

Conformational Angles and Properties of Ω -Amino Acids in Protein Folding

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Introduction

The conformational properties of α -amino acids are defined by three sets of torsion angles ϕ , ψ and ω , while in omega (ω) amino acids, due to the insertion of one or more methylene groups between the N- and C α -atoms into the peptide backbone, the accessible conformational space is greater than α -amino acids. β -, γ -, δ -... amino acid residues belong to the family of ω -amino acids.

While significant work has been done using the alpha, and beta amino acids for the conformational transitions and their importance in the field of nanomaterials and peptide based vaccine adjuvant developments [1-7]. The angles of amino acids and their three dimensional structure play a crucial role in enhancing immune response and vaccine development [5-7].

The conformational properties of β -amino acid residues are based on three degrees of freedom: ϕ (N - C β), θ (C β - C α), ψ (C α - CO). Similarly, the conformational variabilities of γ - and δ - amino acid residues are defined as four [ϕ (N - C γ), θ_1 (C γ - C β), θ_2 (C β - C α), ψ (C α - CO)] and five [ϕ (N - C δ), θ_1 (C δ - C γ), θ_2 (C γ - C β), θ_3 (C β - C α), ψ (C α - CO)] degrees of freedom, respectively [8]. Figure 1a illustrates the comparison of backbone torsion angles in α -, β -, γ - and δ -amino acid residues.

These torsion angles about the polymethylene chains are denoted as $\theta_1, \theta_2, \dots, \theta_n$, with increasing subscript numbers begin from N-terminus to C-terminus. The θ torsion angles lie close to gauche ($\theta \approx \pm 60^\circ$) or trans ($\theta \approx 180^\circ$) conformations. Conventionally for β and higher ω -amino acids the C β / C ω atom precedes the C α -atom, when the chain is read from N-terminus. β Gly (β -homoglycine) is the simplest member of the β -amino acid family. For example, in β -residues, when substituent takes at the C α -carbon atom it is defined as β^2 while at the C β -carbon atom, it is defined as β^3 . Figure 1b illustrates the nomenclature of acyclic substituted β -amino acid residues.

