Aflatoxins are a group of closely related secondary toxic fungal metabolites produced by *Aspergillus flavus* and *A. parasiticus*, of relatively low molecular weight organic compounds characterized by their diversity, their frequent specificity with regard to the taxonomy of the producing organisms and their production during the stationary phase of the batch cultures. During early period of recognition it was considered as a part of storage flora of inadequate post-harvest storage and poor storage conditions during distribution of commodities such as maize, groundnuts, peanuts, barley etc. However, it has now become increasingly recognized that the contamination of some commodities especially peanuts and maize with aflatoxin is a far more complex phenomenon which may involve infection and aflatoxin production in the field. Although contamination of crop in field is undoubtedly influenced by insect damage, *A. flavus* is also known to infect intact kernels of maize by colonizing and growth down the external silk (1). Aflatoxins also decrease the production of vitamin A in the liver. This has secondary effects such as decreased blood calcium levels, decreased bone strength and a decreased tissue and serum tocopherol level. This decrease in tocopherol level can lead to vitamin A and E deficiencies (2). Other pathological features in cattles are blood coagulation defects, which may involve impairment of prothrombin, factors VII and X and possibly factor IX. A single dose of aflatoxin causes an increase in plasma enzymes (aspartate aminotransferase, lactate dehydrogenase, glutamate dehydrogenase, gamma-glutamyltransferase and alkaline phosphatase) and in bilirubin, probably reflecting liver damage. Other abnormal clinical findings are proteinuria, ketonuria, glycosuria and hematuria (3). Similar changes in blood coagulation parameters have been reported in dogs (3). Serum glutamate-pyruvate transaminase and glutamate oxaloacetate transaminase (mitochondrial) activities were elevated. Hypoglycemia and low cerebrospinal fluid glucose were observed. The onset of the illness included coughing, rhinorrhea, sore throat, earache, slightly enlarged, firm yellow liver, and a pale, slightly widened renal cortex. A high rate of mortality (81% of the diagnosed cases) occurred. Since Reye’s Syndrome is characterized by abnormal mitochondrial structure and function (4), it is of interest to note that aflatoxin B1 causes abnormal mitochondrial structure and function (5). Inhibition of protein synthesis caused by aflatoxins alters serum protein composition, resulting in the suppression of the production of non-specific

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**AMELIORATIVE EFFECT OF CURCUMIN ON AFLATOXIN-INDUCED TOXICITY IN SERUM OF MICE**

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**Abstract:** The present investigation was an attempt to evaluate the ameliorative effect of curcumin on aflatoxin-induced toxicity on serum and blood of mice. Aflatoxin was obtained by growing *Aspergillus parasiticus* in SMKY liquid medium. Pure curcumin (97% purity) was purchased from Hi-Media Laboratories Pvt. Ltd., Mumbai, India. Young adult male albino mice were orally administered with low dose and high dose (750 and 1500 µg/kg body weight) with and without curcumin (2 mg/0.2 mL olive oil/animal/day) for 45 days. On 46th day the animals were sacrificed by cervical dislocation. For serum parameters blood was collected in non-EDTA containing vails from heart of the dissected mice. Serum parameters are creatinine, protein, AST and ALT. The results revealed dose dependent increase in creatinine, AST and ALT and decrease in protein in serum parameters of mice. Treatment with curcumin along with aflatoxin ameliorates aflatoxin-induced changes in serum parameters.

**Keywords:** aflatoxin, curcumin, serum, creatinine, protein

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humoral substances important to native defense (6). Curcumin (Diferuloylmethane) was first isolated by Vogel and Pelletier (7) and its chemical structure was determined by Roughley and Whiting (8). It has a melting point at 176-177°C, forms a reddish-brown salt with alkali and is soluble in ethanol, alkali, acetone, acetic acid and chloroform. Curcumin is found to be the biologically active compound in turmeric.

Curcumin reduces carbon tetrachloride and D-galactosamine-induced glutamate oxaloacetate transaminase and glutamate pyruvate transaminase levels (9). Curcumin has capacity of lowering cholesterol, fatty acids and triglycerides in alcohol-induced toxicity (10).

In vitro curcumin can significantly inhibit the generation of reactive oxygen species (ROS) like superoxide anions, H₂O₂ and nitrite radical generation by activated macrophages, which play an important role in inflammation also. Curcumin lowers the production of ROS in vivo (11). Curcumin reduces oxidized proteins in amyloid pathology in Alzheimer transgenic mice (12). It also decreases lipid peroxidation in rat liver microsomes, erythrocyte membranes and brain homogenates (13). Curcumin shows anticoagulant activity by inhibiting collagen and adrenaline-induced platelet aggregation in vitro as well as in vivo in rat thoracic aorta (14). Both turmeric and curcumin decreases blood sugar level in alloxan-induced diabetes in rat (15). Curcumin also decreases advanced glycation end products induced complications in diabetes mellitus (16). In patients undergoing surgery, oral application of curcumin reduces post-operative inflammation (17).

EXPERIMENTAL

Preparation of aflatoxin extract was the same as described in the preceding paper (18). Curcumin was purchased from Hi-Media Laboratories Pvt. Ltd., Mumbai, India.

Young inbred, Swiss strain male albino mice (Mus musculus), weighing approximately 37-40 g, were obtained from Cadila Health Care, Ahmedabad, India. They were provided feed and water ad libitum and maintained under laboratory conditions. Seventy such animals were divided into seven groups and caged separately. Group 1 (control) animals were maintained without any treatment. Animals of Group 2 (vehicle control) received olive oil (0.2 mL/animal/day). Animals of Group 3 received curcumin (2 mg/0.2 mL olive oil/animal/day) for 45 days and served as positive controls. Animals of Group 4 and 5 were orally administered aflatoxins at a dose of 25 (low dose; LD) and 50 (high dose; HD) µg/0.2 mL olive oil/animal/day (750 and 1500 µg/kg body weight), respectively, for 45 days. Group 6 and 7 animals were orally administered low dose and high dose of aflatoxin along with curcumin (2 mg/0.2 mL olive oil/animal/day), respectively, for 45 days. All the treatments were given orally using a feeding tube attached to a hypodermic syringe.

