Inhibition of Tacrolimus Metabolism by Cannabidiol
In Vitro Study

PRESENTER:
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BACKGROUND: Cannabidiol has shown inhibition *in vitro* on CYP3A5 for which tacrolimus is a sensitive substrate.

METHODS

1. Tacrolimus was incubated in five conditions: alone, with 10 µM cannabidiol (CBD), 7-hydroxycannabidiol (7-OH CBD), 7-carboxycannabidiol (7-COOH CBD), and 1 µM ketoconazole with pooled human liver microsomes (HLMs) and recombinant (r) CYP3A4 and CYP3A5.
2. **Depletion rate and half-life** of tacrolimus were obtained with linear regression analysis.

RESULTS

- **CBD** slowed tacrolimus depletion by 1.8-, 6.6-, and 30.3-fold with HLM, rCYP3A4, and rCYP3A5, respectively.
- **7-OH CBD** slowed tacrolimus depletion by 3.3-, 15.2-, and 20.8-fold with HLM, rCYP3A4 and rCYP3A5, respectively.
- **7-COOH CBD** only slowed tacrolimus depletion minimally.
- Observed CYP3A4 selectivity for ketoconazole aligns with the literature.

CONCLUSION

- CBD and 7-OH CBD strongly inhibited tacrolimus metabolism, whereas 7-COOH CBD showed minimal inhibition.
- Results may contribute to CYP3A5 inhibitor selection in drug development

Cannabidiol and 7-hydroxycannabidiol strongly inhibited tacrolimus metabolism mediated by CYP3A4/5 *in vitro*.

Fold-Change in Tacrolimus Depletion Rate Against Control

	Tacrolimus	Tacrolimus + CBD	Tacrolimus + 7-OH CBD	Tacrolimus + 7-COOH CBD	Tacrolimus + Ketoconazole
Pool HLMs	1	1.8	3.3	1.2	11.2
rCYP3A4	1	6.6	15.2	1.1	8.7
rCYP3A5	1	30.3	20.8	1.1	2.7

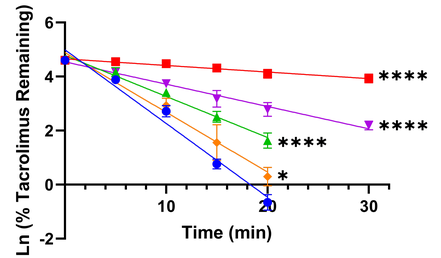
Control = tacrolimus; Depletion rate = k_{dep} (h^{-1})

Trial Design: See Poster TIP-002
Trial Initial Results: See Poster LB-009

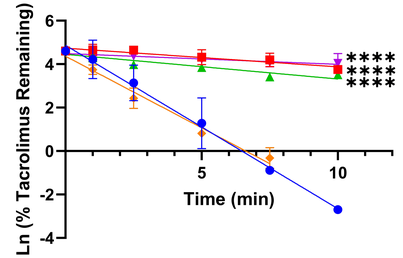
Raw data & Detailed methods

*p<0.05; ****p<0.0001

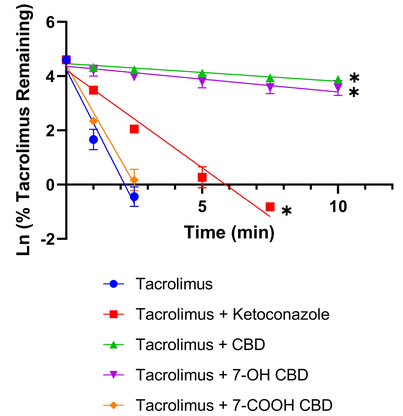
Tacrolimus Depletion with Pooled HLM



Tacrolimus Depletion with rCYP3A4



Tacrolimus Depletion with rCYP3A5



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