Conformational effects of the valine side chain on the $\beta_L\beta_L\beta_L$ extended in the HCO-Gly-L-Val-Gly-NH_2 tripeptide motif : An ab initio and DFT exploratory study

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Abstract— Ab initio and DFT molecular computations were carried out on the HCO-Gly-L-Val-Gly-NH_2 tripeptide at the HF/6-31G(d) and B_3LYP/6-31G(d) levels of theory. The study of conformation in HCO-Gly-L-Val-Gly-NH_2 tripeptide, which is in repeating sequences of parent elastin-mimetic polypeptide, were performed with varying of side chain torsional angle (χ) and backbone dihedral angles (Φ_2,Ψ_2), to finding the most stable conformer.
At first the side chain torsional angle (χ) as a variable of the energy function was changed at 30° intervals from 0° to 360°. Three minima, gauche (-) , gauche (+) and anti, were obtained that among of them, gauche (-) conformer has the lowest energy. Afterward the two terminal glycine moieties were kept in the β_L conformations while the conformation of the central valine was varied for three states, gauche (-), anti and gauche (+).
In addition to electronic energy (E), the key thermodynamic functions: enthalpy (H), Gibbs free energy (G) and entropy (S) were obtained at B_3LYP/6-31G(d) level of theory.
The most stable conformation for three states of valine , gauche (+), anti and gauche (-) is $\beta_L\beta_L\beta_L$ conformation and also in gauche (+), anti and gauche (-) states 8, 7 and 6 conformers were found respectively.
The obtained $\beta_L\gamma_L\beta_L$, $\beta_L\gamma_D\beta_L$, $\beta_L\varepsilon_D\beta_L$ and $\beta_L\alpha_D\beta_L$ Conformations in this three states, are more stable in anti state than other two states. According to obtained results dipole-dipole attraction interactions and also entropy play the main role in forming a more stable conformer.

Keywords: B3LYP, Conformational analysis, Elastine, HF, HCO-Gly-L-Val-Gly-NH2, Ramachandran.

1 INTRODUCTION

During the last two decades the study of peptide and other protein-based materials has faced a renaissance. Most of these studies focus on discovering the rules that govern protein folding. The proteins are categorized with respect to their first, second and third structures and the second and third structures of proteins are the result of the first structure and the protein biological activity is determined by these structures [1].
Two sections of science, drug discovery and nanotechnology require the prediction and control of protein second structure [2]-[3]. *The modification of p*eptides is a general strategy for drug design to increase the resistance to physiological degradation and decrease the conformational flexibility. Countless possibilities of structural changes with respect to peptide structure or amino acid side chains is presented and established to be promising in drug design in future [4]-[10].
A relatively small and emerging class of protein-based materials is elastomeric materials. with respect to the polypeptides that from these materials, they are mainly formed by sequences with regular repetitions and little complications.

Elastin protein is a kind of elastomeric material that is mainly formed by glycine, valine, alanine and proline amino acides. One of the parent repeating polymers in elastin is $(Val\text{-}Pro\text{-}Gly\text{-}Val\text{-}Gly)_n$ [11]-[14]. These polymers have medical and non-medical applications. The study of possible conformations of single amino acide diamids of glycine, alanine, valine and proline and also a number of di- , tri- and oligo-peptides (dialanine, trialanine, tetra-alanine, oligo-analine, tri-glycine) are already investigated extensively [15]-[19].
Also the study of dipeptide pro-Gly-conformational properties in elastin polypeptide was performed to define and describe the relation between proline application relevance with elastomeric mechanical behavior of penta-peptide in this group of materials[20].
Protein Folding is defined as a function of the structure torsional angles(Φ,Ψ,ω). Different interactions between amino acide side chains improves these torsional angles. In order to understand protein folding, it's necessary to study the formed peptide model and their conformation and the effect of one residue on another. Single amino acide diamidse conformation based on Ramachandran plot is shown in Fig (1) in which Φ and Ψ are between 0° and 360° and there are 9 *possible* minima in it.

