

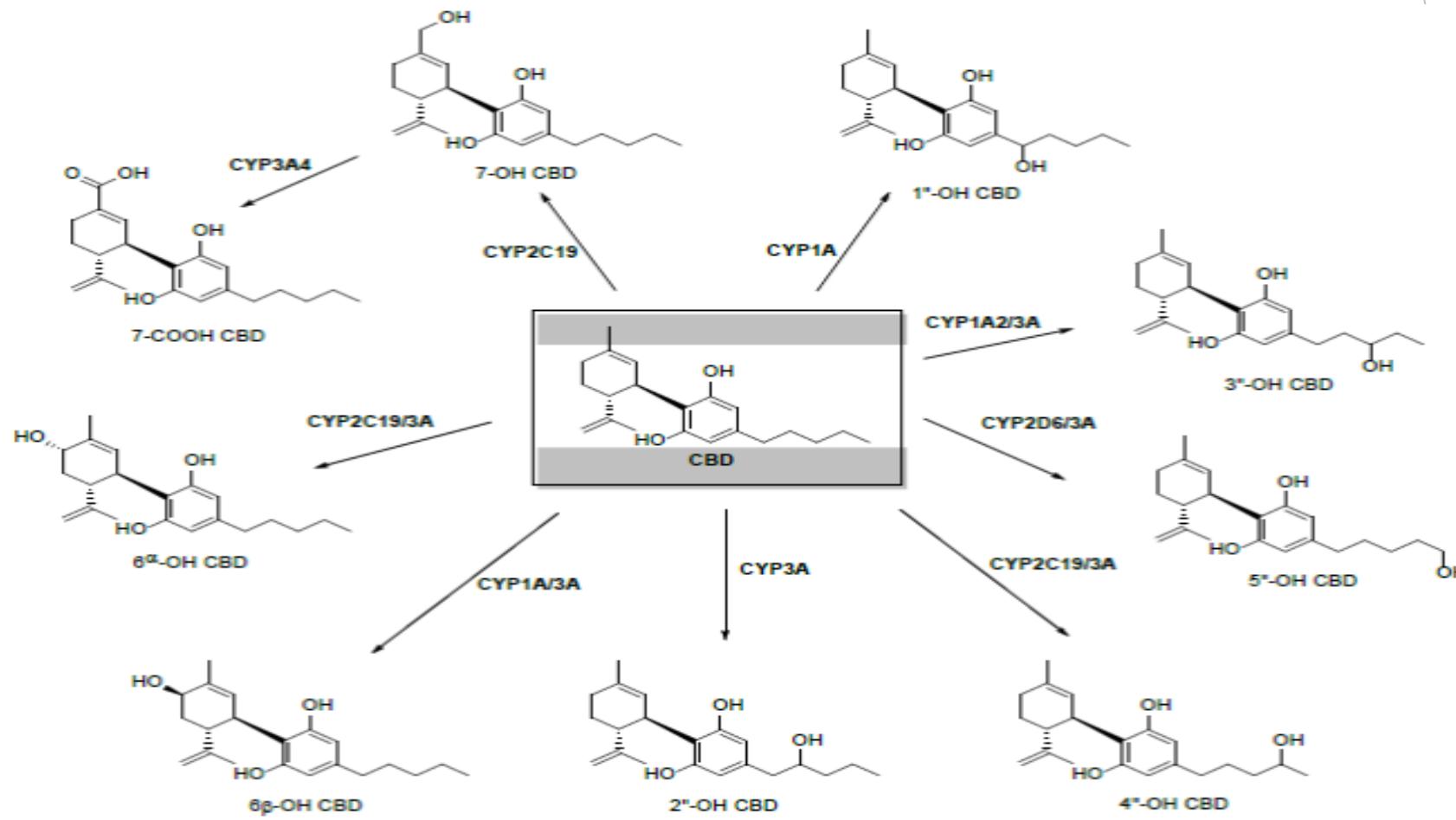
# Drug Interactions with Cannabidiol (CBD): Cause for Concern?

