

<https://doi.org/10.15407/ujpe67.8.602>

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## INTERACTION OF VALINE WITH WATER MOLECULES: RAMAN AND DFT STUDY

*Interaction of non-ionized and zwitterionic forms of valine with water molecules is studied using Raman spectroscopy and quantum chemical calculations. An integral equation formalism for the polarizable continuum model (IEF-PCM) for solvent effects is used at the B3LYP/6-311++G(d,p) level of theory. Hydrogen bonding between valine and water molecules is studied by the Atom in Molecule (AIM) and Non-Covalent Interaction (NCI) methods. By comparing the experimental and theoretical Raman spectra of valine in the aqueous medium, the complex of zwitterionic valine with 4 water molecules is found to be the most probable one.*

*Keywords:* valine, zwitterion, hydrogen bond, Raman spectra, DFT method.

### 1. Introduction

Hydrogen bonding is one of the most important intermolecular interactions and determines the structure of many relatively simple and complex molecules, from water to DNA [1]. Vibrational spectroscopy and quantum chemical calculations are powerful tools for the study of intermolecular hydrogen bonding [2–7]. Recently, such studies were supported with neutron spectrometry methods [8, 9].

Amino acids can be used as a model to study the importance of intermolecular interactions in life processes [10, 11]. Since water is a natural medium for biological molecules, the nature of intermolecular interactions in aqueous solutions of amino acids is of significant interest [12 – 25]. A detailed study of the interaction of amino acids with water is a key step in understanding the solvation process of larger systems such as peptides and proteins. Molecular complexes of various sizes are the main components of aqueous solutions of amino acids, so that it is necessary to start studying such interactions from the formation mechanism of such complexes.

Amino acids are mainly in the non-ionized (neutral) form in the gas phase. In the crystalline phase and in the aqueous medium, they can be found in the zwitterionic form caused by the transfer of the pro-

ton of amino acid molecules from the carboxyl group (–COOH) to the amino group (–NH<sub>2</sub>) [12].

The effect of microsolvation on amino acids was studied using different theoretical methods [13–23]. In this work, the attention is focused on studying the formation mechanism of complexes of valine and water molecules formed in an aqueous medium.

A few years ago, J.K. Gochhayat *et al.* [24] used the second-order Moller–Plesset (MP2) perturbation theory to find the number of water molecules required for the transition from the neutral to the zwitterionic form of several amino acids. As a result, it was shown that, at least three water molecules are necessary for the transition of valine to the zwitterionic form.

Ju-Young Kim *et al.* [25] studied the effect of microsolvation on the relative stability of zwitterionic and canonical forms of valine for complexes formed by valine with up to five water molecules [Val-(H<sub>2</sub>O)<sub>n</sub>] ( $n = 0-5$ ). These authors found that five water molecules are needed to stabilize the zwitterionic form of valine.

Although several theoretical studies have been conducted on the effect of microsolvation of valine in an aqueous medium [24, 25], the mechanisms of interaction of valine with water molecules cannot be said to be fully covered. Therefore, the purpose of this work is to study the interaction of valine with water molecules. These studies contribute to a better understanding of the molecular structure

and vibrational properties of valine in its non-ionized and zwitterionic forms.

## 2. Methods

The Raman spectrum of the aqueous solution of valine (concentration 2 M) was recorded using a Renishaw Invia Raman spectrometer with 1200 line/mm diffraction grating. The spectrum was obtained at room temperature in the spectral range 400–1800  $\text{cm}^{-1}$ . An argon laser with a wavelength of 785 nm and a power of 100 mW was used as a source of excitation light. A standard Renishaw CCD Camera detector was used to record the scattered light.

