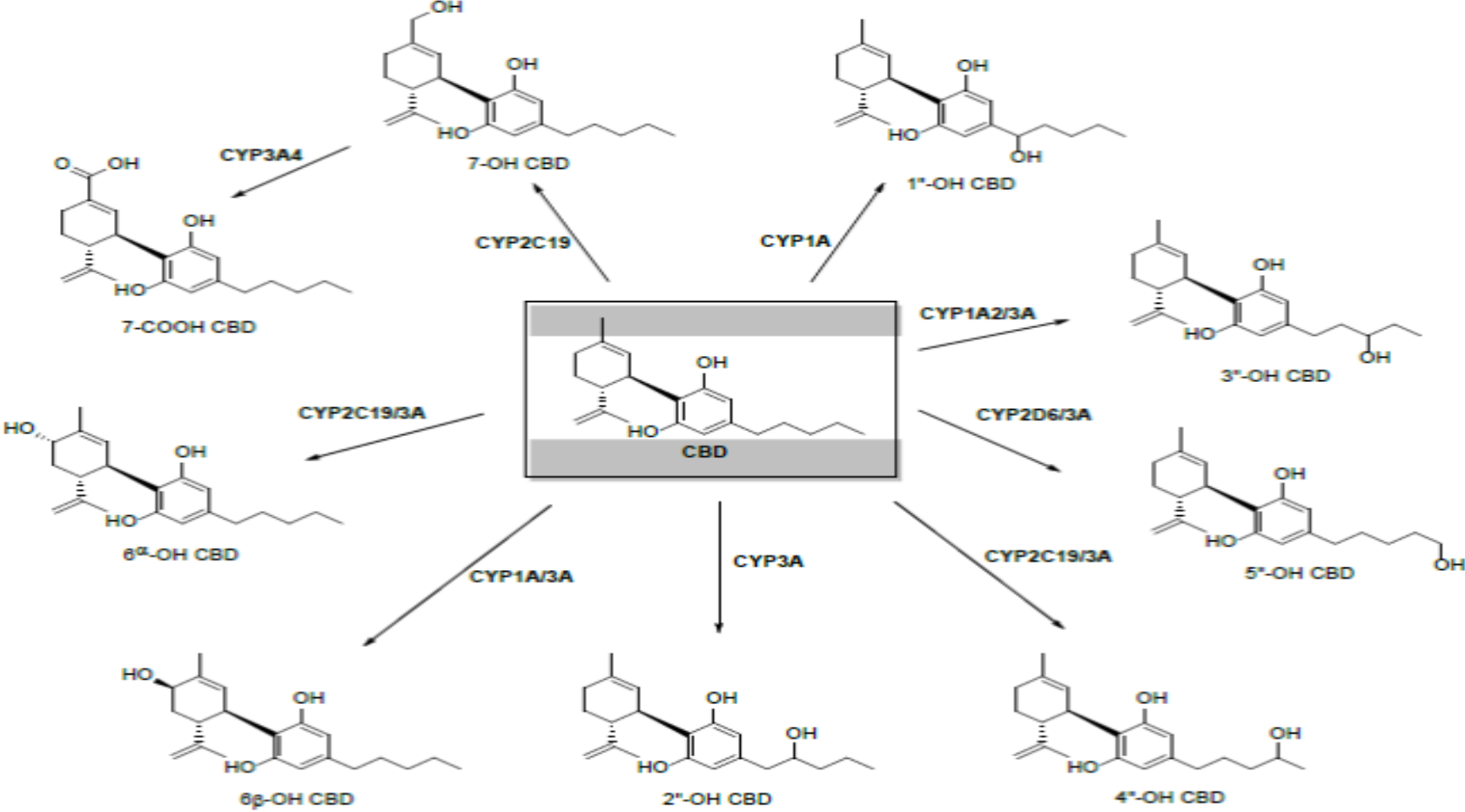


Drug Interactions with Cannabidiol (CBD): Cause for Concern?

