The Hepatoprotective Effect of *Andrographis paniculata* on Sodium Arsenite Induced Toxicity in Albino Wistar Rats.

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Abstract

*Andrographis paniculata* (AP), generally known as king of bitters has various pharmacological as well as medicinal properties which are of great importance to the global world. The present study evaluated the hepatoprotective effect of aqueous extract of AP leaves on sodium arsenite (SA) induced toxicity in albino Wistar rats. Forty male albino rats were randomly divided into eight groups. Group 1 received distilled water only, group 2 was given 5mg/kg body weight (bwt) of sodium arsenite orally on 7th, 14th, 21st and 28th day of the experiment while group 3, group 4 and group 5 were administered daily with 1000mg/kg bwt, 500mg/kg bwt and 200mg/kg bwt of aqueous extracts of AP simultaneously with 5mg/kg bwt of SA once a week. Groups 6, 7 and 8 were treated with only extracts of 1000mg/kg bwt, 500mg/kg bwt and 200mg/kg bwt daily. The results of the study indicated there was a significant (P<0.05) increased in serum ALT, AST and ALP enzymes activities in group 2 as compared to the control group. Administration of AP extracts to the albino wistar rats given SA resulted in a significant reduction (P<0.05) in the activities of these serum enzymes in groups 3, 4 and 5 as compared to group 2. The results of groups 6, 7, 8 showed a remarkable level close to the control (group 1). Histopathological examination of the liver section of the SA induced hepatotoxicity in the albino rats indicated an hepatoprotective effect of aqueous extract of AP.

Keywords: *Andrographis Paniculata*, Hepatoprotective, liver enzymes, sodium arsenite

Introduction

Liver disease is a worldwide problem which is caused by infections and different carcinogenic agents such as aflatoxin, heavy metals like arsenic, cadmium, lead etc. Human are avoidably or unavoidably exposed to hepatotoxic agents especially inorganic arsenic through ground water which is the primary source of drinking water.
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(Saha, 1995 and Waalkes, et al., 2003). Sodium arsenite is the most toxic among the arsenics and has been reported to possess genotoxic, hepatic tumorigenic and carcinogenic potentials. (Mass, 1999 and Nickson et al. 1998). Report has shown that hepatotoxicity has increased as a result of various environmental toxins and hepatotoxic drugs (Jin et al., 2005). In the absence of reliable liver protective drugs in allopathic medical practices, herbs may play a role in the management of various liver disorders (Jaeschke et al., 1996; Essabu et al., 1997).

*Andrographis paniculata* (AP) is also known as king of bitters” from the family Acanthaceae has been shown to possess protective effect against urothelial toxicity (Sheeja and Kutta, 2006) and liver disorders including treatment of hepatitis (Sharmal et al., 1992). Mostly the leaves and roots have been traditionally used for different medicinal purposes in Asia and Europe as a folklore. AP has a surprisingly broad range of pharmacological effect such as anti-inflammatory (Shen et al., 2000, 2002), anti-diarrhoeal (Caupta et al., 1990), anti-microbial (Singha et al., 2003), anti-malarial, (Rahman et al., 1999), Cardiovascular (Tan et al., 2004) anti-cancer (Kumar et al., 2004) and immunostimulatory activities (Iruretagoneya et al. 2005).

Previuos reports have shown that Andrographolide, a major bioactive compound of this plant can inhibit the expression of inducible nitric oxide synthase (Chiou et al., 1998, 2000). Also aqueous extracts of AP has been shown to inhibit hexachlorocyclohexane (BHC) induced toxicity in Swiss male mice (Trivedi and Rawal, 2000, 2011). Hepatoprotective activity of AP against carbon tetrachloride, galactosamine and paracetamol intoxication had been reported (Handa and Sharma, 1990a, 1990b). However, male reproductive toxicity (Akbarsha and Murugaian, 2000) and cytotoxicity (Nanduri et al., 2004) of this plant have been reported. Very few studies on the effects of crude extracts of AP on liver functions are available. To our knowledge, effect of simultaneous administration of AP extracts and SA in albino wistar rats have not been reported, hence the purpose of the present study. In this study we assessed the hepatoprotective effects of AP on sodium arsenite induced liver damage in albino wistar rats using biochemical assays and histopathological observations.

**METHODOLOGY**

**Test animals**

Forty male albino wistar rats (average weight of 180g) were obtained from Central Animal House, University College Hospital, Ibadan, Nigeria. They were acclimatized under a 12:12h light/dark cycle for a week, fed free standard pellets diets with clean tap water ad libitum.

**Preparation of plant materials:**

The fresh AP leaves was obtained from Abadina, University of Ibadan, washed with clean water and air dried under shade for 3 weeks. It was grinded into powder using grinding machine. One
hundred grammes of the powdered plant leaves was soaked in 500ml of distilled water overnight. Thereafter, the mixture was filtered using muslin cloth. The filtrate was pooled and concentrated using rotary evaporator to obtain the crude extract which was later lyophilized.

