Plasma Pharmacokinetics of THC, 11-OH-THC, and THCCOOH

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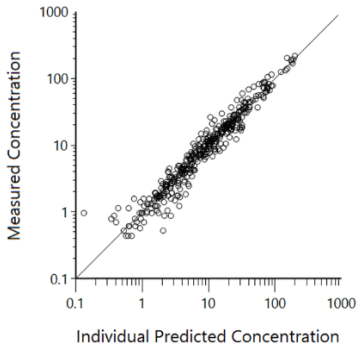
Introduction/Background: Population pharmacokinetic (popPK) modeling of THC, but not including those of the major metabolites, has been performed in a clinical research setting with dense plasma sampling following a closely monitored administration by smoking and vaping.[1] To interpret sparse, observational plasma THC and metabolite concentrations, we aimed to develop a comprehensive popPK model of THC and its metabolites as a Bayesian prior for further modeling of sparse, observational data. We postulated that such a model could estimate daily THC exposure in a cohort of regular cannabis users in Boulder, Colorado.

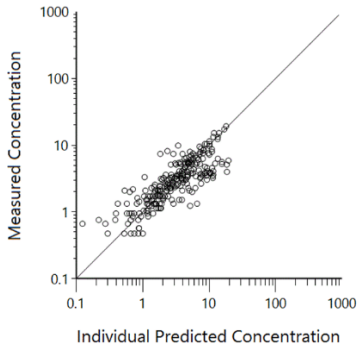
Methods: Six sequestered subjects smoked in a rigorously-paced manner two different concentrations of marijuana cigarettes (1.75% and 3.55% THC) over 10 min one week apart. Frequent blood samples were obtained during and immediately after each smoking event and then less frequently for one week for the measurement of THC, 11-OH-THC and THCCOOH by LC-MS/MS.[2] A multicompartment popPK model was developed using non-linear mixed effects analysis. 16 regular users of cannabis were recruited into a larger study involving psychomotor testing. Blood samples were obtained at recruitment, in a mobile lab immediately before smoking in their home, upon returning to the mobile lab and then again one hour later for analysis of THC/metabolites. These data were analyzed with the prior, dense data and the Bayesian prior for popPK analysis, including estimates of (1) daily THC consumption prior to recruitment, (2) daily THC consumption in the interval between recruitment and home-smoking and (3) the dose consumed during the home-smoking event.

Results: A 3-compartment PK model of THC was developed (Vss=22.6 L/kg, and Cle=1.12 L/min) with extension to metabolite kinetics. Baseline daily THC consumption was estimated to be 2.56$\pm$3.27 (mean$\pm$SD) NIDA cannabis cigarettes (5.6% THC). Consumption dropped to 0.87$\pm$0.97 cigarettes in the interval prior to home-smoking and 0.45$\pm$0.26 while in their home that was estimated to have begun 14 minutes prior to returning to the mobile lab.

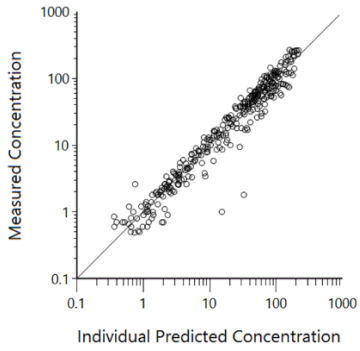
Conclusions: The current study demonstrates the feasibility of developing a popPK model from THC clinical trial studies which when combined with observation plasma THC (and metabolite) data can estimate dose, timing of dose until first blood sample and daily THC consumption.



THC



11-OH-THC



THCCOOH