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Biotransformation of CBD



CBD (Epidiolex) Drug-Drug Interactions

Effect of Other Drugs on CBD

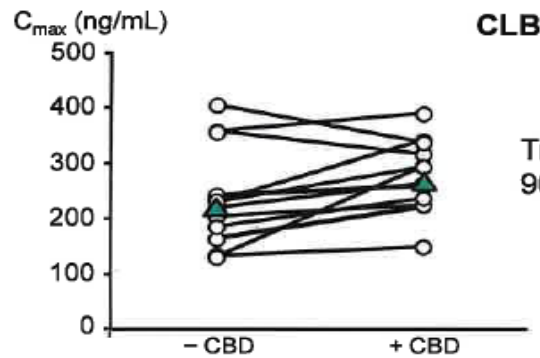
- ▶ CYP3A or CYP2C19 Inhibitors
- ▶ CYP3A4 or CYP 2C19 Inducers

Effect of CBD on Other Drugs

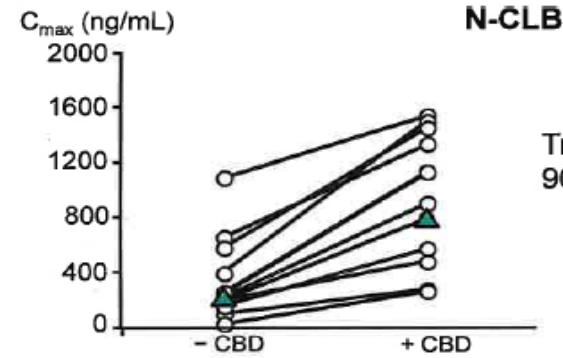
- ▶ CYP1A2, 2C8/9, UGT1A9, UGT2B7 Substrates
 - ▶ In-vitro data suggest potential for inhibition
- ▶ CYP2C19
 - ▶ Inhibition
- ▶ CYP 3A4
 - ▶ No effect on midazolam, however some data suggest inhibition potential

PK Interactions between CBD & Clobazam (CLB)

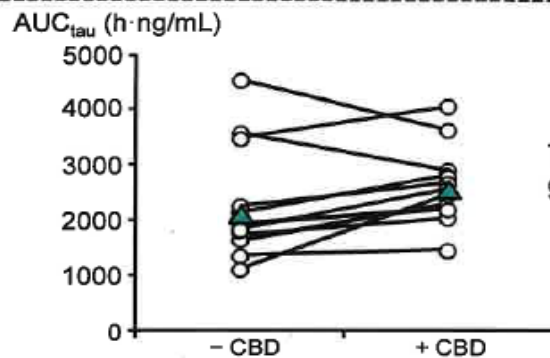
CBD + CLB: Significant Increase in N-CLB C_{max} and AUC_{tau}



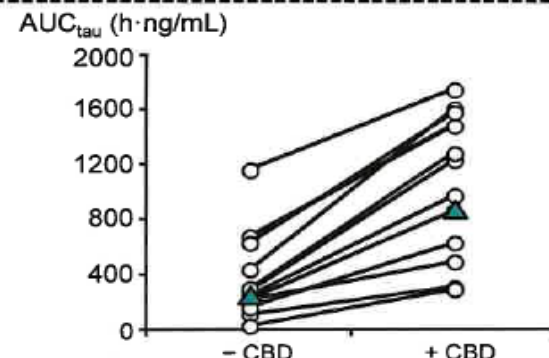
Treatment ratio: 1.20
90% CI: [1.05, 1.38]



Treatment ratio: 3.39
90% CI: [2.61, 4.39]



Treatment ratio: 1.21
90% CI: [1.05, 1.39]



Treatment ratio: 3.38
90% CI: [2.62, 4.36]

▲ Geometric mean

○ Individual values

AUC_{tau} , area under the curve within a dosing interval, tau; CBD, cannabidiol; CI, confidence interval; CLB, clobazam; C_{max} , maximum measured plasma concentration; N-CLB, N-desmethyclobazam