**Experimental Design**
The rats were randomly divided into eight groups. Group 1 received distilled water only for 30 consecutive days, group 2 was given 5mg/kg bwt of sodium arsenite on the 7th, 14th, 21st and 28th day respectively and Groups 3, 4 and 5 were administered daily with 1000mg/kg bwt, 500mg/kg bwt and 200mg/kg bwt of AP simultaneously with 5mg/kg bwt of SA. Also groups 6, 7 and 8 were administered daily with only AP extracts of 1000mg/kg body wt, 500mg/kg body wt and 200mg/kg body wt.

**Assessment of liver function:**
At the end of the experimental period, all the animals were sacrificed by cervical dislocation. Blood samples were collected and centrifuged at 3000rpm for 30 mins. The biochemical parameters like Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) activities were determined by the method of Reitman and Frankel (1957). Also Alkaline phosphatase (ALP) activity was assayed using the reconstituted reagent ALP kit obtained from Randox Company Ltd, UK by the method of King and King (1954).

**Histopathological analysis:**
Immediately after the sacrifice of rats, the livers were removed and stored in 10% formalin for histopathological examination. The livers tissues were fixed with 10% phosphate-buffered neutral formalin, dehydrated in graded alcohol (50-100%) and embedded in paraffin. Thin sections were cut and stained with heamatoxylin and eosin stain for microscopic assessment.

**Statistical Analysis:**
The values were expressed as mean ± standard deviation. Data obtained was subjected to One-way analysis of variances (ANOVA). The values P < 0.05 were considered statistically significant.
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Results and Discussion

Table 1: Liver Enzyme Activities in Albino Wistar Rats Fed With Aqueous Extracts of Andrographis paniculata and Sodium Arsenate.

<table>
<thead>
<tr>
<th>Groups</th>
<th>ALP (Mean ± SD)</th>
<th>AST (Mean ±SD)</th>
<th>ALT (Mean ±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.32±7.30b</td>
<td>13.30±1.08c</td>
<td>20.26±2.27d</td>
</tr>
<tr>
<td>2</td>
<td>40.48±10.50a</td>
<td>26.00±3.37a</td>
<td>29.10±3.32a</td>
</tr>
<tr>
<td>3</td>
<td>18.40±3.19b</td>
<td>18.20±4.2b</td>
<td>23.93±3.74bc</td>
</tr>
<tr>
<td>4</td>
<td>16.56±5.52bc</td>
<td>19.10±5.13b</td>
<td>23.84±3.22bc</td>
</tr>
<tr>
<td>5</td>
<td>12.88±4.22d</td>
<td>17.70±4.8b</td>
<td>24.80±2.64bc</td>
</tr>
<tr>
<td>6</td>
<td>15.64±6.95c</td>
<td>17.38±1.6b</td>
<td>25.05±1.71b</td>
</tr>
<tr>
<td>7</td>
<td>13.80±4.78d</td>
<td>14.73±0.8c</td>
<td>22.92±3.46c</td>
</tr>
<tr>
<td>8</td>
<td>8.28±2.76c</td>
<td>15.74±3.19c</td>
<td>21.56±1.94c</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD n=3. Within column, values with different superscript are significant different (P < 0.05).

The Histopathological Observation:

(A): Control group

(B): Sodium Arsenite (SA) only
SA is a proven carcinogen commonly found in drinking water (Waalkes et al, 2003). It induces free radical damages in tissues which causes inflammation of the hepatic cells thereby resulting in the elevation of liver enzymes. Elevated levels of these enzymes are indicative of cellular leakage and loss of functional integrity of cell membrane in liver (Drotman and Lawhan, 1978). Due to the absence of efficient liver protective drug in modern medicine, a large number of studies searching for hepatoprotective constituents from natural sources have been conducted in recent years (Adnyana et al 2001, Huang et al 2010).

From the results, administration of sodium arsenite only resulted in a significant (p<0.05) increase of the level of ALT, AST and ALP in the serum of rats. The treatment of rats with aqueous AP extracts significantly (p<0.05) reduced the levels of AST, ALT and ALP in rats intoxicated with sodium arsenite to near normal demonstrating that AP extracts has hepatoprotective effect on sodium arsenite induced liver injury. The effects of AP extracts only given to the rats showed a remarkably enzyme activities with values near to normal.
Also histology of the liver sections of control rats showed no visible lesions as compared to group 2 (SA only) which showed severe portal central and venous congestion, moderate hepatic degeneration and necrosis, and also moderate portal cellular infiltration by mononuclear cells. It was observed that the hepatohistological changes induced by SA was ameliorated by the treatment of AP extracts with the absence of portal cellular infiltration mononuclear cells. Result from the present study is suggesting that aqueous extracts of AP contain hepatoprotective agents.

**Conclusion:**
From the above experimental study, we conclude that the extracts of AP produces adequate hepatoprotective activity against sodium arsenite induced toxicity in albino wistar rats.

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