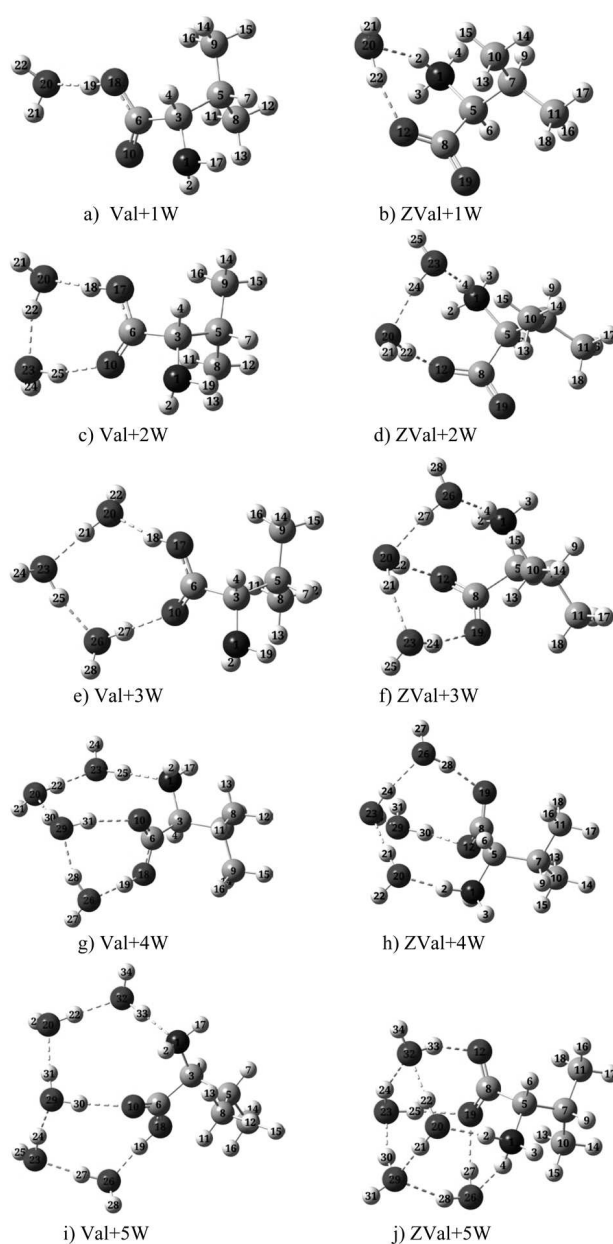
### 2.1. Computational method

All calculations were performed using the DFT method in the Gaussian 09W program [26]. The DFT method, especially with the B3LYP hybrid functional, has been successfully used to calculate the energies and various physicochemical parameters of molecular clusters in different solutions [17, 18]. In this work, we performed calculations using the B3LYP functional and the 6-311++G(d,p) basis set, which includes diffusion and polarization functionals, to consider the intermolecular hydrogen bonding. In order to account for the effect of the aqueous solution as accurately as possible, all calculations were performed using the IEF-PCM approach. In addition, for a more profound understanding of interactions existing in clusters, based on Bader's AIM theory [27], the topological parameters of the electron density distribution in the most stable structure were obtained using the MULTIWFN [28] program. The program VMD [29] was used to visualize the results of the non-covalent interaction (NCI) analysis.

## 3. Results and Discussions

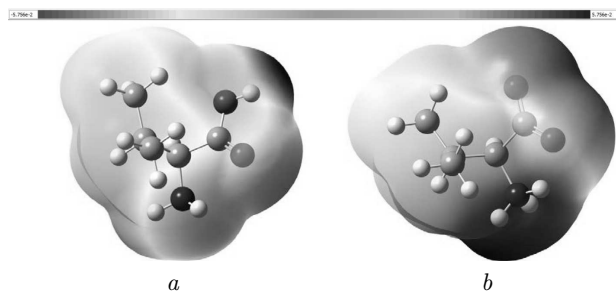
### 3.1. Optimized structures of Val + nW and ZVal + nW (n = 1–5) complexes

It is known that amino acids have several proton acceptor and proton donor centers. Therefore, valine forms various hydrogen-bound complexes with water molecules. In this research, we consider the complexes with the lowest energy. The optimized geometries of non-ionized (Val) and zwitterionic (ZVal) valine molecular complexes with water (W) molecules (Val + nW, ZVal + nW, n = 1–5) are presented in Fig. 1.



**Fig. 1.** Most stable ground state optimized geometries of Val + nW and ZVal + nW (n = 1–5) calculated at the B3LYP/6-311++G(d,p) level theory. Red, grey, white, and blue balls represent oxygen, carbon, hydrogen, and nitrogen atoms, respectively

The ground-state and relative energies of Val + nW and ZVal + nW (n = 1–5) complexes are presented in Table 1. Binding energies of molecular complexes were determined using the formula



**Fig. 2.** MEP surfaces of valine: non-ionized (a) and zwitterion (b)

$BE = E_{\text{complex}} - (E_{\text{ZVal}} + n E_{\text{W}})$  (Table 2). To estimate the thermodynamic stability of the complexes, thermodynamic parameters such as the Gibbs energy, enthalpies, and entropies are determined (Table 3).

When a water molecule approaches the neutral valine's carboxyl group, a molecular complex is formed that is more stable than those generated by other conformers (Fig. 1, a). The zwitterionic form of valine is supported by just one water molecule [18]. Valine's two functional groups (amino and carboxyl) must interact with the water molecule for this to happen (Fig. 1, b). Table 1 shows that the ZVal+1W complex's formation energy is by 1.38 kcal/mol higher than that for the Val+1W complex's. The ZVal+1W is more stable than the Val+1W, as follows from the complex formation energy and Gibbs energy presented in Table 3.

