BMC Pharmacology

Meeting abstract

The peripheral antinociceptive effect of DAMGO and 6β-glycine-substituted 14-O-methyloxymorphone (HS-731) after systemic administration in a mouse visceral pain model

Mahmoud Al-Khrasani*[1], Mariana Spetea[2], Tamás Friedmann[1], Pál Riba[1], Kornél P Király[1], Helmut Schmidhammer[2] and Susanna Fürst[1,3]

Address: [1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Budapest, Hungary, [2]Department of Pharmaceutical Chemistry, Institute of Pharmacy and Center for Molecular Biosciences, University of Innsbruck, Austria and [3]HAS-SE Neuropsychopharmacology Research Group, Budapest, Hungary

Email: Mahmoud Al-Khrasani* - mahmoud@pharma.sote.hu

* Corresponding author

from 13th Scientific Symposium of the Austrian Pharmacological Society (APHAR). Joint Meeting with the Austrian Society of Toxicology (ASTOX) and the Hungarian Society for Experimental and Clinical Pharmacology (MFT)
Vienna, Austria. 22–24 November 2007

Published: 14 November 2007

BMC Pharmacology 2007, **7**(Suppl 2):A50 doi:10.1186/1471-2210-7-S2-A50

This abstract is available from: http://www.biomedcentral.com/1471-2210/7/S2/A50

Inhibition of nociception through activation of peripheral μ opioid receptors (MOR) avoiding the central adverse effects of opioids has added a new possibility to manage pain control. Here we report the antinociceptive effects of the peripherally restricted MOR agonist HS-731, the peptide DAMGO, and morphine in the writhing test in mice. S.c. and i.c.v. HS-731 dose-dependently and completely inhibited writhing, being 24–598 times more potent than the two MOR-selective agonists DAMGO and morphine. However, extremely high s.c./i.c.v. potency ratios were calculated for HS-731 and DAMGO and much lower for morphine. Remarkably, a long duration of action was induced by HS-731 and much shorter by morphine and DAMGO. The antinociceptive effects of systemic opioids were reversed by s.c. naloxone while i.c.v. administration of the MOR selective antagonist CTAP significantly abolished the antinociceptive effect of s.c. morphine but completely failed to antagonize the effects of systemic HS-731 or DAMGO. In addition, in the rat vas deferens HS-731 and DAMGO, but not morphine, showed high intrinsic efficacy and naltrexone-sensitive agonist response at MOR by depressing electrically-evoked contractions of this organ. These data demonstrate that the selectivity and high efficacy of HS-731 and DAMGO at peripheral MOR as well as their inability to cross the blood brain barrier are a cornerstone for producing peripheral antinociception after systemic administration.

Acknowledgements

This work was supported by grants from the European Committee (QLK6-0999; EPILA), Hungarian research grants (OTKA K-60999 and ETT-441/2006) and the Austrian Science Foundation (P15481).