Inhibitory Effects of Cannabinoids on CYP 2C9

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

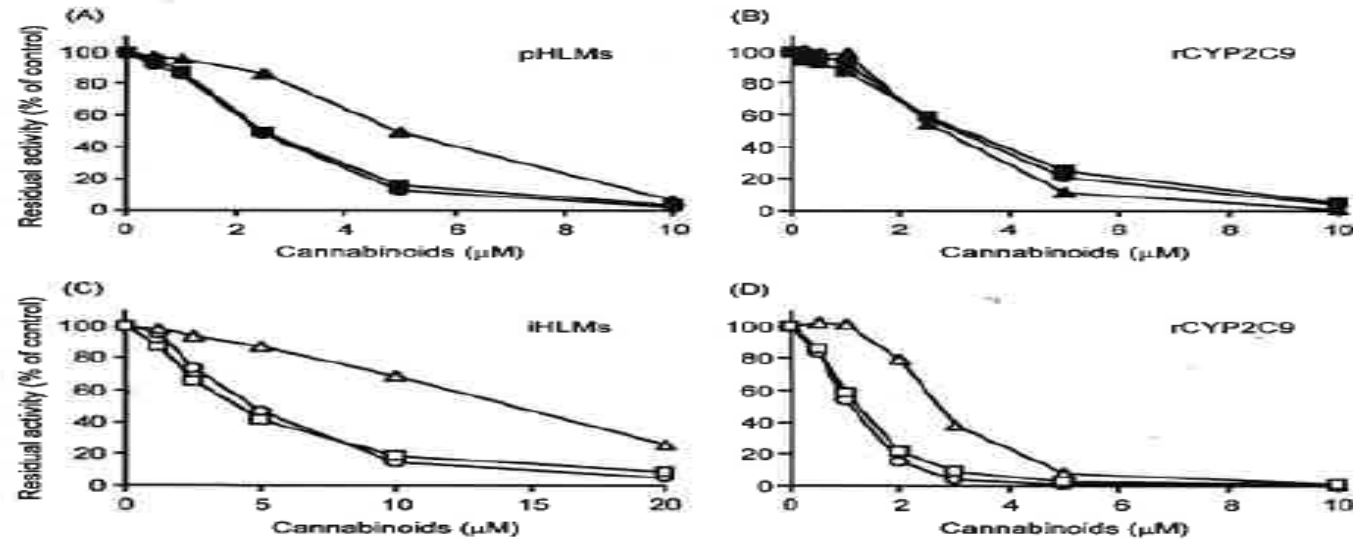
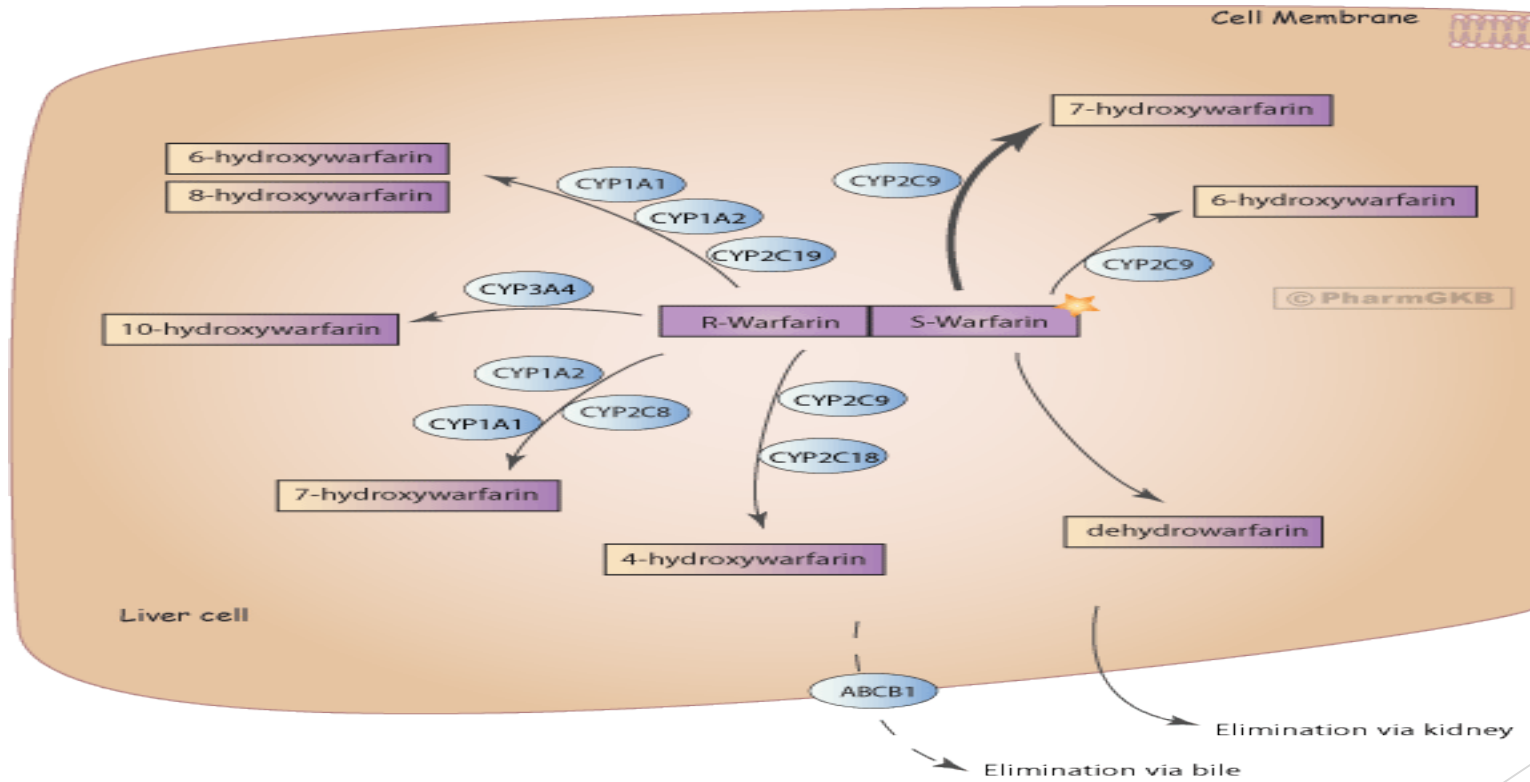