In the complex of neutral valine with two water molecules, the carboxyl group performs both H-donor and H-acceptor functions and has a cyclic structure (Fig. 1, c). The complex formed by two water molecules with zwitterion valine also has a cyclic structure, where the carboxyl group ( $\text{COO}^-$ ) acts as an H-acceptor, and the amino group ( $\text{NH}_3^+$ ) acts as an H-donor (Fig. 1, d). It follows from Table 1 that the formation energy of the ZVal+2W complex is by 1.25 kcal/mol higher than that for the Val+2W complex, so that it is structurally more stable.

The complex formed by neutral valine with three water molecules also has a cyclic form, and water molecules are located around the carboxyl group (Fig. 1, e). The complex formed by zwitterion valine with three water molecules (ZVal+3W) has a bicyclic form (Fig. 1, f) and is structurally more stable by 1.88 kcal/mol compared to the Val+3W complex.

The complex formed by neutral valine with four water molecules is in a bicyclic form (Fig. 1, g), the

amino group of valine acts as an H-acceptor. The ZVal+4W complex is also in a bicyclic form (Fig. 1, h) and is structurally more stable by 3.07 kcal/mol as compared to the Val+4W complex (Table 1).

In the interaction of neutral valine with five water molecules, the amino group acts as an H-acceptor,

**Table 1. Calculated energies of stable Val + nW and ZVal + nW (n = 1–5) complexes at B3LYP/6-311++G(d,p) level of theory**

No	Val + nW energy ( $E_1$ ) (Hartree)	ZVal + nW energy ( $E_2$ ) (Hartree)	$\Delta E = E_1 - E_2$ kcal/mol
1	-478.9870	-478.9892	1.38
2	-555.4664	-555.4684	1.25
3	-631.9427	-631.9457	1.88
4	-708.4236	-708.4285	3.07
5	-784.9018	-784.9052	2.13

**Table 2. Binding energy of Val + nW and ZVal + nW (n = 1–5) complexes**

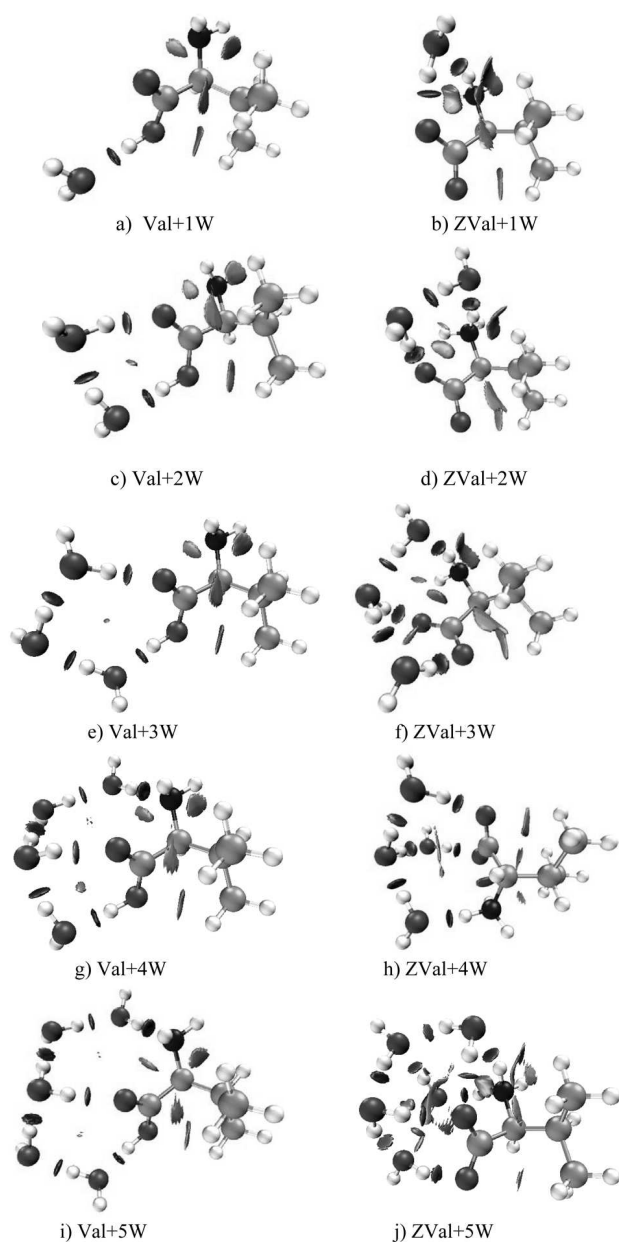
Complex	Binding energy (kcal/mol)	Complex	Binding energy (kcal/mol)
Val + 1W	4.22	ZVal + 1W	5.60
Val + 2W	12.33	ZVal + 2W	13.58
Val + 3W	18.49	ZVal + 3W	20.38
Val + 4W	27.54	ZVal + 4W	30.62
Val + 5W	34.90	ZVal + 5W	37.04

