Supplementary Table 1. THC/cannabinoid interventions vs. placebo

Lead author, year	Population	Intervention	Comparator	Results
Mohammad Aghaei et al.,[12] 2024	n=56 healthy participants (33 women, 23 men), 18-55 years; prior cannabis exposure ≥1 time, no history of CUD (DSM-5). Community recruitment (flyers/ads/word of mouth). Required negative urine toxicology and negative pregnancy test (women). Most had used cannabis <5 times in the month prior to screening (Tables 1-2; Methods/Results).	Oral THC (dronabinol) 10 mg+D3:D6D3:D10	Oral placebo	VAS "high" (peak vs. baseline): dose×sex interaction ATS=3.81, df=1, p=0.05, d=0.43; in women, dose effect ATS=4.76, df=1, p=0.03, d'=0.48; in men ATS=0.49, df=1, p=0.48, d'=0.11. CADSS: main dose (THC) effect in observer ATS=31.3, df=1, p=0.0001 and subjective ATS=42.0, df=1, p=0.0001; no main sex effect (observer ATS=0.47, p=0.49; subjective ATS=2.77, p=0.9) and no dose×sex interaction (observer ATS=0.19, p=0.66; subjective ATS=2.21, p=0.14). PSI: dose effect ATS=52.7, df=1, p<0.0001; no sex (ATS=0.46, p=0.50) or interaction (ATS=0.1, p=0.76). RAVLT: no main dose/sex/interaction effects on immediate, short, or long recall (details in supplement; text: "no main effect..."). Heart rate: dose effect F(1,54)=21.63, p<0.0001; no sex F(1,54)=1.53, p=0.22; no interaction F(1,54)=1.52, p=0.22.
Ganesh et al.,[17] 2023	n=28 healthy volunteers (12 women), with ≥1 prior cannabis exposure (not naïve). Median age 25.5 (IQR 10.25). Seven (25%) used cannabis >2×/week; past 30 days: 18 (65.29%) no use, 3 (10.71%) 1-3 days, 7 (25%) ≥8 days (Table 1).	IV CBD+IV THC (combinations with CBD:THC ratios 1:1, 2:1, 3:1)	THC alone and placebo (plus CBD alone in Phase 1)	PANSS positive (change): • Phase 1 global effect: ATS=16.01, p<0.00001; post hoc THC vs. CBD:THC 2:1: ATS=0.58, p=0.44. • Responders (Phase 1): THC vs. CBD:THC 2:1: ATS=9.73, p=0.0018. • Phase 2 global effect: ATS=8.73, p<0.00001; post hoc THC vs. 1:1: ATS=7.83, corrected p≈0.015 (table shows p=0.005 uncorrected); THC vs. 2:1: ATS=1.696, p=0.19; THC vs. 3:1: ATS=1.25, p=0.26. VAS "high": • Phase 1 global: ATS=43.02, p<0.00001; THC vs. 2:1: ATS=0.13, p=0.72. • Phase 2 global: ATS=17.57, p<0.00001; THC vs. 1:1 ATS=0.15 p=0.71; vs. 2:1 ATS=0.11 p=0.73; vs. 3:1 ATS=0.15 p=0.698 (all NS). Neural noise (LZC): • Phase 1 global: ATS=5.66, p=0.0015 (post hoc THC vs. 2:1 not significant). • Phase 2 global: ATS=2.68, p=0.04; THC vs. 1:1: ATS=8.83, corrected p=0.009; THC vs. 2:1: ATS=0.33 p=0.56; THC vs. 3:1: ATS=0.76 p=0.38. VAS anxious (Phase 2): THC vs. 3:1 ATS=10.41, corrected p=0.004 (largest attenuation).
