

# Scientific Studies Reference List

## PAIN

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Blake DR, et al. Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. *Rheumatology*, 2006;45(1), 50–52

Malfait AM, et al. The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritic therapeutic in murine collagen-induced arthritis. *PNAS*, 2000;97(17), 9561–9566

Hammell DC, Zhang LP, Ma F, Abshire SM, McIlwrath SL, Stinchcomb AL, Westlund KN. Transdermal cannabidiol reduces inflammation and pain related behaviours in a rat model of arthritis. *Eur J Pain* 2016;20(6): 936-948. DOI: 10.1016/j.jveb.2012.05.005

Malfait AM, Gallily R, Sumariwalla PF, Malik AS, Andreakos E, Mechoulam R, Feldmann M. The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritic therapeutic in murine collagen-induced arthritis. *Proceedings of the National Academy of Sciences*. 2000;97 (17) 9561-9566. DOI: 10.1073/pnas.160105897

Mlost J, Bryk M, et al.,. Cannabidiol for Pain Treatment: Focus on Pharmacology and Mechanism of Action. *Int J Mol Sci*. 2020 Nov 23;21(22):8870. doi: 10.3390/ijms21228870

## INFLAMMATION

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Couch DG, et al. The use of cannabinoids in colitis: A systematic review and meta-analysis. *Inflammatory Bowel Diseases*, 2018;24(4), 680–697

De Laurentiis A., Araujo, H.A., Rettori, V. Role of the endocannabinoid system in the neuroendocrine responses to inflammation. *Curr Pharm Des*. 2014;20(29): 4697-4706

Lodzki M, Godin B, Rakou L, Mechoulam R, Gallily R, Touitou E. Cannabidiol- transdermal delivery and anti-inflammatory effect in a murine model. *Journal of Controlled Release* 2003;93: 377-387. DOI: 10.1016/j.jconrel.2003.09.001

## OSTEOARTHRITIS

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Gamble LJ, et al. Pharmacokinetics, safety, and clinical efficacy of cannabidiol treatment in osteoarthritic dogs. *Frontiers in Veterinary Science*, 2018;165(5)

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: 2224-2451. DOI: 10.1097/j.pain.0000000000001052

Kogan et al. The Use of Cannabidiol-Rich Hemp Oil Extract to Treat Canine Osteoarthritis-Related Pain: A Pilot Study. *JAHVMA*. 2020

Verrico, et al. A randomized, double-blind, placebo-controlled study of daily cannabidiol for the treatment of canine osteoarthritis pain. *PAIN*. 2020

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## OSTEOARTHRITIS *continued...*

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Mejia S et al. Evaluation of the Effect of Cannabidiol on Naturally Occurring Osteoarthritis-Associated Pain: A Pilot Study in Dogs. *J Am Anim Hosp Assoc.* 2021 Mar 1;57(2):81-90

Brioschi FA, Di Cesare F, Gioeni D, Rabbogliatti V, Ferrari F, D'Urso ES, Amari M, Ravasio G. Oral Transmucosal Cannabidiol Oil Formulation as Part of a Multimodal Analgesic Regimen: Effects on Pain Relief and Quality of Life Improvement in Dogs Affected by Spontaneous Osteoarthritis. *Animals (Basel).* 2020 Aug 26;10(9):1505

Wallace, J.E., Kogan, L.R., Carr, E.C.J. et al. Motivations and expectations for using cannabis products to treat pain in humans and dogs: a mixed methods study. *J Cannabis Res* 2, 36 (2020)

Mejia S, Duerr FM, Griffenhagen G, McGrath S. Evaluation of the Effect of Cannabidiol on Naturally Occurring Osteoarthritis-Associated Pain: A Pilot Study in Dogs. *J Am Anim Hosp Assoc.* 2021 Mar 1;57(2):81-90. doi: 10.5326/JAAHA-MS-7119. PMID: 33450016.

