Acknowledgement—The technical assistance of Eileen F. Bostwick and Mary Eddy is gratefully acknowledged.

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REFERENCES

1. J. S. BAXTER and J. M. YOFFE, *J. Anat.* **82,** 189 (1948).
2. M. WACHSTEIN and M. BRADSHAW, *J. Histochem. Cytochem.* **13,** 44 (1965).
3. C. M. EDELMANN, JR. and A. SPITZER, *J. Pediat.* **75,** 509 (1969).
4. B. RENNICK, B. HAMILTON and R. EVANS, *Am. J. Physiol.* **201,** 743 (1961).
5. J. B. HOOK, H. E. WILLIAMSON and G. H. HIRSCH, *Can. J. Physiol. Pharmac.* **48,** 169 (1970).
6. G. H. HIRSCH and J. B. HOOK, *Science, N.Y.* **165,** 909 (1969).
7. G. H. HIRSCH and J. B. HOOK, *J. Pharmac. exp. Ther.* **171,** 103 (1970).
8. G. H. HIRSCH and J. B. HOOK, *J. Pharmac. exp. Ther.* **174,** 152 (1970).
9. G. H. HIRSCH, D. F. COWAN and J. B. HOOK, *Proc. Soc. exp. Biol. Med.* **137,** 116 (1971).
10. H. F. CSERR, *Physiol. Rev.* **51,** 273 (1971).
11. D. W. BIERER and S. R. HEISEY, *Brain Res.* **46,** 113 (1972).
12. L. S. HOLLOWAY, JR. and S. CASSIN, *Am. J. Physiol.* **223,** 507 (1972).
13. R. J. CROSS, and J. V. TAGGART, *Am. J. Physiol.* **161,** 181 (1950).
14. H. W. SMITH, N. FINKELSTEIN, L. ALOMINOSA, B. CRAWFORD and M. GRABER, *J. clin. Invest.* **24,** 388 (1945).
15. R. G. D. STEEL, and J. H. TORRIE, *Principles and Procedures of Statistics*, p. 481. McGraw-Hill, New (1960).

Biochemical Pharmacology, Vol. 23, pp. 758–759. Pergamon Press, 1974. Printed in Great Britain.

Potentiating effect of cannabidiol on Δ^9-tetrahydrocannabinol-induced changes in hepatic enzymes

(*Received* 10 *April* 1973; *accepted* 23 *August* 1973)

IN RECENT years, several observations have been made indicating that the pharmacological and behavioural effects of Δ^9-tetrahydrocannabinol (Δ^9-THC), the principle active component of cannabis,[1–3] are influenced to a great extent by the other major components e.g. cannabidiol, cannabinol etc. present in the cannabis preparations.[4–6] Karniol and Carlini[6] observed that Δ^9-THC content by itself did not explain the biological activity of different Brazilian cannabis samples. Previous reports made from this laboratory[7,8] indicated that using the same dosages in terms of Δ^9-THC content, cannabis extract was in all cases found to be more active in biochemical response than pure Δ^9-THC. The present report deals with the effect of cannabidiol (CBD) on Δ^9-THC-induced activities of two hepatic enzymes, tyrosine α-keto glutarate transaminase (TKT) and tryptophan pyrrolase (TPO), of rats.

In the present experiment, the pure Δ^9-THC and cannabidiol (CBD) used, were provided by the United Nations Narcotics Laboratory, Geneva and the National Institute of Mental Health, Washington, U.S.A., respectively.