Sainz-Cort et al.,[15] 2021	Members of a cannabis social club (Barcelona). Recruited 20; 18 completed (10 women, 8 men). Mean age 29.94 (SD 6.92). Criteria: >21 years, current users ≥3 days/week, no chronic/mental/neurologic disease, 12 h abstinence (alcohol/cannabis/other substances) before each session.	Vaporized THC extract, CBD extract, THC+CBD (2:1)	Placebo (hemp) and comparisons across conditions (THC vs. THC+CBD vs. CBD vs. placebo)	Key examples (means, SD; Table 4): VAS AUC "feeling high": Placebo 16.72 (30.88); CBD 25.92 (34.41); THC+CBD 75.83 (73.20); THC 210.68 (104.92); Friedman p<0.001; THC>THC+CBD (p<0.001); THC>CBD (p<0.001); THC>placebo (p<0.001). ARCI Sedation (true/total): Placebo 0.56 (1.20); CBD 0.61 (1.20); THC+CBD 2.17 (1.72); THC 2.89 (1.78); Friedman p<0.001; THC>THC+CBD (p=0.039); THC>CBD (p<0.001); THC>placebo (p<0.001). PSI "cognitive disorganization": Placebo 3.56 (2.87); CBD 3.61 (2.79); THC+CBD 6.61 (6.55); THC 13.78 (8.43); Friedman p<0.001; THC>THC+CBD (p<0.001); THC>CBD (p<0.001); THC>placebo (p<0.001). PSI "paranoia": Placebo 0.56 (0.92); CBD 0.39 (0.78); THC+CBD 1.06 (1.30); THC 1.89 (1.78); Friedman p=0.004; THC>CBD (p=0.001); THC>placebo (p=0.002). Overall pattern: THC increased most VAS/PSI; THC+CBD showed lower scores than THC on several items; CBD≈placebo on most.
Hindocha et al.,[21] 2020	n=48 cannabis users (age 16-23), exposure range from 1 day/month to daily use; recruited from a prior study (n>400) with genotyping; snowball/word-of-mouth sampling. Inclusion: 24 h abstinence (confirmed with saliva/urine), English, normal/corrected vision. Exclusion: current respiratory/physical problems, pregnancy/risk, learning difficulties, schizophrenia/psychosis or substance abuse, and other illicit drugs >1×/week (pp. 3-4).	Vaporized THC, CBD, THC+CBD	Placebo (ethanol vehicle) and comparisons among active conditions	Satiety (BSS "want to smoke a joint"): • CNR1 rs1049353: drug×genotype interaction F(3,105)=4.192, p=0.008, η^2=0.05. In GG: lower "wanting" vs. placebo after THC (p=0.016; d=0.52) and after THC+CBD (p<0.001; d=0.52); not with CBD (p=0.137; d=0.31). In A (AA/AG): no changes (ps=1.000). Main drug effect: vs. placebo, THC M=4.73 (SE 0.41) p=0.047; THC+CBD M=4.45 (SE 0.42) p=0.001; CBD M=4.95 (SE 0.43) p=0.182. Time effect F(1,36)=12.945 p=0.001 (increases over time). • CNR1 rs806378: main drug effect F(3,114)=3.784 p=0.012; vs. placebo (M=5.36 SE 0.43), lower after THC M=4.730 SE 0.40 p=0.043 and THC+CBD M=4.55 SE 0.43 p=0.004; CBD NS (M=5.06 SE 0.43 p=0.254). • FAAH rs324420: time effect only F(1,27)=11.738 p=0.002. Attentional bias (dot-probe): • CNR1 rs1049353: drug×genotype interaction F(3,120)=3.108 p=0.029 η^2=0.03. In GG, lower bias with THC M=4.25 SE 4.79 vs. CBD M=25.93 SE 4.88 (p=0.011; d=0.74); THC+CBD vs. CBD p=0.066; placebo vs. CBD p=0.291. In A: no differences (ps=1.000). • CNR1 rs806378: main genotype effect F(1,43)=5.679 p=0.022 η^2=0.047: CC M=20.21 (SE 2.87)>T (CT/TT) M=11.38 (SE 2.34), independent of drug/stimulus. • FAAH rs324420: drug×genotype interaction F(3,126)=3.385 p=0.020 η^2=0.003. After THC, CC M=5.56 (SE 3.71)<A (AA/AC) M=21.41 (SE 5.42) (p=0.02; d=0.78). In CC, THC<CBD (CBD M=21.14 SE 3.81; p=0.018; d=0.56). Craving (MCQ): no main effects or drug×genotype interactions for any SNP (p. 8).
