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EFFECT OF CANNABIS EXTRACT, Δ^9-TETRAHYDRO-CANNABINOL AND LYSERGIC ACID DIETHYLAMIDE ON RAT LIVER ENZYMES

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Abstract—The effect of intraperitoneal administration of cannabis extract, Δ^9-tetrahydrocannabinol (THC) and lysergic acid diethylamide (LSD), both at high (50 mg/kg, 100 mg/kg and 100 μg/kg respectively) and low (10 mg/kg, 10 mg/kg and 10 μg/kg respectively) doses, on the rat liver tyrosine α-ketoglutarate transaminase and tryptophan pyrrolase activity was studied and found that cannabis extract and Δ^9-tetrahydrocannabinol, but not LSD, increased the above two enzyme activities after 6 hr of injection.

Δ^9-TETRAHYDROCANNABINOL (Δ^9-THC), the major active component of cannabis[1–5] and lysergic acid diethylamide (LSD) are the well-known psychotomimetic agents. Isbell and Jasinski,[6] while making a comparative study of Δ^9-THC and LSD, found that the objective effects of these two agents differed markedly and that patients tolerant to LSD were not cross-tolerant to THC indicating that the mental effects of the two drugs are probably mediated by different mechanisms. Holtzman *et al.*[7] and Pal and Ghosh[8] have also concluded that these two psychotomimetic agents affect the metabolism and/or turn over of 5-hydroxytryptamine in a different manner. It is also well-known that the action of several psychopharmacological agents in animals is accompanied by increased adrenocortical hyperactivity[9–11] with concomitant elevations in the level of several hepatic enzymes.[12–15] Although the mechanism of the different psychotropic drug action in these inductions still remains to be elucidated, the present study mainly deals with the comparative effect of the administration of cannabis extract, Δ^9-THC and LSD on the activities of two liver enzymes, tyrosine-α-ketoglutarate transaminase (TKT) and tryptophan pyrrolase (TPO).

MATERIALS AND METHODS

Four groups of adult male albino rats, weighing about 100–130 g, were used in this experiment. The first group was injected intraperitoneally with suspension of cannabis extract (4·2% Δ^9-THC content) at doses (50 and 10 mg/kg); second group with suspension of pure Δ^9-THC at doses (100 and 10 mg/kg) and the third group with LSD-25 solution of doses (100 and 10 μg/kg) respectively. The last group, used as control, received the saline–tween vehicle in equivalent volume by the same route. The doses of cannabis extract reported in this study were based solely on the total amount of Δ^9-isomer of THC content. The tyrosine-α-ketoglutarate transaminase activity was determined by the method of Chan and Cohen,[16] as modified by Pal, Ray and Ghosh.[15] Tryptophan pyrrolase activity was assayed by the method of Knox and Auerbach.[17] The protein was estimated by the biuret method.[18]

RESULTS AND DISCUSSION

As shown in the Table 1, both high and low doses of cannabis extract as well as of Δ^9-THC, within 6 hr of administration, increased significantly the activity of TKT and TPO in rat liver; but LSD under similar conditions of study, showed no significant change in the activity of the said enzymes. It was further noted that within the same dose range, cannabis extract was more effective than pure Δ^9-THC, towards increasing the activities of TKT and TPO.

TABLE 1. EFFECT OF CANNABIS EXTRACT, Δ^9-THC AND LSD ON LIVER ENZYMES

Treatment	Dosage*	Tryptophan pyrrolase†	Tyrosine α-keto-glutarate transaminase‡
Control (Saline–tween)		0·89 ± 0·06	9·52 ± 0·65
Cannabis extract	10 mg/kg	1·66 ± 0·07	20·32 ± 1·02
	50 mg/kg	2·38 ± 0·13	28·26 ± 3·78
Δ^9-THC	10 mg/kg	1·63 ± 0·03	11·72 ± 0·18
	100 mg/kg	2·18 ± 0·07	20·03 ± 0·44
LSD	10 μg/kg	0·88 ± 0·02	8·41 ± 0·73
	100 μg/kg	1·02 ± 0·04	9·78 ± 0·24

Results expressed in mean ± S.E.M.

* The dose of cannabis extract are expressed in terms of the total content of Δ^9-isomer of THC. Activity was measured 6 hr after administration.

† Specific activity expressed in μmole of kynurenine formed/g protein/hr.

‡ Specific activity expressed in μmole of *p*-hydroxyphenylpyruvate formed/mg protein/hr.

The results in the present study suggest that cannabis extract and its active com ponent, Δ^9-THC, increase the liver TKT and TPO activity like reserpine and other psychotropic drugs,[12–15] but LSD fails to show such effect on the said hepatic enzymes. Hence it is probable that the psychotropic action of LSD and Δ^9-THC on liver enzymes may be mediated through different mechanisms. Since the enhanced activity of the pituitary-adrenocortical axis is implicated in the increased hepatic enzymes level[10,11] it will be of further interest to study the effect of Δ^9-THC and LSD in terms of the neurohormonal factors involved in regulating the hepatic enzymes activity.

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