Δ9-tetrahydrocannabinol Pharmacokinetics of Inhaled Cannabis Market Products in Occasional and Daily Users

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Background/Introduction: Population pharmacokinetic models of Δ9-tetrahydrocannabinol (THC) have been developed for THC plasma concentration data following protocol-driven inhalation regimens with NIDA-supplied, low THC potency cannabis products. Since, most cannabis consumption is now of high concentration, market-derived cannabis and most consumption is *ad libutum*, we performed a pilot study of the population pharmacokinetics of THC in users of high potency flower, (occasional and daily), and users of high concentration THC concentrates.

Methods: THC concentration data were obtained for 135 minutes from 30 subjects stratified to three groups: 10 occasional users (no more than three times per week) and 10 daily users all of whom normally smoked high concentration flower (15-30%) and 10 daily users who normally inhaled THC concentrates (60-90%). On the day of the study, all subjects were instructed to smoke/inhale the product they supplied themselves, *ad libitum,* in the manner they usually employed, and to the endpoint they usually desired. Parameters for a 3-compartment population pharmacokinetic model were estimated along with an estimate of the bioavailable inhaled dose which were compared to the physically measured dose used during the study session.

Results: Central and rapidly equilibrating volumes of distribution of a 3-compartment model were estimated (19.9±1.2 L, 51.6±4.7 L, respectively) as well as intercompartmental clearances to rapid and slow equilibrating peripheral compartments (1.65±0.14 L/min and 1.75±0.10 L/min, respectively). The slow volume of distribution and elimination clearance were fixed to estimates we determined previously from the population pharmacokinetic model of data in other subjects in which blood samples were collected for one week following a single inhalation session (3372 L and 0.72 L/min, respectively). Covariate analysis revealed that occasional cannabis users inhaled significantly less THC than daily users despite similar used, physically weighed THC.

Conclusion: 3-compartment pharmacokinetics of THC did not differ among the 3 groups and the early phase (first 135 minutes after inhalation) kinetics were similar to those previously described using low potency cannabis products. These analyses suggest covariate-driven adjustments can be made to weighed THC doses, based both on product and usage pattern, that would improve the accuracy of THC exposure estimates based on weighed product alone.

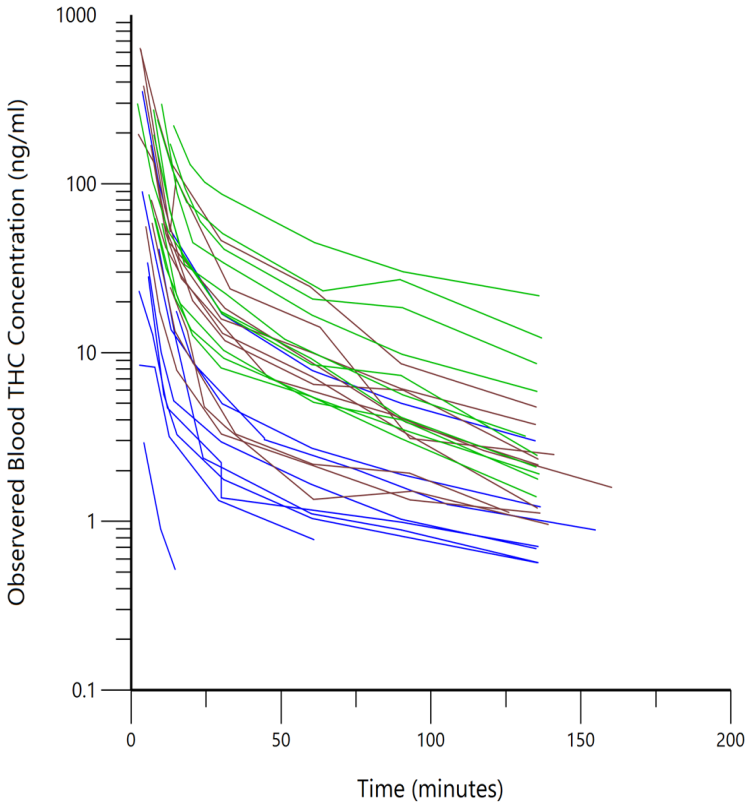

Figure 1. Observed blood THC concentration versus time for all 29 subjects (each line connects the measured concentrations from one subject) after subtraction of the baseline (before inhalation) blood THC concentration. Blue lines are occasional flower users, brown lines are daily concentrate users and green lines are daily flower users.