Woelfl et al.,[20] 2020	Sixty healthy volunteers, male, right-handed, 19-36 years; no severe medical/neurologic illness and no personal/family psychiatric history; excluded: recurrent substance abuse, cannabis use >10 times or <1 time lifetime, or use in the prior 6 months; BMI 18-30; negative urine screen; no caffeine/alcohol/nicotine during the study. Four parallel groups (1:1:1:1), stratified by COMT genotype; n=15/group.	CBD/THC (CBD before THC)	PLA/PLA; CBD/PLA; PLA/THC (and between-arm comparisons)	Emotion (V2-baseline difference): • Performance-related activity: CBD/THC median -8 (0,25,75,100: -12, -9, -5, -4) vs. PLA/PLA median -3 (-12, -5, -1, 2), p=0.002; vs. CBD/PLA median -2 (-18, -7, -1, 8), p=0.035. • Depressiveness: CBD/THC median 1 (-1, 0, 6, 8) vs. PLA/PLA median 0 (-4, 0, 1, 3), p=0.015; vs. CBD/PLA median 0 (-4, 0, 1, 3), p=0.026. • Extraversion: CBD/THC median -3 (-11, -8, -2, 0) vs. PLA/PLA median 0 (-10, -2.5, 1, 6), p=0.013; vs. CBD/PLA median -1 (-7, -3, 0.5, 4), p=0.017. • Emotional excitability: Kruskal-Wallis p=0.058 (not significant). Cognition/attention (V2-baseline differences): • Digit symbol coding: CBD/PLA median 6 (-3, 5, 12, 20) vs. PLA/THC median 2 (-79, -4.5, 6, 20), p=0.039; vs. CBD/THC median -2 (-27, -12.5, 7, 11), p=0.016 (comparisons reported vs. CBD/PLA). • Letter-number sequencing: CBD/THC median 0 (-4, -1.5, 1, 2) vs. CBD/PLA median 2 (-2, 0.5, 3, 4), p=0.005. • d2 "concentration capacity": CBD/THC median -10 (-55, -25, 15, 62) vs. PLA/PLA median 25 (-20, 16, 33.5, 43), p=0.005; vs. CBD/PLA median 29 (-48, 10.5, 35.5, 67), p=0.010. • d2 "error-corrected total number" (global, 3 measures): V1 median 536 (293, 461, 556.25, 618.00) → V2 median 539 (329.0, 456.5, 583.0, 652) → V3 median 593.5 (414.0, 547, 639.5, 653). THC levels (pmol/mL): PLA/THC median 0.954 (0.0, 0.817, 1.615, 9.690) vs. CBD/THC median 2.61 (0.614, 1.032, 3.960, 8.350), difference not significant.
Ranganathan et al.,[13] 2017	Healthy participants recruited from the community. Inclusion: 18-55 years, good physical/mental health, cannabis use ≥1 time lifetime. Not regular daily users (to avoid withdrawal). Two experiments: Exp #1 n=38 (THC after encoding) and Exp #2 n=57 (THC before encoding); 16 participated in both.	IV THC (Δ9-THC)	IV placebo (ethanol vehicle)	RAVLT (Table 2): Exp #1 (post-encoding): immediate total 59.17±10.08 (THC) vs. 59.40±9.41 (placebo), p=0.99; short delayed 13.14±2.24 vs. 12.80±2.62, p=0.54; long delayed 10.79±3.61 vs. 11.00±3.79, p=0.67; rate of learning 6.03±2.08 vs. 5.37±1.77, p=0.18. Exp #2 (pre-encoding): immediate total 44.86±13.09 (THC) vs. 55.50±9.64 (placebo), p<0.0001; short delayed 9.33±4.22 vs. 11.69±2.72, p<0.0001; long delayed 9.04±4.29 vs. 11.45±2.90, p<0.0001; rate of learning 5.91±2.88 vs. 5.52±1.85, p=0.31. VAS "high": Exp #1 61.21±28.64 (THC) vs. 9.97±21.05 (placebo); Exp #2 58.44±28.37 vs. 8.58±15.34; dose effect F(1,92)=204.9, p<0.0001.
