

Cannabinomimetic control of mast cell mediator release: new perspective in chronic inflammation

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Abstract

The present review aims to elucidate the emerging role played by cannabinomimetic compounds in the control of mast cell activation. Mast cells are immune competent cells strategically localised at the sites directly interfacing with the external environment, which, in case of injury, regulate the immune response by the release of a plethora of both pre-formed and newly-synthesised mediators. However, although the main goal of mast cell activation is to initiate the inflammatory reaction, and thus maintain internal homeostasis, the consequences of dysregulated mast cell activation could be to chronically activate the inflammatory response as occurs in arthritis, inflammatory bowel diseases, atherosclerosis and asthma. Therefore, much effort has been made to develop compounds that act to prevent mast cell degranulation. Cannabinomimetic compounds (i.e. agents able to modulate endocannabinoid function) are considered as an emerging class of regulators of mast cell behaviour. We focus on the evidence for a cannabinomimetic control of both acute and chronic inflammatory disease, recognising a common mast cell origin for problems such as dermatitis, inflammatory gastrointestinal syndrome and granuloma formation. Special emphasis is provided for the recent promising results obtained with palmitoylethanolamide in human studies. In the light of evidence suggesting that the control of mast cell activation at an early time during an inflammatory process may account for its resolution, it is reasonable to propose that cannabinomimetic compounds, including palmitoylethanolamide and its congeners, could represent possible candidates for treating several chronic inflammatory diseases.

Similar articles

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Review. Polish.

- [Mast cells and nerves tickle in the tummy: implications for inflammatory bowel disease and irritable bowel syndrome.](#) Rijniere A, Nijkamp FP, Kraneveld AD. Pharmacol Ther. 2007 Nov;116(2):207-35. doi: 10.1016/j.pharmthera.2007.06.008. Epub 2007 Jul 18. PMID: 17719089 Review.
- [\[Effect of dexamethasone on mast cell reaction in inflammation\].](#) Klymenko MO, Kozyrieva HF. Fiziol Zh. 2002;48(3):29-33. PMID: 12125281 Ukrainian.
- [Cannabinoids and the immune system: potential for the treatment of inflammatory diseases?](#) Croxford JL, Yamamura T. J Neuroimmunol. 2005 Sep;166(1-2):3-18. doi: 10.1016/j.jneuroim.2005.04.023. PMID: 16023222 Review.
- [Neutrophil recruitment in mast cell-dependent inflammation: inhibitory mechanisms of glucocorticoids.](#) Schramm R, Thorlacijs H. Inflamm Res. 2004 Dec;53(12):644-52. doi: 10.1007/s00011-004-1307-8. PMID: 15654511 Review.
- [Mast cells and basophils in innate immunity.](#) Abraham SN, Arock M. Semin Immunol. 1998 Oct;10(5):373-81. doi: 10.1006/smim.1998.0140. PMID: 9799712 Review.
- [Mast cells and inflammation.](#) Stassen M, Hültner L, Müller C, Schmitt E. Arch Immunol Ther Exp (Warsz). 2002;50(3):179-85. PMID: 12098933 Review.
- [Palmitoylethanolamide, endocannabinoids and related cannabimimetic compounds in protection against tissue inflammation and pain: potential use in companion animals.](#) Re G, Barbero R, Miolo A, Di Marzo V. Vet J. 2007 Jan;173(1):21-30. doi: 10.1016/j.tvjl.2005.10.003. Epub 2005 Dec 1. PMID: 16324856 Review.
- [Role of mast cells in progressive renal diseases.](#) Holdsworth SR, Summers SA. J Am Soc Nephrol. 2008 Dec;19(12):2254-61. doi: 10.1681/ASN.2008010015. Epub 2008 Sep 5. PMID: 18776124 Review.
- [Role of mast cells in gastrointestinal mucosal defense.](#) Penissi AB, Rudolph MI, Piezzi RS. Biocell. 2003 Aug;27(2):163-72. PMID: 14510234 Review.

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Cited by 18 articles

- [The Mast Cell-SCF-CB1 Interaction Is a Key Player in Seborrheic Keratosis.](#) Yamanaka-Takaichi M, Sugawara K, Sumitomo R, Tsuruta D. J Histochem Cytochem. 2020 Jul; 68(7):461-471. doi: 10.1369/0022155420938031. Epub 2020 Jun 24. PMID: 32578480

