



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. Vandrey is currently a Professor at the Johns Hopkins University Behavioral Pharmacology Research Unit (BPRU) and helps run the Cannabis Science Lab (CSL). Dr. Vandrey's research focuses primarily on the impact of route of administration, dose, and chemical composition of cannabis products on resultant drug effects and pharmacokinetics.

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

Ryan: The most important result is that the study suggests that adding a high dose of d-limonene to inhaled formulations of delta-9-THC can selectively reduce THC-induced anxiety in individuals prone to having such experiences.

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?

Ryan: d-limonene alone did not have an effect on anxiety because this was not an anxious population. These folks only experienced anxiety when we provoked it with high doses of inhaled delta-9-THC. This experiment is specific to how co-administration of delta-9-THC and d-limonene affect anxiety. While this may be part of a larger "entourage effect", such an effect is not operationally defined and involves much more complex chemical interactions beyond what was evaluated in this study.

CBD Oracle: You note that there is a big difference between your test mixture and full spectrum or "whole plant" products - how would you expect the results to change in that case? What is the "real world" significance of the study in that sense?

Ryan: We observed a significant decrease in delta-9-THC induced anxiety with a d-limonene dose that was 3 times the maximum amount we would expect to find naturally in cannabis flower based on chemical analysis of over a 100 different samples of botanical cannabis. There was a qualitative reduction in anxiety at the max d-limonene dose we would expect in cannabis flower, but it was not statistically significant. That is not to say that other chemicals in cannabis may also act similarly as d-limonene and also help mitigate the anxiogenic effects of delta-9-THC, or that a more robust effect of smaller doses of d-limonene could happen in a different population of users, but, in our experiment, we got greater attenuation of anxiety when we pushed doses of d-limonene above what is usually found naturally in the cannabis plant.

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

Ryan: That is was limited to the inhaled route of administration and only to healthy adults.

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

Ryan: We will attempt to replicate our results with an oral dose study and evaluate the interaction between delta-9-THC and other terpenes or cannabinoids using a similar model. **I**