Human Study Abstract - University of Washington

Clinical Pharmacokinetics of a Cannabidiol/Cannabidiolic Acid-Rich Hemp Product

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Background. The prevalence of cannabis products in the United States has increased exponentially due to increasing state legalization. The cannabis plant (Cannabis sativa) contains >500 phytoconstituents, including >100 cannabinoids. Cannabidiol (CBD) is a psychoactive, non-intoxicating cannabinoid commonly extracted from hemp. Both hemp and marijuana are derived from cannabis, but hemp contains a much lower content (≤0.3%) of tetrahydrocannabinol (THC), the psychoactive cannabinoid that produces euphoric effects. The 2018 Farm Bill further increased availability and usage of hemp products, which are commonly used to self-treat pain, anxiety, and sleep disorders. Clinical pharmacokinetic studies involving CBD-containing products typically evaluate the pharmacokinetics of CBD and downstream metabolites, including 7-OH-CBD and 7-COOH-CBD, but not the precursor, cannabidiolic acid (CBDA). The purpose of this study was to characterize the clinical pharmacokinetics of these and other cannabinoids administered as a novel CBD/CBDA-rich hemp product.

Methods. Five healthy adults participated in an open label study during which they were administered a hemp oil soft gel (~1 mg/kg) once daily for 8 days. Plasma samples collected on Day 1 and Day 8 were analyzed for CBD and related cannabinoids, as well as THC, tetrahydrocannabinolic acid (THCA), 11-OH-THC, and 11-COOH-THC by LC-MS/MS. Pharmacokinetics were obtained via non-compartmental analysis using Phoenix WinNonlinTM.

Results. Day 1: the doses of CBD and CBDA were comparable (~50 mg), yet the AUC0-12h and Cmax of CBDA ranged from ~8-50x and ~20-100x those of CBD, respectively. Comparable doses of THC and THCA (~2.5 mg) showed similar trends (20-60x and 15-35x, respectively). Day 8: the profiles for CBD, CBDA, THC, and THCA were comparable to those on Day 1. The Day 8/Day 1 AUC0-12h and Cmax ratios for the inactive 7-COOH-CBD and 11-COOH-THC ranged from 1.7-2.1 and 1.2-1.5, respectively. The active 7-OH-CBD and 11-OH-THC were near or below quantification limits.

Conclusions. This study is the first to characterize the human pharmacokinetics of CBDA contained in a novel CBD/CBDA-rich hemp product. Systemic exposure to CBDA was much higher than that to CBD despite comparable doses, necessitating further investigation of the clinical impact of CBDA.

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