Pharmacokinetics of cannabidiolic acid in cattle following oral dosing of industrial hemp (*Cannabis sativa*)

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Introduction

Industrial hemp (IH) (*Cannabis sativa* containing < 0.3% tetrahydrocannabinol [THC]) has gained recent traction as a novel agricultural commodity. Hemp plants and by-products are considered to have nutritional and potentially therapeutic value. The presence of bioactive cannabinoid compounds including cannabidiol (CBD), cannabidiolic acid (CBDA), and 9-tetrahydrocannabolic acid (THCA-A) in hemp may result in drug residues in edible tissues that pose a food safety risk to the consumer. The absence of published data describing the pharmacokinetics of cannabinoids in livestock is a significant impediment to research.

Materials and Methods

Eight castrated male Holsteins weighing an average 473 lb (215 kg) were enrolled onto the study. Female IH flowers with a known cannabinoid profile was placed into gelatin capsules. Each calf received 35 g of IH in pre-weighed gelatin capsules to achieve a dose of 5.4 mg/kg CBDA. Blood samples for plasma CBDA, cannabidiol (CBD), cannabidivarinic acid (CBDVA), cannabichromenic acid (CBCA) and 9tetrahydrocannabolic acid (THCA) concentrations were taken prior to IH dosing and at predetermined time points out to 96 h. Plasma was stored frozen at -112°F (-80°C) until analyzed. Plasma cannabinoid concentrations were determined using high-pressure liquid chromatography coupled with mass spectroscopy (HPLC-MS). Serum was collected prior to IH administration and at 96 h for serum biochemical analysis

Results

No adverse reactions were noted. Cannabidiolic acid (CBDA), tetrahydrocannabinolic acid-A (THCAA), cannabidivarinic acid (CBDVA), and cannabichromenic acid (CBCA) were detected in all cattle after IH dosing. The geometric mean maximum concentration of CBDA of 72.7 ng/mL was observed at 14 h after IH administration. The geometric mean half-life of CBDA was 14.1 h. Cannabidiol (CBD) was only detected in 4 samples from 2 calves. The mean observed maximum concentrations of THCA-A, CBCA, and CBDVA were 12.1 ng/mL, 12.3 ng/mL, and 13.1 ng/mL, respectively. The times of the mean maximum concentrations were observed at 25.2 h, 23.2 h, and 13.6 h for THCA-A, CBCA, and CBDVA. No changes in serum biochemistry analysis were observed following IH dosing compared to baseline values.

Significance

Cannabinoids are absorbed from the rumen following oral administration of industrial hemp. Further research is needed to determine the oral bioavailability and tissue residue profile of cannabinoids after oral dosing of IH.