- [μ-opioid receptor, β-endorphin, and cannabinoid receptor-2 are increased in the colonic mucosa of irritable bowel syndrome patients.](#) Dothel G, Chang L, Shih W, Barbaro MR, Cremon C, Stanghellini V, De Ponti F, Mayer EA, Barbara G, Sternini C. *Neurogastroenterol Motil.* 2019 Nov;31(11):e13688. doi: 10.1111/nmo.13688. Epub 2019 Jul 23. PMID: 31336406 Free PMC article.
- [N-palmitoylethanolamide Prevents Parkinsonian Phenotypes in Aged Mice.](#) Crupi R, Impellizzeri D, Cordaro M, Siracusa R, Casili G, Evangelista M, Cuzzocrea S. *Mol Neurobiol.* 2018 Nov;55(11):8455-8472. doi: 10.1007/s12035-018-0959-2. Epub 2018 Mar 19. PMID: 29552727
- [Endo-cannabinoids system and the toxicity of cannabinoids with a biotechnological approach.](#) Niaz K, Khan F, Maqbool F, Momtaz S, Ismail Hassan F, Nobakht-Haghighi N, Rahimifard M, Abdollahi M. *EXCLI J.* 2017 May 15;16:688-711. doi: 10.17179/excli2017-257. eCollection 2017. PMID: 28827985 Free PMC article. Review.
- [Sweat lipid mediator profiling: a noninvasive approach for cutaneous research.](#) Agrawal K, Hassoun LA, Foolad N, Pedersen TL, Sivamani RK, Newman JW. *J Lipid Res.* 2017 Jan;58(1):188-195. doi: 10.1194/jlr.M071738. Epub 2016 Nov 8. PMID: 27875258 Free PMC article.
- [Pharmacological treatment options for mast cell activation disease.](#) Molderings GJ, Haenisch B, Brettner S, Homann J, Menzen M, Dumoulin FL, Panse J, Butterfield J, Afrin LB. *Naunyn Schmiedebergs Arch Pharmacol.* 2016 Jul;389(7):671-94. doi: 10.1007/s00210-016-1247-1. Epub 2016 Apr 30. PMID: 27132234 Free PMC article. Review.
- [Mast Cell-Mediated Mechanisms of Nociception.](#) Aich A, Afrin LB, Gupta K. *Int J Mol Sci.* 2015 Dec 4;16(12):29069-92. doi: 10.3390/ijms161226151. PMID: 26690128 Free PMC article. Review.
- [Circulating tryptase as a marker for subclinical atherosclerosis in obese subjects.](#) Moreno M, Puig J, Serrano M, Moreno-Navarrete JM, Ortega F, Ricart W, Fernandez-Real JM. *PLoS One.* 2014 May 15;9(5):e97014. doi: 10.1371/journal.pone.0097014. eCollection 2014. PMID: 24830464 Free PMC article.
- [Inhibitory effect of topical adelmidrol on antigen-induced skin wheal and mast cell behavior in a canine model of allergic dermatitis.](#) Cerrato S, Brazis P, Della Valle MF, Miolo A, Puigdemont A. *BMC Vet Res.* 2012 Nov 26;8:230. doi: 10.1186/1746-6148-8-230. PMID: 23181761 Free PMC article.
- [Identification of sites in apolipoprotein A-I susceptible to chymase and carboxypeptidase A digestion.](#) Usami Y, Kobayashi Y, Kameda T, Miyazaki A, Matsuda K, Sugano M, Kawasaki K, Kurihara Y, Kasama T, Tozuka M. *Biosci Rep.* 2012 Dec 6;33(1):49-56. doi: 10.1042/BSR20120094. PMID: 23072735 Free PMC article.

- [Mast cell chymase and tryptase as targets for cardiovascular and metabolic diseases.](#) He A, Shi GP. *Curr Pharm Des.* 2013;19(6):1114-25. doi: 10.2174/1381612811319060012. PMID: 23016684 Free PMC article. Review.
- [Neuroprotective activities of palmitoylethanolamide in an animal model of Parkinson's disease.](#) Esposito E, Impellizzeri D, Mazzon E, Paterniti I, Cuzzocrea S. *PLoS One.* 2012;7(8):e41880. doi: 10.1371/journal.pone.0041880. Epub 2012 Aug 17. PMID: 22912680 Free PMC article.
- [Emerging role of mast cells and macrophages in cardiovascular and metabolic diseases.](#) Xu JM, Shi GP. *Endocr Rev.* 2012 Feb;33(1):71-108. doi: 10.1210/er.2011-0013. Epub 2012 Jan 12. PMID: 22240242 Free PMC article. Review.
- [Is lipid signaling through cannabinoid 2 receptors part of a protective system?](#) Pacher P, Mechoulam R. *Prog Lipid Res.* 2011 Apr;50(2):193-211. doi: 10.1016/j.plipres.2011.01.001. Epub 2011 Feb 2. PMID: 21295074 Free PMC article. Review.
- [Palmitoylethanolamide reduces granuloma-induced hyperalgesia by modulation of mast cell activation in rats.](#) De Filippis D, Luongo L, Cipriano M, Palazzo E, Cinelli MP, de Novellis V, Maione S, Iuvone T. *Mol Pain.* 2011 Jan 10;7:3. doi: 10.1186/1744-8069-7-3. PMID: 21219627 Free PMC article.
- [Immunoactive effects of cannabinoids: considerations for the therapeutic use of cannabinoid receptor agonists and antagonists.](#) Greineisen WE, Turner H. *Int Immunopharmacol.* 2010 May;10(5):547-55. doi: 10.1016/j.intimp.2010.02.012. Epub 2010 Feb 25. PMID: 20219697 Free PMC article. Review.
- [Endocannabinoids anandamide and its cannabinoid receptors in liver fibrosis after murine schistosomiasis.](#) Liu H, Gao X, Duan R, Yang Q, Zhang Y, Cheng Y, Guo Y, Tang W. *J Huazhong Univ Sci Technolog Med Sci.* 2009 Apr;29(2):182-6. doi: 10.1007/s11596-009-0209-y. Epub 2009 Apr 28. PMID: 19399401
- [Cannabinoids reduce granuloma-associated angiogenesis in rats by controlling transcription and expression of mast cell protease-5.](#) De Filippis D, Russo A, D'Amico A, Esposito G, Pietropaolo C, Cinelli M, Russo G, Iuvone T. *Br J Pharmacol.* 2008 Aug;154(8):1672-9. doi: 10.1038/bjp.2008.211. Epub 2008 Jun 16. PMID: 18552882 Free PMC article.