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Clinical studies on the disposition and metabolism of Δ^9-THC and their correlation with its pharmacologic effects

Plasma levels of ^{14}C-Δ^9-THC declined in a biphase manner after its intravenous administration to non-users, or chronic users of marihuana. The t½ of the second phase was 56 h in non-users and 27 h in chronic users. Urinary excretion of radioactivity was significantly greater in users than non-users. However, total radioactivity excreted in urine and feces did not differ significantly. 11-Hydroxy-THC was present in plasma within 10 min and was excreted in urine and feces. 8,11-Dihydroxy-THC was also excreted in feces. The major urinary metabolites in man appear to be acidic and very polar, perhaps being identical to the metabolites present in rabbit urine (Agurell, *et al. Biochem. Pharmacol.*, 1970). After oral ingestion of a pharmacologic dose of ^{14}C-Δ^9-THC, the psychologic effects had their onset within 30 to 60 min, reached their peak at 2 to 3 h, and had a duration of 4 to 6 h. Plasma radioactivity correlated well, with the psychologic effects increasing to a peak at about 3 h then gradually declining. The finding that at the peak "high" unchanged Δ^9-THC plasma levels account for only a relatively small percentage of total radioactivity is consistent with the hypothesis that 11-OH-Δ^9-THC or some other metabolite is responsible for the pharmacologic activity. After the inhalation of a marihuana cigarette containing ^{14}C-Δ^9-THC, plasma levels of radioactivity were initially high and then gradually declined. The psychologic effects were manifested within 6 to 12 min and were largely dissipated by 3 h, at which time the plasma levels of radioactivity had decreased considerably.

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The role of vehicles in cannabis application and interaction between cannabis and central active drugs

The administration of cannabis compounds is complicated by the extreme insolubility in aqueous media. We applicated a single dose of cannabis resin (containing 10 mg/kg THC, 9 mg/kg cannabinol, 20 mg/kg canna-