Fig. 2. Effects of major phytocannabinoids on *S*-warfarin 7-hydroxylase and diclofenac 4'-hydroxylase activities of HLMs and rCYP2C9

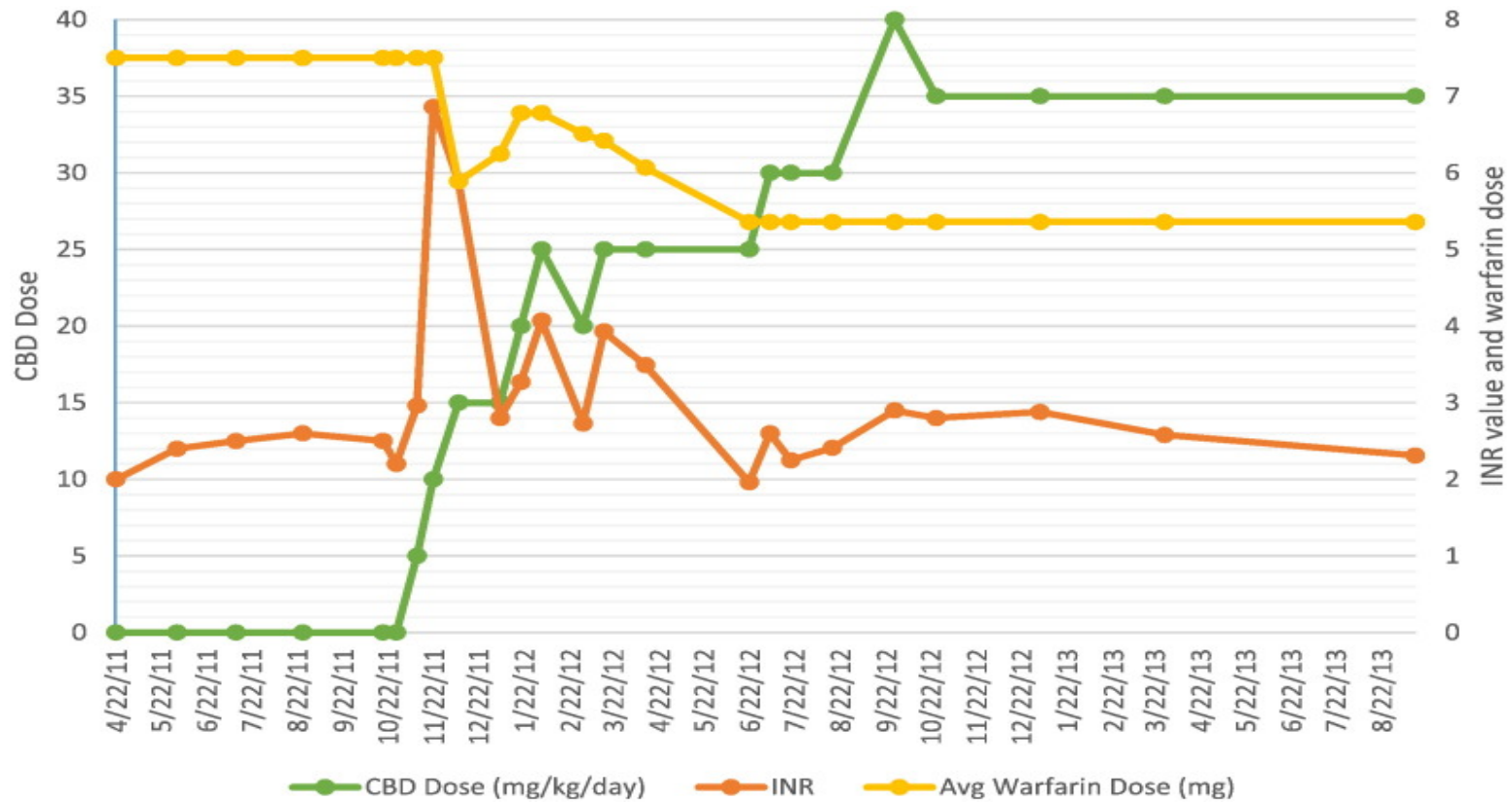
pHLMs (A) and rCYP2C9 (B) were incubated with $3 \mu\text{M}$ *S*-warfarin in the presence of various amounts of Δ^9 -THC (closed circles), CBD (closed triangles), and CBN (closed squares). iHLMs (C) and rCYP2C9 (D) were incubated with diclofenac (10 and $2 \mu\text{M}$, respectively) in the presence of various amounts of Δ^9 -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>