γ_D	δ_D	α_L
ε_D	β_L	ε_L
α_D	δ_L	γ_L

$$\mathbf{E = E(\phi,\psi)}$$

Fig 1. Topological features of the Ramachanran map E=E(ϕ,ψ), associated with an amino acid residue

The complexity increases as peptide chain alongates and the plot dimensions also increases. In the case of tripeptide derivatives (see Fig 2), which A and B can be regarded as CH_3 or H there are nine conformers for each amino acide according to Ramachandaran plot which results in $9\times 9\times 9=729$ conformers.

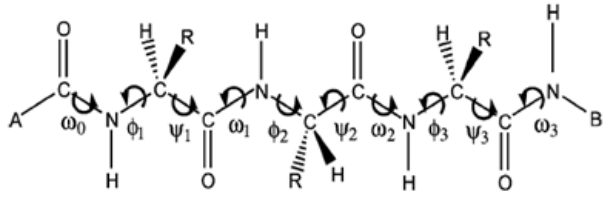

Fig 2. The conformational structure of diamides of tripeptides.

Protein chemists have simplified their approach to the study of protein folding by separating the problem of backbone conformation from side chain conformation , as well as form the problems of nearest neighbors and long-range interactions. The simplest amino acids, such as glycine [21-26]and alanine [15],[21]-[25],[27]-[28] were among the first studied, followed by valine [23],[29], which has one sidechsin torsional angle was next. In addition conformational studies have been performed on proline [30],aspartate [31], aspargine [32], cytosine and selenocytosine [33]. And also ab initio studies have been performed on dialanine [15]-[17],[34],[35] trialanine [36],tetra- alanine [37-40], as well as oligoalanine [41], triglycine [42],[43], Ala-Gly-Ala tripeptide [44],[45] and other tripeptides [46].
Biophysical studies and computational analysis of native elastine mimetic polypeptides have indicated the presence of $\beta-$sheet conformation and have postulated a functional role for this conformation in the development of elastomeric behavior [47],[48]. Although proline and glycine amino acids prefer spiral structures β turn (II) in elastin, but valine amino acid existence with a large side chain can play an important role in forming pleated sheet β (extended) structure [42].
In the present work we study the different conformers that obtained from the rotation of valine side chain around $<N_5C_6C_{16}C_{18}$ dihedral angle (χ) and backbone torsional angle (Φ_2,Ψ_2) of valine amino acide in protected tripeptide " $HCO-Gly-L-val-Gly-NH_2$ " in elastin penta – peptide which has a chiral center and one prochiral side chain.(see Fig 3)

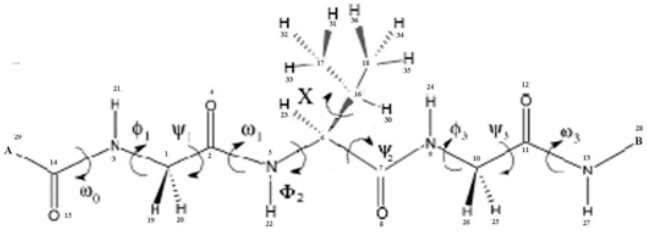

Fig 3.Schematic of the numbering system applied to the tripeptide HCO-Gly-L-Val-Gly-NH_2. showing all side chain and backbone torsional angles

The pervious researches show that protein folding is governed by the law of thermodynamics [49], therefore using computational methods the optimized geometries, energies and other thermodynamic properties such as Gibbs free energy, enthalpy and entropy were determined and we found the most stable conformer that obtained from rotation around torsional angles (Φ_2,Ψ_2) of valine amino acid.

2 COMPUTATIONAL METHODS

Ab initio and DFT calculations were carried out on the selected conformations of the tripeptide model HCO – Gly – L – Val – Gly – NH_2 shown in Fig 3, at the HF/6-31G(d) and B_3LYP/6-31G(d) levels in gas phase at 1 atm and 298K. In all cases, the steady –state nature (minimum on the potential energy surface) of the optimized complexes have been confirmed by calculating the corresponding frequencies at the same computational level. The Gaussian 98 program [50] was used for the geometry optimization of the gauche (-) (g^-), gauche (+) (g^+) and anti (a) conformers of HCO – Gly – L – Val – Gly – NH_2 tripeptide. For this purpose the side chain torsional angle (χ) as a variable of the energy function was changed at 30° intervals from 0 to 360°. The corresponding bond angles, bond lengths and dihedral angles were compared among g^+, g^- and anti (a) conformers. Afterward two of the glycine residues were chosen at a time to be in the fully extended, or β conformation, and valine amino acid was placed at 9 possible minima in Ramachandran plot for the g^+, g^- and anti conformers and then optimization calculation carried out at B_3LYP/6-31G(d) level.

