LETTER TO THE EDITOR

SUBSTITUTED QUINAZOLONES AS ANTICONVULSANTS

Sir,

The discovery of 2-methyl-3-(o-toly)-4-quinazolone (methaqualone) and its anticonvulsant and hypnotic properties have aroused interest in the quinazolone heterocycle. The ability of quinazolone derivatives to show anticonvulsant, central nervous system depressant and monoamine oxidase inhibitory properties (1-5) prompted the synthesis (6-11) of some new 2-aryl-3-(5'-chloro-1'-benzophenone-2'-yl)-4-quinazolones, and evaluation of their anticonvulsant activity.

Anticonvulsant activity: This was determined against pentylenetetrazol-induced seizures (12) in albino mice of either sex weighing 20-25 g. The test compounds at a dose of 100 mg/kg were injected intraperitoneally to a group of 10 mice. Pentylenetetrazol (90 mg/kg) was injected subcutaneously 4 hr after the administration of the compounds. Mice were observed for 60 min for the occurrence of seizures. Animals free from even threshold convulsions were considered protected and their mortality was recorded after 24 hr.

All quinazolones at a dose of 100 mg/kg, ip afforded protection against pentylenetetrazol-induced seizures ranging from 20 to 80%. Maximum protection (80%) was observed with compound 5. The bromo (compound 2) and iodo (compound 3) substituents at position 6 in the quinazolone nucleus decreased the anticonvulsant activity compared with the parent compound (compound 1). A marked decrease in activity was seen when two chloro groups (compound 4) were introduced at position 6 and 8. However, the replacement of chloro groups by bromo groups (compound 5) produced the most potent anticonvulsant amongst the present series of the compounds. Iodo substitution at position 6 and 2-chlorophenyl group at position 2 of quinazolone nucleus, considerably decreased the anticonvulsant activity (to 20%) as in the case of compound 6. The presence of three chloro group (compound 7) enhanced the capacity of the compound to afford protection against pentylenetetrazol-induced seizures. All compounds reduced pentylenetetrazol-induced mortality during the 24 hr experimental period.
P-nitrophenyl substitution at position 2 and 6,8-Dichloro groups in substituted quinazolone (compound 8) showed 40% anticonvulsant activity which was comparatively lower than unsubstituted and bromosubstituted derivative.

Table 1 - 2-Aryl-3-(5'-Chloro-1'-Benzophenone-2'-yl)-4-Quinazolone and their anticonvulsant activity

<table>
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<tr>
<th>Sl No</th>
<th>X</th>
<th>X₁</th>
<th>Y</th>
<th>Yield</th>
<th>M.P.</th>
<th>Molecular</th>
<th>Anticonvulsant activity</th>
<th>Mortality after 24 hours</th>
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Values were taken in open capillaries and are uncorrected. The compounds were analysed for N and % error is within limit.

Mono and di-bromo substituted quinazolones (Compound 9,10) also showed 40% anticonvulsant activity with 20% mortality 24 hr after the injection of pentylenetetrazol. These values are lower in comparison with those observed with other analogues.
ACKNOWLEDGEMENTS

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