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Impact of solvation on the geometrical parameters of some amino acids

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ABSTRACT

The impact of the utilized solvent is of an important concern. Eliminating the effect of solvents and other factors is a crucial point in order to get more accurate results. Therefore, density functional theory DFT calculations at B3LYP/ 6-31G(d,p) level were carried out for a number of amino acids in the gaseous state and also under the effect of various solvation processes using different solvents; DMSO, acetonitrile (AN), nitromethane (NM) and methanol (Meth). Geometrical parameters of both N and C terminals were investigated. Results demonstrate that different solvation processes affect the studied parameters that should be considered for future applications.

Keywords: *amino acids; valine; alanine; solvation; dft; geometrical parameters.*

1. INTRODUCTION

Living bodies comprise of various macromolecules; proteins, carbohydrates, lipids and nucleic acids. Proteins are considered one of the most important macromolecules where they perform several vital functions. They may be hormones, enzymes, receptors, signaling compounds, structural units of muscles and many more roles. Proteins are composed of many polypeptide chains that contain hundreds of amino acids. Amino acids are the main building block for proteins and polypeptides that have crucial applications in our lives and in diverse scientific fields [1]. There are twenty amino acids in all livings. They are common in their chemical structure where they all composed of a central alpha carbon atom bonded to four moieties; a hydrogen atom, a carboxyl group (called C-terminal), amino group (called N-terminal) and R-group, by single covalent bonds. Twenty different R groups result in twenty different amino acids. Alanine is the second simple amino acid regarding its chemical structure where its R group is a methyl one (CH_3) [2]. Depending on the nutrition point of view, alanine is one of the non-essential amino acids, which the body can produce, in the protein synthesis and also can be used as an energy fuel. It is always synthesized from the "glucose-alanine cycle" via the action of alanine aminotransferase (ALT) enzyme which catalyzes the transamination processes between pyruvate and glutamate structures to alanine in both directions, regulated by Peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1α) [3]. Alanine amino acid is responsible for carrying ammonia group (NH_3) from the muscles, as a metabolic waste, to the liver acting as a precursor for the gluconeogenesis process as well as acting as an ergogenic aid in exercise performance [4]. In addition, its isomer called β-alanine combines with histidine amino acid in order to form carnosine (dipeptide) that act as an H^+ buffer in muscles [5]. Valine amino acid is similar to alanine one in its chemical structure where its R group is a propane group instead of a methyl one in alanine. Being hydrophobic make it always buried in the inner parts of pro1teins escaping from the outer aqueous environment. In addition, it is not involved in any catalytic reactions. However, it is vital in ligand recognition especially those involve hydrophobic interactions [6]. One of the reported physical properties of valine is that it has two transition states at 80°C and 100°C [7]. Serine is one of the polar amino acids. Its R group contains a terminal hydroxyl group. It is one of the early discovered amino acids. Serine is one of the essential amino acids that must be supplied in diets. It is one of the polar entities among protein structure, hence it is found on their external parts where it can form hydrogen bonds with surrounding aqueous solution. Lysine is a basic amino acid, containing a carboxyl group and two amino groups [8]. Lysine is one of the amino acids that have many applications including industrial and biological ones. A simple, cheap, rapid and highly sensitive electrochemical sensor was fabricated based on Poly-L-Lysine, Multi walled carbon nanotubes and Al_2O_3 composite for determination of 17β-E2 in clinical whole blood samples [9]. In additional, DFT calculations revealed that Serine-Lysine peptides can be used as a mediator in production of titanium dioxide using silicification methods depending on its enrichment with amino groups in lysine [10]. DFT studies confirmed the utilization of Poly-L-Lysine coated with Ag nanoparticles in the presence of cetyltrimethylammonium bromide (CTAB) as a stabilizing agent for colorimetric sensing of Hg^{2+} ions [1]. Many articles showed that L-lysine has corrosion inhibition on mid steel using electrochemical techniques [8].

Molecular modeling at a different level of theories could be utilized to understand the structural and chemical properties of amino acids as well as many structure and systems [11-13]. It is widely utilized for understanding the interaction between chitosan and amino acids [14]. To follow the effect of Hydrated Dioxin on the physical and geometrical parameters of amino acids [15]. To study the effect of Alkaline Elements on the Structure and Electronic properties of Glycine [16]. To study between Aspartic Acid and Iron [17]. It is also documented that molecular modeling is confirming the experimental findings and paves the way toward understanding important phenomena in biology and chemistry and environment [13, 18-20]. Based upon the above findings the present computational work is conducted to elucidate the impact of solvation on the geometrical parameters of some amino acids using DFT level of theory.

