



# Cannabinoids in the Management of Acute Pain: A Systematic Review and Meta-analysis

Objective: To synthesize the best evidence surrounding the efficacy of cannabinoids for acute pain in the clinical setting based on subjective pain scores and observed adverse effects. Design: Systematic review with meta-analysis. Data Sources: PubMed, ...

[View original](#)

1. Aggarwal SK. Cannabinergic pain medicine: a concise clinical primer and survey of randomized-controlled trial results. Clin J Pain. 2013;29:162–171 [[PubMed](#)] [[Google Scholar](#)]
2. Lynch ME, Campbell F. Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials. Br J Clin Pharmacol. 2011;72:735–744 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
3. Whiting PF, Wolff RF, Deshpande S, et al.. Cannabinoids for medical use: a systematic review and meta-analysis. JAMA. 2015;313:2456–2473 [[PubMed](#)] [[Google Scholar](#)]

4. Madden K, van der Hoek N, Chona S, et al.. Cannabinoids in the management of musculoskeletal pain: a critical review of the evidence. *JBJS Rev.* 2018;6:e7 [[PubMed](#)] [[Google Scholar](#)]
5. Reiman A, Welty M, Solomon P. Cannabis as a substitute for opioid-based pain medication: patient self-report. *Cannabis Cannabinoid Res.* 2017;2:160–166 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
6. Aviram J, Samuelly-Leichtag G. Efficacy of cannabis-based medicines for pain management: A systematic review and meta-analysis of randomized controlled trials. *Pain Physician.* 2017;20:E755–E796 [[PubMed](#)] [[Google Scholar](#)]
7. Stevens A, Higgins M. A systematic review of the analgesic efficacy of cannabinoid medications in the management of acute pain. *Acta Anaesthesiol Scand.* 2017;61:268–280 [[PubMed](#)] [[Google Scholar](#)]
8. Liberati A, Altman DG, Tetzlaff J, et al.. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med.* 2009;6:e1000100. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
9. Higgins JPT, Green S. *Cochrane handbook for systematic reviews of interventions.* John Wiley & Sons: Chichester, UK, 2008 [[Google Scholar](#)]

10. Cooper ZD, Comer SD, Haney M. Comparison of the analgesic effects of dronabinol and smoked marijuana in daily marijuana smokers.

Neuropsychopharmacology. 2013;38:1984. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

11. Kalliomäki J, Philipp A, Baxendale J, et al.. Lack of effect of central nervous system-active doses of nabilone on capsaicin-induced pain and hyperalgesia.

Clin Exp Pharmacol Physiol. 2012;39:336–342

[[PubMed](#)] [[Google Scholar](#)]

12. Kraft B, Frickey NA, Kaufmann RM, et al.. Lack of analgesia by oral standardized cannabis extract on acute inflammatory pain and hyperalgesia in volunteers. Anesthesiology. 2008;109:101–110

[[PubMed](#)] [[Google Scholar](#)]

13. Lee MC, Ploner M, Wiech K, et al.. Amygdala activity contributes to the dissociative effect of cannabis on pain perception. Pain. 2013;154:124–134 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

14. Redmond WJ, Goffaux P, Potvin S, et al.. Analgesic and antihyperalgesic effects of nabilone on experimental heat pain. Curr Med Res Opin. 2008;24:1017–1024 [[PubMed](#)] [[Google Scholar](#)]

2008;24:1017–1024 [[PubMed](#)] [[Google Scholar](#)]

15. Rukwied R, Watkinson A, McGlone F, et al.. Cannabinoid agonists attenuate capsaicin-induced responses in human skin. Pain. 2003;102:283–288

[[PubMed](#)] [[Google Scholar](#)]

[\[PubMed\]](#) [\[Google Scholar\]](#)

16. Cooper ZD, Bedi G, Ramesh D, et al.. Impact of co-administration of oxycodone and smoked cannabis on analgesia and abuse liability.