3 RESULTS AND DISCUSSION

The studied tripeptide structure is shown in Fig 3 which is presented by an internal coordinate system of z-matrix, numbering atoms and every possible torsional angle of the structure and the side chain (χ) dihedral angle. In this study A and B are considered as H atom.We added HCO and NH_2 groups to tripeptide separately for keeping α-carbon during the peptide bond and modeling the bigger polypeptide structures.
Adding these groups doesn't change the special internal parameters of the main structure of tripeptide. At first the effect of changes in torsional angle of side chain on structure conformation was studied as a variable of energy function. For this the optimized geometries that obtained from the rotation of side chain around (χ) dihedral angle at 30° intervals from 0° to 360° were determined. The HF/6-31G(d) and B_3LYP/6-31G(d) geometries of various conformers that obtained from rotation around (χ) are shown in Tables 1 and 2.

According to the results in both B_3LYP and HF levels three minima conformers were seen in χ=+60°, χ=180° and χ=-60° which are in uncoated state and were named gauche (+) (g^+), anti (a) and gauche(-) (g^-) respectively (see Fig 4). The order of stability of these conformers is $Eg^- < Eg^+ < Ea$ (see Tables 1 and 2).

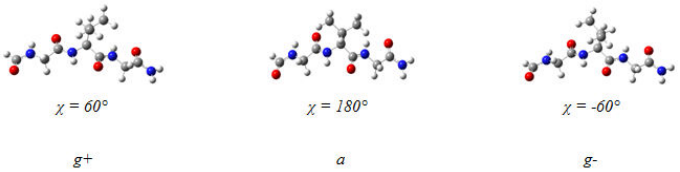

Fig 4. optimized structures of three stable conformers g^+, g^- and anti

In ideally the α -carbon bond angle for HCO – Gly – L – Val – Gly – NH_2 , N – $\hat{C}_\alpha$ – C (5-6-7 in Fig 3) is 109.5° which according to our results it can be seen that this bond angle in both HF and B_3LYP levels for g^- conformer has less deviation than 109.5° comparing to other conformers g^+ and anti. In addition the values of dihedral angles (Φ_1,Ψ_1,$\Phi_3$$\Psi_3$) have less deviation than 180° but Φ_2 and Ψ_2 have more deviation than 180°. The largest changes in dihedral angles are found for the Φ_2 and Ψ_2 of anti conformer. The calculated results for anti conformer show the dihedral angles Φ_2 and Ψ_2 are (-128.25 and 131.45°) and (-131.96 and 131.94°) at HF/6-31G(d) and B_3LYP/6-31G(d) respectively. deviation from 180° in HF and B_3LYP levels are 52° and 49° respectively and dihedral angle Ψ_2 Deviation in HF and B_3LYP levels are 49° and 40° respectively. (see Tables 1 and 2).
The calculated relative energies for interactive transformation of various conformations of tripeptide as a function of dihedral angle (χ) show that the barrier energies of between them are 3 to 6.8 $kcalmol^{-1}$ for transform to extended conformation or $\beta_L\beta_L\beta_L$ (see Fig 5).
So valine side chain rotation has a great effect on tripeptide structure conformation specially the adjacent amino acid dihedral angles.
What with the valine side chain can be oriented in g^- , a and g^+ conformers, So generally according to Ramachandran plot for the studied tripeptide 9×9×9×3=2187 conformers is expected.

Table 1. Optimized geometries and energies for HCO-Gly-L-Val-Gly-NH_2 (g+, a and g- states) varying side chain torsional angel (χ) of L-Valine at HF/6-31G (d) level of theory