**Table 3. Gibbs energies (G), enthalpies (H) and entropies (S) of Val + nW and ZVal + nW (n = 1–5) complexes (T = 298 K)**

Complex	G (kcal/mol)	H (kcal/mol)	S (kcal/mol) K
Val + 1W	92.56	126.34	113.27
ZVal + 1W	95.57	127.52	107.14
Val + 2W	107.31	143.77	122.28
ZVal + 2W	144.80	108.88	120.48
Val + 3W	119.12	160.97	140.34
ZVal + 3W	123.20	162.31	131.17
Val + 4W	133.87	178.52	149.77
ZVal + 4W	134.91	179.39	149.20
Val + 5W	146.66	195.75	164.63
ZVal + 5W	153.19	197.70	149.31

Table 4. Topological parameters at the BCP of the valine-water complexes. All calculations are performed at the B3LYP/6-311++G(d,p) level of theory

Complex	BCP	Electron density, $\rho$	Laplacian of electron density, $\nabla^2\rho$	Lagrangian kinetic energy, $G$	Hamiltonian kinetic energy, $H$	Potential energy density, $V$	H-bond energy, $E_{\text{int}}$
Val + 1W	O <sub>18</sub> -H <sub>19</sub> ... O <sub>20</sub>	0.0406	0.1295	0.0345	0.0021	-0.0366	11.48
Val + 2W	O <sub>23</sub> -H <sub>25</sub> ... O <sub>10</sub>	0.0303	0.1113	0.0263	-0.0015	-0.0247	7.75
	O <sub>17</sub> -H <sub>18</sub> ... O <sub>20</sub>	0.0245	0.1358	0.0401	0.0062	-0.0463	14.53
Val + 3W	O <sub>26</sub> -H <sub>27</sub> ... O <sub>10</sub>	0.0301	0.1182	0.0275	-0.0021	-0.0254	7.97
	O <sub>23</sub> -H <sub>25</sub> ... O <sub>26</sub>	0.0380	0.1259	0.0324	0.0009	-0.0334	10.48
	O <sub>20</sub> -H <sub>21</sub> ... O <sub>23</sub>	0.0408	0.1282	0.0343	0.0023	-0.0366	11.48
	O <sub>17</sub> -H <sub>18</sub> ... O <sub>20</sub>	0.0502	0.1416	0.0420	0.0066	-0.0485	15.22
Val + 4W	O <sub>18</sub> -H <sub>19</sub> ... O <sub>26</sub>	0.0497	0.1357	0.0405	0.0066	-0.0470	14.75
	O <sub>26</sub> -H <sub>28</sub> ... O <sub>29</sub>	0.0387	0.1208	0.0318	0.0016	-0.0335	10.51
	O <sub>29</sub> -H <sub>30</sub> ... O <sub>20</sub>	0.0339	0.1148	0.0285	-0.0002	-0.0283	8.88
	O <sub>20</sub> -H <sub>22</sub> ... O <sub>23</sub> O	0.0371	0.1242	0.0317	0.0006	-0.0324	10.16
	O <sub>29</sub> -H <sub>31</sub> ... O <sub>10</sub>	0.0246	0.0923	0.0209	-0.0022	-0.0187	5.87
	O <sub>23</sub> -H <sub>25</sub> ... N <sub>1</sub>	0.0424	0.0943	0.0289	0.0053	-0.0342	10.73
Val + 5W	O <sub>18</sub> -H <sub>19</sub> ... O <sub>26</sub>	0.0522	0.1326	0.0432	0.0076	-0.0508	15.94
	O <sub>26</sub> -H <sub>27</sub> ... O <sub>23</sub>	0.0417	0.1297	0.0350	0.0026	-0.0376	11.80
	O <sub>23</sub> -H <sub>24</sub> ... O <sub>29</sub>	0.0418	0.1292	0.0349	0.0026	-0.0375	11.76
	O <sub>29</sub> -H <sub>30</sub> ... O <sub>10</sub>	0.0256	0.1012	0.0227	-0.0026	-0.0200	6.27
	O <sub>29</sub> -H <sub>31</sub> ... O <sub>20</sub>	0.0349	0.1169	0.0293	0.0001	-0.0295	9.25
	O <sub>20</sub> -H <sub>22</sub> ... O <sub>32</sub>	0.0388	0.1272	0.0331	0.0013	-0.0344	10.79
	O <sub>32</sub> -H <sub>33</sub> ... N <sub>1</sub>	0.0439	0.0955	0.0300	0.0061	-0.0361	11.33
