



INTERVIEW REGARDING

D-limonene Impact on THC-induced Anxiety Effects

This interview was conducted by CBD Oracle via email in June 2024 and is provided here for full transparency. Learn more about [CBD Oracle's Editorial Policy](#).

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Dr. Tory Spindle obtained his PhD in Experimental Health Psychology from Virginia Commonwealth University. Broadly, Dr. Spindle utilizes human laboratory studies to characterize the behavioral pharmacology of cannabis and nicotine/tobacco products. His cannabis research seeks to understand how factors such as route of administration (oral, vaped, smoked, topical), dose, product formulation/chemical composition profile, and user factors (e.g., puffing topography, sex, tolerance) impacts the pharmacokinetic and pharmacodynamic effects of cannabis.

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CBD Oracle: What would you say is the most important result of your study?

Tory: Perhaps this is obvious, but the most important result was that we saw a mitigation of THC-induced anxiety by co-administering limonene and this effect was dose-dependent. This is one of the first demonstrations of the cannabis entourage effect in humans, which is very important because there is little to no empirical clinical data to support many claims made by the industry regarding the influence of minor cannabinoids/terpenes on cannabis effects.

CBD Oracle: Does the fact that d-limonene had no effect on anxiety alone but did in combination with THC offer evidence for the entourage effect?



Tory: The fact that d-limonene had no effect on its own simply demonstrates this constituent doesn't produce discernable effects. The fact that THC + limonene resulted in reduced anxiety compared with THC alone is the better demonstration of the entourage effect, at least for limonene. That said, it is important to note that this finding doesn't necessarily mean that all cannabis constituents will meaningfully influence the effects of cannabis so it should not be viewed as a universal validation of the entourage effect.

CBD Oracle: You note in the paper that 30 mg THC + 15 mg d-limonene produced higher plasma THC levels than 30 mg THC alone - could you comment on why this might be? Could it be related to the fact there were fewer participants in that session?

Tory: It is possible this was due to increased variability from having fewer participants in that study condition. In other words, if someone is an outlier and happened to have higher THC blood concentrations in a particular condition, they would have a greater impact on the mean value because there were fewer other participants to balance this effect out.

CBD Oracle: What would you say was a major limitation of the study?

Tory: I think there are a couple key limitations we highlight in the manuscript. One notable one is that the 30 mg THC + 15 mg d-limonene condition always occurred last.

Ideally, this condition would have occurred in random order for all participants, but when we started the study, we did not yet have safety data on limonene doses that high, so we had to wait until we ran a few participants and had the proper safety data to incorporate that condition. The other main limitation is that we used a vaporized route of administration only.

CBD Oracle: What's the next step for research into d-limonene and the entourage effect overall?

Tory: We have several studies planned or ongoing to extend this line of research including studies on interactions between THC and other terpenes (pinene and myrcene) and a study to evaluate oral THC and oral limonene combinations (the preferred method among those who use cannabis for medical purposes).

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