FURNER, R. L., MCCARTHY, J. S., STITZEL, R. E. & ANDERS, M. W. (1969). *J. Pharmac. exp. Ther.*, **169**, 153–158.
KNABE, J. & KRÄUTER, R. (1965). *Arch. Pharm.*, **298**, 1–4.
ROWLAND, M. (1972). *J. pharm. Sci.*, **61**, 70–74.
RUMMEL, W., BRANDENBURGER, U. & BÜCH, H. (1967). *Med. Pharmac. exp.*, **16**, 496–504.
WAHLSTRÖM, G. (1966). *Life Sci.*, **5**, 1781–1790.
WAHLSTRÖM, G., BÜCH, H. & BUZELLO, W. (1970). *Acta pharmac. tox.*, **28**, 493–498.

Reduction of audiogenic seizure by Δ^8- and Δ^9-tetrahydrocannabinols

That marihuana extract exerts an anticonvulsant effect in rats was first reported by Loewe & Goodman (1947), and in 1971 Sofia, Soloman & Barry reported that Δ^9-tetrahydrocannabinol (Δ^9-THC) protects mice against minimal and maximal electroshock convulsions. We have found that Δ^9-THC possesses an anticonvulsant effect in audiogenic seizure-susceptible rats (Man & Consroe, 1973) and we now present evidence that Δ^8-tetrahydrocannabinol (Δ^8-THC) also has antiseizure activity against sound-induced convulsions. Additional data on the anticonvulsant property of Δ^9-THC is also included and a comparison has been made of the relative anticonvulsive potency of the two compounds.

Female rats, 180 to 195 g from the University of Arizona colony of audiogenic seizure-susceptible rats, were screened several days before the experiment in a sound chamber and ranked on audiogenic response score; animals with scores of 5 or higher were used for the experiment. The audiogenic response score, which ranges from 0 (absence of seizure) to 9 (maximal seizure), and the audiogenic testing procedure have been described by Jobe, Picchioni & Chin (1973). The tetrahydrocannabinols were prepared as stable emulsions with 10% polysorbate 80 (Tween 80) in saline according to Phillips, Turk & Forney (1971). The emulsions or vehicle was injected via a lateral tail vein in equivalent volumes and tests for audiogenic seizure were made 30 min later.

In doses of 1·25, 2·5 and 5 mg kg^{-1} Δ^8-THC caused significant reductions in seizure severity, i.e., decreases in the response score (Fig. 1A). Additional statistical evaluation of the data revealed that the decreases in the scores are dose-related ($F = 3{\cdot}5$, df $= 29$, $P < 0{\cdot}05$). Identical graded doses of Δ^9-THC caused similar significant

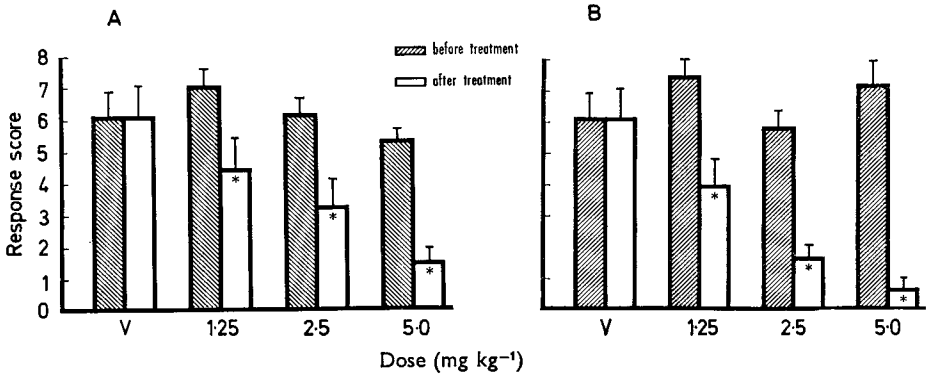

FIG. 1A. Effect of Δ^8-tetrahydrocannabinol (Δ^8-THC) on the audiogenic response score. Each bar represents the mean response of 10 animals; the verticle line represents ± standard error of the mean. An asterisk denotes statistically significant difference from corresponding control value, i.e., before treatment (Student *t*-test, $P < 0{\cdot}05$). v = 10% polysorbate 80-saline vehicle.