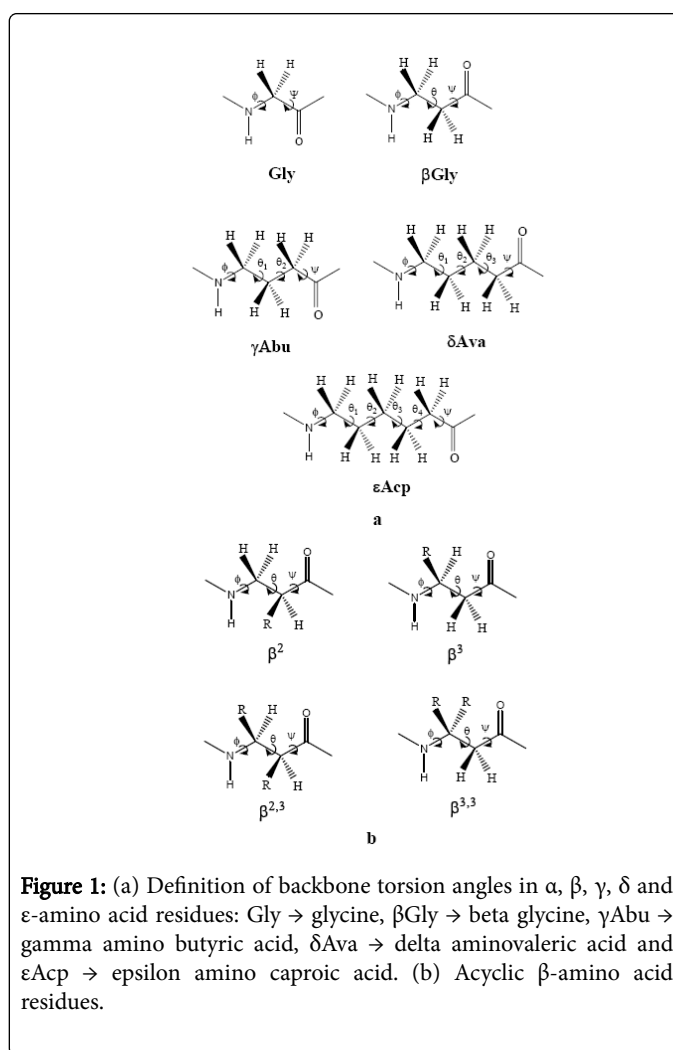


Figure 1: (a) Definition of backbone torsion angles in α , β , γ and δ and ϵ -amino acid residues: Gly \rightarrow glycine, β Gly \rightarrow beta glycine, γ Abu \rightarrow gamma amino butyric acid, δ Ava \rightarrow delta aminovaleric acid and ϵ Acp \rightarrow epsilon amino caproic acid. (b) Acyclic β -amino acid residues.

Figure 2 shows the definition of β^3 -HAla, β^3 -HVal, β^3 -HPhe, β^3 -HLeu and β^3 -HPro residues. β^3 -HAla, β^3 -HVal, β^3 -HPhe, β^3 -HLeu and β^3 -HPro residues are referred in this thesis as β Ala, β Val, β Phe, β Leu and β Pro, respectively. γ Abu (gamma aminobutyric acid) and δ Ava (delta aminovaleric acid) are the simplest members of the γ - and δ -families, respectively.

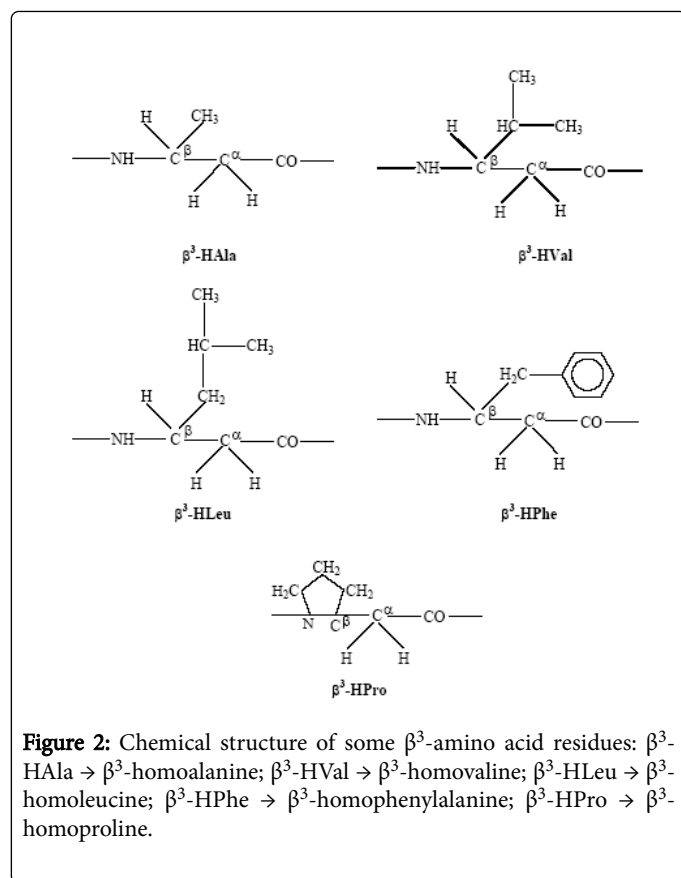


Figure 2: Chemical structure of some β^3 -amino acid residues: β^3 -HAla \rightarrow β^3 -homoalanine; β^3 -HVal \rightarrow β^3 -homovaline; β^3 -HLeu \rightarrow β^3 -homoleucine; β^3 -HPhe \rightarrow β^3 -homophenylalanine; β^3 -HPro \rightarrow β^3 -homoproline.

Currently, small molecule based drug increasingly interest in development of anti-cancer therapy molecules like Bortezomib, gold nanoparticles platinum based inorganic molecules for anti-tumor therapy [9]. The homologation alpha amino acids to beta amino acids or gamma amino acids would enhance the penetration of drug molecules inside the cellular lever to develop the anticancer drugs. The incorporation of inorganic drug molecules co-ordination with protein

secondary structures would help for development for vaccines for cancer treatment [10,11].

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