THE PEPTIDE CONFORMATION ANALYSES REGULATING THE CATECHOLAMINE SYNTHESIS PROCESSES

L.I. VELIYEVA, E.Z. ALIYEV
Baku State University
AZ-1148, Z. Khalilov str., 23, Baku, Azerbaijan

The spatial structure and mobility of side chains of proline-containing peptide are studied by the method of theoretical conformational analysis. The influence of side chains on formation of peptide spatial structure is analyzed on the calculation result.

Keywords: neuropeptides; structure; conformation analysis
PACS: 87.80.-y

INTRODUCTION

The proline-containing peptide (PR-peptide) is related to number of compounds regulating the processes of synthesis, secretion and reception of catecholamine, firstly isolated from neurosecretory granules of bull hypothesis [1]. It is known that many low-molecular peptide compounds containing the proline residuals along with ferment inhibition influence on central nervous system (CNS), increase the hormone concentration in blood, cause antibacterial action and other effects [2,4]. The peptide specific spatial organization in formation and stabilization of which the molecule chemical structure plays the important role, is on the base of wide range of such peptide biochemical properties. The spatial organization of PR-peptide, the chemical structure of which contains the proline four residuals is studied in the given work by the method of theoretical conformation analysis. The presence of proline in peptide chain causes the significant limits of frame conformation mobility [2]. That's why the mobility of side chains of amino-acid residuals is studied and their role in formation of PR-peptide spatial organization is revealed along with establishment of set of peptide low-energy conformation states. The investigations are carried out by the technique described in [4,5] and they include the step-by-step study of fragment conformation states and their overlapping sections (fig.1).

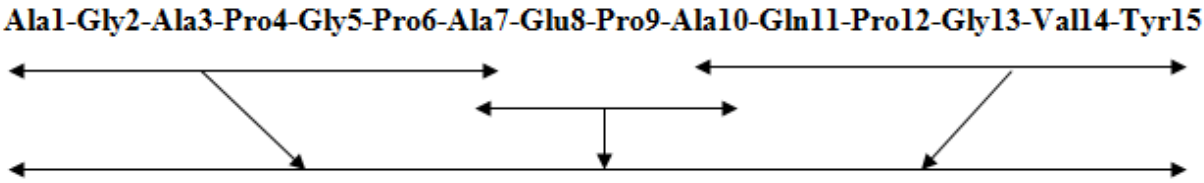

Fig.1. The calculation scheme of PR-peptide.

RESULTS AND CALCULATIONS

Ala1-Ala7 fragment

According to calculation results Ala1- Gly2-Ala3 fragment of PR-peptide of peptide chain is presented by big number of low-energy conformation states (~20). They are related to all admissible shapes of three-peptide frame with equal probability, i.e. can form the both wrapped and unwrapped forms of peptide chain. The summary contribution from energy of dipeptide interactions in first case is ~-3kkal/mol, in second case is ~2,2 kcal/mol. Pro4-Gly5-Pro6 section forms the identical conformation states belonging mainly to ff shape (90% of all admissible structures) in investigated fragment. In many low-energy conformations Pro4 is in R frame shape (83%) whereas Pro6 can be in both R and B shapes (43% and 57% correspondingly). The dipeptide interactions between Gly5 and Pro6 9-2,8 kcal/mol are the main stabilizing factor in the given section. The formation of β-bend in Ala3-Pro4-Gly5-Pro6 section is the character for Ala1-Ala7 fragment. The distance between C^{α} atoms of Ala3 and Pro6(≤6,2 Å) is the general criterion.

Ala7-Ala10 fragment

Only B and L forms of proline main chain are permitted for Glu8 because of steric collisions of ionized side chain of glutaminic acid with γ-methylene group of proline pyrrolidine ring. Alanine can be in R, B and L sections of conformation space. That's why the general number of initial variants for procedure of minimization of total conformation energy is 18. They describe the all possible forms and shapes of fragment peptide frame. The calculation results show on preference of two shape types fef and fee the each of which contains 9 conformations with relative energy ≤ 6 kcal/mol. The dipeptide interactions between Glu8 and Pro9 (on the average ~3,3 kcal/mol) make the big contribution in stabilization of all low-energy structures.

131 H.Javid ave, AZ-1143, Baku
ANAS, G.M.Abdullayev Institute of Physics
E-mail: jophphysics@gmail.com

Table 1.

Low-energy conformations of RP-peptide.