ZVal + 1W	N <sub>1</sub> -H <sub>2</sub> ... O <sub>20</sub>	0.0337	0.1097	0.0273	-0.0002	-0.0271	8.50
	O <sub>20</sub> -H <sub>22</sub> ... H <sub>12</sub>	0.0401	0.1318	0.0347	0.0018	-0.0365	11.45
ZVal + 2W	O <sub>20</sub> -H <sub>22</sub> ... O <sub>12</sub>	0.0379	0.1332	0.0338	0.0006	-0.0344	10.79
	O <sub>23</sub> -H <sub>24</sub> ... O <sub>20</sub>	0.0373	0.1216	0.0313	0.0009	-0.0322	10.10
	N <sub>1</sub> -H <sub>4</sub> ... O <sub>23</sub>	0.0366	0.1125	0.2905	0.0009	-0.0300	9.41
ZVal + 3W	O <sub>23</sub> -H <sub>24</sub> ... O <sub>19</sub>	0.0348	0.1159	0.0290	0.00002	-0.0290	9.10
	O <sub>20</sub> -H <sub>21</sub> ... O <sub>23</sub>	0.0273	0.0929	0.0220	-0.0012	-0.0208	6.53
	O <sub>20</sub> -H <sub>22</sub> O <sub>12</sub>	0.0310	0.1091	0.0263	-0.0009	-0.0254	7.97
	O <sub>26</sub> -H <sub>27</sub> ... O <sub>20</sub>	0.0369	0.1165	0.0302	0.0010	-0.0312	9.79
	N <sub>1</sub> -H <sub>4</sub> ... O <sub>26</sub>	0.0364	0.1122	0.0289	0.0008	-0.0297	9.32
ZVal + 4W	O <sub>26</sub> -H <sub>28</sub> ... O <sub>19</sub>	0.0336	0.1201	0.0293	-0.0007	-0.0286	8.97
	O <sub>23</sub> -H <sub>24</sub> ... O <sub>26</sub>	0.0319	0.1084	0.0265	-0.0006	-0.0259	8.13
	O <sub>23</sub> -H <sub>25</sub> ... O <sub>19</sub>	0.0327	0.1104	0.0272	-0.0004	-0.0268	8.41
	O <sub>29</sub> -H <sub>30</sub> ... O <sub>12</sub>	0.0380	0.1271	0.0327	0.0009	-0.0336	10.54
	O <sub>20</sub> -H <sub>21</sub> O <sub>23</sub>	0.0431	0.1285	0.0355	0.0033	-0.0388	12.17
	N <sub>1</sub> -H <sub>2</sub> ... O <sub>20</sub>	0.0442	0.1288	0.0359	0.0037	-0.0396	12.42
	N <sub>1</sub> -H <sub>4</sub> ... O <sub>12</sub>	0.0242	0.0995	0.0216	-0.0033	-0.0182	5.71
ZVal + 5W	O <sub>32</sub> -H <sub>33</sub> ... O <sub>12</sub>	0.0322	0.1126	0.0273	-0.0008	-0.0265	8.31
	O <sub>20</sub> -H <sub>22</sub> ... O <sub>32</sub>	0.0268	0.0957	0.0223	-0.0016	-0.0206	6.46
	O <sub>23</sub> -H <sub>24</sub> ... O <sub>32</sub>	0.0229	0.0824	0.0187	-0.0019	-0.0169	5.30
	O <sub>29</sub> -H <sub>30</sub> ... O <sub>23</sub>	0.0388	0.1194	0.0316	0.0017	-0.0033	1.03
	O <sub>23</sub> -H <sub>25</sub> ... O <sub>19</sub>	0.0321	0.1085	0.0267	-0.0004	-0.0263	8.25
	O <sub>26</sub> -H <sub>27</sub> ... O <sub>19</sub>	0.0309	0.1083	0.0263	-0.0008	-0.0255	8.00
	O <sub>26</sub> -H <sub>28</sub> ... O <sub>29</sub>	0.0247	0.0883	0.0203	-0.0018	-0.0185	5.80
	O <sub>20</sub> -H <sub>21</sub> ... O <sub>29</sub>	0.0279	0.0986	0.0232	-0.0014	-0.0218	6.84
	N <sub>1</sub> -H <sub>2</sub> ... O <sub>10</sub>	0.0398	0.1161	0.0312	0.0022	-0.0334	10.48



**Fig. 3.** The coloring isogram for Val +  $n$ W and ZVal +  $n$ W ( $n = 1-5$ ) complexes

and the resulting complex is in a bicyclic form (Fig. 1, *i*). The complex of the zwitterion with five water molecules is in the form of a cage (Fig. 1, *j*), and, as compared to the Val + 5W complex, is structurally more stable by 2.13 kcal/mol energy (Table 1).

