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Human Pharmacokinetic Parameters of Orally Administered Δ ^{9}–Tetrahydrocannabinol Capsules Are Altered by Fed Versus Fasted Conditions and Sex Differences

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Abstract

Background: There is variability in the reported Δ^{9}-tetrahydrocannabinol (THC) and 11-hydroxy-tetrahydrocannabinol (11-OH-THC) pharmacokinetic (PK) and pharmacodynamic (PD) parameters between studies and there is limited investigation into how the presence of food or sex affect these parameters. In this study, we examined the PK and PD parameters of an encapsulated THC extract and its major active metabolite, 11-OH-THC, under different fed states. **Methods:** The study was a single-dose, randomized, double-blinded, four-way crossover investigation. THC capsules (1 or 2×5 mg) were administered to 28 healthy adults (13 females: 15 males) under a fasted condition or after a high-fat meal. Blood samples were collected and PK parameters were determined through noncompartmental analysis. Adverse events (AEs), cognitive function (through completion of digit symbol substitution tests), blood pressure, and heart rate were also recorded. **Results:** The presence of high-fat food significantly enhanced time to peak plasma concentration (T_{max}) and area under the curve (AUC_{0-24}) for both THC and 11-OH-THC and reduced THC's apparent volume of distribution (V_z/F) and apparent clearance (Cl/F). Females had a significantly greater peak plasma concentration (C_{max}) compared with males after 5 mg THC in a fasted state. No cardiovascular or cognitive effects and only mild AEs (somnolence, fatigue, and euphoric mood) were reported. **Conclusion:** These findings may help to inform the guidelines provided by governing health bodies on the effects of cannabis, such as time to onset and duration of action, and aid health care practitioners in their prescribing practices. Furthermore, the doses used in this study are safe to consider for future interventional studies in disease conditions where THC has been shown to have therapeutic efficacy.

Keywords: 11-OH-THC; THC; fasted; fed; pharmacokinetic; sex.