χ	E	ΔE	Gly_1		L-Val_2		Gly_3		
	Hartree	Kcal/mol	Φ_1	Ψ_1	Φ_2	Ψ_2	Φ_3	Ψ_3	$N\ddot{C}_\alpha C$
0	-906.3765	6.8398	179.92	179.50	-142.59	143.47	-177.74	-179.63	105.523
30	-906.4814	3.7650	179.37	-177.77	-151.30	135.005	-177.42	-179.13	104.512
60	**-906.4865**	**0.5647**	**-179.56**	**179.28**	**-151.19**	**147.42**	**-179.49**	**-179.79**	**105.945**
90	-906.4849	1.5688	-179.70	179.05	-154.11	158.01	-178.83	178.54	106.838
120	-906.4803	4.4553	-179.85	-179.99	-153.76	151.046	-177.75	-179.62	106.141
150	-906.4833	2.5728	-178.75	178.21	-127.65	137.79	-178.27	-179.84	105.825
180	**-906.4863**	**0.6903**	**-179.79**	**179.71**	**-128.25**	**131.46**	**-178.74**	**-179.97**	**106.184**
210	-906.4835	2.4473	179.92	179.26	-136.97	141.67	-178.47	179.25	106.398
240	-906.4816	3.6395	-179.17	178.42	-151.11	156.40	-179.68	179.83	106.391
270	-906.4846	1.7570	-179.48	177.43	-139.84	153.38	179.80	-179.8	106.382
300(-60)	**-906.4874**	**0**	**-179.02**	**177.61**	**-130.49**	**160.99**	**179.45**	**179.10**	**107.524**
330	-906.4827	2.9493	-178.87	177.92	-130.50	157.70	-179.108	179.25	107.866
360	-906.4765	6.8398	179.92	179.50	-142.59	143.47	-177.74	-179.63	105.523

Table 2. Optimized geometries and energies for HCO-Gly-L-Val-Gly-NH_2 (g+, a and g- states) varying side chain torsional angel (χ) of L-Valine at $B_3LYP/6\text{-}31G$ (d) level of theory

χ	E	ΔE	Gly_1		$L\text{-}Val_2$		Gly_3		
	Hartree	Kcal/mol	Φ_1	Ψ_1	Φ_2	Ψ_2	Φ_3	Ψ_3	$NC_\alpha C$
0	-911.860223	6.0216	178.049	-177.165	-142.855	147.582	-173.676	-179.725	105.118
30	-911.86412	3.5763	-179.424	179.561	-151.092	139.064	-176.309	-179.147	104.193
60	**-911.86933**	**0.31**	**-176.827**	**178.350**	**-152.716**	**153.370**	**179.959**	**-179.835**	**105.311**
90	-911.867731	1.3105	179.926	179.195	-156.620	161.010	-178.124	179.531	106.280
120	-911.863834	3.7558	-178.626	178.367	-155.115	153.812	-176.012	-178.786	105.478
150	-911.865967	2.4174	179.047	179.625	-132.626	141.468	179.942	-178.306	105.273
180	**-911.8684764**	**0.8424**	**-177.695**	**176.878**	**-131.959**	**139.940**	**-169.048**	**176.558**	**105.547**
210	-911.86658	2.0331	177.024	179.648	-136.803	150.119	-171.414	178.463	106.071
240	-911.864663	3.2355	-179.447	176.442	-151.766	163.615	178.335	-178.666	105.666
270	-911.867347	1.5512	179.476	178.084	-143.513	158.758	-179.920	179.884	105.458
300(-60)	**-911.869819**	**0**	**-179.120**	**-179.968**	**-133.525**	**162.765**	**178.663**	**179.715**	**106.666**
330	-911.865778	2.5357	-179.655	178.521	-133.557	159.289	-179.234	179.962	106.874
360	-911.860223	6.0216	178.049	-177.165	-142.855	147.582	-173.676	-179.725	105.118

In the current research according to the changes in torsional angles of central amino acid, valine, we have determined the most stable conformer. For this purpose two terminal amino acids "Gly" has been kept fix in β_L conformation and the central amino acid, valine, was considered for 9 possible minima in Ramachanran plot in three variable states g^-, a and g^+, so 3×9=27 possible conformations were studied for tripeptide HCO – GLY – L – Val – GLY – NH_2.