The calculations show that, in the solvated phase, ZVal +  $n$ W complexes are structurally more stable

than Val +  $n$ W complexes. It is also found that the interaction of neutral valine with water molecules increases the binding energy with the increase in the number of water molecules, and the fragments of ZVal +  $n$ W complexes more strongly interact than those of Val +  $n$ W complexes (Table 2).

### 3.2. Molecular electrostatic potential surface analysis

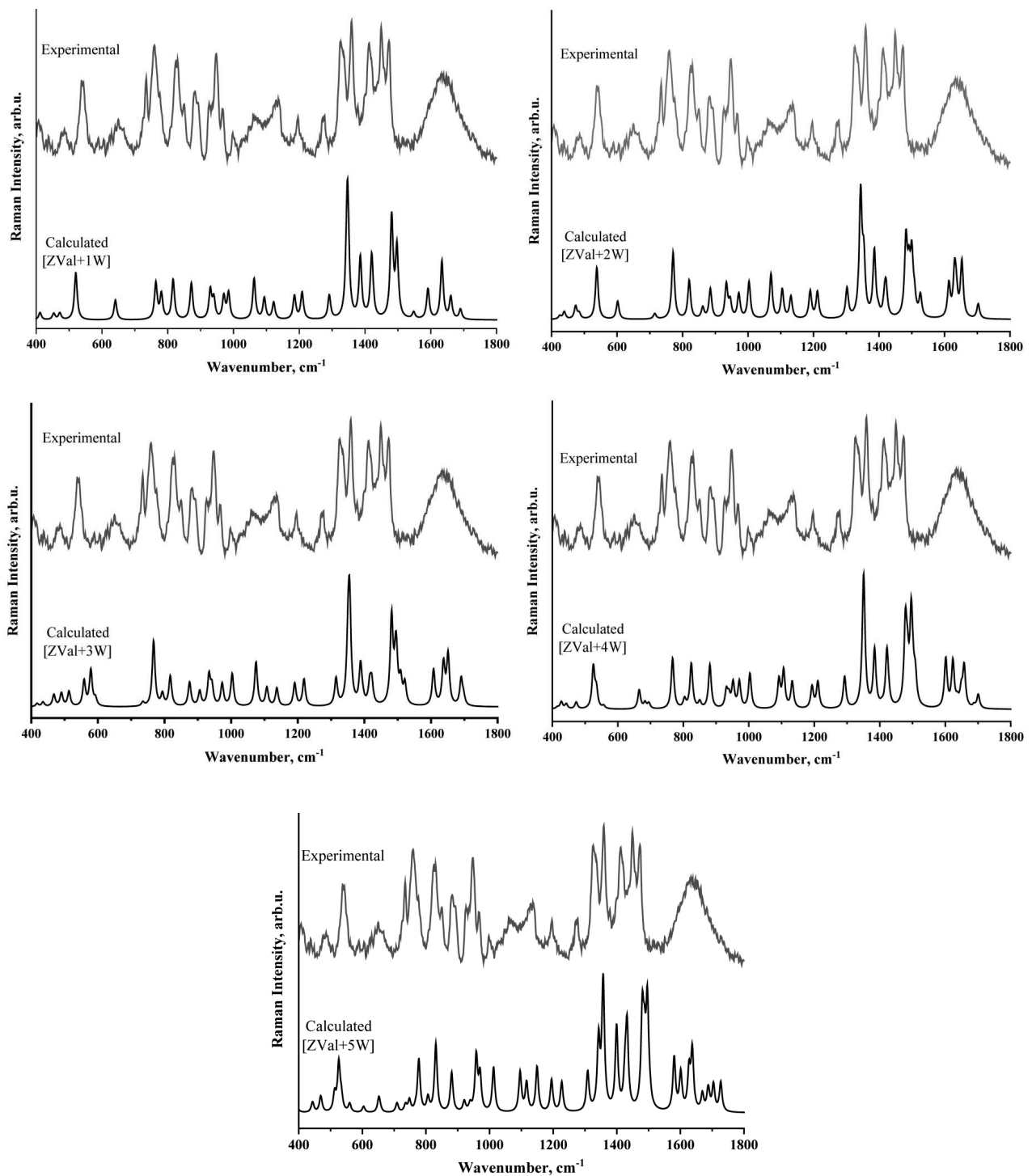
The molecular electrostatic potential (MEP) surface is characterized by the electron density distribution of the atoms in the molecule. Its analysis allows obtaining the information about the size, shape, charge density, and chemical reactivity properties of molecules. Figure 2 shows the MEP surfaces of non-ionized and zwitterionic forms of valine. Depending on the level of MEP, the surfaces are represented in different colors. The red < yellow < green < blue order is shown in the ascending order of the electrostatic potential of the molecule.

