bidiol, 1 mg/kg unknown substances) i.p. in different vehicles to male rats in order to get some information about the influence of these agents. Onset of hypothermia was rapid in propylene glycol (30 Vol. %) and polyethylene glycol (60 Vol. %) and somewhat delayed in cremophor (10 %). No decrease in body temperature was observed after cannabis in rape oil. Cannabis in rape oil enhanced hexobarbitone sleeping time up to four days following a single injection. Using the other vehicles the effect lasted two days at most. Similar the route of administration is of interest. Experiments are in progress to determine pharmacological response by different routes.

Interaction of cannabis with other drugs seems to be important in view of polytoxicomania. We studied the effect of cannabis given one hour prior i.p. on the LD_{50} of various agents (see table). LD_{50} values are estimations by the method of Speerman and Kärber. Cannabis enhances the toxicity of morphine and pentobarbitone, decreases the toxicity of *d*-amphetamine sulfate. Almost no effect can be detected in ethanol LD_{50}. The effect on amphetamine toxicity is less pronounced after 8 day-pretreatment with cannabis.

	Control LD_{50} 1 h after 10 % cremophor 0.2 ml/100 g	LD_{50} 1 h after i.p. application of cannabis extract (25 % Δ^9-THC)	
		40 mg/kg = 10 mg/kg THC	80 mg/kg = 20 mg/kg THC
d-Amphetamine sulfate, s.c.	17 mg/kg	54 mg/kg	66 mg/kg
Pentobarbitone, s.c.	108 mg/kg	73 mg/kg	64 mg/kg
Morphine sulfate, s.c.	159 mg/kg	94 mg/kg	67 mg/kg
Ethanol, p.o.	10.9 g/kg	8.4 g/kg	8.6 g/kg

L. MAITRE

Biological Research Laboratories of the Pharmaceutical Division of Ciba-Geigy Limited, Basle, Switzerland

Effects of some cannabinols on biosynthesis of brain amines and on pituitary response in the rat

Δ^9-Tetrahydrocannabinol (Δ^9-THC), Δ^8-tetrahydrocannabinol (Δ^8-THC) and dimethylheptyltetrahydrocannabinol (DMHP) were injected i.p. into male albino rats (190—220 g body weight) as suspensions in physiological saline containing 6.5 % Tween 80. The effects of single injections (10—30 mg/kg) on catecholamine biosynthesis and on serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) concentrations were studied in the

whole brain or in selective brain regions (C. striatum, hypothalamus). The biosynthesis of ^{3}H-dopamine and ^{3}H-noradrenaline from intravenously injected ^{3}H-tyrosine was enhanced in the whole brain by all three cannabinols. Concomitantly an increased concentration of ^{3}H-dihydroxyphenylacetic acid (DOPAC) was found. DMHP was more active than Δ^8 or Δ^9-THC, but no qualitative differences were observed. Biosynthesis was also studied *in vitro* with slices of C. striatum and of hypothalamus obtained from rats pretreated with these cannabinols. Measurements of tritiated water, noradrenaline and dopamine formed from ^{3}H-tyrosine added to the incubation medium showed a particular enhancement of tyrosine hydroxylation in the C. striatum by Δ^9-THC and in the hypothalamus by DMHP. No striking effects on 5-HT and 5-HIAA concentrations were observed.

All three cannabinols elevated plasma corticosterone and at the same time lowered the cholesterol ester content of the adrenals in intact rats but not after hypophysectomy. Δ^9-THC (30 mg/kg) displayed a longer duration of action than the other two analogs. It increased the concentration of plasma free fatty acids for at least two hours.

These results indicate that the cannabinols enhance noradrenaline and dopamine turnover in the rat brain most probably by stimulating tyrosine hydroxylase activity. On the other hand the cannabinols obviously stimulate the pituitary gland to release ACTH as demonstrated by the adrenal and lipolytic activities.

C. J. MIRAS

Department of Biological Chemistry, Goudi, Athens, (609), Greece

The effect of hashish on noradrenaline concentration and uptake in the brain

1. Hashish extract was injected i.p. into rabbits. Ninety minutes following the injection the animals were killed and noradrenaline (NA) content of various parts of the brain estimated fluorometrically.

It was found that hashish extract causes changes in the amine content of the brain which vary both in magnitude and sign, depending upon the particular area examined. Thus endogenous NA content of the quadrigeminal area and hypothalamus postero-superior increased significantly while that of cerebellum was inversely affected in the hashish treated animals.

2. An investigation of the NA content of hypothalamus in hashish sublimate treated animals was carried out using histochemical fluorescence