## EPILEPSY

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Devinsky O, Verducci C, Thiele EA, et al.,. Open-label use of highly purified CBD (Epidiolex) in patients with CDKL5 deficiency disorder and Aicardi, Dup15q, and Doose syndromes. *Epilepsy & Behavior* 2018;86: 131-137. DOI:10.1016/j.yebeh.2018.05.013

Vega-Garcia A, Fera-Romero I, et al.,. Cannabinoids: A New Perspective on Epileptogenesis and Seizure Treatment in Early Life in Basic and Clinical Studies. *Front. Behav. Neurosci.*, 2021; doi.org/10.3389/fnbeh.2020.610484

McGrath S, Bartner LR, Rao S, Packer RA, Gustafson DL. Randomized blinded controlled clinical trial to assess the effect of oral cannabidiol administration in addition to conventional antiepileptic treatment on seizure frequency in dogs with intractable idiopathic epilepsy, *Journal of the American Veterinary Medical Association*, 2019;254(11), 1301-1308

Rosenberg EC, Patra PH, Whalley BJ. Therapeutic effects of cannabinoids in animal models of seizures, epilepsy, epileptogenesis, and epilepsy-related neuroprotection. *Epilepsy Behav.* 2017 May;70(Pt B):319-327. doi: 10.1016/j.yebeh.2016.11.006

Bialer M, Perucca E. Does cannabidiol have antiseizure activity independent of its interactions with clobazam? An appraisal of the evidence from randomized controlled trials. *Epilepsia.* 2020;61(6) DOI:10.1111/epi.16542

Devinsky O, et al.,. Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome. *N Engl J Med* 2017;376:2011-20 DOI: 10.1056/NEJMoa1611618

Scuderi C, Filippis D, Juvone T, Blasio A, Steardo A, Esposito G. Cannabidiol in Medicine: A Review of its Therapeutic Potential in CNS Disorders. *Phytotherapy Research* 2009;23: 597-602. DOI: 10.1002/ptr.2625

## ENDOCANNABINOIDS / CANNABINOIDS / CANNABIS / TOXICITY

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Di Marzo V, Melck D, Bisogno T, De Petrocellis L. Endocannabinoids: endogenous cannabinoid receptor ligands with neuromodulatory action. Trends Neurosci. 1998;21(12): 521-528

Hartsel JA, Boyar K, Pham A, Silver RJ, Makriyannis A. Cannabis in Veterinary Medicine: Cannabinoid Therapies for Animals. Nutraceuticals in Veterinary Medicine. 2019; 121-155. DOI:10.1007/978-3-030-04624-8\_10

Hartsel JA, Eades J, Hickory B, Makriyannis A. Cannabis sativa and Hemp. In R.C. Gupta (Ed.), Nutraceuticals Efficacy, Safety and Toxicity. 2016; (pp. 735-751). DOI: 10.1016/B978-0-12-802147-7.00053-X

Howlett AC, Barth F, Bonner TI, Cabral G, Casellas P, Devane WA, et al. International Union of Pharmacology. XXVII. Classification of cannabinoid receptors. Pharmacol. Rev 2002 54:161-202. doi.org/10.1124/pr.54.2.161

Landa L, Sulcova A, Gbelec. The use of cannabinoids in animals and therapeutic implications for veterinary medicine: a review. Vet. Med. 2016;61, 111-122. DOI:10.17221/8762-VETMED

Mackie K. Cannabinoid receptors: where they are and what they do. J Neuroendocrinol. 2008;20 Suppl 1:10-14. DOI:10.1111/j.1365-2826.2008.01671.x

McPartland JM, Matia I, Di Marzo V, Glass M. Evolutionary origins of the endocannabinoid system. Gene. 2005;370:64-74. DOI: 10.1016/j.gene.2005.11.004

Pertwee RG. The pharmacology of cannabinoid receptors and their ligands: an overview. Int J Obes. 2006;30:S13-S18. DOI: 10.1038/sj.ijo.0803272

Sallaberry CA, Astern L. The Endocannabinoid System, Our Universal Regulator. JYI. 2018;34(6): 48-55. DOI: 10.22186/jyi.34.5.48-55

Vaughn D, Kulpa J, Paulionis L. Preliminary Investigation of the Safety of Escalating Cannabinoid Doses in Healthy Dogs. Front. Vet. Sci., 11 February 2020; doi.org/10.3389/fvets.2020.00051