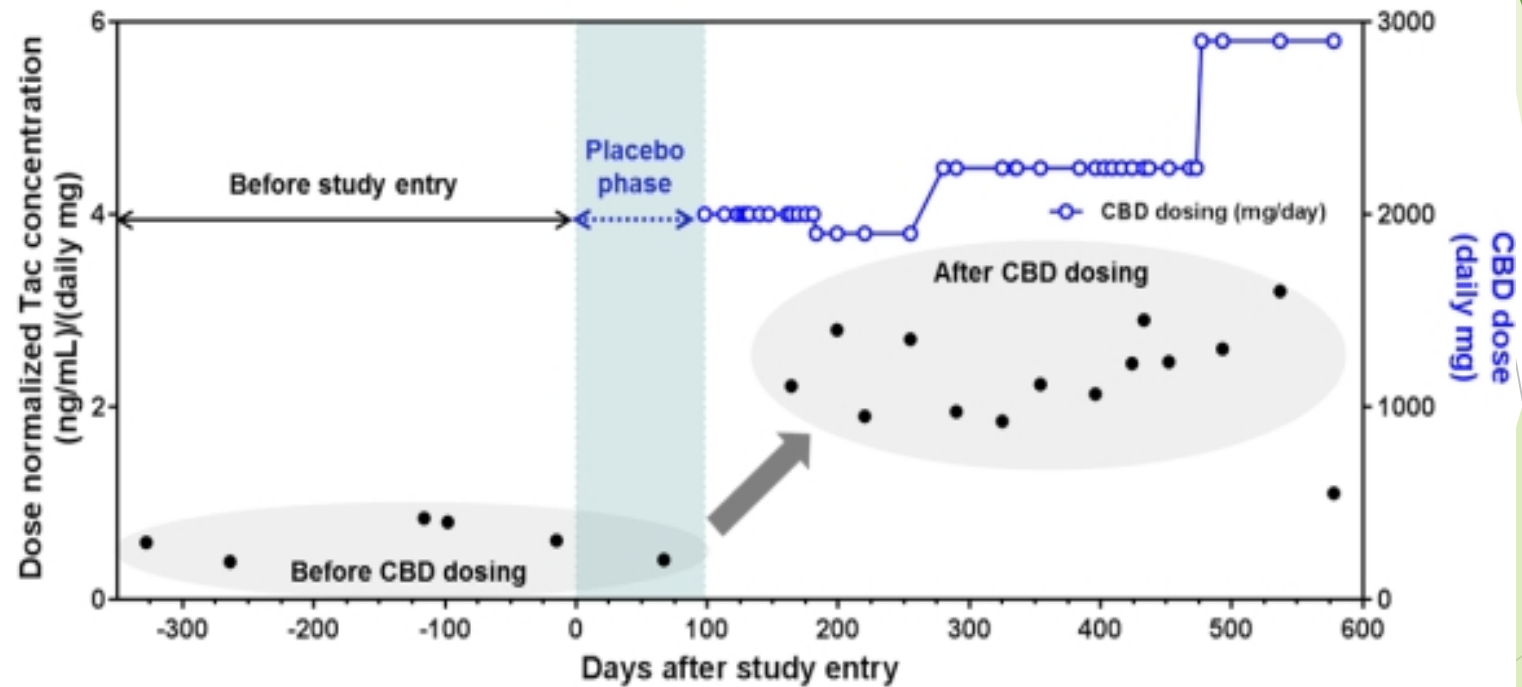
CBD & Warfarin: Case Report



[Grayson et al. Epilepsy Behav Case Rep. 2018; 9: 10-11](#)

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

Figure 2: Tacrolimus Dose Normalized Trough Concentration



Leino A, Emoto C, Fukuda T, Privitera M, Vinks A, Alloway R.

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

[abstract]. <https://atcmeetingabstracts.com/abstract/evidence-of-a-clinically-significant-drug-drug-interaction-between-cannabidiol-and-tacrolimus-/>.

Accessed May 23, 2019.

Summary

- ▶ 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