SHORT COMMUNICATION

CHRONIC TOXICITY STUDY OF PASPALUM SCROBICULATUM EXTRACT IN RATS

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INTRODUCTION

Dried ethanol extract of *Paspalum scrobiculatum* grain has powerful tranquillizing action in animals (1, 2). It has been successfully used as a major tranquillizer, in short-term clinical trials, in acutely agitated schizophrenic patients (3–7). These clinical trials were conducted on the basis of acute and subacute toxicity studies carried out by Bhide (8) in mice and dogs, and by Shah *et al.* (6) in rats and mice. To assess the safety of this extract in connection with long-term clinical trials, chronic toxicity study in rats was planned. The results are reported here.

MATERIALS AND METHODS

Fresh *Paspalum scrobiculatum* grain samples of proved potency (9) were kept in rectified spirit at room temperature for 15 days. Rectified spirit was decanted off, filtered and evaporated to dryness at room temperature. The thick viscous residue was used throughout this experiment. It was preserved at O°C.

Sixty albino rats (weight about 70 gm) of CDRI colony were divided into 3 equal groups each having 10 male and 10 female animals. Group I served as a control and received only gum acacia suspension. Animals of group II received 62 mg/kg (1.5 times the tranquillizing dose in rats) and those of group III received 125 mg/kg (3 times the tranquillizing dose in rats) of the extract. The extract was administered as freshly prepared gum acacia emulsion in water. All substances were administered to the animals by stomach tube every day, for 90 days.

The animals were observed daily for their general condition; the body weight was recorded at weekly intervals. Surviving animals were sacrificed after 90 days and hematological and biochemical tests of liver and kidney functions were conducted. Their tissues were examined for macroscopic changes and, tissue sections prepared by routine method (Haematoxylin-Eosin-Stain preparations) were examined under microscope.

RESULTS

After 90 days’ feeding of gum acacia suspension to the animals of the control group, their general health and behaviour appeared normal. Also, their food intake was normal and weight gain steady (Fig. 1).

After about 10 weeks of feeding of the drug, animals in groups II and III showed ataxia which was particularly marked immediately after administration of drug. It lasted for about 40 minutes and hind limbs were more affected. Mortality was about the same in control and
Fig. 1. Graph showing body weight of rats

- ▲ Control
- ○ Low dose
- ● High dose

Male rats
Female rats

Days
7 14 21 28 35 42 49 56 63 70 77 84 91

Fig. 1.

% Age mortality

- Male
- Female

Control Low dose High dose

Fig. 2.
low dose groups; it was somewhat less in the high dose group (Fig. II). Blood study details are given in Table 1.

Table 1

Average values of the various studies done in rats sacrificed after 90 days’ feeding schedule

<table>
<thead>
<tr>
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<th>High Dose Group</th>
<th>Low Dose Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>13.4 ± 0.41</td>
<td>13.1 ± 0.35</td>
<td>13.3 ± 0.32</td>
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<tr>
<td>White cell count</td>
<td>5,313.0 ± 172.0</td>
<td>4,918.0 ± 110.0</td>
<td>5,044.0 ± 128.0</td>
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<tr>
<td>Blood sugar</td>
<td>118.0 ± 8.1</td>
<td>104.0 ± 4.1</td>
<td>81.0 ± 2.1</td>
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<tr>
<td>Blood urea</td>
<td>37.2 ± 5.28</td>
<td>68.2 ± 6.2</td>
<td>43.8 ± 6.1</td>
</tr>
<tr>
<td>Serum Transaminase</td>
<td>35.2 ± 5.7</td>
<td>31.0 ± 3.4</td>
<td>35.0 ± 3.8</td>
</tr>
<tr>
<td>Serum proteins</td>
<td>5.06 ± 0.09</td>
<td>5.08 ± 0.19</td>
<td>4.38 ± 0.11</td>
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</table>

At autopsy, the animals were found to be free of parasites. No neoplasms were encountered. Lung infections of varying severity were seen in the majority of surviving animals. These ranged from solidification of the lung parenchyma by acute inflammatory exudate in very severe cases, to a few patchy areas showing aggregates of mononuclear and polymorphonuclear cells as well as clusters of large foamy cells with small nuclei (histiocytes) in mild cases. The lung changes were found nearly equally distributed in all the 3 groups. Sections of rest of the organs appeared normal under the microscope.

Discussion and Summary

In its early stage, work on natural products has to be necessarily conducted on crude extracts. Biological data on such crude preparations serve as the indispensable base line to results obtained on purified fractions. The dried ethanol extract of *Paspalum scrobiculatum* was used as such in the previous animal experiments and clinical trials (1—7). Therefore, it was important to use the same crude extract for this toxicity study, although it contained many other substances besides the tranquilizing principle.

No evidence of gross tissue toxicity in white CDRI rats was encountered after the administration of the drug in this study. The 2 doses of the extract used in this work are about 100 and 200 times the effective oral human dose. After 10 weeks of its administration, both doses produced ataxia in rats; this could be a cumulative extrapyramidal effect induced by the tranquilizing principle in the extract. Each rat in the high dose group received, in all, about 11 gm of the extract/kg body weight; which produced late retardation of weight gain.
The mortality, blood value changes and lung pathology are comparable in the control and extract treated groups. Therefore, those changes cannot be attributed to the administration of the extract. The histology of the remaining tissues was quite within the normal range. These facts suggest considerable safety margin in the use of the crude extract of *Paspalum scrobiculatum*.

**ACKNOWLEDGEMENT**

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**REFERENCES**