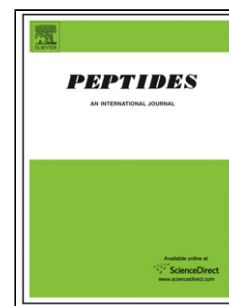


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C-terminal hydrazide modification changes the spinal antinociceptive profiles of endomorphins in mice

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Highlights

- 1. Analog EM-1-NHNH₂ 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-NHNH₂ and EM-2-NHNH₂ 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-NHNH₂, EM-2-NHNH₂ given spinally in the radiant heat paw withdrawal test. Following intrathecal (i.t.) administration, EM-1, EM-2, EM-1-NHNH₂ and EM-2-NHNH₂ dose-dependently increased the latency for paw withdrawal response. EM-1-NHNH₂ displayed the highest antinociceptive effects, with the ED₅₀ values being 1.63 nmol, more potent than the parent EM-1 (1.96 nmol), but with no significant difference. By contrast, the

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