

Delta-9-tetrahydrocannabinol produces analgesia in the formalin foot assay in mice

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Introduction: There is significant interest in the therapeutic potential of Δ^9 -tetrahydrocannabinol (THC) as an analgesic. Although a previous study investigated THC in the formalin foot assay in rats, the dose-dependence for analgesia remains unclear¹. The aim of this study was to establish a dose-response curve for analgesia as well as investigate potential behavioural and respiratory effects for THC.

Method: All procedures were approved by the Animal Care Committee at The University of British Columbia. Naïve female CD-1 mice weighing 25-30 g were used. On the day of experiments, animals were habituated to the testing apparatus for 2 h. Animals were randomly assigned to receive intravenous (i.v) 0-10 mg/kg THC (n = 8/dose) in a volume of 2 ml/kg. THC was dissolved in a vehicle composed of ethanol, ethoxylated castor oil, and saline in a ratio of 1:1:18. Animals were subjectively assessed for normal or abnormal behaviour during testing. 20 μ l of 5% formalin was then injected into the right hindpaw. Animals were video recorded for 45 min and resulting videos were analyzed by a blinded observer to record the length of time the animal exhibited nocifensive responses. For effects on respiratory rate, animals were injected i.v. with THC and placed in a well-ventilated, darkened restraint chamber for 9 min before counting the number of breaths taken. Data are expressed as mean with 95% confidence interval and fit using a log[inhibitor] vs response four parameter model.

Results: THC reduced nocifensive responses in phase I (0 - 5 min) with an IC_{50} of 0.9 mg/kg (95% CI, 0.5, 1.4) and Hill slope of -2.4 (95% CI, -5.7, 0.8) and in phase II (15 - 45 min) with an IC_{50} of 0.8 mg/kg (95% CI, very wide) and Hill slope of -9.1 (95% CI, very wide). The number of animals classified as normal decreased with an IC_{50} of 2.3 mg/kg (95% CI, 1.3, 4.0) and Hill slope of -2.9 (95% CI, -6.8, 1.1). THC reduced nocifensive behaviours in phase II, but not phase I in a time dependent manner with a $t_{1/2}$ of 3.6 h (95% CI, very wide). Respiratory rate decreased with an IC_{50} of 0.6 mg/kg (95% CI, 0.4, 1.0) and Hill slope of -1.8 (95% CI, -3.1, -0.6).

Conclusions: Intravenous THC produces dose-dependent analgesia in the formalin foot assay in mice with accompanying adverse effects on behaviour and respiration.

References:

1. Moss DE and Johnson RL (1980). *Eur J Pharmacol* **61**: 313-315.