Cortes-Briones et al.,[14] 2015	Randomized, double-blind crossover trial in healthy humans. Analyzed n=20 with complete EEG (of 56 consented; 30 completed 3 days; exclusions for artifacts/outliers). Age 18-35 (in analysis: 25.7±7.6), 14 men/6 women; education 15.2±2.1; estimated IQ 116.9±3.9; BMI 24.25±2.99. Subgroups: recent users (≤30 days) n=9 vs. non-users n=11. Cannabis-naïve excluded; cannabis dependence and DSM-IV Axis I disorders excluded (except tobacco/cannabis), etc.	IV Δ9-THC	Placebo (vehicle)	Table 2 [means (SD)]: ITC: 40 Hz placebo 0.149 (0.082); 0.015 0.142 (0.073); 0.03 0.104 (0.073). 30 Hz: 0.027 (0.042); 0.042 (0.044); 0.043 (0.043). 20 Hz: 0.038 (0.040); 0.030 (0.040); 0.039 (0.041). Evoked power (μV^2): 40 Hz placebo 0.288 (0.209); 0.015 0.269 (0.167); 0.03 0.196 (0.167). 30 Hz: 0.075 (0.122); 0.114 (0.137); 0.107 (0.100). 20 Hz: 0.252 (0.393); 0.134 (0.178); 0.184 (0.194). Dose effect (ITC 40 Hz): Wald(2)=12.677, pAdj=0.006; 0.03<0.015 (pAdj=0.005) and 0.03<placebo (pAdj=0.002). Evoked power: no significant effect after correction; trend at 40 Hz [Wald(2)=5.023, p=0.081]. PANSS: Δ9-THC increased PANSS positive/negative/general/total (all p<0.001); all doses differed at 10 min post-infusion (all p<0.01). (PANSS means/SD not shown in the extracted fragments.) ITC-PANSS (active conditions only): ITC inversely associated with PANSS positive β=-0.385 (pAdj=0.028), negative β=-0.358 (pAdj=0.021), general β=-0.383 (pAdj=0.036), total β=-0.453 (pAdj=0.002). Exploratory (recent use): recent users had lower ITC at trend level (p=0.07) and lower evoked power [Wald(1)=5.188, p=0.023]; no significant group×dose interaction.
Schoedel et al.,[16] 2011	n=23 frequent recreational cannabis users (completed all sessions); 20-45 years (mean 28.9±7.48), 83.3% men. "Frequent" defined as non-medical use ≥1×/week in 3 months+≥4×/week at least once; urine THC+ at screening and rating session; excluded alcohol/drug dependence, heavy caffeine use/smokers, etc.	Nabiximols (Sativex®) oromucosal spray (THC:CBD ~1:1)	Placebo and oral dronabinol (synthetic THC) 20 mg and 40 mg	Primary [LS mean (95% CI), N=23; Table 2]: drug liking VAS (E_{max}/E_{min}/AUE24) • Placebo: 43.8 (34.4-53.3)/23.8 (14.5-33.1)/699.9 (454.4-945.5) • Nabix 10.8: 53.1 (43.7-62.6)/27.1 (17.7-36.4)/860.4 (614.8-1105.9) • Nabix 21.6: 60.5 (51.0-69.9)/24.9 (15.5-34.2)/917.4 (671.9-1163.0) • Nabix 43.2: 72.8 (63.4-82.3)/29.8 (20.5-39.1)/1284.9 (1039.3-1530.4) • Dronabinol 20: 