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# Biotransformation of CBD



# CBD (Epidiolex) Drug-Drug Interactions

## Effect of Other Drugs on CBD

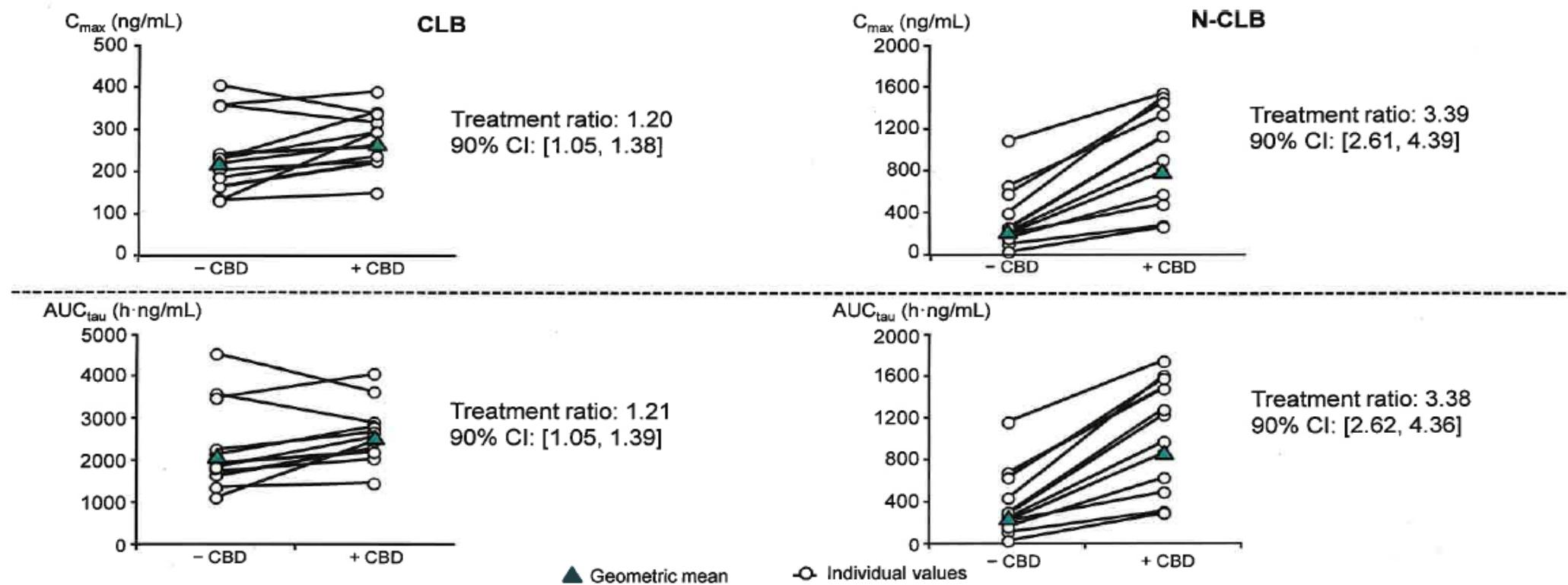
- ▶ CYP3A or CYP2C19 Inhibitors
- ▶ CYP3A4 or CYP 2C19 Inducers

## 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)

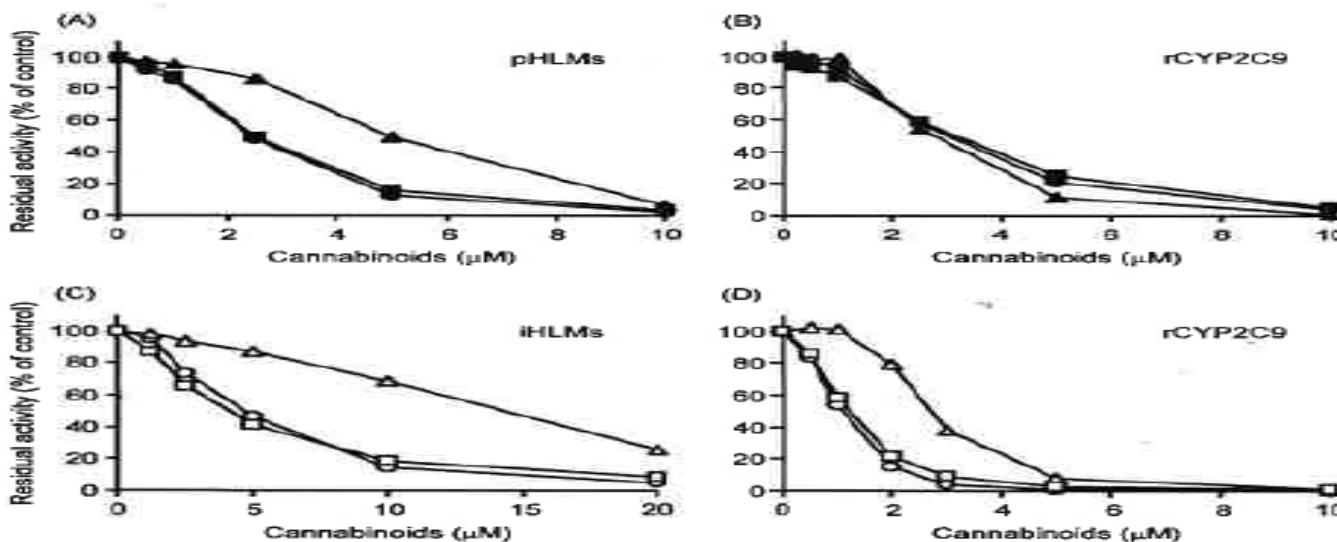
CBD + CLB: Significant Increase in N-CLB  $C_{max}$  and  $AUC_{tau}$



