INTERNATIONAL JOURNAL OF ADVANCED BIOLOGICAL RESEARCH

www.scienceandnature.org

BIOCHEMICAL VARIATION FOLLOWING EXPOSURE OR RATS WITH ARSENIC TRIOXIDE AND ALPHA LIPOIC ACID

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ABSTRACT
Four groups of rat treated I/P with Arsenic trioxide (1.5mg / Kg. b. wt), alphalipoic acid (100 mg /Kg.b.wt), or both arsenic trioxide and alpha lipoic acid and control group treated with phosphate buffer saline (0.2ml) for 3 months the results showed a significant increase ($P \leq 0.05$) in the levels of liver enzymes (SGPT, SGOT and A/P) in comparison with control group, whereas group received both arsenic trioxide and alpha lipoic acid showed no significant increase in the level of liver enzymes in comparison with control group and a significant decrease ($P \leq 0.05$) as compared with group received Arsenic trioxide.

KEYWORDS: Arsenic trioxide, alphalipoic acid in rats, biochemical effect.

INTRODUCTION

Arsenic is ubiquitous element in the environment, weathering of rocks converts sulphite to arsenic trioxide which enters the arsenic cycle as dust or by dissolution in rain , rivers or ground water[1]. Arsenic is a very toxic metal and also an environmental and industrial pollutant which is present in soil , water , air and food[2]. Arsenic induce actue and chronic toxicity associated with degenerative changes and inflammatory lesions and neoplastic abnormalities in the tissues of skin, respiratory system cardiovascular system, nervous, renal, hepatic and endocrine[3]. Also arsenic cause oxidative stress through lipid peroxidation and consumption of some antioxidant system[4].

Some workers found that the Arsenic exposure in mice cause an immune suppression , reduce macrophage and neutrophils abundance[5] some studies have shown reduce lymphocyte proliferation $CD4^+$, $CD8^+$, and their ratio together with decrease T regulatory cells in exposed adult and children to arsenic[6]. Aim of the study to evaluate biochemical variation of liver enzymes in rats treated with arsenic trioxide and alpha lipoic acid.

MATERIAL AND METHODS

Biochemical Tests

Alkaline phosphatase (ALP)

AlP is an enzyme originated mainly in the bone, liver and placenta, with some activity in the kidney and intestine , It is called alkaline because it functions best at a PH OF 9[7].

Serum ALP concentration was enzymatically measured using standard assay (ALP-kit) (Biomerieux/France) alkaline phosphates activity in serum samples was estimated spectrohotometrically by employing (king and Armstrong) method , in which the disodium phenyl phosphate is hydrolysed with liberation of phenol and formation of sodium phosphate .The amount of liberated Phenol is read on absorbance at 510 Nm, by using the following equation:

$$\text{ALP} = \frac{\text{Test} - \text{blank}}{\text{Standard} - \text{blank}} \times 20 = \text{IU} \backslash \text{Di}$$

AST and ALT:

AST and ALT concentrations were enzymatically measured using standard assay (AST, ALT-Kit) (Biomerieux /France) [1].

AST and ALT enzymes catalyze the transfer of the amino group of glutamic acid to oxalacetic acid and pyruvie acid in reversible reaction.

The transaminase activity is proportional to the amount of oxaloacetate or pyruvate formed over a definite period of time and is measured by a reaction with 2,4-Dinitrophenhydrazin (DNPH) in alkaline solution at wave length of 510 Nm.

The following formula indicated these reactions :-

AST: Aspartate + α' Keto glutarate $\xrightleftharpoons{\text{ALT}}$ xalocetate + glutamate

ALT: Alanine + α' Keto glutarate $\xrightleftharpoons{\text{AST}}$ /rovate + glutamate

RESULTS

Biochemical Test

Serum Glutamate Pyruvate Transaminase (SGPT) or ALT: Daily administration of arsenic alone (1.5mg\kg B.W) for 3 months on the SGPT (IU/ d' L) in ATO group rats are shown in table (1) .The SGPT values increased significantly ($P< 0.05$) in the ATO group (51.52 ± 8.99) in comparison with that of control group which showed normal values ($P< 0.05$)(23.82 ± 1.81) .But there is non – significant difference in the ATO +ALA group (received arsenic trioxide and supplemented with 100 mg \ kg B.W

of alpha lipoic acid for 3 months) (30.27 ±.98) in comparison with that of control group .Also the result of SGPT of ALA group (received alpha lipoic acid alone for 3 months) , showed non–significant change (28.92 ±3.05) in relation to control group .

