**Supplemental Materials**

**Overview of studies included in this systematic review (N=60)**

Studies found through the PubMed search (n=49)

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**Figure S1.** PRISMA flow diagram for systematic review

**Table S1.** Overview of side effects and drop-out rates

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| First Author | Start sample | Drop-out | Analyzing sample | Bedrocan | Bediol  | Bedrolite | Combinationtreatment | Placebo |
| van de Donk et al. (2019) | 25 | 1 = unknown reasons3 = nausea during visit\*\*1 = fear of needles | 20 | 16 = drug high 14 = coughing 5 = bad taste 3 = nausea 3 = dizzy 2 = sore throat 1 = headache 1= sleepy  | 16 = drug high 14 = coughing 7 = sore throat 6 = bad taste 6 = nausea 4 = dizzy 2 = headache 1 = dyspnoea  | 13 = coughing8 = drug high5 = bad taste 3 = headache 2 = dizzy 1 = sore throat 1 = nausea 1 = vomiting 1 = sleepy  | NA | 2 = drug high1 = headache |
| Almog et al. (2020) | 27 | 1 = did not complete all sessions due to technical failure1 = consent withdrawal | 27 | **0.5 mg**12 = drug high 8 = dry mouth7 = pain7 = weakness 7 = restlessness 6 = sleepiness4 = cough2 = dizziness2 = nausea 2 = BP reduced**1.0 mg**16 = drug high 11 = cough 8 = dizziness6 = weakness 5 = dry mouth4 = sleepiness4 = nausea 3 = pain3 = restlessness 2 = BP reduced2 = hunger | NA | NA | NA | 9 = drug high 7 = restlessness6 = pain5 = weakness 3 = hunger2 = dry mouth2 = sleepiness2 = cough2 = nausea 2 = BP reduced1 = dizziness |
| Aviram et al. (2022) | 215 | **excluded from analysis**25 = stopped treatment before achieving a balanced regimen25 = pilot program13 = stopped during titration period9 = requested to not respond to questions**reasons for stopping treatment**8 = worsening of medical condition7 = financial reasons5 = ineffectiveness of treatment3 = deceased (unrelated to treatment)3 = no longer need treatment1 = adverse event\*\*1 = regulatory reasons | 143 | 25 = dizziness15 = headache11 = sleepiness8 = anxiety6 = dry mouth4 = nausea4 = cough3 = heartburn3 = confusion3 = concentration impairment2 = memory impairment2 = restlessness2 = palpitations1 = vomiting1 = tinnitus1 = muscle pain | NA | NA | NA | NA |
| Baraldi et al. (2021)\* | 32 | after 6 months 2 = vertigo\*\*2 = NR | 32 | NA | NA | NA | 10 = drowsiness2 = postural instability1 = vertigo1 = weight gain**baseline (n=32)**30 = nausea and/or vomiting19 = photophobia and/or phonophobia**3 months (n=32)**20 = nausea and/or vomiting19 = photophobia and/or phonophobia**6 months (n=28)**19 = nausea and/or vomiting19 = photophobia and/or phonophobia | NA |
| Eisenberg et al. (2014) | 10 | 2 = failed device | 8 | 7 = lightheadedness for the first 10 minutes | NA | NA | NA | NA |
| Giorgi et al. (2020) | 102 | 25 = lost to follow-up3 = lack of benefit effect6 = adverse events (mainly nausea, palpitations and dizziness)\*\*2 = high cost of treatment | 66 | NA | NA | NA | 14 = dizziness 11= sleepiness 8 = palpitations 6 = nausea6 = xerostomia 5 = blurred vision5 = stypsis3 = headache3 = hunger1 = dyspnea | NA |
| Mazza et al. (2021)\* | 38 | **before start of the treatment**1 = did not start due to unpleasant scent1 = difficulty to retrieve cannabis1 = long period of hospitalization following prescription**1 month follow-up (n=30)**4 = vomiting after intake\*\*1 = experienced several side effects\*\***3 months follow-up (n=18)**12 = different side effects\*\***12 months follow-up (n=12)**6 = personal reasons, moving or pharmacy no longer supplied cannabis | 35 | NA | NA | NA | **after one day to 1 month (n=35)**13 = mental confusion5 = nausea/vomiting5 = vertigo/dizziness5 = restlessness/irritation4 = palpitations4 = somnolence2 = dry mouth2 = insomnia1 = nightmares1 = increased hunger1 = euphoria1 = headache1 = increased sexual drive1 = abdominal distension1 = erect nipples1 = fatigue1 = anger**after 3 months (n=18)**1 = headache1 = decreased creativity**after 12 months (n=12)**2 = memory impairment | NA |
| Nunnari et al. (2022)\* | 186 | 6 = different formulations20 = discontinuation of cannabis-based oil before six months 104 = lack of a follow-up visit after at least six months from the first consumption  | 56 | NA | NA | NA | NR | NA |
| Palmieri et al. (2019) | 20 | NA | 20 | 3 = somnolence | NA | NA | NA | NA |
| Poli et al. (2018) | 338 | **1 month follow-up**79 = inefficacy33 = side effects (sleepiness 30%; mental confusion 25%)\*\* | 338 | 10 = sleepiness8 = mental confusion15 = other side effects | NA | NA | NA | NA |
| Vulfsons et al. (2020) | 22 | 1 = preferred not to use the inhaler | 21 | 3 = mild cough after inhalation | NA | NA | NA | NA |
| Sacca et al. (2016) | 13 | 1 = dizziness\*\* 1 = drug cost | 13 | 3 = dizziness  | NA | NA | NA | NA |
| Engels et al. (2007) | 24 | NA | 24 | NR | NA | NA | NA | NA |
| Zafar et al. (2020) | 10 | NA | 10 | NA | NA | NA | No adverse side effects occurred | NA |
| Zafar et al. (2021)\* | 10 | NA | 10 | NA | NA | NA | No adverse side effects occurred | NA |
| Pane et al. (2020) | 5 | NA | 5 | NA | NA | NA | 1 = panic attack | NA |
| Palmieri et al. (2023) | 30 | NA | 30 | No adverse side effects occurred | NA | NA | NA | NA |
| De Wit et al. (2023) | 18 | 3 = discontinued cannabis use | 18 | NA | NA | NA | 4 = drug high1 = starvingfeeling anxious, depressed, or drowsy at times | NA |

\*Combination treatment with medicinal cannabis from different companies, only Bedrocan products and dosing are reported. NR = Not Reported; NA = Not apllicable DB = Double Blind; PC = Placebo Controlled; Ra = Randomized; Cr = Crossover; OL = Open-Label; RE = Retrospective; PR = Prospective; QU = Qualitative. \*\*drop-out related to side effects