For every conformation at $B_3LYP/6\text{-}31G^*$ level we determined the optimized geometries and energies and also by using frequency calculations at this level we obtained Gibbs free energy (G), enthalpy(H) and entropy(S). All structure have been verified to be energy minima through vibrational analysis (no imaginary frequencies). Of all conformations studied, the $\beta_L\beta_L\beta_L$ conformation of HCO-Gly-L-Val-Gly-NH_2 has the lowest energy value, being the most stable structure. Thus, the energy values of other conformations of HCO-Gly-L-Val-Gly-NH_2 were compared to the energy value of the $\beta_L\beta_L\beta_L$ structure which is the reference conformation. Our results turnout

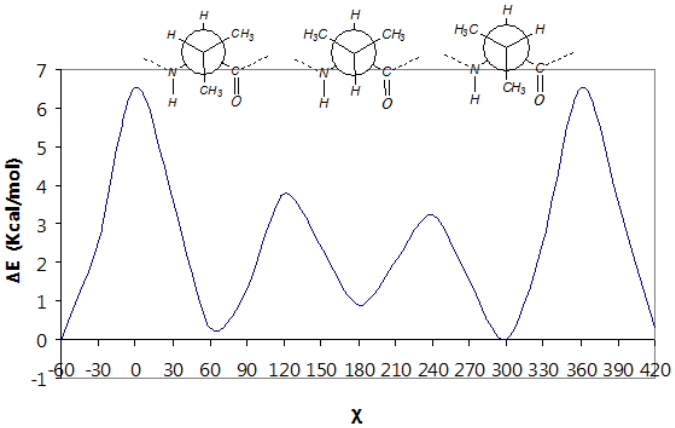

Fig 5. Relative energy of HCO-Gly-L-Val-Gly-NH_2 conformations as a function of χ

that observed conformers for g^+, a and g^- states, are $\beta_L\beta_L\beta_L$, $\beta_L\gamma_L\beta_L$, $\beta_L\gamma_D\beta_L$, $\beta_L\alpha_D\beta_L$ and $\beta_L\varepsilon_D\beta_L$. In g^+ state only $\beta_L\varepsilon_L\beta_L$ Conformer was absent and 8 other conformers obtained (see Tables 3, 4 and 5).

In anti state $\beta_L\varepsilon_L\beta_L$ and $\beta_L\delta_L\beta_L$ were absent and 7other conformers obtained, and in g^- state $\beta_L\varepsilon_L\beta_L$, $\beta_L\delta_D\beta_L$ And $\beta_L\alpha_L\beta_L$ Were absent and 6 other conformers obtained. So $\beta_L\varepsilon_L\beta_L$ conformer was absent in every three states .

Among the absent conformesr, $\beta_L\alpha_L\beta_L$, $\beta_L\varepsilon_L\beta_L$ and $\beta_L\delta_L\beta_L$ conformers incline toward $\beta_L\beta_L\beta_L$ conformer, in other word they find their stability in $\beta_L\beta_L\beta_L$ State, and also $\beta_L\delta_D\beta_L$ conformer inclines toward $\beta_L\delta_L\beta_L$, so it can be seen that not only $\beta_L\beta_L\beta_L$ conformer is the most stable conformer, but also most of the absent conformer find their stability in $\beta_L\beta_L\beta_L$ state in good agreement with experimental and pervious theoretical studies [47],[48].

$\beta_L\gamma_L\beta_L$, $\beta_L\gamma_D\beta_L$, $\beta_L\varepsilon_D\beta_L$ and $\beta_L\alpha_L\beta_L$ conformers have less energy in anti state in comparing to other states, g^+ and g^- , then they are more stable .

Table 3. [B3LYP/6-31G(d)] Optimized geometries and energies for HCO-Gly-L-Val-Gly-NH_2 (g+ state) varying the backbone conformation of L-Valine

Backbone conformation	Energy (Hartree)	ΔE (Kcalmol⁻¹)	Gly_1		$L\text{-}Val_2$		Gly_3	
			Φ_1	Ψ_1	Φ_2	Ψ_2	Φ_3	Ψ_3
$\beta_L\beta_L\beta_L$	-911.8696	0	-179.2733	177.7993	-154.3444	156.9292	179.9279	179.7652
$\beta_L\gamma_L\beta_L$	-911.8650	2.8737	175.081	-176.8972	-87.1741	75.1857	174.4044	178.7223
$\beta_L\gamma_D\beta_L$	-911.8582	7.1489	-173.2580	163.4510	67.7447	-34.2700	-174.8796	175.1399
$\beta_L\delta_L\beta_L$	-911.8647	3.0789	-176.3404	-176.5911	-120.1713	11.0364	-176.0986	-179.1454
$\beta_L\delta_D\beta_L$	-911.8605	5.6874	180.000	175.8850	-159.3346	-36.4532	159.9042	172.8533
$\beta_L\varepsilon_L\beta_L$	Not found	–	–	–	–	–	–	–
$\beta_L\varepsilon_D\beta_L$	-911.8548	9.2624	174.2435	-168.8282	73.3631	162.0373	-145.130	177.6515
$\beta_L\alpha_L\beta_L$	-911.8644	3.2326	-173.4291	-179.5013	-101.6964	-1.4546	-171.1523	-178.5286
$\beta_L\alpha_D\beta_L$	-911.8585	6.9236	171.2522	-174.8257	47.8655	45.2630	155.4225	177.4487

