Review > Pain Res Manag. Autumn 2005;10 Suppl A:15A-22A. doi: 10.1155/2005/242516.

Pharmacokinetics of cannabinoids

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PMID: 16237477 DOI: 10.1155/2005/242516

Abstract

Delta-9-tetrahydrocannabinol (Delta-9-THC) is the main psychoactive ingredient of cannabis (marijuana). The present review focuses on the pharmacokinetics of THC, but also includes known information for cannabinol and cannabidiol, as well as the synthetic marketed cannabinoids, dronabinol (synthetic THC) and nabilone. The variability of THC in plant material (0.3% to 30%) leads to variability in tissue THC levels from smoking, which is, in itself, a highly individual process. THC bioavailability averages 30%. With a 3.55% THC cigarette, a peak plasma level of 152±86.3 ng/mL occured approximately 10 min after inhalation. Oral THC, on the other hand, is only 4% to 12% bioavailable and absorption is highly variable. THC is eliminated from plasma in a multiphasic manner, with low amounts detectable for over one week after dosing. A major active 11-hydroxy metabolite is formed after both inhalation and oral dosing (20% and 100% of parent, respectively). THC is widely distributed, particularly to fatty tissues, but less than 1% of an administered dose reaches the brain, while the spleen and body fat are long-term storage sites. The elimination of THC and its many metabolites (from all routes) occurs via the feces and urine. Metabolites persist in the urine and feces for several weeks. Nabilone is well absorbed and the pharmacokinetics, although variable, appear to be linear from oral doses of 1 mg to 4 mg (these doses show a plasma elimination half-life of approximately 2 h). As with THC, there is a high first-pass effect, and the feces to urine ratio of excretion is similar to other cannabinoids. Pharmacokinetic-pharmacodynamic modelling with plasma THC versus cardiac and psychotropic effects show that after equilibrium is reached, the intensity of effect is proportional to the plasma THC profile. Clinical trials have found that nabilone produces less tachycardia and less euphoria than THC for a similar antiemetic response.

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