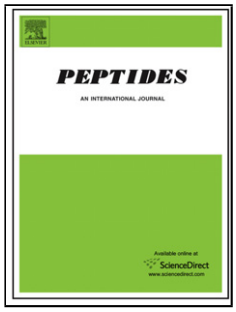

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Authors: Chang-lin Wang, Dai-jun Yang, Bi-yu Yuan, Yu Wang

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C-terminal hydrazide modification changes the spinal antinociceptive profiles of endomorphins in mice

Chang-lin Wang [a,b,*], Dai-jun Yang [a], Bi-yu Yuan [a], Yu Wang [a]

[a] *School of Life Science and Technology, State Key Laboratory of Urban Water Resource and Environment, Harbin Institute of Technology, 92 West Dazhi Street, Harbin 150001, China*

[b] *State Key Laboratory of Medicinal Chemical Biology, Nankai University, Tianjin, China.*

[*] **Corresponding author.**

Tel.: +86 451 86403992, E-mail address: wangcl@hit.edu.cn. (C.L. Wang).

Highlights

- 1. Analog EM-1-$NHNH_2$ displayed the highest antinociception after i.t. (change to: intrathecal) administration.
- 2. C-terminal hydrazide modification changed the (add: antinociceptive opioid) mechanisms of EM-2 but not EM-1.
- 3. Both EM-1-$NHNH_2$ and EM-2-$NHNH_2$ decreased the acute antinociceptive tolerance (change to: development of acute tolerance).

Abstract

Previously, we have demonstrated that endomorphins (EMs) analogs with C-terminal hydrazide modification retained the μ-opioid receptor affinity and selectivity, and exhibited potent antinociception after intracerebroventricular (i.c.v.) administration. In the present study, we extended our studies to evaluate the antinociceptive profiles of EMs and their analogs EM-1-$NHNH_2$, EM-2-$NHNH_2$ given spinally in the radiant heat paw withdrawal test. Following intrathecal (i.t.) administration, EM-1, EM-2, EM-1-$NHNH_2$ and EM-2-$NHNH_2$ dose-dependently increased the latency for paw withdrawal response. EM-1-$NHNH_2$ displayed the highest antinociceptive effects, with the ED_{50} values being 1.63 nmol, more potent than the parent EM-1 (1.96 nmol), but with no significant difference. By contrast, the