Table 4. [B3LYP/6-31G (d)] Optimized geometries and energies for HCO-Gly-L-Val-Gly-NH_2 (anti state) varying the backbone conformation of L-Valine

Backbone conformation	Energy (Hartree)	ΔE (Kcalmol⁻¹)	Gly_1		$L\text{-}Val_2$		Gly_3	
			Φ_1	Ψ_1	Φ_2	Ψ_2	Φ_3	Ψ_3
$\beta_L\beta_L\beta_L$	-911.86856	0	-178.4706	178.48175	-129.55981	138.71765	179.22121	-179.53745
$\beta_L\gamma_L\beta_L$	-911.8668	1.1258	174.2039	-177.4764	-87.09808	88.88939	179.1988	175.01209
$\beta_L\gamma_D\beta_L$	-911.86282	3.6025	178.52624	175.88197	74.17020	-61.6689	176.01610	-175.5255
$\beta_L\delta_L\beta_L$	Not found	—	—	—	—	—	—	—
$\beta_L\delta_D\beta_L$	-911.86075	4.9003	179.78891	177.24002	-125.18338	-64.23455	164.16544	176.11975
$\beta_L\varepsilon_L\beta_L$	Not found	—	—	—	—	—	—	—
$\beta_L\varepsilon_D\beta_L$	-911.85754	6.9204	170.52336	-168.04083	76.78468	140.60697	-176.87855	-178.3917
$\beta_L\alpha_L\beta_L$	-911.86342	3.2255	-168.1809	172.52004	-78.82294	-27.66006	-153.73941	179.36147
$\beta_L\alpha_D\beta_L$	-911.86104	4.7186	156.40055	-164.19934	56.88729	42.17325	133.17856	-175.4254

The calculated thermodynamic properties such as Gibbs free energy, enthalpy and entropy indicate that when energy, Gibbs free energy and enthalpy have the least values, entropy increases, and the most stable conformers have the highest entropy in every state (see Tables 6, 7, and 8)

Although $\beta_L\beta_L\beta_L$ conformer has the minimum total energy but it has less entropy than some of conformers and it doesn't have the maximum value so dipole-dipole attraction plays the main role in producing this stability (see Fig 6).

According to Fig 5 when Φ_2= 0° and Ψ_2=180° there is a coupling between two oxygen atoms in peptide plane and if Φ_2=180° And Ψ_2=0° There is an interference between two Hydrogen atoms, and this fact prevents the formation of such angles. If both Φ_2 and Ψ_2 are 180° and Φ_2=Ψ_2=0° we'll have an interference between carbonyl oxygen atoms and Hydrogen atom which is the favorable factor. So dipole-dipole attraction interactions and entropy play the main role in forming a stable conformer.