$AUC_{tau}$ , 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-desmethylclobazam

# Inhibitory Effects of Cannabinoids on CYP 2C9

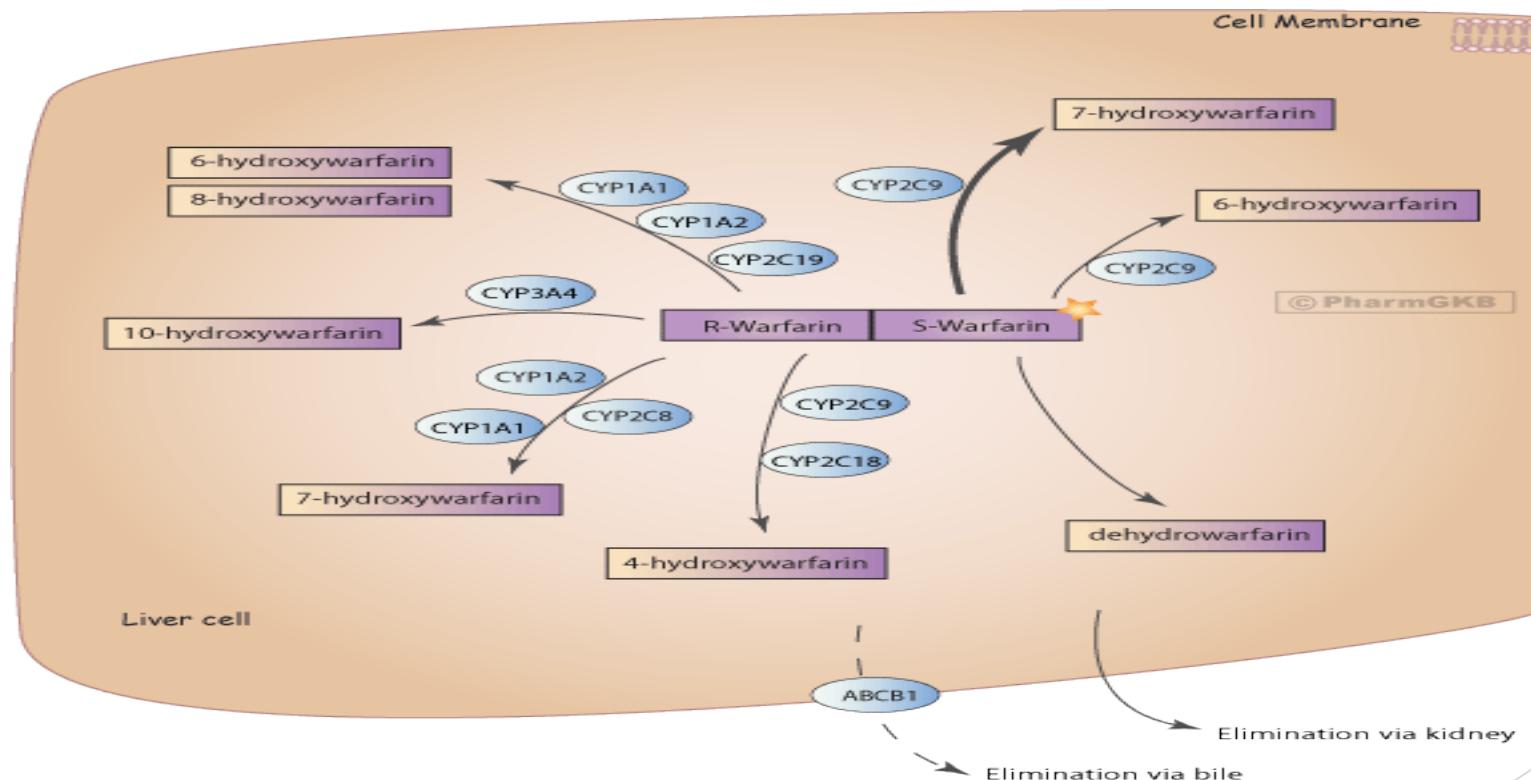
**(Table 2).** The inhibitory effect of CBD on the liver microsomal activities ( $IC_{50} \approx 4.8 \mu M$ ) was less potent than those of  $\Delta^9$ -THC and CBN. In contrast,  $\Delta^9$ -THC, CBD, and



