# EFFECT OF ANTI-INFLAMMATORY DRUGS ON CENTRAL EFFECTS OF BARBITURATES

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Experiments on albino mice showed that preliminary administration of amidopyrin, phenylbutazone, and certain of its $C_4$-substituted derivatives considerably increases the duration of hexobarbital sleep, and potentiates the central muscle-relaxant action of barbital and the anticonvulsant activity of phenobarbital.

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In this investigation the effect of amidopyrin, sodium salicylate, hydrocortisone, phenylbutazone and its $C_4$-derivatives with substitution of the radicals: o-carboxyanilinobenzyl (preparation No. 782), o-carboxyanilino-$\alpha$-thienyl (preparation No. 17), p-toluidino-parafluorobenzyl (preparation No. 17-K), and $\beta$-naphthylamino-$\alpha$-thienyl (preparation No. 13)* was studied on the sedative activity of hexobarbital, the anticonvulsant action of phenobarbital, and the central muscle-relaxant activity of barbital.

## EXPERIMENTAL METHOD

Experiments were carried out on 420 albino mice of both sexes weighing 20-30 g. The sedative effect was assessed by means of the 30-second lateral position test [4], the anticonvulsant activity from changes in the electric shock reaction [5], and the central muscle-relaxant action was determined by Dunham's method. The character of the observed potentiation of the combined substances was determined by Brody's method [3]. The preparations were injected intraperitoneally in the form of a suspension in 2% starch mucilage, and hexobarbital and sodium salicylate were given in aqueous solution. The anti-inflammatory substances were injected 1-3 h before the barbiturates.

*The synthesis was carried out under Professor N. S. Kozlov's direction in the Department of Chemistry of Perm' Agricultural Institute.

TABLE 1. Effect of Anti-Inflammatory Drugs on Central Effects of Barbiturates

| Anti-inflammatory drugs | Dose of anti-inflammatory drug (in mg/kg) | Sedative effect of hexobarbital (80 mg/kg)—duration of sleep (in min) with confidence limits | Anticonvulsant effect of phenobarbital (10 mg/kg)—% of animals protected | Central muscle-relaxant effect of barbital (70 mg/kg)—% of animals falling from rod |
|---|---|---|---|---|
| Barbiturate | | 21.5 ± 9.7 | 20 | 10 |
| Barbiturate + amidopyrine | 100 | 265 ± 45.5 | 70 | 70 |
| Barbiturate + preparation No. 782 * | 207 | 146 ± 18.7 | 60 | 70 |
| Barbiturate + phenylbutazone | 120 | 142 ± 14.8 | 60 | 60 |
| Barbiturate + salicylate | 200 | 110 ± 44.5 | 30 | 90 |
| Barbiturate + preparation No. 17-K | 203 | 74.5 ± 9.5 | 30 | 80 |
| Barbiturate + preparation No. 17 | 201 | 35.5 ± 3.3 | 30 | 40 |
| Barbiturate + preparation No. 13 | 210 | 34.5 ± 7.0 | 50 | 50 |
| Barbiturate + hydrocortisone | 10 | 33.2 ± 7.6 | 20 | 50 |

*Phenylbutazone and its derivatives were injected in equimolecular doses.

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## EXPERIMENTAL RESULTS

Amidopyrin, phenylbutazone, preparations Nos. 782 and 17-K, and sodium salicylate considerably increased the duration of hexobarbital sleep (Table 1), while amidopyrin and preparation No. 17-K also reduced ($P < 0.05$) the frequency of barbiturate hyperkinesia. In experiments carried out by Brody's method [3], the observed potentiation was found to be indirect and possibly dependent on changes in detoxication of hexobarbital in the liver. It accordingly appeared desirable to study the effect of anti-inflammatory drugs on the activity of barbiturates which undergo practically no breakdown in the liver (barbital), or which are only partially detoxicated in it, such as phenobarbital [1, 2].

Amidopyrin, preparations Nos. 13 and 782, and phenylbutazone potentiated the anticonvulsant action of phenobarbital, increasing the number of animals in which protection against the tonic extensor phase of an electroconvulsive fit was observed from 20 to 60-70%. The first two of these drugs also prolonged this effect from 60 min, when phenobarbital was given alone, to 210-390 min.

Under the influence of all the anti-inflammatory drugs tested the intensity of the central muscle-relaxant action of barbital increased considerably: 80-90% of the mice in this case were unable to stay on a rotating rod, while after administration of barbital alone, only 10% of the animals fell off the rod.

The results obtained indicate that the potentiation effect is not connected with any effect of the anti-inflammatory substances on inactivation of barbiturates in the liver.

## LITERATURE CITED


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