Four groups of adult male albino rats weighing about 100–120 g were used in this experiment. The first group was injected intraperitoneally (i.p.) with the suspension of pure Δ^9-THC at doses 5 mg/kg and 25 mg/kg, the second group with the suspension of pure CBD at doses 2 mg/kg and 10 mg/kg and the third group with Δ^9-THC and CBD simultaneously at doses 5 mg/kg + 2 mg/kg and 25 mg/kg + 10 mg/kg respectively. The control group received the saline tween vehicle in equivalent volume by the same route. Activities of tyrosine α-ketoglutarate transaminase (TKT) and tryptophan pyrrolase (TPO) and the protein concentration were determined as previously described.[7]

Table 1 shows that the intraperitoneal administration of Δ^9-THC (5 mg/kg and 25 mg/kg), significantly increased the activity of hepatic enzymes, tyrosine-α-ketoglutarate transaminase (TKT) and tryptophan pyrrolase (TPO), of rat. The administration of cannabinol (CBD) (2 mg/kg and 10 mg/kg) alone did not produce any significant changes in the activities of the above two enzymes under similar conditions of treatment. On the other hand, when CBD was administrated along with Δ^9-THC, the activities of the two enzymes were significantly increased from 30 to 100 per cent corresponding to their respective controls. The results of the present finding indicate that while CBD alone has no effect it can potentiate the effect of Δ^9-THC on the induced TKT and TPO activities in liver.

TABLE 1. EFFECT OF Δ^9-TETRAHYDROCANNABINOL AND CANNABIDIOL ON LIVER TRYPTOPHAN PYRROLASE AND TYROSINE α-KETO GLUTARATE TRANSAMINASE

Treatment	Dosage* (mg/kg body wt)	Tryptophan pyrrolase†	Tyrosine α-keto glutarate transaminase‡
Control (saline-tween)	—	0·808 ± 0·07	8·28 ± 0·45
Δ^9-THC	5	1·17 ± 0·09	10·00 ± 0·98
	25	1·75 ± 0·12	15·75 ± 0·87
CBD	2	0·785 ± 0·06	8·40 ± 0·58
	10	0·990 ± 0·04	10·81 ± 0·65
Δ^9-THC + CBD	5 + 2	1·45 ± 0·06	19·23 ± 1·02
	25 + 10	1·98 ± 0·15	24·16 ± 1·12

* Δ^9-THC and CBD were injected simultaneously.
† Specific activity expressed in μmoles of kynurenine formed/g of protein/hr.
‡ Specific activity expressed in μmoles of *p*-hydroxyphenyl pyruvate formed/mg of protein/hr.
Results expressed in mean ± S.E.M. of 12 determinations.

From the present observations along with our earlier report[7,8] it may be stated that the potentiating effect of CBD on Δ^9-THC induced activities of two liver enzymes may be explained by either: (a) inhibition of metabolism of Δ^9-THC or its more active metabolites and thereby maintaining a higher concentration of Δ^9-THC or its active metabolite within the system for a longer time; and/or (b) by changing the cellular permeability and thereby sensitizing the site of action of Δ^9-THC within the system.

Acknowledgements—Our best thanks are due to Dr. Olav J. Braenden, Narcotic Division, United Nations, Geneva and to Dr. Monique C. Braude of National Institute of Mental Health, Washington, U.S.A. for kindly supplying us the pure Δ^9-THC and CBD, used for the present investigation.

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REFERENCES

1. R. MAECHOULAM, *Science, N.Y.* **168,** 1159 (1970).
2. L. E. HOLLISTER, *Nature, Lond.* **227,** 968 (1970).
3. L. E. HOLLISTER, R. K. RICHARDS and H. H. GILLESPIE, *Clin. Pharmac. Ther.* **9,** 783 (1968).
4. G. JONES and R. G. PERTWEE, *Br. J. Pharmac.* **45,** 375 (1972).
5. W. D. M. PATON and R. G. PERTWEE, *Br. J. Pharmac.* **44,** 250 (1972).
6. G. K. KARNIOL and E. A. CARLINI, *J. Pharm. Pharmac.* **24,** 833 (1972).
7. M. K. PODDAR and J. J. GHOSH, *Biochem. Pharmac.* **21,** 3301 (1972).
8. M. K. PODDAR and J. J. GHOSH, *Science and Culture* **38,** 377 (1972).