Effect of 2',6'-dimethyl-L-tyrosine (Dmt) on pharmacological activity of cyclic endomorphin-2 and morphiceptin analogs.

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Kolekcja

Naukowa

Streszczenie

This study reports the synthesis and biological evaluation of a series of new side-chain-to-side-chain cyclized endomorphin-2 (EM-2) and morphiceptin analogs of a general structure Tyr-c(Xaa-Phe-Phe-Yaa)NH_2 or Tyr-c(Xaa-Phe-d-Pro-Yaa)NH_2, respectively, where Xaa and Yaa were l/d Asp or l/d Lys. Further modification of these analogs was achieved by introduction of 2′,6′-dimethyl-l-tyrosine (Dmt) instead of Tyr in position 1. Peptides were synthesized by solid phase method and cleaved from the resin by a microwave-assisted procedure.

Dmt^1-substituted analogs displayed high affinity at the μ-opioid receptors, remained intact after incubation with the rat brain homogenate and showed remarkable, long-lasting μ-opioid receptor-mediated antinociceptive activity after central, but not peripheral administration.

Our results demonstrate that cyclization is a promising strategy in the development of new opioid analgesics, but further modifications are necessary to enhance the blood–brain barrier permeability.

Słowa kluczowe

Binding studies, μ- and δ- opioid receptors, Hot plate test, Antinociception, Solid phase peptide synthesis

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