ANTIPYRETIC EFFECT OF GLYCYRRHETIC ACID AND IMIPRAMINE

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Many of the anti-inflammatory agents have been shown to possess antipyretic activity viz. acetyl salicylic acid, ACTH and cortisone (1). Since glycyrrhetic acid and imipramine have been shown to possess potent anti-inflammatory activity (2, 3), it was thought, therefore, worthwhile to investigate the antipyretic activity of these compounds.

METHODS

Healthy albino rats weighing 150-200 g were used in groups of six each. Normal rectal temperature was recorded by a clinical thermometer and its hourly variation was noted over a period of 4 hours at the beginning of the experiments. Pyrexia was produced by injecting 15% suspension of dried Brewer's yeast in 2% Gum acacia in normal saline subcutaneously at 5 p.m. and volume injected was 1 ml suspension per 100 g body weight according to the method of Gujral, Kohli, Bhargava and Saxena (4). However in our hands, a fairly stabilized temperature was obtained after 18 hours.

Glycyrrhetic acid and imipramine were injected in doses of 40 and 20 mg/kg i.p. respectively in pyretic rats, whereas, sodium salicylate was used as a reference standard in dose of 600 mg/kg of body weight. The temperatures were recorded at two hourly interval. The results were statistically analysed, and 'p' values of significance were found out.

RESULTS

Perusal of Table 1 indicates the effect of the subcutaneous injection of Brewer's yeast in albino rats. The mean temperature of apyretic rats was found to be 99.4 ± 0.19 . The mean temperature 18 hours after the injection was 101.9 ± 0.07 which was statistically significant ($p < 0.001$). At 20 and 22 hours the mean temperatures were 101.8 ± 0.15 and

TABLE 1. Pyrexia induced by Brewer's yeast.

Groups	Temperature (°F)	"p" value
A. Apyretic control	99.4 ± 0.19	—
B. Brewer's yeast induced pyrexia		
18 hr	101.9 ± 0.07	< 0.001
20 hr	101.8 ± 0.15	< 0.001
22 hr	101.9 ± 0.07	< 0.001

TABLE 2. Antipyretic effects of glycyrrhetic acid and imipramine.

Drugs	Dose mg/kg i.p.	Mean initial temp. of apyretic rats	Mean temp. of pyretic rats + SE (Control)	Mean temp. after drug treatment			
				2 hr	'p'	4 hr	'p'
Control	—	99.4±0.19	101.9±0.07	101.8±0.14	0.05	101.9±0.06	—
Sodium salicylate	600	99.6±0.08	101.6±0.14	99.4±0.14	0.001	99.3±0.18	0.001
Glycyrrhetic acid	40	99.2±0.12	101.6±0.15	99.0±0.30	0.001	99.0±0.22	0.001
Imipramine	20	99.6±0.06	101.6±0.21	101.6±0.28	—	101.9±0.19	0.8-0.09

TABLE 3. Hypothermic activity of glycyrrhetic acid and imipramine.

Drugs	Dose mg/kg	0 hr (Control)	2 hr	p	4 hr	p
Control	—	99.3±0.15	99.2±0.05	0.5~0.6	99.8±0.27	0.1~0.2
Glycyrrhetic acid	40	99.4±0.28	99.4±0.22	—	99.6±0.19	0.4~0.5
Imipramine	20	99.1±0.21	98.6±0.25	0.1~0.2	98.1±0.24	0.01~0.02

101.9±0.07 respectively and the values when compared with the control were found to be highly significant ($p<0.001$). However, the rise in temperature from 18 to 22 hours was constant and there was no significant difference.

The antipyretic effect of glycyrrhetic acid, imipramine and sodium salicylate are shown in Table 2.

The mean temperature values two and four hours after the pretreatment with sodium salicylate (600 mg/kg) were found to be 99.4±0.14 and 99.3±0.18 respectively as compared to the control mean value of 101.6±0.14 in the pyretic rats ($p<0.001$). Similarly glycyrrhetic acid (40 mg/kg) produced a significant fall in temperature from 101.6±0.15 to 99.0±0.30 and 99.0±0.22 at two and four hours ($p<0.001$). However, imipramine (20 mg/kg) did not show any antipyretic effect.

Table 3 shows the hypothermic activity of glycyrrhetic acid and imipramine. Glycyrrhetic acid did not show any hypothermic activity upto 4 hours in doses of 40 mg/kg whereas imipramine showed hypothermic activity at 4 hours ($p<0.01-0.02$).

DISCUSSION

Many non-steroidal and steroidal anti-inflammatory agents are known to possess antipyretic activity viz. indomethacin (5), salicylate, cortisone, desoxycorticosterone, ACTH (1). On the same basis non-steroidal imipramine and steroidal glycyrrhetic acid were tested for their antipyretic and hypothermic activities in the present study. Gujral, Kohli, Bhargava and Saxena (4) found the rise in temperature 15 hours after the subcutaneous injection of Brewer's yeast in albino rats. However, in our hands the rise in temperature was found 18 hours after the injection of Brewer's yeast. The validity of the same has been confirmed statistically at 18, 20 and 22 hours. The temperature remains fairly stabilized during these 4 hours without showing any significant variation. Glycyrrhetic acid showed almost similar antipyretic activity as is present in sodium salicylate (Table 2). However,

imipramine failed to show such an antipyretic response, although imipramine was found to possess hypothermic activity after 4 hours of its administration, the effect which was lacking in glycyrrhetic acid (Table 3).

The antipyretic and hypothermic effects of glycyrrhetic acid on temperature resemble with those of ACTH (2) which indicates the possible mode of action of the former mediated through pituitary adrenal axis. Structural resemblance of glycyrrhetic acid with steroids might be responsible for such a response *per se* or it might be by preserving endogenous corticoids (6).

SUMMARY

The effects of glycyrrhetic acid and imipramine on rectal temperature of normal and pyretic rats have been studied. Glycyrrhetic acid showed an antipyretic activity similar to that of sodium salicylate whereas imipramine is devoid of such a response. Imipramine could only show hypothermic effect in 4 hours, the response which was not shared by glycyrrhetic acid.

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