2. EXPERIMENTAL SECTION

2.1. Calculation Details.

A computational study of some amino acids; alanine, serine, valine and lysine, was performed using GAUSSIAN 09 software that is implemented at Spectroscopy department, National Research Centre (NRC) [21]. Calculations were conducted via Density Functional Theory (DFT) level at Becke-style 3-Parameter Density Functional Theory (using the Lee-Yang-Parr correlation functional) (B3LYP) [22-24] and 6-31g(d,p) as a basis set. The geometrical parameters of the proposed amino acids were investigated in both gaseous state as well as under solvation with different solvents such as dimethylsulfoxide (DMSO), nitromthane (NM), acetonitrile (AN) and methanol (Meth).

3. RESULTS SECTION

Although many research works describes the process of solvation of amino acids as an important step for studying protein [25, 26] the topic still open for molecular modeling analyses as in the following steps. First the building of the studied structure are described then the electronic properties are also described for different amino acids at different solvents at B3LYP/ 6-31G(d,p) level of theory.

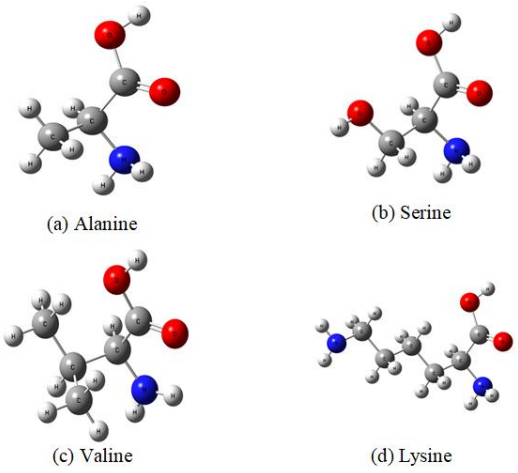

Figure 1. Model molecules of (a) alanine, (b) serine, (c) valine and (d) lysine amino acids.

3.1. Building Model Molecules.

Four amino acids were built up as illustrated in figure 1. All amino acids have the same chemical structure except for their R group where they all composed of a central alpha carbon atom bonded to four moieties; a hydrogen atom, a carboxyl group (called C-terminal), amino group (called N-terminal) and R-group, by single covalent bonds. Alanine is the simplest built up molecule; its R group is a methyl CH_3 group. It makes it one of hydrophobic amino acids. Serine amino acid has CH_2OH group in its R side chain. Having OH group enhance its hydrophilicity. Valine is similar to alanine in being hydrophobic. Its side chain composed of propane terminal group. Lysine is a basic amino acid; its R group contains an additional amine group.

3.2. Energy Optimization Calculations.

Energy optimization calculations were carried out for the proposed amino acids via DFT calculations at B3LYP level and 6-31G(d,p) basis set. The calculations were conducted for the amino acids in both gaseous states and under solvation with several solvents such as DMSO, nitromthane (NM), acetonitrile (AN) and methanol (Meth) and geometrical parameters are investigated in both cases. Table 1 presents the resultant geometrical parameters of the proposed structures. Bond lengths and bond angles of both C as well as N terminals of the studied structures are considered. Solvation of amino acids with various solvents seem to affect the geometrical parameters of their terminals, as illustrated in table 1, which should be considered in further applications. Regarding alanine amino acid, its two NH bonds are slightly different in their lengths, however they have the same chemical nature. Solvation of alanine increases the length of its two NH bonds that may be attributed to the solvation of alanine at its N terminal is a favored process. However, the solvation processes lowered the HNH angle. It decreases from 107.0971^o in the gaseous state to 105^o under solvation effects with the chosen solvents except for acetonitrile one in which HNH bond reaches to 106.2814^o. Five geometrical parameters are considered for the C terminal of alanine. Three bond lengths include C=O, CO and OH. Since, CO contains a single sigma bond so its length is longer than that of the C=O that has a shorter pi bond. OH bond is shorter than both of them. The added different solvents to alanine nearly have the same impact on the studied bond lengths. They all increase the length of both C=O and OH to nearly the same extent, however the decrease the length of the CO one. Two bond angles for the C terminal are studied; HOC and OCO. Solvation of alanine increases the HOC bond angle. It reaches a maximum value of 108^o using acetonitrile solvent. However, solvation with various solvents has little impact on the OCO bond angle where it slightly increases to have a

largest value for acetonitrile as well. For serine amino acid, the lengths of the two NH bonds are also different like for alanine. The HNH bond angle is smaller than that in alanine where it equals 103.888°. However, the bond length of C=O bond equal to that one in alanine. Results of C terminal parameters demonstrate that they are different from those in alanine. Both CO and OCO are smaller, but OH as well as HOC are larger.