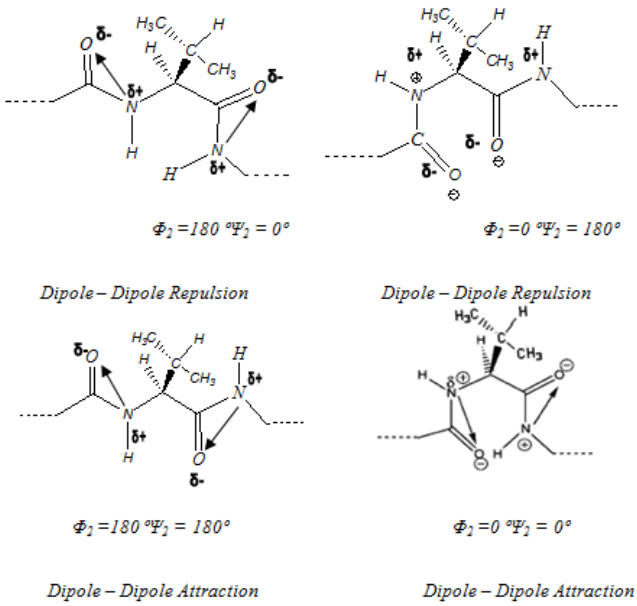

Fig 6. A schematic illustration of Dipole – Dipole Repulsion and Attraction Interactions for certain conformers of amino acid diamides

Table 5. [B3LYP/6-31G (d)] Optimized geometries and energies for HCO-Gly-L-Val-Gly-NH_2 (g^- state) varying the backbone conformation of L-Valine

Backbone conformation	Energy (Hartree)	ΔE (Kcal/mol)	Gly_1		$L\text{-}Val_2$		Gly_3	
			Φ_1	Ψ_1	Φ_2	Ψ_2	Φ_3	Ψ_3
$\beta_L\beta_L\beta_L$	-911.86925	0	-175.294	178.784	-133.942	162.798	177.953	-179.647
$\beta_L\gamma_L\beta_L$	-911.86580	2.5376	174.687	-171.190	-87.566	59.606	169.264	-176.431
$\beta_L\gamma_D\beta_L$	-911.85886	6.8952	178.453	172.189	61.778	-29.221	-171.266	174.001
$\beta_L\delta_L\beta_L$	-911.86668	1.9842	-176.290	175.193	-123.006	15.839	178.699	-178.193
$\beta_L\delta_D\beta_L$	Not found	–	–	–	–	–	–	–
$\beta_L\varepsilon_L\beta_L$	Not found	–	–	–	–	–	–	–
$\beta_L\varepsilon_D\beta_L$	-911.85726	7.89643	173.475	-173.454	44.452	-145.470	-168.790	-178.579
$\beta_L\alpha_L\beta_L$	Not found	–	–	–	–	–	–	–
$\beta_L\alpha_D\beta_L$	-911.86025	6.0221	158.034	-166.428	45.755	44.504	137.062	-175.043

Table 6. Enthalpy, Gibbs-free energy and entropy values for the optimized geometries of HCO-Gly-L-Val-Gly-NH_2 (g+ state) at the B3LYP/6-31G (d) level of theory

Backbone conformation	Gibbs-free energy (Hartree)	ΔG (Kcal/mol)	Enthalpy (Hartree)	ΔH (Kcal/mol)	Entropy ($cal.mol^{-1}.K^{-1}$)	ΔS ($cal.mol^{-1}.K^{-1}$)
$\beta_L\beta_L\beta_L$	-911.62603	0	-911.54938	0	161.313	0
$\beta_L\gamma_L\beta_L$	-911.62183	2.6544	-911.54480	2.8747	162.118	-0.805
$\beta_L\gamma_D\beta_L$	-911.61421	7.4235	-911.53775	7.2974	160.923	0.39
$\beta_L\delta_L\beta_L$	-911.62015	3.6879	-911.54441	3.1213	159.417	1.896
$\beta_L\delta_D\beta_L$	-911.61587	6.3768	-911.54024	5.7361	159.170	2.143
$\beta_L\varepsilon_L\beta_L$	Not found	—	—	—	—	—
$\beta_L\varepsilon_D\beta_L$	-911.60929	10.5071	-911.53433	9.4472	157.763	3.55
$\beta_L\alpha_L\beta_L$	-911.62054	3.4444	-911.54424	3.2255	160.584	0.729
$\beta_L\alpha_D\beta_L$	-911.61294	8.21727	-911.53824	6.9899	157.201	4.112

Table 7. Enthalpy, Gibbs-free energy and entropy values for the optimized geometries of HCO-Gly-L-Val-Gly-NH_2 (anti state) at the B3LYP/6-31G (d) level of theory