69.6 (60.1-79.0)/39.5 (30.2-48.8)/1271.1 (1025.5-1516.6) • Dronabinol 40: 76.1 (66.6-85.5)/36.5 (27.2-45.9)/1360.9 (1115.4-1606.45) SDV (E_{max}; Canadian $): placebo 0.93 (-3.5-5.4); Nabix 10.8 5.68 (1.2-10.2); Nabix 21.6 7.42 (3.0-11.9); Nabix 43.2 13.80 (9.3-18.3); Dron 20 10.34 (5.9-14.8); Dron 40 17.32 (12.8-21.8). ARCI MBG (E_{max}/AUE24): Placebo 4.4 (2.6-6.2)/60.2 (43.1-77.3); Nabix 10.8 5.2 (3.4-6.9)/63.2 (46.2-80.3); Nabix 21.6 5.9 (4.1-7.6)/69.4 (52.4-86.5); Nabix 43.2 7.1 (5.3-8.9)/81.6 (64.6-98.7); Dron 20 6.8 (5.1-8.6)/68.5 (51.4-85.6); Dron 40 8.1 (6.3-9.8)/81.7 (64.6-98.7). Secondary [E_{max} LS mean (SE), Table 3; examples]: High VAS: placebo 23.7 (7.5); Nabix 21.6 44.2 (7.4); Nabix 43.2 69.4 (7.4); Dron 20 60.9 (7.4); Dron 40 75.2 (7.4). Stoned VAS: placebo 14.6 (7.3); Nabix 21.6 38.5 (7.3); Nabix 43.2 61.4 (7.3); Dron 20 55.8 (7.3); Dron 40 75.1 (7.23). Cognition/psychomotor: no significant global effects on CRT or DAT; on STM, dronabinol 40 mg increased E_{max} "reaction time" vs. placebo (p=0.010). PK (1.5 h): higher peak THC with dronabinol vs. nabiximols at comparable doses: difference 3.0 ng/mL (dron 20 vs. nabix 21.6) and 10.2 ng/mL (dron 40 vs. nabix 43.2), p<0.001. AEs (Table 4; ≥2 subjects): "Any AE" 50% placebo; 50% nabix 10.8; 67% nabix 21.6; 85% nabix 43.2; 71% dron 20; 84% dron 40. "Euphoric mood" 17% placebo vs. ~54-56% in dronabinol/nabix 43.2.

THC: Tetrahydrocannabinol, CBD: Cannabidiol, CUD: Cannabis use disorder, DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th edition, VAS: Visual analog scale, AUC: Area under the curve, "Peak vs. baseline": Difference between the maximum value and the baseline value, ANOVA: Analysis of variance, ATS: ANOVA-type statistic, df: Degrees of freedom, d/d': Effect size (Cohen's), CADSS: Clinician-administered dissociative states scale, PSI: Psychotomimetic states inventory, RAVLT: Rey auditory verbal learning test, PANSS: Positive and negative syndrome scale, LZC: Lempel-Ziv complexity (a measure of "neural noise"), BSS: Behavioral satiety scale, *CNR1: Cannabinoid receptor type 1* gene, FAAH: Fatty acid amide hydrolase, SNP: Single-nucleotide polymorphism, EEG: Electroencephalography, ITC: Inter-trial coherence, SD: Standard deviation, SE: Standard error, E_{max}/E_{min}: Maximum/minimum effect value, AUE24: Area under the effect curve up to 24 h, SDV: Street drug value (perceived economic value), ARCI MBG: Morphine-benzedrine group subscale of the addiction research center inventory, PK: Pharmacokinetics, AE(s): Adverse event(s), IV: Intravenous, PLA: Placebo