Similar to alanine, solvation of serine leads to some geometrical changes in its terminals. Different solvents have nearly the same effect on the two NH bonds Solvation of serine also increase the angle of HNH one. Little changes can be observed for C terminal parameters upon solvation except for C=O and OCO ones. Solvation processes result in decreasing the length of C=O bond but increasing the OCO angle. They have no significant impact on other parameters. Unlike both alanine and serine amino acids, the lengths of the two NH bonds in valine are equal. Different solvents increase each one of them to nearly equal values except for methanol whose results are smaller than others. However, they decrease the values of HNH angle except for methanol which increases its value by about two degrees. They also decrease the values of both C=O and CO bonds to the same extent. However, they have no effect on the results of OH and HOC. On the other hand they cause increases in the values of OCO angle. The geometrical parameters of lysine amino acid have the same behavior as others, however the HOC angle is larger than OCO one unlike those in other amino acids. Solvation using various solvents has a different impact on the C and N terminals where some values increase others decrease while the rest still unchanged. All of the two NH bonds, OH and OCO angle increase to the same extent for each one. However, both HNH and CO decrease due to solvation processes. While C=O and HOC keep unchanged except for little variations.

Table 1. Geometrical parameters of C and N terminals of alanine (Ala), serine (Ser), valine (Val) and lysine (Lys) amino acids in the gaseous state and under solvation with DMSO, nitromethane (NM), acetonitrile (AN) and methanol (Meth) solvents calculated at DFT using B3LYP/6-31G(d,p) level.

		Amino group			Carboxyl group				
Amino Acid	**Solvation**	**NH(1)**	**NH(2)**	**HNH**	**C=O**	**CO**	**OH**	**HOC**	**OCO**
Ala	**No Solvation**	1.0164	1.0170	107.0971	1.2096	1.3576	0.9720	106.1465	122.3635
	DMSO	1.0208	1.0225	105.5234	1.2183	1.3423	0.9929	107.9218	122.8446
	NM	1.0209	1.0225	105.5044	1.2179	1.3430	0.9925	107.9635	122.8339
	AN	1.0223	1.0220	106.2814	1.2177	1.3425	0.9927	108.0036	123.3192
	Meth	1.0209	1.0225	105.5298	1.2180	1.3429	0.9924	107.9286	122.8294
Ser	**No Solvation**	1.0193	1.0170	103.8880	1.2095	1.3447	0.9937	108.0666	121.7808
	DMSO	1.0231	1.0225	105.830	1.2198	1.3397	0.9937	108.0641	123.3426
	NM	1.0232	1.0226	106.369	1.2189	1.3383	0.9939	107.9752	123.4562
	AN	1.0231	1.0227	106.311	1.2192	1.3375	0.9823	108.6215	123.5935
	Meth	1.0232	1.0224	105.8014	1.2198	1.3397	0.9932	108.0367	123.3400
Val	**No Solvation**	1.0000	1.0000	109.4700	1.2580	1.4300	0.9600	109.4712	120.0000
	DMSO	1.0203	1.0221	106.7940	1.2193	1.3415	0.9600	109.4712	123.0590
	NM	1.0203	1.0221	106.7895	1.2190	1.3416	0.9600	109.4712	123.0470
	AN	1.0203	1.0221	106.7844	1.21909	1.3415	0.9600	109.4712	123.0540
	Meth	1.0153	1.0163	111.5456	1.24022	1.3410	0.9600	109.4712	122.1993
Lys	**No Solvation**	1.0172	1.0159	107.3702	1.2108	1.3560	0.9724	122.4155	105.9422
	DMSO	1.0227	1.0203	106.1345	1.21933	1.3410	0.9933	123.0261	107.8423
	NM	1.0227	1.0204	106.1268	1.21926	1.3413	0.9930	122.9637	107.7900
	AN	1.0227	1.0204	106.1249	1.2194	1.3410	0.9931	122.9823	107.7684
	Meth	1.0226	1.0204	106.1355	1.21934	1.3413	0.9929	122.9740	107.7526

4. CONCLUSIONS

The electronic properties due to the surrounding solvent in computer simulations of biological macromolecules such as proteins remains a scientific challenge as it is the first step toward understanding the behaviors of such molecules. Accordingly, DFT calculations were carried out for a number of amino acids in the gaseous state and also under the effect of various solvation processes using different solvents; DMSO, AN, NM and Meth. DFT was conducted at B3LYP level and 6-31G(d,p) basis set. Geometrical parameters of both N and C terminals were investigated. Solvation processes seem to affect the studied parameters that should be considered for future applications. Choosing the appropriate solvent is a crucial point when beginningnew research to eliminate the impact of solvent and get accurate results.

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