The Proteolytic Stability and Cytotoxicity Studies of l-Aspartic Acid and l-Diaminopropionic Acid derived β-Peptides and a Mixed α/β-Peptide

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Abstract:

The use of peptides as drugs in pharmaceutical applications is hindered by their susceptibility to proteolysis and therefore low bioavailability. β-Peptides that contain an additional methylene group in the backbone, are gaining recognition from a pharmaceutical standpoint as they are considerably more resilient to proteolysis and metabolism. Recently, we reported two new classes of β-peptides, β3- and β2-peptides derived from l-aspartic acid and l-diaminopropionic acid, respectively. Here, we report the proteolytic stability of these β-peptidic compounds and a mixed α/β-peptide against three enzymes (pronase, trypsin and elastase), as well as, human serum. The stability of these peptides was compared to an α-peptide. Peptides containing β-linkages were resistant to all conditions. The mixed α/β-peptide, however, exhibited proteolysis in the presence of trypsin and pronase but not elastase. The rate of degradation of the mixed α/β-peptide was slower than that would be expected for an α-peptide. In addition, these β-peptides were not toxic to HeLa and COS-1 cell lines as observed by MTT cytotoxicity assay. These results expand the scope of mixed α/β-peptides containing β-amino acids or small β-peptide fragments as therapeutic peptides.

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