As can be seen from Fig. 2, the MEP surfaces of non-ionized and zwitterion structures of valine are different. In non-ionized valine, the nucleophilic region is located on the hydrogen atom of the O–H group, and the electrophilic region is located on the oxygen atom of the C=O group. In zwitterionic valine, the nucleophilic sphere is located on the hydrogen atoms of the  $\text{NH}_3^+$  group, and the electrophilic sphere is located on the oxygen atoms of the  $\text{COO}^-$  group.

### 3.3. AIM topological analysis

The analysis of atoms in molecules (AIM) proposed by Bader [30] is an effective tool for the analysis of intermolecular interactions in molecular complexes. The properties of hydrogen bonds between complexes are characterized by the electron density  $\rho(r)$ , electron density Laplacian  $\nabla^2\rho(r)$ , Lagrangian kinetic energy  $G(r)$ , potential energy density  $V(r)$ , Hamiltonian kinetic energy  $H(r) = G(r) + V(r)$ , and the H-bond energy can be described using topological parameters such as  $E_{\text{int}} = V(r)/2$ . The topological parameters of the Val +  $n$ W and ZVal +  $n$ W complexes at the bond critical point (BCP) of the molecular interactions obtained with the MULTIWFN program are presented in Table 4.

The strength of the hydrogen bond is characterized by the Laplacian of the electron density and the energy density at critical points. According to I. Rozas



**Fig. 4.** Simulated Raman spectra of ZVal +  $n$ W ( $n = 1-5$ ) complexes along with the experimentally recorded Raman spectrum of valine in aqueous medium

Table 5. The experimentally observed Raman line positions of valine in aqueous medium along with the calculated values for different hydrogen bonded complexes of zwitterionic valine (ZVal) and water (W)

Observed Raman line position (cm <sup>-1</sup> )	Calculated Raman line positions (cm <sup>-1</sup> )				
	ZVal + 1W	ZVal + 2W	ZVal + 3W	ZVal + 4W	ZVal + 5W
407	411	424	416	414	442
437	452	438	434	442	444
538	520	537	558	534	533
735	763	714	734	694	735
759	780	770	766	766	766
824	816	820	816	824	830
850	871	861	874	849	880
948	939	945	942	951	957
967	970	971	972	970	969
1062	1062	1069	1074	1091	1095
1125	1122	1130	1136	1106	1116
1138	1185	1189	1190	1132	1149
1277	1291	1301	1314	1292	1308
1326	1345	1343	1350	1349	1342
1359	1347	1353	1355	1351	1356
1413	1419	1416	1415	1421	1425
1449	1480	1481	1421	1426	1432
1473	1483	1491	1481	1478	1480
1634	1633	1635	1636	1636	1637

et al. [31], hydrogen bonding interactions can be classified as follows:

- Weak hydrogen bond ( $E_{HB} < 50$  kJ/mol)  $\nabla^2\rho(r) > 0, H(r) > 0$ ;
- Medium hydrogen bond ( $50 < E_{HB} < 100$  kJ/mol)  $\nabla^2\rho(r) > 0, H(r) < 0$ ;
- Strong hydrogen bond ( $100 < E_{HB}$  kJ/mol)  $\nabla^2\rho(r) < 0, H(r) < 0$ .

Table 4 shows that the values of the electron density ( $\rho$ ) at the critical points of bonding are in the interval of 0.0245–0.0522 au and 0.0229–0.0442 au for clusters Val +  $n$ W and ZVal +  $n$ W ( $n = 1-5$ ). These values are in the hydrogen bond interval (0.0033–0.168 au) [32]. The Laplacian of the electron density ( $\nabla^2\rho$ ) values are all positive and lie between 0.0923–0.1357 au and 0.0824–0.1332 au. All of them are in the interval of hydrogen bonding (0.020–0.139 au) and confirm the presence of hydrogen bonding in the clusters.

