

<b>Author Year</b> <b>Country</b> <b>PEdro Score</b> <b>Research Design</b> <b>Total Sample Size</b>	<b>Methods</b>	<b>Outcome</b>
<p>Wilsey et al. 2016 USA RCT Crossover PEdro=8 N=42</p>	<p><b>Population:</b> Mean age=46.4±13.6 yr; Gender: males=29, females=13; Level of injury: C=22, T=14, L=6; Severity of injury; Type of pain=neuropathic.  <b>Intervention:</b> Participants completed all conditions over the course of 3 8 hr sessions, during which were given either a placebo cannabis vapor, 2.9%, or 6.7% delta-9 THC with assessments taken at time of administration and hourly after for 7 hrs. Crossover design was used so each session they were given a different treatment condition.  <b>Outcome Measures:</b> Pain intensity numeric rating scale (NRS), pain relief (patient global impression of change (PGIC)), neuropathic pain scale (NPS), allodynia visual analog scale (VAS), heat-pain threshold, drug effect VAS, spasticity NRS and PGIC, modified Ashworth scale (MAS) for spasticity, vital signs (heart rate (HR), blood pressure (BP)), neurocognitive assessments (attention and concentration, fine motor speed processing speed and learning and memory (Wechsler adult intelligence scale digit symbol test (DST), (trail marking test (TMT), grooved pegboard test (GBT), paced auditory serial addition test (PASAT), Hopkins verbal learning test revised (HVLT)).</p>	<ol style="list-style-type: none"> <li>1. Significant dose effect on pain intensity was observed after controlling for baseline pain (p&lt;0.0001) and a significant stairstep effect between conditions was observed where significantly less pain was felt at the 2.9% delta 9-THC dose compared to baseline, and significantly less pain was felt at the 6.7% dose compared to baseline and the 2.7% dose.</li> <li>2. Pain intensity was observed to be significantly lower for both dosages of delta 9-THC compared to baseline (p&lt;0.05), but only the 6.7% dose showed significance over the following 2 hrs (p&lt;0.01).</li> <li>3. Four sided effects (“bad drug effect,” “nauseous,” “changes perceiving time,” and “difficulty remembering things”) showed no significant effect on pain, but others did (p ranged from &lt;0.0001 to p=0.02), but main effect for delta 9-THC treatment remained significant above all effects of psychomimetic measures (p&lt;0.0004).</li> <li>4. 18 participants achieved a 30% pain reduction (clinically important while using placebo, while 26 and 35 reached 30% for the lower and higher dosages respectively.</li> <li>5. Significantly more pain relief with active cannabis compared to placebo (p&lt;0.0001) and the effect was observed immediately after vaporization (p&lt;0.005) and 1 hr (p&lt;0.04), but not 2 hrs later (p&gt;0.2).</li> <li>6. For second vaporization, but active cannabis doses provided greater pain relief than placebo immediately (p&lt;0.001) and one hour later (p&lt;0.05), but only one dose remained effective in reducing pain significantly compared to placebo (2.9% at time 360, p=0.03; 6.7% at time 420, p=0.03) with no time showing a significant difference in pain relief between active delta 9-THC doses.</li> <li>7. Across all timepoints, measurements of NPS showed that vaporized cannabis positively and significantly affected all measured multidimensional pain descriptors associated with neuropathic pain, even after controlling for baseline</li> </ol>

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<p>Andresen et al. 2016 Denmark RCT PEDro= N=73</p>	<p><b>Population:</b> Mean age=56.3±11.6 yr; Gender: males=54, females=19; Time since injury=10.3±11.7 yr; Level of injury: tetraplegia=32, paraplegia=41; Severity of injury: AIS A=24, B=3, C=15, D=31; Type of pain=neuropathic. <b>Intervention:</b> Participants were randomized to a ultramicronized (Normast) group or a placebo group taking dosages 2 times daily with 12 h between dosages, for 12 wks. <b>Outcome Measures:</b> Change in neuropathic pain intensity from baseline wk to wk 12 and analysis and effects on spasticity, evoked pain, sleep problems, anxiety, depression and global impression of change.</p>	<p>levels (p&lt;0.0001 except for itching: p=0.04).</p> <ol style="list-style-type: none"> <li>1. No significant difference between change in neuropathic pain intensity observed between the Normast and placebo groups (p=0.46).</li> <li>2. No significant difference over time between the two groups when using covariates (p=0.82).</li> <li>3. Normast group had a significant reduction in their use of rescue medication compared to the placebo group (p=0.02).</li> <li>4. Normast group showed a significant increase in intensity of spasticity observed in the pain diary recordings compared to a decrease in the placebo group (p=0.013).</li> <li>5. No significant differences observed in any of the other outcome measures (p&gt;0.05).</li> </ol>
<p>Rintala et al. 2010 USA RCT PEDro=5 N=7</p>	<p><b>Population:</b> Mean age: 50.1 yr. Severity of injury: AIS A=4, B=1, D=2. Level of injury: paraplegia=4, tetraplegia=3. Mean time since injury was 21.9 yr. Type of pain=neuropathic, <b>Treatment:</b> Participants were randomized into two groups: 1) 5 mg dronabinol titrated every third day (max 20 mg/day) ; 2) 25 mg diphenhydramine day one then titrated up to 75 mg/day. Participants remained in a seven day stabilization phase once titration was complete and then a 28 day maintenance phase. Next participants completed a nine day weaning-off phase followed by a seven day washout period. Each participant then crossed over to the other group. <b>Outcome Measures:</b> Brief Pain Inventory (BPI)</p>	<ol style="list-style-type: none"> <li>1. Pain intensity was not significantly different between the dronabinol and diphenhydramine groups.</li> <li>2. No significant difference was seen in side effects between the groups.</li> <li>3. Most common side effects included dry mouth, constipation, fatigue and drowsiness.</li> </ol>
<p>Hagenbach et al. 2007 Switzerland  Phase 1-2 Non-RCT N=25  Phase 3 RCT PEDro=4 N=13</p>	<p><b>Population:</b> SCI (N=15): Age=29-66 yr; Gender: males=11, females=2; Level of injury: C4-T11; Severity of injury: AIS: A,B,C,D Type of pain=neuropathic. <b>Treatment:</b> Phase 1-2: Patients received 10 mg oral tetra hydrocannabinol (THC) on day one. Dose titration began on day two until the maximum tolerated dose or treatment aim was achieved and maintained for 6 wk. Phase 3: In a double blind manner, SCI patients from phase 1 of the study were randomly assigned to either maximum oral THC doses (6 participants) or placebo doses (7 participants) for 6 weeks. <b>Pain Scale:</b> Self ratings</p>	<ol style="list-style-type: none"> <li>1. Significant improvement in pain was seen on day one compared to baseline measures (p=0.047).</li> <li>2. No significant improvement in pain post SCI was seen compared to placebo on day 8 and 43.</li> <li>3. Individuals in the oral THC group showed no significant difference in mood or attention compared to the placebo group or to baseline.</li> </ol>