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

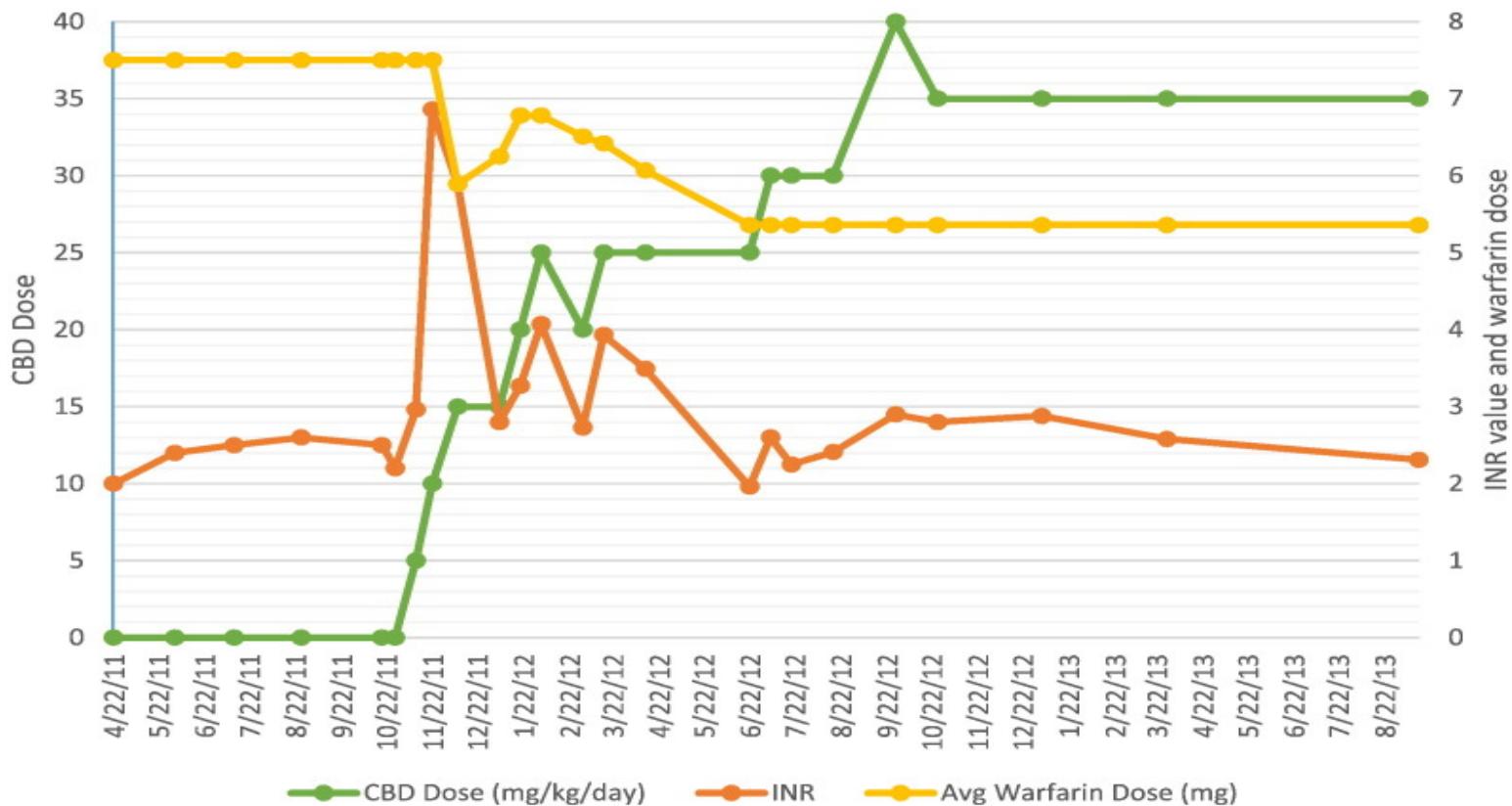
pHLMs (A) and rCYP2C9 (B) were incubated with 3  $\mu M$  S-warfarin in the presence of various amounts of  $\Delta^9$ -THC (closed circles), CBD (closed triangles), and CBN (closed squares). iHLMs (C) and rCYP2C9 (D) were incubated with diclofenac (10 and 2  $\mu M$ , respectively) in the presence of various amounts of  $\Delta^9$ -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/PA14501113>

