N-terminal guanidinylation of the cyclic 1,4-ureido-deltorphin analogues: the synthesis, receptor binding studies, and resistance to proteolytic digestion.

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Streszczenie

The synthesis of a series of N-guanidinylated cyclic ureidopeptides, analogues of 1,4-ureido-deltorphin/dermorphine tetrapeptide is described. The δ- and μ-opioid receptor affinity of new guanidinylated analogues and their non-guanidinylated precursors was determined by the displacement radioligand binding experiments. Our results indicate that the guanidinylation of cyclic 1,4-ureidodeltorphin peptide analogues does not exhibit a uniform influence on the opioid receptor binding properties, similarly as reported earlier for some linear peptides. All analogues were also tested for their in vitro resistance to proteolysis during incubation with large excess of chymotrypsin, pepsin, and papain by means of mass spectroscopy. Guanidinylated ureidopeptides 1G-4G showed mixed μ agonist/δ agonist properties and high enzymatic stability indicating their potential as therapeutic agents for treatment of pain.

Słowa kluczowe

cyclic opioid peptides, peptide guanidinylation, dermorphin/deltorphin analogues, binding to opioid receptors, stability to proteolytic enzymes

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