Neuropsychopharmacology. 2018;43:2046–2055 [\[PMC free article\]](#) [\[PubMed\]](#) [\[Google Scholar\]](#)

17. Cooper ZD, Haney M. Sex-dependent effects of cannabis-induced analgesia. Drug Alcohol Depend.

2016;167:112–120 [\[PMC free article\]](#) [\[PubMed\]](#) [\[Google Scholar\]](#)

18. Esfandyari T, Camilleri M, Busciglio I, et al.. Effects of a cannabinoid receptor agonist on colonic motor and sensory functions in humans: a randomized, placebo-controlled study. Am J Physiol Gastrointest Liver Physiol. 2007;293:G137–G145 [\[PubMed\]](#) [\[Google Scholar\]](#)

19. Greenwald MK, Stitzer ML. Antinociceptive, subjective and behavioral effects of smoked marijuana in humans. Drug Alcohol Depend. 2000;59:261–275 [\[PubMed\]](#) [\[Google Scholar\]](#)

20. Naef M, Curatolo M, Petersen-Felix S, et al.. The analgesic effect of oral delta-9-tetrahydrocannabinol (THC), morphine, and a THC-morphine combination in healthy subjects under experimental pain conditions. Pain. 2003;105:79–88 [\[PubMed\]](#) [\[Google Scholar\]](#)

21. Roberts JD, Gennings C, Shih M. Synergistic affective analgesic interaction between delta-9-

tetrahydrocannabinol and morphine. *Eur J Pharmacol.* 2006;530:54–58 [[PubMed](#)] [[Google Scholar](#)]

22. van Amerongen G, Siebenga P, de Kam ML, et al.. Effect profile of paracetamol,  $\Delta$ 9-THC and promethazine using an evoked pain test battery in healthy subjects. *Eur J Pain.* 2018;22:1331–1342 [[PubMed](#)] [[Google Scholar](#)]

23. Wallace M, Schulteis G, Atkinson JH, et al.. Dose-dependent effects of smoked cannabis on capsaicin-induced pain and hyperalgesia in healthy volunteers. *Anesthesiology.* 2007;107:785–796 [[PubMed](#)] [[Google Scholar](#)]

24. Walter C, Oertel BG, Felden L, et al.. Brain mapping-based model of  $\Delta$ (9)-tetrahydrocannabinol effects on connectivity in the pain matrix. *Neuropsychopharmacology.* 2016;41:1659–1669 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

25. De Vita MJ, Moskal D, Maisto SA, et al.. Association of cannabinoid administration with experimental pain in healthy adults: a systematic review and meta-analysis. *JAMA Psychiatry.* 2018;75:1118–1127 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

26. Ouzzani M, Hammady H, Fedorowicz Z, et al.. Rayyan—a web and mobile app for systematic reviews. *Syst Rev.* 2016;5:210. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

27. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. John Wiley & Sons: Chichester, UK, 2011 [[Google Scholar](#)]
28. Welch VA, Akl EA, Guyatt G, et al.. GRADE equity guidelines: 1. Considering health equity in GRADE guideline development: introduction and rationale. J Clin Epidemiol. 2017;90:59–67 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
29. Balshem H, Helfand M, Schünemann HJ, et al.. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011;64:401–406 [[PubMed](#)] [[Google Scholar](#)]
30. Higgins JPT, Thompson SG, Deeks JJ, et al.. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557–560 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
31. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21:1539–1558 [[PubMed](#)] [[Google Scholar](#)]
32. Beaulieu P. Effects of nabilone, a synthetic cannabinoid, on postoperative pain. Can J Anaesth. 2006;53:769–775 [[PubMed](#)] [[Google Scholar](#)]
33. Buggy DJ, Toogood L, Maric S, et al.. Lack of analgesic efficacy of oral delta-9-tetrahydrocannabinol

in postoperative pain. *Pain*. 2003;106:169–172

[[PubMed](#)] [[Google Scholar](#)]

34. Jain AK, Ryan JR, McMahon FG, et al.. Evaluation of intramuscular levonantradol and placebo in acute postoperative pain. *J Clin Pharmacol*. 1981;21:320S–326S [[PubMed](#)] [[Google Scholar](#)]

35. Kalliomaki J, Segerdahl M, Webster L, et al.. Evaluation of the analgesic efficacy of AZD1940, a novel cannabinoid agonist, on post-operative pain after lower third molar surgical removal. *Scand J Pain*. 2013;4:17–22 [[PubMed](#)] [[Google Scholar](#)]

36. Levin DN, Dulberg Z, Chan A, et al.. A randomized controlled trial of nabilone for the prevention of postoperative nausea and vomiting in elective surgery. *Can J Anaesth*. 2017;64:385–395 [[PubMed](#)] [[Google Scholar](#)]

37. Ostfeld T, Price J, Albanese M, et al.. A randomized, controlled study to investigate the analgesic efficacy of single doses of the cannabinoid receptor-2 agonist GW842166, ibuprofen or placebo in patients with acute pain following third molar tooth extraction. *Clin J Pain*. 2011;27:668–676 [[PubMed](#)] [[Google Scholar](#)]