Backbone conformation	Gibbs-free energy (Hartree)	ΔG (Kcal/mol)	Enthalpy (Hartree)	ΔH (Kcal/mol)	Entropy ($cal.mol^{-1}.K^{-1}$)	ΔS ($cal.mol^{-1}.K^{-1}$)
$\beta_L\beta_L\beta_L$	-911.6249	0	-911.5483	0	161.241	0
$\beta_L\gamma_L\beta_L$	-911.6234	0.9413	-911.5466	1.0668	161.639	-0.398
$\beta_L\gamma_D\beta_L$	-911.6192	3.5768	-911.5426	3.5768	161.305	-0.064
$\beta_L\delta_L\beta_L$	Not found	—	—	—	—	—
$\beta_L\delta_D\beta_L$	-911.6180	4.3298	-911.5407	4.7691	162.047	-0.806
$\beta_L\varepsilon_L\beta_L$	Not found	—	—	—	—	—
$\beta_L\varepsilon_D\beta_L$	-911.6135	7.1536	-911.5373	6.9026	160.378	0.863
$\beta_L\alpha_L\beta_L$	-911.6197	3.2631	-911.5432	3.2003	161.029	0.212
$\beta_L\alpha_D\beta_L$	-911.6145	6.5261	-911.5406	4.8319	155.433	5.808

Table 8. Enthalpy, Gibbs-free energy and entropy values for the optimized geometries of HCO-Gly-L-Val-Gly-NH_2 (g^- state) at the B3LYP/6-31G (d) level of theory

Backbone conformation	Gibbs-free energy (Hartree)	ΔG (Kcal/mol)	Enthalpy (Hartree)	ΔH (Kcal/mol)	Entropy ($cal.mol^{-1}.K^{-1}$)	ΔS ($cal.mol^{-1}.K^{-1}$)
$\beta_L\beta_L\beta_L$	-911.6252	0	-911.5496	0	159.202	0
$\beta_L\gamma_L\beta_L$	-911.6218	2.1335	-911.5456	2.5100	160.391	-1.189
$\beta_L\gamma_D\beta_L$	-911.6148	6.52606	-911.5385	6.9653	160.702	-1.5
$\beta_L\delta_L\beta_L$	-911.6226	1.6315	-911.5465	1.9453	160.214	-1.012
$\beta_L\delta_D\beta_L$	Not found	—	—	—	—	—
$\beta_L\varepsilon_L\beta_L$	Not found	—	—	—	—	—
$\beta_L\varepsilon_D\beta_L$	-911.6118	8.4086	-911.5369	7.9694	157.601	1.601
$\beta_L\alpha_L\beta_L$	Not found	—	—	—	—	—
$\beta_L\alpha_D\beta_L$	-911.6133	7.4673	-911.5398	6.1496	154.641	4.561

4 CONCLUSION

1- The results obtained from HF/6-31G(d) and B_3LYP/6-31G(d) for different conformers of HCO – Gly – L – Val – Gly – NH_2 that have been concluded due to the rotation of valine amino acid side chain around dihedral angle (χ), show three minima at χ=+60°, χ =180° and χ = - 60° which were labeled g^+, a and g^- respectively, and order of their stability is $g^- > g^+ > a$.

2- The calculated relative energies for interactive transformation of various conformations of tripeptide as a function of dihedral angle (χ) show that the barrier energies of between them are 3 to 6.8 $kcalmol^{-1}$ for transform to extended conformation or $\beta_L\beta_L\beta_L$.

3- The rotaion of valine side chain has a great effect on tripeptide conformation, special on dihedral angles of neighbor amino acids. Therefore whatever the side chain becomes larger, diviation of dihedral angles from 180º inclines toward less values.

4- The results of calculations show that the most stable conformer for three states of valine , g^+, a and g^- , is $\beta_L\beta_L\beta_L$ conformer and also in g^+, a and g^- states 8, 7 and 6 conformers were found respectively.

5- The obtained $\beta_L\gamma_L\beta_L$, $\beta_L\gamma_D\beta_L$, $\beta_L\varepsilon_D\beta_L$ and $\beta_L\alpha_D\beta_L$ Conformers in this three states, are more stable in anti state than other two states. According to obtained results dipole-dipole attraction interactions and also entropy play the main role in forming a more stable conformer.

6- In good agreement with experimental and pervious theoretical studies [42,47-48] we found that the $\beta_L\beta_L\beta_L$ conformation of HCO-Gly-L-Val-Gly-NH_2 is the most stable among all of conformations.

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