

Molecular Mechanics Study of Antihypertensive Val-Tyr Dipeptide

G.A. Akverdieva¹, N.M. Godjayevev^{1,2}, S. Akyuz³, N.E. Dogan³, T. Akyuz³

¹Institute for Physical Problems, Baku State University, Z.Khalilov st.23, AZ-1148, Baku, Azerbaijan, ²Qafqaz University, Baku-Sumqayit Road, 16 km, Khirdalan, AZ-0101, Baku, Azerbaijan, ³Istanbul Kultur University, Science and Letters Faculty, Physics Department, Atakoy Campus, 34156 Bakirkoy, Istanbul, Turkey

Antihypertensive peptides received much interest over the last decade. Val-Tyr dipeptide is known to be angiotensin converting enzyme (ACE) inhibitory peptide in vitro [1]. In order to understand the mechanism of the activity of a drug it is necessary explore its conformational possibilities and determine physiologically active conformations.

In this study conformational behavior of antihypertensive dipeptide Val-Tyr has been investigated by molecular mechanics. The analysis of dipeptide is based on universal sets of low-energy conformational states of free amino acids. For χ_1 of the side chains of both Val and Tyr, all three values of torsion minima 60, 180, -60° were considered. The value 180° for χ_2 and χ_3 of Val and the values 90° and 180° for χ_2 and χ_3 of Tyr, which correspond to stable states of side chains of these residues, were taken. Thus, 72 conformations, belonging to the folded and extended shapes of backbone were calculated. Calculation results reveal that 20% of the examined conformations have the relative energy up to 2 kcal/mol and both shapes are equally probable for this dipeptide. The optimal conformations of folded ($E_{rel.} = 0.0$ kcal/mol) and extended ($E_{rel.} = 0.5$ kcal/mol) backbone shapes are illustrated in Figure 1. Massivity of side chains of amino acid residues is an important factor, which form the stabilizing forces-dispersion interactions of side chains of Val and Tyr. The energy of dipeptide is very sensitive to positions of the side chains of the amino acid residues. Though the extended shape of this dipeptide is the best, from the point of view of mono-peptide energy, in the conformations with the folded backbone, the side chains are more close to each other and form effective dispersion contacts. In addition, the folded structures are also favourable as regards dispersion contacts of the backbone elements, which result in the density packing of mono-peptide links. So, the distance from atom CG1 of side chain of Val to atom O of side chain of Tyr is 4.1 and 7.7 Å, the distance from atom CG2 of side chain of Val to atom O of side chain of Tyr is 6.3 and 8.6 Å and the distance between N and C atoms of the opposite terminals of the molecule is 4.7 and 6.0 Å in the mentioned optimal folded and extended structures, respectively.

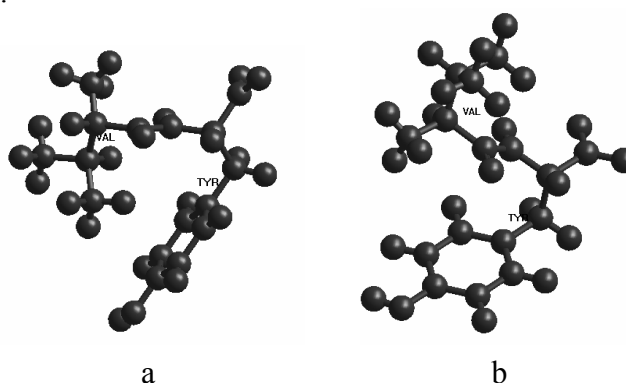


Fig. 1: The optimal folded (a) and extended (b) structures of Val-Tyr dipeptide

- [1] T. Matsui, X. L. Zhu, K. Watanabe, K. Tanaka, Y. Kusano, K. Matsumoto, Life Sciences 79 (2006) 2492-2498.
[2] L. Vercruysse, N. Morel, J. Van Camp, J. Szust, G. Smaghe, Peptides 29 (2008) 261-267.