Drug Interactions with Cannabidiol (CBD): Cause for Concern?

Barry E. Gidal, PharmD, FAES
Professor of Pharmacy
University of Wisconsin-Madison
Biotransformation of CBD
CBD (Epidiolex) Drug-Drug Interactions

**Effect of Other Drugs on CBD**
- CYP3A or CYP2C19 Inhibitors
- CYP3A4 or CYP 2C19 Inducers

**Effect of CBD on Other Drugs**
- CYP1A2, 2C8/9, UGT1A9, UGT2B7 Substrates
  - In-vitro data suggest potential for inhibition
- CYP2C19
  - Inhibition
- CYP 3A4
  - No effect on midazolam, however some data suggest inhibition potential
PK Interactions between CBD & Clobazam (CLB)

CBD + CLB: Significant Increase in N-CLB $C_{\text{max}}$ and $\text{AUC}_{\text{tau}}$

- **CLB**
  - $C_{\text{max}}$ (ng/mL)
  - Treatment ratio: 1.20
  - 90% CI: [1.05, 1.38]

- **N-CLB**
  - $C_{\text{max}}$ (ng/mL)
  - Treatment ratio: 3.39
  - 90% CI: [2.61, 4.39]

- **AUC$_{\text{tau}}$ (h ng/mL)**
  - Treatment ratio: 1.21
  - 90% CI: [1.05, 1.39]

- **AUC$_{\text{tau}}$ (h ng/mL)**
  - Treatment ratio: 3.38
  - 90% CI: [2.62, 4.36]

$\text{AUC}_{\text{tau}}$: area under the curve within a dosing interval, $\text{tau}$; CBD, cannabidiol; CI, confidence interval; CLB, clobazam; $C_{\text{max}}$, maximum measured plasma concentration; N-CLB, N-desmethyloclobazam

Inhibitory Effects of Cannabinoids on CYP 2C9

(Table 2). The inhibitory effect of CBD on the liver microsomal activities (IC\textsubscript{50} \approx 4.8 \mu M) was less potent than those of \Delta^9\textsubscript{-}THC and CBN. In contrast, \Delta^9\textsubscript{-}THC, CBD, and

Fig. 2. Effects of major phytocannabinoids on S-warfarin 7-hydroxylase and diclofenac 4'-hydroxylase activities of HLMs and rCYP2C9. pHLMs (A) and rCYP2C9 (B) were incubated with 3 \mu M S-warfarin in the presence of various amounts of \Delta^9\textsubscript{-}THC (closed circles), CBD (closed triangles), and CBN (closed squares). iHLMs (C) and rCYP2C9 (D) were incubated with diclofenac (10 and 2 \mu M, respectively) in the presence of various amounts of \Delta^9\textsubscript{-}THC (open circles), CBD (open triangles), and CBN (open squares). Each point is the mean of two determinations.
Warfarin Enantiomer Metabolism

https://www.pharmgkb.org/pathway/PA145011113
CBD & Warfarin: Case Report

Evidence of a Clinically Significant Drug-Drug Interaction between Cannabidiol and Tacrolimus: A Case Report

The potential exists for multiple pharmacokinetic interactions between CBD (and THC) and numerous FDA approved medications.

The exact concentration-effect relationship underlying these interactions is still unclear.

Some patients may be at risk if certain CBD drug combinations go undocumented and are not appropriately monitored by HCPs.