Supplementary Table 2. THC/cannabinoid interventions vs. active comparator

Lead author, year	Population	Intervention	Active comparator	Results
Oliver et al.,[18] 2024	n=46 healthy volunteers; infrequent cannabis users (<1 time/week); 21-50 years; recruited at King's College London; multiple exclusions (major psychiatric/physical disorders or SUD, psychotropic medication, first-degree relative with psychosis, positive drug test, recent alcohol/tobacco, pregnancy/lactation, BMI<18 or >30, etc.).	Vaporized cannabis with fixed THC+variable CBD (CBD:THC ratios 0:1, 1:1, 2:1, 3:1)	(1) Baseline vs. THC-only (0:1). (2) Between-ratio comparisons (0:1 vs. 1:1 vs. 2:1 vs. 3:1).	THC effect (0:1 vs. baseline; Table 2): • Total cannabis AB: Δ=12.2 (95% CI 1.20 to 23.3), d=0.41, p=0.03 • Short cannabis AB: Δ=15.1 (-3.2 to 33.4), d=0.38, p=0.10 • Long cannabis AB: Δ=9.8 (-7.0 to 26.6), d=0.26, p=0.25 • Total food AB: Δ=6.3 (-5.4 to 18.0), d=0.21, p=0.29 • Short food AB: Δ=11.3 (-3.0 to 25.7), d=0.27, p=0.12 • Long food AB: Δ=0.3 (-11.7 to 12.3), d=0.02, p=0.96 • PR cannabis: Δ=0.3 (-0.1 to 0.7), d=0.23, p=0.12 • PR food: Δ=0.3 (-0.02 to 0.7), d=0.21, p=0.06 CBD effect (mixed models; Table 3; all p>0.05 after correction): Cannabis AB (EMM diff; 95% CI; p): 0:1-1:1 1.657 (-10.777, 14.092) 0.993; 0:1-2:1 -1.991 (-14.344, 10.363) 0.988; 0:1-3:1 2.327 (-10.192, 14.846) 0.982; 1:1-2:1 -3.648 (-16.083, 8.787) 0.935; 1:1-3:1 0.670 (-11.931, 13.271) 1.000; 2:1-3:1 4.318 (-8.202, 16.837) 0.899. Food AB: 0:1-1:1 -1.203 (-14.547, 12.141) 0.998; 0:1-2:1 -1.079 (-14.340, 12.181) 0.998; 0:1-3:1 1.247 (-12.183, 14.677) 0.998; 1:1-2:1 0.123 (-13.221, 13.467) 1.000; 1:1-3:1 2.450 (-11.063, 15.963) 0.983; 2:1-3:1 2.327 (-11.104, 15.757) 0.985. PR cannabis: 0:1-1:1 0.330 (0.041, 0.620) 0.104; 0:1-2:1 0.197 (-0.093, 0.486) 0.521; 0:1-3:1 0.137 (-0.153, 0.426) 0.778; 1:1-2:1 -0.133 (-0.423, 0.156) 0.790; 1:1-3:1 -0.194 (-0.483, 0.096) 0.535; 2:1-3:1 -0.060 (-0.350, 0.229) 0.975. PR food: 0:1-1:1 0.214 (-0.134, 0.562) 0.604; 0:1-2:1 0.126 (-0.221, 0.474) 0.884; 0:1-3:1 -0.032 (-0.380, 0.315) 0.998; 1:1-2:1 -0.087 (-0.435, 0.260) 0.958; 1:1-3:1 -0.246 (-0.594, 0.102) 0.486; 2:1-3:1 -0.159 (-0.506, 0.189) 0.795. Correlations (p. 9): cannabis AB vs. THC peak r=-0.06, p=0.43; THC AUC r=-0.08, p=0.31; CBD peak r=-0.01, p=0.88; CBD AUC r=-0.02, p=0.79 (others not significant).