In Figure 3, non-covalent interactions between valine and water molecules are depicted by a colored isogram. Blue represents hydrogen bonding, green represents Van der Waals interactions, and red repre-

sents strong repulsion (steric effect). The results of the analysis confirmed that hydrogen bonding is dominant in the formation of Val +  $n$ W and ZVal +  $n$ W complexes.

### 3.4. Vibrational analysis

Raman spectra of zwitterionic valine complexes with water molecules (ZVal +  $n$ W,  $n = 1-5$ ) simulated by DFT: B3LYP/6-311++G(d,p) method along with the experimentally registered Raman spectrum of valine in the aqueous medium are presented in Fig. 4. These spectra were then cross-compared to determine the number of water molecules involved in the hydrogen-bonding interactions with one zwitterionic valine molecule. Table 5 presents several experimentally observed wave numbers of different vibrational modes of the zwitterionic valine molecule in an aqueous medium and the theoretically calculated wave numbers of five most stable conformers [ZVal +  $n$ W,  $n = 1-5$ ]. Calculated wavenumbers are given without any scaling factor. It should be noted that DFT calculations yield Raman scattering amplitudes, which cannot be taken directly as Raman intensities. The

Raman intensity is proportional to the scattering cross-section ( $\partial\sigma/\partial\nu$ ) and can be calculated using the Raman scattering amplitude and wavenumbers calculated for each normal mode using the following formula [22]:

$$\frac{\partial\sigma_i}{\partial\nu_i} = \left(\frac{2^4\pi^4}{45}\right) \left(\frac{(\nu_0 - \nu_i)^4}{1 - \exp\left[\frac{-hc\nu_i}{kT}\right]}\right) \left(\frac{h}{8\pi^2c\nu}\right) S_i,$$

where  $\nu_0$  is the frequency of excitation light,  $\nu_i$  is the frequency of the  $i$ -th normal vibration mode,  $h$  is Planck's constant,  $c$  is the speed of light in vacuum,  $k$  is Boltzmann's constant,  $S_i$  is Raman activity.

The analysis of Fig. 4 implies that the simulated Raman spectrum of the ZVal + 4W complex is in better agreement with the experimental spectra of valine in the aqueous medium compared to other complexes. Moreover, the positions of the calculated Raman lines of the ZVal + 4W complex are close to the positions of the experimentally observed Raman lines. Therefore, one should draw conclusion that the ZVal + 4W complex is present in the aqueous solution of valine, and this form is dominating among all other possible complexes.

#### 4. Conclusion

In this work, the ground state geometries of the hydrogen-bound Val +  $n$ W and ZVal +  $n$ W ( $n = 1-5$ ) complexes were optimized at the B3LYP/6-311++G(d,p) level by the DFT method. The results of calculations show that the zwitterionic form of valine is structurally more stable in the aqueous medium than its neutral (non-ionized) form. Comparing the binding energy of a valine molecule with water molecules, it is found that water molecules bind more strongly to the zwitterionic structure of valine. Based on the carried out AIM topological analysis, it is found that valine forms complexes with water molecules by hydrogen bonds. In addition, the Raman spectra of ZVal +  $n$ W ( $n = 1-5$ ) complexes are theoretically calculated and compared with the experimentally observed Raman spectrum of valine in the aqueous medium. It is also found that the calculated Raman spectrum of the [ZVal + 4W] complex is in the best agreement with the experimentally observed Raman spectrum of valine in the aqueous medium. Thus, it has been concluded that this structure is the most probable hydrogen-bound complex of valine with water molecules.

*This work was supported by Ministry of Innovative Development of the Republic of Uzbekistan in the frame of the State scientific and technical program for fundamental research.*

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Received 28.09.22

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#### ВЗАЄМОДІЯ ВАЛІНУ З МОЛЕКУЛАМИ ВОДИ: ДОСЛІДЖЕННЯ МЕТОДАМИ DFT ТА РАМАНІВСЬКОЇ СПЕКТРОСКОПІЇ

Взаємодію неіонізованої та цвітеріонної форм валіну з молекулами води досліджено методами раманівської спектроскопії та квантово-хімічного моделювання. Формалізм інтегрального рівняння для моделі поляризаційного континууму (IEF-PCM) для врахування впливу розчинника використовувався на рівні теорії V3LYP/6-311++G(d,p). Водневі зв'язки між молекулами валіну та води вивчалися методами квантової теорії атомів у молекулах (AIM) і нековалентної взаємодії (NCI). Шляхом порівняння експериментальних і теоретичних раманівських спектрів валіну у водному середовищі встановлено, що найбільш імовірним є комплекс цвітеріонного валіну з 4 молекулами води.

*Ключові слова:* валін, цвітеріон, водневий зв'язок, раманівські спектри, метод DFT.