Serum Glutamate Oxaloacetate Transaminase (SGOT) or AST:

The result of SGOT values increased significantly (P< 0.05) in the ATO group (276 ±15.84) in relation to control group. But there is non-significant difference in the SGOT values of ATO + ALA group in comparison with the control group, whereas the SGOT values of ALA group showed non- significant difference in comparison with the control group as listed in table (1) .

Serum Alkaline Phosphatase (ALP):

Our result showed significant diffence (P< 0.05) in the values of ALP (IU\dl) of ATO group animals (434 ± 33.41) in comparison with the control group

The ALP values of ATO +ALA were showed non – significant change (333.6 ±52.58) in relation to control group .Also the ALP values of ALA group demonstrated non- significant change (296.6 ±35.1) in comparison with the control group as listed in table (1)

TABLE 1: Serum liver enzyme tests (GPT, GOT and ALP) in different rat groups

Groups	GPT IU/dl (Mean ± SE)	GOT IU /dl (Mean ± SE)	ALT IU/dl (Mean ± SE)
Control	23.82 ± 1.81 a	163.6 ± 17.24 a	302 ± 26.88 a
ATO alone	51.52 ± 8.99 b	276 ± 15.84 b	434 ± 33.41 b
ATO+ALA	30.27 ± 3.98 a	174.4 ± 8.77 a	333.6 ± 52.58 a
ALA alone	28.92 ± 3.05 a	160.4 ± 21.01 a	296.6 ± 35.1 a

The similar letters refers to the non–significant differences while the different letters refers to the significant differences at ($P \leq 0.05$), [ATO: arsenic trioxide, ALA : alpha lipoic acid] .

DISCUSSION

There are three liver enzymes that are commonly used in the diagnosis of liver disease, they are Glutamate Pyruvate transaminase (GPT\ALT), Glutamate Oxaloacetate transaminase (GOT\AST) and Alkaline phosphatase (ALP). Injury to liver, whether is acute or chronic by toxic substances eventually results in an increase in serum concentrations of aminotransferases [9]. The abnormal elevation of liver enzymes such as SGOT, SGPT and ALP can be taken as an index for liver injury or disease .These enzymes are normally present in the serum and tissues of the body, espically the tissues of liver , the researchers related the cause of increase serum activities of ALT and AST to the increased cellular basal metabolic rate , irritability and destructive changes of liver and skeletal muscles cells [10].

In the present study ,Administration of intraperitoneally (1.5mg\kg B.W) of arsenic trioxide for 3 months caused significant increase (P< 0.05) In the levels of hepatic marker enzymes in serum (SGOT, SGPT and ALP), this may be due to the leakage of the enzymes to the blood stream. The increase in the levels of these enzymes in the serum indicates the liver damage and alteration in the liver function due to exposure to arsenic trioxide , the exact mechanism of arsenic trioxide involved in elevationof these enzymes may be due to the hepato cellular damage with severe necrosis and vacuolation of hepatocytes (provided by the histopathological changes of liver sections in the current study) resulting in increased plasma membrane permeability led to leakage of these enzymes from the liver tissue into the blood stream. This is because arsenic trioxide is known to produce oxidative damage in the liver tissue via production of reactive oxygen species (ROS). Treatment or supplementation with alpha lipoic acid significantly decreased (P< 0.05) (compared with ATO alone group in the levels of these liver enzymes (SGOT, SGPT and ALP) in the serum suggesting that it offers protection by preserving the structural integrity of the hepatocytes .Also , these results provided with histopathological changes of liver sections in the current study) Adimintration of alpha lipoic acid preserved the integrity of the hepatocellular membrane via decreased production of reactive oxygen species and amelioration the oxidative damage *i.e.* the leakage of liver enzymes because of liver injury was preserved by the liver cell membrane stability via action of alpha lipoic acid .These results coincide with previous studies[11] reported that SGPT and SGOT values increased significantly (P<0.05) in arsenic treated rats. Similarly[12] also observed that SGOT, SGPT and ALP increased in arsenic treated group of Swiss albino mice .Other studies the protective role of alpha lipoic acid for the liver tissue[13] indicate that alpha lipoic acid enhanced free radical scavenging and antioxidant status ,further ameliorated the Aflatoxin BI (AFBI) – induced oxidative stress[14] who showed the possibility that alpha lipoic acid offers protection against oxygen species - mediated damage by enhancing cellular antioxidant defense and reducing severe physiological and histopathological alteration in rat exposed to malathion.

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