

Grossman (1968) it can be calculated that in dogs caerulein is less active than gastrin I or II on a molar basis.

Gastrin I was purchased from the American Gastroenterological Association, caerulein was kindly donated by Professor Bertaccini (Parma, Italy) and supplied as a methanolic extract from the skin of *Hyla caerulea* containing 55 µg/ml caerulein.

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On the mechanism of lipomobilizing effect of chlordiazepoxide

Previously, Arrigoni Martelli & Tóth (1968) have shown that chlordiazepoxide provokes hyperglycaemia possibly through an activation of adrenergic mechanisms. The potentiation of hyperglycaemia observed in rats treated with chlordiazepoxide and theophylline or with chlordiazepoxide and cyclic 3',5'-AMP led us to suppose that chlordiazepoxide, like theophylline (Butcher & Sutherland, 1962), interferes in some of the biochemical steps connecting the release of noradrenaline with phosphorylase activation. Since theophylline, through a blockade of phosphodiesterase, enhances lipolysis (Hynie, Krishna & Brodie, 1966), we decided to examine the effects of chlordiazepoxide on free fatty acid mobilization.

Female albino rats, Wistar strain, weighing about 250 g were used. Plasma free fatty acids (FFA) were determined according to Dole (1966). The experimental design and the results obtained are reported in Table 1. Chlordiazepoxide (40 mg/kg, i.p.) produced a sustained elevation of the plasma FFA levels; a similar effect was elicited by theophylline (20 mg/kg, i.p.).

The lipomobilizing effect of noradrenaline was potentiated by pretreatment of rats with chlordiazepoxide or with theophylline. Cyclic 3',5'-AMP (10 mg/kg, i.p.) had no effect on plasma FFA levels. When the same dose was given to rats pretreated with chlordiazepoxide the FFA levels rose about 3-fold. Likewise, in rats pretreated with theophylline, cyclic 3', 5'-AMP produced a significant elevation of plasma FFA. The

Table 1. *Effect of chlordiazepoxide and theophylline on plasma FFA*

1st treatment mg/kg	Time interval min	2nd treatment mg/kg	Time interval min	FFA μ -equiv/ml \pm s.e.*	
				Plasma level	Δ due to treatment
None	None	None	None	0.29 \pm 0.05	
Chlordiazepoxide, 40, i.p.	"	"	60	0.68 \pm 0.07	0.39 \pm 0.06
"	"	"	90	0.53 \pm 0.06	0.24 \pm 0.04
"	"	"	120	0.47 \pm 0.05	0.18 \pm 0.06
Theophylline, 20, i.p.	"	"	60	0.69 \pm 0.06	0.40 \pm 0.05
"	"	"	90	0.57 \pm 0.04	0.28 \pm 0.09
"	"	"	120	0.50 \pm 0.05	0.21 \pm 0.06
Noradrenaline, 0.05, s.c.	"	"	60	0.76 \pm 0.08	0.47 \pm 0.06
Chlordiazepoxide, 40, i.p.	30	Noradrenaline, 0.05, s.c.	60	1.23 \pm 0.12	0.94 \pm 0.11
Theophylline, 20, i.p.	30	Noradrenaline, 0.05, s.c.	60	1.31 \pm 0.06	1.02 \pm 0.05
Cyclic 3',5'-AMP 10, i.p.	—	—	60	0.30 \pm 0.04	0.01 \pm 0.003
Chlordiazepoxide, 40, i.p.	60	Cyclic 3',5'-AMP, 10, i.p.	60	0.85 \pm 0.09	0.56 \pm 0.07
Theophylline, 20, i.p.	60	Cyclic 3',5'-AMP 10, i.p.	60	0.86 \pm 0.09	0.57 \pm 0.08
Theophylline, 20, i.p.	30	Chlordiazepoxide, 40, i.p.	60	1.03 \pm 0.10	0.74 \pm 0.09
Chlordiazepoxide, 40, i.p.	30	Theophylline, 20, i.p.	60	0.97 \pm 0.08	0.68 \pm 0.07

* Mean from 12 rats.

lipomobilizing effect of chlordiazepoxide was almost double in rats pretreated with theophylline, and vice versa.

Noradrenaline raises the cyclic 3',5'-AMP and hence lipase activity: theophylline, by blocking phosphodiesterase, prevents the inactivation of cyclic 3',5'-AMP and hence of adipose tissue lipase (Hynie & others, 1966). The surprising similarity of the effects of chlordiazepoxide and theophylline on plasma FFA levels, like that observed on blood glucose levels (Arrigoni Martelli & Tóth, 1968), suggests that these two drugs act through a similar mechanism.

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