CNS Drugs
2014 Apr;28(4):319-29.
doi: 10.1007/s40263-014-0151-9.

The mu-opioid receptor agonist/ noradrenaline reuptake inhibition (MOR-NRI) concept in analgesia: the case of tapentadol

Thomas M Tzschentke [1], Thomas Christoph, Babette Y Kögel
Affiliations

- PMID: **24578192**
- DOI: 10.1007/s40263-014-0151-9

Abstract

Tapentadol is a novel, centrally-acting analgesic drug, with an analgesic efficacy comparable to that of strong opioids such as oxycodone and morphine. Its high efficacy has been demonstrated in a range of animal models of acute and chronic, nociceptive, inflammatory, and neuropathic pain as well as in clinical studies with moderate to severe pain arising from a number of different etiologies. At the same time, a favorable gastrointestinal tolerability has been demonstrated in rodents and humans, and advantages over morphine regarding tolerance development and physical dependence were shown in animal studies. Furthermore, a low level of abuse and diversion is beginning to emerge from first post-marketing data. Tapentadol acts as a μ-opioid receptor (MOR) agonist and noradrenaline reuptake inhibitor (NRI). Both mechanisms of action have been shown to contribute to the analgesic activity of tapentadol and to produce analgesia in a synergistic manner, such that relatively moderate activity at the two target sites (MOR and noradrenaline reuptake transporter) is sufficient to produce strong analgesic effects. It has been suggested that tapentadol is the first representative of a proposed new class of analgesics, MOR-NRI. This review presents the evidence that has led to this suggestion, and outlines how the pharmacology of tapentadol can explain its broad analgesic activity profile and high analgesic potency as well as its favorable tolerability.

Similar articles

- [Tapentadol: with two mechanisms of action in one molecule effective against nociceptive and neuropathic pain. Preclinical overview]. Tzschentke TM, Christoph T, Schröder W, Englberger W, De Vry J, Jahnel U, Kögel BY. Schmerz. 2011 Feb;25(1): 19-25. doi: 10.1007/s00482-010-1004-1. PMID: 21258822 Review. German.

- Tapentadol - A representative of a new class of MOR-NRI analgesics. Zajączkowska R, Przewłocka B, Kocot-Kępska M, Mika J, Leppert W, Wordliczek J. Pharmacol Rep. 2018

Aug;70(4):812-820. doi: 10.1016/j.pharep.2018.01.005. Epub 2018 Jan 31. PMID: 29921501 Review.

- Synergistic interaction between the two mechanisms of action of tapentadol in analgesia. Schröder W, Tzschentke TM, Terlinden R, De Vry J, Jahnel U, Christoph T, Tallarida RJ. J Pharmacol Exp Ther. 2011 Apr;337(1):312-20. doi: 10.1124/jpet.110.175042. Epub 2011 Jan 24. PMID: 21262850 Free PMC article.

- Spinal-supraspinal and intrinsic μ-opioid receptor agonist-norepinephrine reuptake inhibitor (MOR-NRI) synergy of tapentadol in diabetic heat hyperalgesia in mice. Christoph T, Schröder W, Tallarida RJ, De Vry J, Tzschentke TM. J Pharmacol Exp Ther. 2013 Dec;347(3):794-801. doi: 10.1124/jpet.113.207704. Epub 2013 Sep 19. PMID: 24051022

- (-)-(1R,2R)-3-(3-dimethylamino-1-ethyl-2-methyl-propyl)-phenol hydrochloride (tapentadol HCl): a novel mu-opioid receptor agonist/norepinephrine reuptake inhibitor with broad-spectrum analgesic properties. Tzschentke TM, Christoph T, Kögel B, Schiene K, Hennies HH, Englberger W, Haurand M, Jahnel U, Cremers TI, Friderichs E, De Vry J. J Pharmacol Exp Ther. 2007 Oct;323(1):265-76. doi: 10.1124/jpet.107.126052. Epub 2007 Jul 26. PMID: 17656655

See all similar articles

Cited by *19 articles*

- Repeated Administration of Clinical Doses of Tramadol and Tapentadol Causes Hepato- and Nephrotoxic Effects in Wistar Rats. Barbosa J, Faria J, Garcez F, Leal S, Afonso LP, Nascimento AV, Moreira R, Queirós O, Carvalho F, Dinis-Oliveira RJ. Pharmaceuticals (Basel). 2020 Jul 10;13(7):149. doi: 10.3390/ph13070149. PMID: 32664348 Free PMC article.

- Tapentadol Prolonged Release for Severe Chronic Osteoarthritis Pain in the Elderly-A Subgroup Analysis of Routine Clinical Practice Data. Schwittay A, Sohns M, Heckes B, Elling C. Pain Res Manag. 2020 Apr 14;2020:5759265. doi: 10.1155/2020/5759265. eCollection 2020. PMID: 32351639 Free PMC article.

- Population pharmacokinetic modeling to facilitate dose selection of tapentadol in the pediatric population. Watson E, Khandelwal A, Freijer J, van den Anker J, Lefeber C, Eerdekens M. J Pain Res. 2019 Oct 14;12:2835-2850. doi: 10.2147/JPR.S208454. eCollection 2019. PMID: 31686902 Free PMC article.

