

Supplemental Online Content

Zamarripa CA, Spindle TR, Surujunaraian R, et al. Assessment of orally administered Δ 9-tetrahydrocannabinol when coadministered with cannabidiol and Δ 9-tetrahydrocannabinol pharmacokinetics and pharmacodynamics in healthy adults: a randomized clinical trial. *JAMA Netw Open*. 2023;6(2):e2254752. doi:10.1001/jamanetworkopen.2022.54752

eTable 1. Mean Δ 9-THC, 11-OH- Δ 9-THC, and Δ 9-THC-COOH Maximum Concentrations, Time to Maximum Concentration, and Total Area Under-the-Curve Following Δ 9-THC and Δ 9-THC+CBD Administration

eTable 2. Statistical Analyses Results for Pharmacodynamic Outcomes Using Change-From Baseline Data

eFigure. Change From Baseline Mean Ratings for the Visual Analog Scale Items on Adverse Outcomes

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Mean Δ 9-THC, 11-OH- Δ 9-THC, and Δ 9-THC-COOH Maximum Concentrations, Time to Maximum Concentration, and Total Area Under-the-Curve Following Δ 9-THC and Δ 9-THC+CBD Administration

	<u>20mg Δ9-THC + 0mg CBD</u>			<u>20mg Δ9-THC + 640mg CBD</u>		
	C_{max}, Mean (SD)	T_{max}, h (Range)	AUC (SD)	C_{max}, Mean (SD)	T_{max}, h (Range)	AUC (SD)
Δ 9-THC	8.2 (4.0)	2.2 (0.5-4)	33.3 (16.9)	14.8 (5.5)	2.7 (1-6)	84.9 (28.4)
11-OH- Δ 9-THC	4.5 (1.9)	2.2 (1-4)	34.0 (16.4)	53.9 (22.6)	2.6 (2-4)	349.0 (137.1)
Δ 9-THC-COOH	45.1 (18.5)	2.6 (1-4)	445.7 (196.2)	118.6 (44.8)	4.1 (2-6)	1030.0 (456.4)

Abbreviations: SD = Standard Deviation, h = Hours

eTable 2. Statistical Analyses Results for Pharmacodynamic Outcomes Using Change-From Baseline Data

Outcome Measure	Drug Condition (D) <i>F</i>	<i>p</i>	Time (T) <i>F</i>	<i>p</i>	D x T <i>F</i>	<i>p</i>
Subjective Measures						
DEQ						
Drug Effect	25.72	<0.0001	31.19	<0.0001	12.29	<0.0001
Unpleasant	9.67	0.0012	11.03	<0.0001	5.71	0.0050
Pleasant	18.43	<0.0001	21.06	<0.0001	5.76	<0.0001
Drug Liking	11.86	0.0002	13.79	<0.0001	3.19	0.0075
Sick	4.34	0.028	4.76	0.0024	2.51	0.040
Heart Racing	9.28	0.0016	6.22	0.0023	3.4	0.013
Anxious/Nervous	5.29	0.011	4.96	0.0022	2.71	0.037
Relaxed	0.80	0.45	2.07	0.075	1.51	0.16
Paranoid	6.42	0.0065	6.31	0.004	3.13	0.045
Sleepy/Tired	11.25	0.0004	5.45	0.0004	1.38	0.22
Alert	1.16	0.33	2.29	0.07	1.18	0.32
Irritable	3.39	0.046	2.38	0.10	2.07	0.11
Vigorous/Motivated	1.44	0.25	3.32	0.02	1.05	0.40
Restless	3.27	0.051	2.80	0.031	1.51	0.18
Hungry/Had	4.49	0.026	6.78	<0.0001	2.05	0.072
Cannabis Craving	1.48	0.24	3.16	0.051	0.71	0.57
Dry Mouth	12.11	0.0004	8.11	0.0001	4.53	0.0016
Dry/Red Eyes	5.98	0.0096	6.35	0.0022	4.32	0.0045
Memory Impairment	8.34	0.0038	8.23	0.0004	5.13	0.0010
Throat Irritation/Coughing	2.30	0.13	3.81	0.018	2.02	0.11
Difficulty Performing Routine Tasks	18.38	<0.0001	11.46	<0.0001	5.25	0.002
Cognitive Measures						
DSST	1.97	0.17	16.89	<0.0001	5.62	<0.0001
PASAT	8.51	0.0038	3.24	0.028	2.92	0.021
DAT	14.12	0.0001	8.00	0.0015	4.70	0.0084
Physiological Measures						
Heart Rate, beats/min	13.50	<0.0001	3.64	0.0065	7.76	0.0002
Diastolic Blood Pressure, mmHg	0.12	0.88	5.42	<0.0001	1.034	0.41
Systolic Blood Pressure, mmHg	1.08	0.35	2.75	0.023	1.24	0.28
Abbreviations: DEQ = drug effect questionnaire, DSST = digit symbol substitution task, DAT = divided attention task, PASAT = paced serial addition task. SD = standard deviation. N=18 for total sample.						

eFigure. Change From Baseline Mean Ratings for the Visual Analog Scale Items on Adverse Outcomes

○ CYP Cocktail+Placebo □ CYP Cocktail+Δ9-THC ▲ CYP Cocktail+Δ9-THC+CBD

VAS Score (Δ from baseline)

