# Synthesis and activity of opioid peptidomimetics with $\beta^2$- and $\beta^3$-amino acids.

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Streszczenie

Morphiceptin (Tyr-Pro-Phe-Pro-$NH_2$) is a selective ligand of the mu opioid receptor, an important target in pain regulation. In this study, morphiceptin was modified at positions 2 or 3 by introduction of $\beta^2$- or $\beta^3$-amino acids and additionally in position 1 by replacing Tyr by Dmt (2',6'-dimethyltyrosine), which resulted in obtaining enzymatically stable analogs with mixed opioid receptor affinity profiles. An analog of the sequence Dmt-d-Ala-(R)-$\beta^2$-1-Nal-Pro-$NH_2$ [Nal=3-(1-naphthyl)-alanine] showed very high activity at the mu and delta receptors in the calcium mobilization functional test but did not cross the artificial membrane imitating the blood-brain barrier. In the in vivo test this analog induced strong antinociceptive effect in the writhing test in mice after intraperitioneal but also oral administration and inhibited diarrhea similarly to loperamide. Therefore, it may become an interesting lead compound in the development of peripherally restricted drugs for the treatment of gastrointestinal disorders.

Słowa kluczowe

Binding assay, calcium mobilization assay, Enzymatic degradation, Peptide synthesis, Writhing test, β-amino acids

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