- Evaluation of Abuse and Route of Administration of Extended-Release Tapentadol Among Treatment-Seeking Individuals, as Captured by the Addiction Severity Index-Multimedia Version (ASI-MV). Vosburg SK, Beaumont J, Dailey-Govoni ST, Butler SF, Green JL. Pain Med. 2020 Sep 1;21(9):1891-1901. doi: 10.1093/pm/pnz250. PMID:

31617931 Free PMC article.

- Tapentadol vs oxycodone/naloxone in the management of pain after total hip arthroplasty in the fast track setting: an observational study. D'Amato T, Martorelli F, Fenocchio G, Simili V, Kon E, Di Matteo B, Scardino M. J Exp Orthop. 2019 Jul 29;6(1):36. doi: 10.1186/s40634-019-0204-6. PMID: 31359202 Free PMC article.

- First evaluation of tapentadol oral solution for the treatment of moderate to severe acute pain in children aged 6 to <18. Finkel JC, Goldberg J, Rosenburg R, Ariyawansa J, Sun T, Ochs-Ross R, Zannikos P, Zhang L, Etropolski M. J Pain Res. 2019 Jun 28;12:1925-1936. doi: 10.2147/JPR.S197348. eCollection 2019. PMID: 31303784 Free PMC article.

- The challenge of developing pain medications for children: therapeutic needs and future perspectives. Eerdekens M, Beuter C, Lefeber C, van den Anker J. J Pain Res. 2019 May 23;12:1649-1664. doi: 10.2147/JPR.S195788. eCollection 2019. PMID: 31213880 Free PMC article.

- Tapentadol: an overview of the safety profile. Polati E, Canonico PL, Schweiger V, Collino M. J Pain Res. 2019 May 16;12:1569-1576. doi: 10.2147/JPR.S190154. eCollection 2019. PMID: 31190968 Free PMC article. Review.

- Pharmacological rationale for tapentadol therapy: a review of new evidence. Romualdi P, Grilli M, Canonico PL, Collino M, Dickenson AH. J Pain Res. 2019 May 16;12:1513-1520. doi: 10.2147/JPR.S190160. eCollection 2019. PMID: 31190962 Free PMC article. Review.

- Tapentadol: a new option for the treatment of cancer and noncancer pains. Dickenson AH, Kress HG. J Pain Res. 2019 May 16;12:1509-1511. doi: 10.2147/JPR.S190171. eCollection 2019. PMID: 31190961 Free PMC article. No abstract available.

- Tapentadol Prolonged Release: A Review in Pain Management. Deeks ED. Drugs. 2018 Nov;78(17):1805-1816. doi: 10.1007/s40265-018-1007-2. PMID: 30471002 Free PMC article. Review.

- Does 'Strong Analgesic' Equal 'Strong Opioid'? Tapentadol and the Concept of 'μ-Load'. Raffa RB, Elling C, Tzschentke TM. Adv Ther. 2018 Oct;35(10):1471-1484. doi: 10.1007/s12325-018-0778-x. Epub 2018 Sep 11. PMID: 30206823 Free PMC article.

- Improving the oral bioavailability of tapentadol via a carbamate prodrug approach: synthesis, bioactivation, and pharmacokinetics. Li Y, Wang Y, Zhang R, Liu C, Wei Y, Sun J, He Z, Xu Y, Zhang T. Drug Deliv Transl Res. 2018 Oct;8(5):1335-1344. doi: 10.1007/s13346-018-0524-6. PMID: 29777509

- Updates in palliative care - overview and recent advancements in the pharmacological management of cancer pain. Wood H, Dickman A, Star A, Boland JW. Clin Med (Lond).

2018 Feb;18(1):17-22. doi: 10.7861/clinmedicine.18-1-17. PMID: 29436434 Free PMC article. Review.

- Review of Post-Marketing Safety Data on Tapentadol, a Centrally Acting Analgesic. Stollenwerk A, Sohns M, Heisig F, Elling C, von Zabern D. Adv Ther. 2018 Jan;35(1): 12-30. doi: 10.1007/s12325-017-0654-0. Epub 2017 Dec 21. PMID: 29270779 Free PMC article. Review.

- Dezocine exhibits antihypersensitivity activities in neuropathy through spinal μ-opioid receptor activation and norepinephrine reuptake inhibition. Wang YX, Mao XF, Li TF, Gong N, Zhang MZ. Sci Rep. 2017 Feb 23;7:43137. doi: 10.1038/srep43137. PMID: 28230181 Free PMC article.

- Effectiveness of tapentadol prolonged release for the management of painful mucositis in head and neck cancers during intensity modulated radiation therapy. Rosario M, Francesco R, Sergio F, Niccolò GL, Alba F, Maurizio N, Sergio A, Stefania G, Filippo A. Support Care Cancer. 2016 Oct;24(10):4451-5. doi: 10.1007/s00520-016-3351-7. Epub 2016 Jul 22. PMID: 27448104

- Oral tapentadol for cancer pain. Wiffen PJ, Derry S, Naessens K, Bell RF. Cochrane Database Syst Rev. 2015 Sep 25;2015(9):CD011460. doi: 10.1002/14651858.CD011460.pub2. PMID: 26403220 Free PMC article. Review.

- Tapentadol prolonged release for severe chronic cancer-related pain: effectiveness, tolerability, and influence on quality of life of the patients. Schikowski A, Krings D, Schwenke K. J Pain Res. 2014 Dec 22;8:1-8. doi: 10.2147/JPR.S72150. eCollection 2015. PMID: 25565884 Free PMC article.

References

1. Anesth Analg. 2002 Jun;94(6):1553-7, table of contents - PubMed
2. Anesth Analg. 2008 Apr;106(4):1309-15, table of contents - PubMed
3. Brain Res. 2005 Mar 15;1038(1):76-82 - PubMed
4. Trends Pharmacol Sci. 2004 Dec;25(12):613-7 - PubMed
5. Clin Pharmacokinet. 2002;41(1):31-57 - PubMed