Metabolism of (-)-Δ^9-Tetrahydrocannabinol (THC) in Chicken and Potential Exposure of THC and Its Metabolites to Humans

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One recent study reported fewer cases of avian bronchitis and higher quality of meat when chicken were fed daily supplementation of cannabis. The exposure to primary substances of cannabis, namely (-)-Δ^9-tetrahydrocannabinol (THC) and its psychoactive metabolite, 11-OH-THC, in meat and egg of these supplemented chickens rarely received attention. Notably, these substances could be consumed by humans, raising health and legal issues. To explore the potential impact, we aimed to comprehensively investigate the pharmacokinetics (PK) of THC and 11-OH-THC in chicken and humans via in vitro and in silico approaches.

In vitro metabolism experiments were performed to characterize metabolism of THC and 11-OH-THC using chicken liver microsomes (CLM). Kinetic parameters were calculated and compared with those derived from human liver microsomes (HLM). Thermal stabilities of THC and 11-OH-THC were further assessed by mimicking the cooking process. PK of THC and 11-OH-THC and their distribution to muscle and egg were predicted via physiologically-based pharmacokinetic (PBPK) modeling. Oral consumption of 11-OH-THC in meat or egg was simulated under fed condition to predict its exposure to humans.

The depletion of THC in CLM was slower than that in HLM (Fig. 1A). Intrinsic clearances (CL_int) were estimated as 0.49 and 54.03 ml/min/g of chicken and human liver, respectively. Similarly, 11-OH-THC was more metabolically stable in CLM than in HLM, where UGT and P450 enzymes accounted for 67.5% and 32.5% of 11-OH-THC depletion in CLM, with CL_int of 0.33 and 0.16 ml/min/g liver, respectively (Fig. 1B). PBPK modeling predicted elimination half-lives of THC and 11-OH-THC in chicken as 79.3 and 27.2 h, respectively, demonstrating that both compounds were slowly eliminated (Fig. 1C and D). Their extensive distribution to chicken muscle and egg were simulated as well. However, high temperature incubation degraded most THC within 30 min, suggesting its substantial loss in a cooked chicken meal. Conversely, 11-OH-THC remained thermally stable (Fig. 1E). Subsequent PBPK modeling in humans simulated 1.68-fold increase in systemic exposure of 11-OH-THC in the presence of meal, suggesting food effect on systemic absorption of 11-OH-THC (Fig. 1F).

Our study established the PK of THC and 11-OH-THC in chicken, and revealed that 11-OH-THC may reside in chicken products even after cooking. Oral absorption of 11-OH-THC in humans could be significantly augmented by food. Considering the comparative pharmacology between 11-OH-THC and THC in men, our findings hold important implications for potential human consumption of and exposure to psychoactive 11-OH-THC in the real-world. Further research is warranted to support the safe use of cannabis-supplemented chicken feeds.

References:
Figure 1. Metabolic stability of (A) THC and (B) 11-OH-THC in CLM and HLM incubation systems. Lines represent linear regression when Y-axis is natural logarithmic transformed. Simulated mean concentration-time profiles of (C) THC and (D) 11-OH-THC in plasma, muscle and eggs in chicken after oral gavage administration. (E) Stability of THC and 11-OH-THC in CLM incubation system at 90 °C. (F) Simulated mean plasma concentration-time profile of 11-OH-THC in humans after oral consumption in the presence/absence of meal.