

Synthesis of artificial collagen-mimetic peptide derived from β -amino acids

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We synthesized a collagen-mimetic peptide for the purpose of increasing of biological and physical stability. Collagen is one of the most important proteins in mammalian body that maintains structural integrity of the organs and tissues. It has been used for a biomaterial such as regenerative medicine because of excellent biological compatibility. The consensus sequence of a general collagen model peptide is known as (X-Y-Gly)_n (for X and Y, it corresponds to proline (Pro) or hydroxyproline (Hyp)), however, it is unstable to hydrolytic enzymes. Most collagen used as biomaterials derived from animals, which can be supplied inexpensively and in large quantities. But many problems such as immune reactions and contamination of pathogens are existed. In order to increase the stability to hydrolytic enzyme and its thermodynamic stability and overcome those problems, we synthesized a collagen mimetic by converting one of the basic sequence Pro-Hyp-Gly into β -amino acid. In short, our mimetic contains one of β -proline (β Pro), β -hydroxyproline (β Hyp) and β -alanine (β Ala), which is substituted from one of Pro, Hyp, and Gly in the consensus sequence.

The synthetic strategy was following. First, three amino acid residues of the basic sequence Pro-Hyp-Gly containing β -amino acid such as Pro- β Hyp-Gly, β Pro-Hyp-Gly and Pro-Hyp- β Ala were respectively synthesized, and then they were repeatedly elongated to 30 amino acids residues such as (Pro-Hyp-Gly)₁₀, (Pro- β Hyp-Gly)₁₀, (β Pro-Hyp-Gly)₁₀, and (Pro-Hyp- β Ala)₁₀ by a solid-phase synthesis method. The resulting collagen mimetics were investigated the helical formation and stabilities for application to biomaterials. Furthermore, we also studied an anti-skin cancer activity of those tripeptide residue to apply for a biologically active agent.