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EFFECT OF CHLORPROMAZINE ON INDUCTION OF DIFFERENT HEPATIC ENZYMES

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Abstract—Following a single high dose of intraperitoneal administration of chlorpromazine (50 mg/kg) into adult male albino rats, tyrosine-α-ketoglutarate transaminase (TKT) and tryptophan pyrrolase (TP) activity of rat liver are increased near about 3-fold within 5 hr whereas threonine dehydrase (TD) activity increases maximally within 2 hr. Actinomycin D (Act. D) inhibits the chlorpromazine induced stimulation of all the three enzymes.

THE ACTION of phenothiazine group of tranquillizer in animals is accompanied by increased adrenocortical secretions.[1–5] It has been further reported that several hepatic enzymes *viz.* alanine-α-ketoglutarate transaminase,[6,7] tyrosine-α-ketoglutarate transaminase[8](TKT) and tryptophan pyrrolase[9] etc. are elevated by adrenocorticosteroids. Previous work in this laboratory has shown some characteristic differences in the time course of induction of TKT by different types of tranquillizer drugs like reserpine, chlorpromazine, prochlorpromazine and trifluopromazine.[10] The present communication reports the effect of chlorpromazine (CPZ) administration on the relative responses in the activity of three different hepatic enzymes.

MATERIALS AND METHODS

Male albino rats weighing 90–110 g were used for the study and maintained on laboratory stock diet *ad lib.* Chlorpromazine (50 mg/kg), saline (control) and actinomycin D (50 μg/kg) were injected intraperitoneally. Rats were sacrificed at different time intervals.

Analytical procedures. Tyrosine-α-ketoglutarate transaminase was assayed as described previously,[10] by following the method of Chan and Cohen.[11] Tryptophan pyrrolase and threonine dehydrase activity were measured according to the method of Mehler and Knox[12] and Pitot *et al.*[13] respectively. Protein was estimated by the biuret method.[14]

RESULTS AND DISCUSSION

The results in Table 1 illustrate the effect of chlorpromazine administration on the activity of three different enzymes of rat liver. In agreement with the previous findings,[10] the administration of CPZ gives a maximum response within 5 hr by 3-fold increase in the activity of TKT and TP. In contrast, threonine dehydrase activity is increased maximally in 2 hr. In all the cases the increased activity of the enzyme falls near the basal value within a few hours. From the nature of CPZ induced stimulation in the activity of the enzymes, it may be concluded that TKT and TP respond through

Table 1. Activity of rat liver enzymes in control and drug treated conditions

Time of sacrifice (hr)	Enzyme activity								
	TKT (μmoles of p^{HPP} formed/mg protein/hr)			TP (μmoles of Kynurenine/mg protein/hr)			TD (α-ketoglutarate/mg protein/$\frac{1}{2}$ hr)		
	Control	Effect of CPZ	Effect of CPZ + Act. D	Control	Effect of CPZ	Effect of CPZ + Act. D	Control	Effect of CPZ	Effect of CPZ + Act. D
2	35 ± 2	66 ± 5	31 ± 3	1·63 ± 0·34	3·27 ± 0·54	1·62 ± 0·26	3·00 ± 0·12	5·25 ± 0·14	3·20 ± 0·08
5	33 ± 2	110 ± 7	35 ± 6	1·64 ± 0·38	4·92 ± 0·47	1·60 ± 0·12	3·00 ± 0·24	3·13 ± 0·05	3·00 ± 0·02
14	36 ± 4	72 ± 6	32 ± 2	1·62 ± 0·25	1·64 ± 0·42	1·64 ± 0·34	3·25 ± 0·32	3·05 ± 0·11	3·15 ± 0·12

N.B. Control rats were injected with equal volume of saline. Actinomycin D (50 μg/kg) and CPZ (50 mg/kg) were injected simultaneously.
Results are expressed as the mean of five experiments ±S.D.

a common type of mechanism. The response of threonine dehydrase activity on the other hand, suggests the probable involvement of a different control mechanism regulating the level of this enzyme.[15,16]

Another point worth noting, is that in all the cases, the increased enzyme activities were found to be abolished with simultaneous administration of actinomycin D, suggesting that the CPZ induced increase in hepatic enzyme activity is dependent on concomitant RNA synthesis.[17]

Further studies may elucidate the pharmacological action of this drug in relation to the selective response of different hepatic enzymes.

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