38. Bruni N, Della Pepa C, Oliaro-Bosso S, et al.. Cannabinoid delivery systems for pain and inflammation treatment. *Molecules*. 2018;23:2478

[[PubMed](#)] [[Google Scholar](#)]

[\[Google Scholar\]](#)

39. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. Clin Pharmacokinet. 2003;42:327–360 [\[PubMed\]](#) [\[Google Scholar\]](#)

40. Hartman RL, Brown TL, Milavetz G, et al.. Controlled cannabis vaporizer administration: blood and plasma cannabinoids with and without alcohol. Clin Chem. 2015;61:850–869 [\[PubMed\]](#) [\[Google Scholar\]](#)

42. Hickernell TR, Lakra A, Berg A, et al.. Should cannabinoids be added to multimodal pain regimens after total hip and knee arthroplasty? J Arthroplasty. 2018;33:3637–3641 [\[PubMed\]](#) [\[Google Scholar\]](#)

43. Holdcroft A, Maze M, Dore C, et al.. A multicenter dose-escalation study of the analgesic and adverse effects of an oral cannabis extract (Cannador) for postoperative pain management. Anesthesiology. 2006;104:1040–1046 [\[PubMed\]](#) [\[Google Scholar\]](#)

44. Prabhu AJ. Weeding out the problem: the impact of preoperative cannabinoid use on pain in the perioperative period. Pain. 2018;16:17 [\[PubMed\]](#) [\[Google Scholar\]](#)

45. Shi Y. Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever. Drug Alcohol Depend. 2017;173:144–150 [\[PMC free article\]](#) [\[PubMed\]](#) [\[Google Scholar\]](#)



46. Donvito G, Nass SR, Wilkerson JL, et al.. The endogenous cannabinoid system: a budding source of targets for treating inflammatory and neuropathic pain. *Neuropsychopharmacology*. 2018;43:52. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

47. Nagarkatti P, Pandey R, Rieder SA, et al.. Cannabinoids as novel anti-inflammatory drugs. *Future Med Chem*. 2009;1:1333–1349 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

48. Cabral GA, Griffin-Thomas L. Emerging role of the cannabinoid receptor CB 2 in immune regulation: therapeutic prospects for neuroinflammation. *Expert Rev Mol Med*. 2009;11:1–31 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

49. Chang YH, Lee ST, Lin WW. Effects of cannabinoids on LPS-stimulated inflammatory mediator release from macrophages: involvement of eicosanoids. *J Cell Biochem*. 2001;81:715–723 [[PubMed](#)] [[Google Scholar](#)]

50. Klein TW. Cannabinoid-based drugs as anti-inflammatory therapeutics. *Nat Rev Immunol*. 2005;5:400. [[PubMed](#)] [[Google Scholar](#)]

51. Guindon J, Hohmann AG. The endocannabinoid system and pain. *CNS Neurol Disord Drug Targets*. 2009;8:403–421 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

52. Urits I, Borchart M, Hasegawa M, et al.. An update of current cannabis-based pharmaceuticals in pain medicine. *Pain Ther.* 2019;8:41–51 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
53. Ward SJ, McAllister SD, Kawamura R, et al.. Cannabidiol inhibits paclitaxel-induced neuropathic pain through 5-HT(1A) receptors without diminishing nervous system function or chemotherapy efficacy. *Br J Pharmacol.* 2014;171:636–645 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
54. Rodríguez-Muñoz M, Onetti Y, Cortés-Montero E, et al.. Cannabidiol enhances morphine antinociception, diminishes NMDA-mediated seizures and reduces stroke damage via the sigma 1 receptor. *Mol Brain.* 2018;11:51. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
55. Li H, Kong W, Chambers CR, et al.. The non-psychoactive phytocannabinoid cannabidiol (CBD) attenuates pro-inflammatory mediators, T cell infiltration, and thermal sensitivity following spinal cord injury in mice. *Cell Immunol.* 2018;329:1–9 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
56. Machado Bergamaschi M, Helena Costa Queiroz R, Waldo Zuardi A, et al.. Safety and side effects of cannabidiol, a cannabis sativa constituent. *Curr Drug Saf.* 2011;6:237–249 [[PubMed](#)] [[Google Scholar](#)]

57. Hammell D, Zhang L, Ma F, et al.. Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis. Eur J Pain. 2016;20:936–948 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

58. Philpott HT, O'Brien M, McDougall JJ. Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in rat osteoarthritis. Pain. 2017;158:2442. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]