On completion of the treatment, the mice were weighed and were sacrificed by cervical dislocation. The blood from heart was collected in non-EDTA added bulbs, allowed to clot and centrifuged at 1000 g for 10 min to collect non-hemolyzed serum. The serum was diluted and used for various biochemical analyses such as creatinine, estimated by method of Varley (19), AST and ALT, by the method of Reitman and Frankel (20) and protein by the method of Lowry et al. (21).

For all the parameters a minimum of 10 replicates were used and the data were statistically analyzed using one way analysis of variance (ANOVA) followed by Tukey test. The levels of significance were accepted at p < 0.05. Comparisons of p-values between different groups were performed.

RESULTS AND DISCUSSION

Table 1 shows the effect of aflatoxin as well as aflatoxin plus curcumin treatment on serum parameters in mice. Also percent changes from vehicle control (Group 2) are shown in Figures 1.1 ñ 1.4. No significant change was observed between different control groups (Groups 1 ñ 3).

Aflatoxin treatment for 45 days caused, as compared to vehicle control (Group 2), a dose-dependent increase in creatinine (LD: 60.04%; HD: 165.58%; Fig. 1.1) and activities of serum aspartate aminotransferase (AST) (LD: 38.94%; HD: 62.01%; Fig.1.2) and serum alanine aminotransferase (ALT) (LD: 54.12%; HD: 126.30%; Fig. 1.3), however, protein content was significantly decreased (LD: 48.83%; HD: 60.26%; Fig. 1.4) in serum of mice.

Oral administration of curcumin along with aflatoxin caused significant amelioration in aflatoxin-induced effects in the serum parameters as compared to the aflatoxin alone treated groups. This amelioration was almost complete in curcumin plus low dose aflatoxin-treated group (Group 6), while it was partial in curcumin plus high dose aflatoxin-treated group (Group 7).

A significant decrease in serum protein was noted in aflatoxin-fed mice (Table 1). Almost all
Table 1. Effect of curcumin on aflatoxin-induced changes in the serum parameters of mice.

<table>
<thead>
<tr>
<th>Experimental Groups</th>
<th>Parameters</th>
<th>1 Untreated control</th>
<th>2 Vehicle control</th>
<th>3 Curcumin control</th>
<th>4 Low dose aflatoxin</th>
<th>5 High dose aflatoxin</th>
<th>6 Low dose aflatoxin + curcumin</th>
<th>7 High dose aflatoxin + curcumin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Creatinine (mg/100 mL)</td>
<td>3.427 ± 0.006</td>
<td>3.469 ± 0.006</td>
<td>3.392 ± 0.001</td>
<td>5.552 ± 0.056</td>
<td>9.213 ± 0.002</td>
<td>3.925 ± 0.012</td>
<td>5.302 ± 0.038</td>
</tr>
<tr>
<td></td>
<td>Protein (mg/100 mL)</td>
<td>63.51 ± 0.09</td>
<td>63.86 ± 0.01</td>
<td>63.46 ± 0.28</td>
<td>32.68 ± 0.01</td>
<td>25.38 ± 0.04</td>
<td>58.06 ± 0.18</td>
<td>50.67 ± 0.14</td>
</tr>
<tr>
<td></td>
<td>Serum aspartate aminotransferase activity (mU/mL)</td>
<td>39.61 ± 0.95</td>
<td>40.31 ± 0.29</td>
<td>40.01 ± 1.89</td>
<td>56.01 ± 0.47</td>
<td>65.31 ± 0.73</td>
<td>43.51 ± 0.22</td>
<td>58.21 ± 0.38</td>
</tr>
<tr>
<td></td>
<td>Serum alanine aminotransferase activity (mU/mL)</td>
<td>13.81 ± 0.51</td>
<td>14.41 ± 0.42</td>
<td>13.21 ± 0.51</td>
<td>22.21 ± 0.48</td>
<td>32.61 ± 0.71</td>
<td>17.51 ± 0.31</td>
<td>23.41 ± 0.22</td>
</tr>
</tbody>
</table>

Values are the mean ± S.E.M.; n = 10. * as compared to group 1, p < 0.05; † as compared to group 2, p < 0.05; ‡ as compared to group 3, p < 0.05; § as compared to group 4, p < 0.05; ¶ as compared to group 5, p < 0.05; # as compared to group 6, p < 0.05; †‡ as compared to group 7, p < 0.05.
changes could be due to amelioration in aflatoxin-induced histopathological changes in kidney.

The enzymes: serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) are present in the cytosol of the hepatocytes. The GPT is also localized in the mitochondria. Whenever liver hepatocytes are damaged, these enzymes are released into the blood. A significant increase in AST and ALT activities indicates the damage to the cytosol and also to mitochondria. The results obtained in the present study indicate significant increase in ALT and AST activities in the aflatoxin alone treated mice (Table 1). On the other hand, aflatoxin treatment with curcumin showed marked recovery. Similar results have been reported by Koul and Kapil (27) with CCl₄ and Trivedi (28) with hexachlorobenzene.

CONCLUSION

It can be concluded that curcumin, being an active component of turmeric, plays efficient role in ameliorating the toxicity induced by aflatoxin in serum of mice.

REFERENCES


Received: 26.09.2007