B. Effect of Δ^9-tetrahydrocannabinol (Δ^9-THC) on the audiogenic response score. Each bar represents the mean response of 10 animals; the verticle line represents ± standard error of the mean. An asterisk denotes statistically significant difference from corresponding control value, i.e., before treatment (Student *t*-test, $P < 0{\cdot}05$). v = 10% polysorbate 80-saline vehicle.

reductions in the score (Fig. 1B). These decreases are also dose-related ($F = 8{\cdot}21$, $df = 29$, $P < 0{\cdot}01$). The 10% polysorbate 80-saline vehicle has no effect on the severity of audiogenic seizure, as indicated by lack of change in score (Fig. 1 A, B).

The median effective dose (ED50) for complete suppression of audiogenic seizure was determined for Δ^8- and Δ^9-THC according to the method of Litchfield & Wilcoxon (1949). The ED50 and corresponding 95% fiducial limits for Δ^8-THC and Δ^9-THC are 6·5 mg kg^{-1} (3·5 — 11·8) and 3·3 mg kg^{-1} (2·0 — 5·5), respectively. Despite the fact that the ED50 of Δ^8-THC is almost twice that of Δ^9-THC, statistical comparison of the relative potency of the two tetrahydrocannabinols (Litchfield & Wilcoxon, 1949) indicate that the ED50s are not significantly different from each other ($P > 0{\cdot}05$).

The data presented clearly show that Δ^8-THC and Δ^9-THC have anticonvulsive activity and that such activity is dose-related. Furthermore, the anticonvulsant potencies for the two cannabinols are similar in the test system used.

The Δ^8- and Δ^9-THC was provided through the courtesy of the FDA-NIMH psychotomimetic agents advisory committee. Partial support of these studies was provided by NIMH Grant IR01–MH 23414–01.

Department of Pharmacology and Toxicology,
College of Pharmacy,
University of Arizona,
Tucson, Arizona 85721 U.S.A.

PAUL F. CONSROE
DOREEN P. MAN
LINCOLN CHIN
ALBERT L. PICCHIONI

March 11, 1973

REFERENCES

JOBE, P. C., PICCHIONI, A. L. & CHIN, L. (1973). *J. Pharmac. exp. Ther.*, **184**, 1–10.
LITCHFIELD, J. T. & WILCOXON, F. (1949). *Ibid.*, **96**, 99–113.
LOEWE, S. & GOODMAN, L. S. (1947). *Fedn Proc. Fedn Am. Socs exp. Biol.*, **6**, 352.
MAN, D. P. & CONSROE, P. F. (1973). *J. Int. Res. Comm.*, **1**, No. 1, 12.
PHILLIPS, R. N., TURK, R. F. & FORNEY, R. B. (1971). *Proc. Soc. exp. Biol. Med.*, **136**, 260–263.
SOFIA, R. D., SOLOMON, T. A. & BARRY, H. (1971). *Pharmacologist*, No. 2, 246.

The fluorescence of paracetamol—a re-examination

During a recent literature search on the physical and chemical properties of paracetamol, it became apparent that the only paper in which the fluorescent properties of this pharmaceutically important compound had been reported in any depth was that of Nang & Pitet (1965), although Child, Bedford & Tomich (1962) had earlier described paracetamol as fluorescent.

In view of the paucity of published work on the fluorescence of paracetamol, attempts were made in our laboratories to repeat some of the work of Nang & Pitet.

Freshly prepared solutions of paracetamol B.P. in 10^{-3}M sodium hydroxide (3×10^{-3}M), in 1% aqueous ethanol (50 μg ml^{-1}), and in ethanol (3×10^{-3}M) were examined for fluorescence with a Baird Fluorispec SF1 spectrofluorimeter equipped with an EMI 9781B photomultiplier. With the emission monochromator set at 400 nm, the excitation monochromator was adjusted until a maximum meter response was noted. With the excitation monochromator set at this maximum, the emission monochromator was adjusted to a maximum meter response. The fluorescence excitation and emission spectra were then recorded in a conventional manner.

For both the alkaline and aqueous ethanol solutions of paracetamol, a very weak emission was observed at 405 nm with an excitation maximum at 355 nm. An identical response was obtained from the solvents alone. Further examination showed