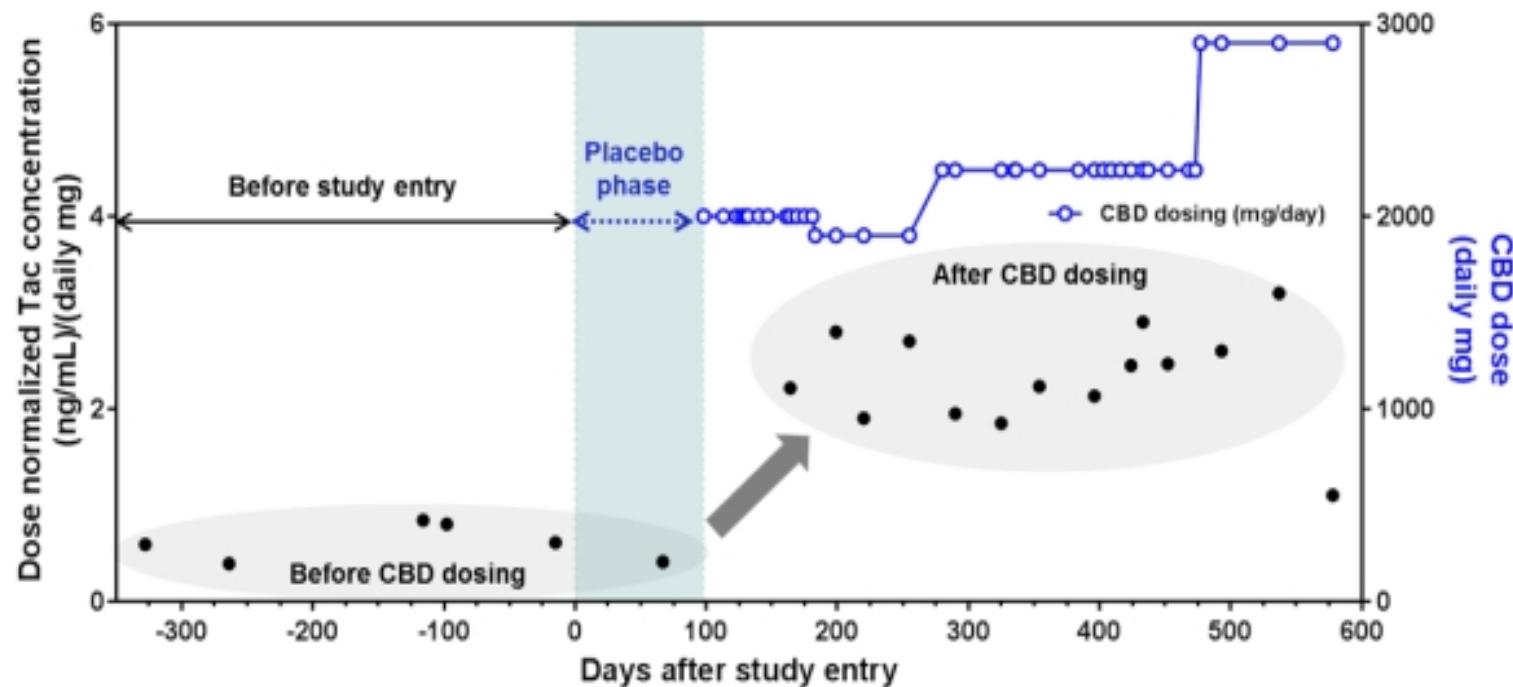
# CBD & Warfarin: Case Report



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-a-case-report/>

. 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