/Kg body weight garlic extract /mice concurrently every day. Garlic was extracted as follows: 30g of garlic bulbs were crushed in 60ml distilled water and squeezed through a double cheesed cloth and the aliquots stored in freezer following Flora et al (2009).This garlic dose (100 mg kg-1 bw) approximately corresponds to the daily dietary intake of 7g of fresh garlic by a person weighing 65 kg. The aqueous extract of garlic and L-ascorbic acid were administered 30 minutes prior to the As_2O_3 dose. The doses were administered for 15 days through gavage.

On the 16th day mice were weighed and sacrificed after giving light anesthesia. Weight of kidneys, liver and uterus were taken. Blood was collected through cardiac puncture and sent to a reputed laboratory for analysis. Following parameters were analysed: Serum glutamic pyruvic transaminase (SGPT) and Serum glutamic oxaloacetic transaminase (SGOT) Initial and final weights of mice and the relative weights of control and treated mice were compared with Student's t-test. Different blood parameters of the four groups of mice were compared by one-way analysis of variance (ANOVA) followed by Tukey's test. P value less than 0.05 was considered statistically significant.

Results and Discussion :

There was no significant change in the behaviour of mice treated with Arsenic trioxide. There was no significant difference in the initial ($F_{3,19}$=2.09, NS) and final ($F_{3,19}$=1.13, NS) weights between the control and treated mice (Table 1). Arsenic treatment in mice for 15 days did not show any significant changes in the weights of liver ($F_{3,19}$=0.235,NS), kidneys ($F_{3,19}$=1.276,NS) and uterus ($F_{3,19}$=0.099,NS), (Table 2).

Haematological analysis revealed significant changes in the SGOT ($F_{3,19}$=6.79,P<0.05) and SGPT ($F_{3,19}$=7.36,P<0.05) levels of treated groups of mice as compared to the control group (Table 3). Unfortunately the administered doses of ascorbic acid and garlic extract were not found to ameliorate the influence of arsenic. Pathological changes were found in the arsenic treated mice. The liver showed necrosis, appearance of vacuoles in the hepatocytes, nuclear degenerative changes

in experimental animals. Besides, central veins showed necrosis of epithelium (Fig a,b & c).

Table 1 : Initial & final weights (in g) of control and experimental mice. Values are Mean ± S.E.

	Control	Arsenic treated	Arsenic + vit C	Arsenic + Garlic extract
Initial weight	27.7 ± 1.23	28.31 ± 0.94	29.5 ± 0.82	25.38 ± 1.65
Final weight	28.42 ± 1.75	27.38 ± 0.57	28.32 ± 1.07	25.38 ± 1.45

Table 2.Comparison of organ weights (in g) of control & experimental mice. Values are Mean ± S.E.

GROUP	Liver	Kidney	Uterus
Control	1.5 ± 0.2	0.2 ± 0.01	0.9 ± 0.03
Arsenic treated	1.3 ± 0.1	0.2 ± 0.01	1.0 ± 0.05
Arsenic + Ascorbic acid	1.4 ± 0.2	0.2 ± 0.02	1.1 ± 0.1
Arsenic+ garlic extract	1.3 ± 0.1	0.17 ± 0.01	1.1 ± 0.1

Table 3. Comparison of SGOT & SGPT level of control and treated mice. Values are Mean ± S.E.

	Control	Arsenic treated	Arsenic + vit C	Arsenic + Garlic extract
SGOT (IU/ml)	20.4 ± 0.8	24.6 ± 0.9	26.8 ± 2.9	32.2 ± 2.1
SGPT (IU/ml)				4 ± 2.4

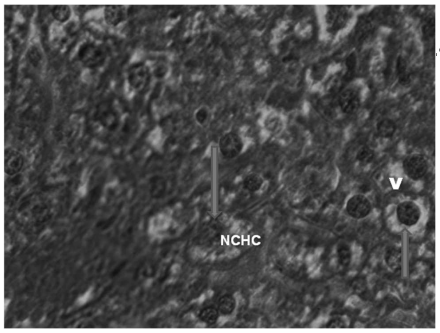

Fig a. Mi necrosis

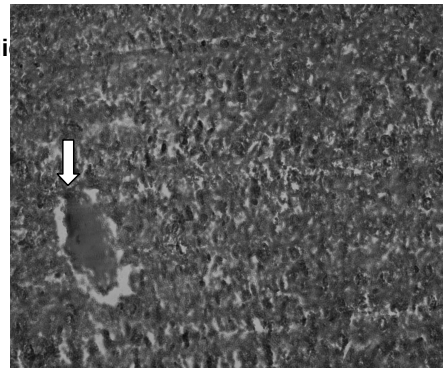

Fig b . M l nuclear 00 X

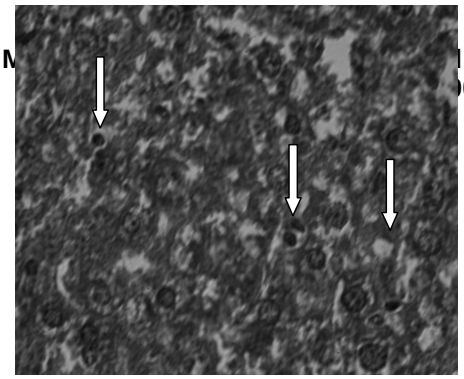

Fig c. Necrosis in the epithelium of central vein (CV) – H & E. 400 X

Arsenic is known to produce disturbance in liver function (Fowler et al., 1977). SGPT and SGOT are reliable determinants of liver parenchymal injury (Moss et al., 1987). The increment of the activities of SGPT and SGOT in plasma may be mainly due to the leakage of these enzymes from the liver cytosol into the blood stream (Navarro et al., 1993), which gives an indication on the hepatotoxic effect of arsenic. It is further recommended that 25mg of L-ascorbic acid (Singh and Rana 2007) and 500mg/kg BW garlic extract (Flora et al 2009) may be helpful in preventing arsenic poisoning by reducing arsenic burden, oxidative stress and hepatic apoptosis in mice.

Conclusion :

The study concluded that arsenic trioxide could have direct toxic effects on liver even when it is consumed in minimal quantity (3mg/kg body weight) for a short period of time i.e; 15 days. The present study also concluded that a low dose of L-ascorbic acid and garlic juice may not exert any significant effect to counteract arsenic toxicity.

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