PROTECTIVE EFFECTS OF B.W. 501 C 67 AND B.W. 204 C 67 AGAINST LETHAL EFFECTS OF EXUDATES FROM BURNT RAT SKIN

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Received for publication October 26, 1971

Rocha e Silva and Rosenthal (1) have reported that the exudates from burnt rat skin contain histamine, bradykinin, adenosine derivatives and possibly serotonin and other as yet unidentified pharmacologically active and toxic substances. Hodson (2) has reported the peripheral antiserotonin activity of B.W. 501 C 67 (α-anilino-N-2-m-chlorophenoxypropyl acetamide monohydrochloride) and B.W. 204 C 67 (S-m-methylanilino-N-2-m-methoxy phenoxy propyl acetamide hydriodide) and Rao (3) reported on the presence of central antiserotonin activity of these compounds. Rao (4) also reported that two newer antihistaminic and antiserotonin compounds, cyproheptadine and BC 105, possess significant protective effect against the lethal effects of exudates from burnt rat skin. In the present communication, an attempt has been made to determine whether or not B.W. 501 C 67 and B.W. 204 C 67 have got any protective effect against the toxicity of the exudates.

MATERIALS AND METHODS

The method of Rocha e Silva and Rosenthal (1) was utilized to obtain the exudates. Albino rats weighing between 120 and 150 g were anaesthetized with nembutal sodium (30 mg/kg intraperitoneally) and then 30 ml of air was injected beneath the dorsal skin to raise a pouch of 7 × 4 × 3 cm. This done of the pocket was submerged in water at 95°C for 15 to 20 sec. After scalding, the animal was suspended by its paws and 5 ml of Tyrode's solution was injected into the pouch. The animal was then shaken for 2 min after which the fluid was withdrawn by syringe and needle. The washing was repeated at regular intervals after burning and a maximum of 5 washings were done to each animal. The fluids thus obtained were mixed and injected intraperitoneally into albino rats taken in groups of ten and the percentage mortality at three different dose levels were determined during the next 24 hr. Results were taken as control readings.

B.W. 501 C 67 and B.W. 204 C 67 were injected intraperitoneally in different doses one hour before administration of the exudate in a dose of 5 ml/100 g of body weight to each rat and at least three dose levels between 0 and 100% mortality were determined for each drug.
RESULTS

Table 1 shows the percentage mortality of rats when three different dose levels of the exudate were administered. A dose of 7.5 ml per 100 g of body weight was found to produce 100% mortality.

<table>
<thead>
<tr>
<th>Control dose of exudate (ml/100 g)</th>
<th>Number of animals</th>
<th>% mortality in 24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>5.0</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>7.5</td>
<td>10</td>
<td>100</td>
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**DISCUSSION**

Exudate obtained from the pouch after scalding was found to contain histamine, bradykinin, serotonin, adenosine derivatives and possibly other as yet unidentified toxic substances which contribute to the death of the animals (5). B.W. 501 C 67 and B.W. 204 C 67 are being developed as antihistaminic antiserotonin compounds (2). The fact that these compounds decreased the percentage mortality of the animals due to the lethal effects of exudates from burnt rat skin may be significant. It may, therefore, be anticipated that the histamine and serotonin contents of the exudates are the major cause of death in animals and the two compounds protect the animals due to their antihistaminic antiserotonin properties only. It may also be suggested that they have a protective action against bradykinin, adenosine derivatives or other yet unidentified substances. In acute toxicity studies, doses of up to 400 mg/kg given orally in rats produced no toxic effect or death (2). In clinical cases of extensive burns, antihistaminic and antiserotonin drugs are rarely used. Antihistaminic antiserotonin compounds are, therefore, possibly therapeutically important in the management of cases of extensive burns.

When the results of toxicity studies of B.W. 501 C 67 and B.W. 204 C 67 and their protective effects against the lethal effects of exudates from burnt rat skin are analysed, it is evident that, on the basis of efficacy, potency and safety, these compounds show sufficient promise to warrant further experimental and perhaps clinical trials in case of extensive burns.
SUMMARY

1. Two newer acetamidine Compounds, B.W. 501 C 67 and B.W. 204 C 67, which are being developed as antihistaminic antiserotonin agents, have been tested for their protective effect against mortality due to the exudates from burnt rat skin.

2. It has been observed that both compounds have significant protective action decreasing the percentage of mortality.

3. The significance of these findings and the possible therapeutic importance of antihistaminic antiserotonin agents in clinical cases of burns have been discussed.

Acknowledgement: The author is grateful to Prof. V.R. Rao, Principal, S.V. Medical College, Tirupati for his permission to undertake this research work and publication.

REFERENCES