Englund et al.,[19] 2023	N=46 healthy volunteers (21-50 years), infrequent users: used cannabis ≥1 time, but not >1/week in past 12 months; never used synthetics; no substance use disorder. Crossover: baseline visit+4 experimental visits; minimum washout 1 week (mean 24 days). Screened 80, randomized 64, completed 46.	Vaporized cannabis with 10 mg THC and variable CBD (0/10/20/30 mg): CBD:THC ratios 0:1, 1:1, 2:1, 3:1	Primary: between-ratio comparisons (CBD:THC). Secondary: baseline vs. THC-only (0:1).	HVLT-R (baseline vs. 0:1 THC): immediate t(45)=5.580, d=0.82, p=1.31×10^{-6}; delayed t(45)=3.399, d=0.50, p=0.001; intrusions t(45)=-3.824, d=0.56, p=4.02×10^{-4} and t(45)=-3.322, d=0.49, p=0.002. Between ratios: no differences (p>0.008). PANSS positive (baseline vs. 0:1): t(45)=-4.709, d=0.69, p=2.41×10^{-5}. "PANSS response" (≥3 points): 24/46 (52.2%) at least one visit; by condition: 0:1 n=12 (26.1%), 1:1 n=10 (21.7%), 2:1 n=15 (32.6%), 3:1 n=10 (21.7%). Between ratios: PANSS p>0.008; response χ^2(3,n=46)=2.202, p=0.532. Digit span (baseline vs. 0:1): forward t(45)=3.309, d=0.49, p=0.002; reverse t(45)=2.361, d=0.35, p=0.023. Between ratios: no differences. CAPE/PSI/SSPS: CAPE baseline vs. 0:1 t(45)=-4.088, d=0.60, p=0.0002; PSI baseline vs. 0:1 t(39)=-7.461, d=1.18, p=5.025×10^{-9}; SSPS between ratios t(45)=-1.096, d=0.16, p=0.279 (overall, between ratios p>0.008). Physiology: heart rate baseline vs. 0:1 t(44)=-9.35, d=1.39, p=5.06×10^{-12}; systolic BP t(44)=-1.19, p=0.240 and diastolic BP t(44)=0.312, p=0.756 (NS). Between ratios: no differences (p>0.008). PK: no differences in THC peak/AUC (p>0.008); CBD peak/AUC increases with dose (p<0.001). 7-OH-CBD peak: 3:1 vs. 0:1 EMM=2.686 (95% CI 1.888-3.483), p=1.25×10^{-9}; 3:1 vs. 1:1 EMM=2.206 (1.551-2.861), p=0.002. 7-OH-CBD AUC: 2:1 vs. 0:1 EMM=4.676 (3.287-6.064), p=0.003; 3:1 vs. 0:1 EMM=8.898 (6.256-11.540), p=1.71×10^{-9}; 3:1 vs. 1:1 EMM=6.843 (4.811-8.875), p=3.57×10^{-6}.

THC: Tetrahydrocannabinol, CBD: Cannabidiol, CBD:THC (0:1, 1:1, 2:1, 3:1): Cannabidiol:tetrahydrocannabinol ratio in the administered product, AB: Attentional bias toward cannabis- or food-related cues (cannabis AB/food AB), PR: Pleasantness/preference rating for cannabis or food cues (cannabis PR/food PR), AUC: Area under the curve, EMM: Estimated marginal means, EMM diff: Difference in EMMs, 95% CI: 95% Confidence interval, HVLT-R: Hopkins verbal learning test-revised, PANSS: Positive and negative syndrome scale, CAPE: Community assessment of psychic experiences, PSI: Psychotomimetic states inventory, SSPS: State social paranoia scale, HR: Heart rate, BP: Blood pressure, 7-OH-CBD: 7-Hydroxycannabidiol (metabolite), t: Student's t statistic, χ^2: Chi-square, d: Effect size (Cohen's d), NS: Not significant

Supplementary Table 3. Overall risk of bias (RoB 2)

Study	Overall risk of bias
Oliver et al.[18]	High
Mohammad Aghaei et al.[12]	High
Ganesh et al.[17]	High
Sainz-Cort et al.[15]	High
Hindocha et al.[21]	High
Woelfl et al.[20]	High
Ranganathan et al.[13]	Some concerns
Cortes-Briones et al.[14]	High
Schoedel et al.[16]	High
Englund et al.[19]	High

Overall judgments were based on RoB 2. "High": High risk of bias; "Some concerns": Some concerns. The most common reasons for "High" judgments were limitations in the measurement of subjective outcomes, missing data/attrition, deviations from intended interventions or protocol, and multiplicity of analyses/reporting