№	Ala1-Gly2-Ala3-Pro4-Gly5-Pro6-Ala7-Glu8-Pro9-Ala10-Gln11-Pro12-Gly13-Val14-Tyr15	Number of conformations in shape	Relative energy interval, kkal/mol	The distance between C^{α} atoms of amino-acid residuals, Å
1	eee / efe / fee / ffe → ff → efef → ee → fff	1	0	Ala1- Pro9 (5,2) Ala10-Tyr15 (6,7)
2		1	4,3	Ala1- Glu8 (5,8) Ala10-Tyr15 (6,7)
3		1	6,7	Ala1- Pro4 (4,5) Ala10-Tyr15 (6,7)
4		7	2,1-9,9	Ala1- Glu8 (5,2) Ala1-Tyr15 (6,7)
5	eee / ffe / fee / efe → ff → efee → ee → fff	4	5,7-8,9	Ala1- Pro9 (5,9) Ala10-Tyr15 (6,7)
6		11	6,3-10	Ala1- Glu8 (6,7) Pro9-Tyr15 (6,3)
7		1	9,5	Ala1-Tyr15 (6,7)
8		1	9,8	Ala1- Glu8 (5,8) Pro9-Tyr15 (6,4)
9	fee / eee → ff → ffef → ee → fff	2	7,1-7,5	Ala1-Tyr15 (6,3)
10		1	7,5	Ala1- Ala7 (6,5) Ala10-Tyr15 (6,7)

Ala10-Tyr15 fragment

Only L and B sections of conformation space are sterically permitted near proline residual as in the case of previous fragment Gln11. The general number of initial approximations for minimization procedure of conformation energy is 126 variants belonging to 8 shapes of peptide frames. As it follows from calculation results Pro12-Tyr15 section forms the totally wrapped structures (shape fff) for all admissible conformations on fragment (relative energy varies in interval 0-5kcal/mol). Pro12 realizes only R shape of peptide frame (in difference from Pro6 for which R and B frame shapes are practically similar) in all calculated conformations. The stabilizing contribution in formation of these structures make the influences between Gln11 and following residuals of peptide chain Pro12, Val14, Tyr15 (-3,5; -3,3 and -2,9 kcal/mol, correspondingly). The formation of β-bend on Gln11-Val14 section is character for fragment that is shown by the distance between C^{α} atoms Gln11 and Val14 (~6,5 Å). Gly13 is in the top of such bend.

Conformation states of PR-peptide.

The conformation calculations are carried out for 778 initial approximations on the base of combinations of low-energy fragment states (fig.1). According to investigation results (table 1) in spatial organization of PR-peptide we can emphasize the two conformationally elastic sections: Ala3-Pro4-Gly5-Pro6 and Ala10- Tyr15 fragments including β-bend conformations. Ala1-Pro9 section also forms the wrapped structure in which the closeness of C^{α} atoms of Ala1 and Gln8, Pro9 residuals varies in limit 5,2-6,7Å. As it is seen from the calculations the side chains of all amino-acid residuals are on the surface of compact structures and are oriented in environment.

CONCLUSION

Generalizing the investigation results we can form the following conclusions:

1. The native conformation of PR-peptide can be presented by the structure containing β-rotations on two tetrapeptide sections Ala3-Pro6 and Gln11-Val14 (all of them are satisfy to condition C_i^{α}-$_{Ci+1}^{\alpha}$, C_{i+2}^{α}, $C_{i+3}^{\alpha} \leq 60°$).
2. Ala7-Glu8-Pro9-Ala10 section is conformationally mobile and can realize the set of low-energy states. The side chain of Glu8 residual is oriented in environment and can participate in realization of intermolecular interaction.

[1] *M.F. Minocva et al.* Journal of Neurochemistry, 1999, vol.73, p.1154

[2] *E.M. Popov.* V kn. «Strukurnaya orqanizasiya belkov», M. «Nauka», 1989, 352 s. (In Russian).

[3] *G.I. Chipens, L.K. Polevaya, M. Veretennikova, A.Yu. Krikis.* Vkn. «Struktura i funkchii nizkomolekulyarnix peptidov», Riqa, Zinatie, 1980, 328 s. (In Russian).

[4] *I.N. Alieva, L.I. Veliyeva, D.I. Aliev, N.M. Godjaev.* Journal of Peptide Science, vol. 8, 2002, p.385-397.

[5] *L.I. Veliyeva, I.N. Alieva, M.A. Musayev, N.M. Godjaev.* Protein and Peptide Letters, 2006, vol.13, n.10, p.1007-1015.

Received: 12.06.2017