Asim et al. BMC Pharmacology 2011, 11(Suppl 2):A4
http://www.biomedcentral.com/1471-2210/11/S2/A4

BMC Pharmacology

MEETING ABSTRACT Open Access

Efficacy of systemic HS-198, an analogue of oxymorphone, on cancer pain-related behaviour in mice

Muhammad F Asim[1], Catalina R Bohotin[1], Cristina E Constantin[2], Helmut Schmidhammer[1], Michaela Kress[2], Mariana Spetea[1*]

From 17th Scientific Symposium of the Austrian Pharmacological Society (APHAR). Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT)
Innsbruck, Austria. 29-30 September 2011

Background

Cancer pain is a significant clinical problem being one of the first symptoms of disease with 75–90% of the patients experiencing chronic pain syndromes in advanced stages [1]. The management of cancer pain is mainly based on the use of opioid drugs; however their clinical use is limited by high incidence of adverse effects. There is a continued search for highly efficacious opioid analgesics with reduced complications and improved patient compliance. An analogue of the clinically used oxymorphone, 5-methyl-substituted 14-*O*-methyloxymorphone (HS-198), is a selective μ opioid agonist and a potent antinociceptive agent in animal models of nociceptive and inflammatory pain, while exhibiting a favourable dissociation between analgesia and the occurrence of side effects [2]. We report data on efficacy of this opioid agonist after subcutaneous administration (s.c.) in a murine model of cancer pain. The opioid receptor-mechanistic basis of the antinociceptive action was also investigated.

Methods

Cancer pain was induced in C57BL/6J mice by s.c. implantation of lung carcinoma cells, in the plantar and dorsal side of the right hindpaw [3]. Mechanical sensitivity was determined using von Frey monofilaments. Heat sensitivity was assessed using the Hargreaves test. *In vitro* biological activities were evaluated using binding and functional assays.

Results

On day 9 post-inoculation, s.c. HS-198 produced a dose-dependent inhibition with significant effects in attenuating cancer pain-related behaviour (thermal and mechanical hypersensitivity) on the tumour side. Pre-treatment with the opioid receptor antagonist naloxone reversed the antinociceptive effects induced by HS-198 in mice with cancer-induced pain. *In vitro*, HS-198 showed high affinity and selectivity for both mouse and rat μ opioid receptors, and it displayed potent μ-agonism through inhibition of G proteins.

Conclusions

Systemic s.c. administration of the μ opioid receptor agonist HS-198 induces potent antinociceptive effects in mice with cancer pain via opioid receptor-specific mechanisms.

Acknowledgements
Supported by the Austrian Science Fund (FWF: TRP 19-B18).

Author details
[1]Department of Pharmaceutical Chemistry, Institute of Pharmacy and Center for Molecular Biosciences, University of Innsbruck, 6020 Innsbruck, Austria. [2]Division of Physiology, Department of Physiology and Medical Physics, Innsbruck Medical University, 6020 Innsbruck, Austria.

Published: 5 September 2011

References
1. Mantyh PW: **Cancer pain and its impact on diagnosis, survival and quality of life.** *Nat Rev Biosci* 2006, **7**:797-809.
2. Schmidhammer H, Spetea M: **Synthesis of 14-alkoxymorphinan derivatives and their pharmacological actions.** *Top Curr Chem* 2011, **299**:63-91.

* Correspondence: mariana.spetea@uibk.ac.at
[1]Department of Pharmaceutical Chemistry, Institute of Pharmacy and Center for Molecular Biosciences, University of Innsbruck, 6020 Innsbruck, Austria
Full list of author information is available at the end of the article

3. Constantin CE, Mair N, Sailer CA, Andratsch M, Xu ZZ, Blumer MJ, Scherbakov N, Davis JB, Bluethmann H, Ji RR, Kress M: **Endogenous tumor necrosis factor α (TNFα) requires TNF receptor type 2 to generate heat hyperalgesia in a mouse cancer model.** *J Neurosci* 2008, **28**:5072-5081.

doi:10.1186/1471-2210-11-S2-A4
Cite this article as: Asim *et al.*: Efficacy of systemic HS-198, an analogue of oxymorphone, on cancer pain-related behaviour in mice. *BMC Pharmacology* 2011 **11**(Suppl 2):A4.