

The effect of Δ^1 -tetrahydrocannabinol on the noradrenaline and dopamine content of the brain and heart of the rat

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Female Wistar rats weighing 250 to 300 g were treated with either an aqueous solution of Tween 80 (25 mg/kg, orally) or Δ^1 -THC (10 mg/kg) in Tween 80, 60 min before being killed. The brain and heart were quickly removed, washed free of

($P < 0.001$) and the difference between Tween 80 and Δ^1 -THC in Tween 80 is significant ($P < 0.01$). These results indicate that Δ^1 -THC reduced the net DA levels of the heart and brain.

Δ^1 -THC caused a concentration-related inhibition of [3 H]-(-)-noradrenaline ([3 H]-NA) uptake in the isolated perfused heart of the rat (Graham, Lewis & Li, 1974a). The amount of tritium released upon transmural stimulation of the rat vas deferens pre-incubated with [3 H]-NA was also reduced in a dose-dependent fashion by Δ^1 -THC (Graham, Lewis & Li, 1974b). The failure of Δ^1 -THC to alter net NA levels in the heart does not exclude alterations in turnover.

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Table 1 Effects of orally administered Tween 80 (25 μ g/kg) and Δ^1 -THC (10 mg/kg) in Tween 80 on the noradrenaline (NA) and dopamine (DA) content of the brain and heart of the rat, expressed as ng/g tissue \pm s.e. mean; n , number of rats used

Tissue		Control	n	Tween 80	n	Δ^1 -THC + Tween 80	n
Brain	NA	286 \pm 12	12	184 \pm 26 Tw < C**	10	186 \pm 15 THC < C*	11
	DA	499 \pm 4	12	444 \pm 24	10	344 \pm 17 THC < C*	11
Heart	NA	506 \pm 32	15	487 \pm 72	12	477 \pm 34	12
	DA	468 \pm 34	13	311 \pm 60 Tw < C***	11	26 \pm 2 THC < C* THC < Tw*	12

Student's t test, comparison of control values (c) with Tween 80 (Tw) and with Δ^1 -THC in Tween 80 (THC); also of Tw v. THC.

* $P < 0.001$; ** $P < 0.01$; *** $P < 0.05$.

blood and transferred to liquid nitrogen. The noradrenaline (NA) and dopamine (DA) contents were assayed by the photofluorimetric methods of Haggendal (1963) and Carlsson & Waldeck (1958) respectively and expressed as ng/g wet wt of tissue.

Oral Tween 80 caused a reduction ($P < 0.01$) in the NA content of the whole brain as did the combination of Δ^1 -THC and Tween 80 ($P < 0.001$). The effects of the two treatments were not significantly different. Neither Tween 80 nor Δ^1 -THC in Tween 80 had an effect on the NA content of the whole heart. Tween 80 alone caused a significant reduction ($P < 0.05$) in the DA content of the heart, but a non-significant reduction in the brain. However, the combination of Δ^1 -THC and Tween 80 produced marked decreases in the DA level in both heart and brain

References

- CARLSSON, A. & WALDECK, B. (1958). A fluorimetric method for the determination of dopamine (3-hydroxytryptamine). *Acta physiol. scand.*, **44**, 293-298.
- GRAHAM, J.D.P., LEWIS, M.J. & LI, D.M.F. (1974a). The effect of Δ^1 -tetrahydrocannabinol on the uptake of [3 H]-(-)-noradrenaline by the isolated perfused heart of the rat. *Br. J. Pharmac.* (in press).
- GRAHAM, J.D.P., LEWIS, M.J. & LI, D.M.F. (1974b). The effect of Δ^1 -tetrahydrocannabinol on the release of [3 H]-(-)-noradrenaline from the isolated vas deferens of the rat. *Br. J. Pharmac.* (in press).
- HAGGENDAL, J. (1963). An improved method for fluorimetric determination of small amounts of adrenaline and noradrenaline in plasma and tissues. *Acta physiol. scand.*, **59**, 242-254.