

An intravenous formulation of Δ^9 -tetrahydrocannabinol using a non-ionic surfactant

The suitability of a mixed solvent system of ethanol-polyethoxylated vegetable oil (PEVO)* and physiological saline (5:5:90) previously used for the solubilization of two antineoplastic nitrosources (Davignon, Wood & Craddock, 1972), has been evaluated for solubilization of Δ^9 -tetrahydrocannabinol (Δ^9 -THC). Appropriate amounts of Δ^9 -THC (as a 10 mg ml⁻¹ solution in ethanol, stored at 4°) were evaporated to dryness under nitrogen in the dark. Equal volumes of ethanol and PEVO were added either sequentially or as a mixed solvent and then agitated and the solution further diluted with 9 volumes of physiological saline. The resulting solutions were clear, tan coloured and contained 0.5–10 mg of Δ^9 -THC ml⁻¹.

The utility of this formulation depends to a large extent on the pharmacological effects of PEVO and ethanol. Haemolysis and hypotension have been associated with Tween-type surfactants (Krantz, Carr & others, 1948). Tween-induced hypotension is a serious problem in canines and appears related to histamine release. In other animals and man this effect is slight or absent (Krantz & others, 1948). Although PEVO is essentially not haemolytic (Macek, 1963), similar species differences in susceptibility to hypotension have been observed (Schaepfi & Phelan, 1972).

We administered the vehicle alone and with Δ^9 -THC intravenously to New Zealand rabbits (1.3–1.6 kg). Two of three rabbits died during injection of Δ^9 -THC 100 mg kg⁻¹ as a 14 mg ml⁻¹ formulation. The rabbits exhibited convulsions, twitches, and striking vasodilation and went through a period of rapid deep breathing followed by shallow intermittent breathing before death. At 40 mg kg⁻¹ Δ^9 -THC (as 7 mg ml⁻¹ solution) all (4) animals were hyperactive, exhibited mild tonic extensions of hind limbs and survived a 24 h observation period. All Δ^9 -THC-treated rabbits at both dose levels exhibited marked miosis. These effects are attributed at least in part to Δ^9 -THC since equal volumes of vehicle alone produced none of these effects. Only slight ataxia and depression were evident in control animals.

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