Design, Synthesis and Biological Evaluation of Triptorelin Analogs Containing Tetrazole Moiety

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Abstract

The design and synthesis of novel bioisosteric analogues of triptorelin acetate containing tetrazole moiety at C- or N-terminus of the peptides is described. Tetrazole acetic acid was synthesized through the reaction of an alkyl cyanoacetate and sodium azide, after that, it was coupled to the N-terminus of triptorelin instead of pyroglutamic acid. In another approach, tetrazole acetohydrazide was prepared and conjugated to the C-terminus of triptorelin instead of the amide bond. The synthesized peptides containing tetrazole moiety at the C- or N-terminus of the peptide sequence are peptidomimetics of triptorelin acetate. The docking results of the designed derivatives showed the same interaction of triptorelin with the receptor but with a higher score.The peptide that has tetrazole moiety in its C-terminus, restricted the testosterone level during four weeks of in vivo study and led to keep testosterone at a moderate level during the first week compared to control.

Keywords

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