Iffland K, Grotenhermen F. An Update on Safety and Side Effects of Cannabidiol: A Review of Clinical Data and Relevant Animal Studies. Cannabis Cannabinoid Res. 2017;2(1):139-154. doi: 10.1089/can.2016.0034

De Briyne N, Holmes D, et al.,. Cannabis, Cannabidiol Oils and Tetrahydrocannabinol—What Do Veterinarians Need to Know? Animals (Basel). 2021;11(3): 892. doi: 10.3390/ani11030892

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# Scientific Studies Reference List

## ENDOCANNABINOIDS / CANNABINOIDS / ETC. *continued...*

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Vaughn DM, Paulionis LJ, et al,. Randomized, placebo-controlled, 28-day safety and pharmacokinetics evaluation of repeated oral cannabidiol administration in healthy dogs. Am J Vet Res. 2021;82(5):405-416. doi: 10.2460/ajvr.82.5.405

Hazzah et al. Cannabis in Vet Med; A Critical Review, JAHVMA 2020

Bartner LR et al. Pharmacokinetics of cannabidiol administered by 3 delivery methods at 2 different dosages to healthy dogs. Can J Vet Res. 2018;82(3):178-183

McGrath S et al. A Report of Adverse Effects Associated with the Administration of Cannabidiol in Healthy Dogs, AHVMA J. 2018; 52, 34-38

Wakshlag JJ et al. Pharmacokinetics of Cannabidiol, Cannabidiolic Acid,  $\Delta$ 9-Tetrahydrocannabinol, Tetrahydrocannabinolic Acid and Related Metabolites in Canine Serum After Dosing With Three Oral Forms of Hemp Extract. Front Vet Sci. 2020 Sep 4; 7:505

Russo EB, McPartland JM. Cannabis is more than simply delta(9)-tetrahydrocannabinol. Psychopharmacology (Berl) 2002;165(4):431-432

Deabold KA, et al. Single-Dose Pharmacokinetics and Preliminary Safety Assessment with Use of CBD-Rich Hemp Nutraceutical in Healthy Dogs and Cats. Animals (Basel). 2019;9(10):832

Mechoulam, R. et al. Pharmacokinetics of Cannabidiol in dogs. Drug Metabolism and Disposition. 1987 Vol (16) No. 3

Brutlag A, Hommerding H. Toxicology of marijuana, synthetic cannabinoids, and cannabidiol in dogs and cats. VCNA-Small Animal Practice. 2018;8:1087–1102

Wakshlag JJ, Schwark WS, Deabold KA, Talsma BN, Cital S, Lyubimov A, Iqbal A, Zakharov A. Pharmacokinetics of Cannabidiol, Cannabidiolic Acid,  $\Delta$ 9-Tetrahydrocannabinol, Tetrahydrocannabinolic Acid and Related Metabolites in Canine Serum After Dosing With Three Oral Forms of Hemp Extract. Front Vet Sci. 2020 Sep 4;7:505

Chicoine A, Illing K, Vuong S, Pinto KR, Alcorn J, Cosford K. Pharmacokinetic and Safety Evaluation of Various Oral Doses of a Novel 1:20 THC:CBD Cannabis Herbal Extract in Dogs. Front Vet Sci. 2020 Sep 29;7:583404

Morris EM, Kitts-Morgan SE, Spangler DM, McLeod KR, Costa JHC, Harmon DL. The Impact of Feeding Cannabidiol (CBD) Containing Treats on Canine Response to a Noise-Induced Fear Response Test. Front Vet Sci. 2020;7:569565. Published 2020 Sep 22

Corsetti S, Borruso S, Malandrucchio L, Spallucci V, Maragliano L, Perino R, D'Agostino P, Natoli E. Cannabis sativa L. may reduce aggressive behaviour towards humans in shelter dogs. Sci Rep. 2021 Feb 2;11(1):2773. doi: 10.1038/s41598-021-82439-2. Erratum in: Sci Rep. 2021 Dec 9;11(1):24029