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An FT-IR and DFT Study of Solvent Effects on Molecular Parameters and Vibrational Frequencies of 3,5-diamino-1,2,4-triazole

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ABSTRACT: In this paper, solvent environments effects on structural and spectroscopic properties of 3,5-diamino-1,2,4-triazole (Guanazole) antitumor agent have been investigated. Optimized molecular structures were obtained in solvent media. Conformational structures of Guanazole in the gas phase were investigated and the relative population distributions of the conformations were obtained using the Boltzmann distribution. Moreover, the experimental FT-IR spectrum of Guanazole were recorded. In addition, vibrational frequencies and its intensities were calculated for each environment by using of optimized structures and they compared with the experimental data. Density Functional Theory and 6311++G (d,p) basis set were used in the theoretical calculations. Based on the solid phase IR spectrum of pure Guanazole, it was seen that Guanazole is dimeric structure in solid phase. For this reason, the dimer structure of Guanazole has been investigated in detail.

Keywords: Density functional theory, guanazole, solvent effects, vibrational spectroscopy

3,5-diamino-1,2,4-triazole Molekülünün Titreşim Frekanslarının ve Moleküler Parametrelerinin Üzerine Çözücü Etkilerinin bir DFT ve FT-IR Çalışması

ÖZET: Bu çalışmada, 3,5-diamino-1,2,4-triazole (Guanazole) anti tümör ajanın yapısal ve spektroskopik özellikleri üzerine çözücü etkileri araştırıldı. Çözücü ortamlar içerisinde optimize edilmiş moleküler yapılar elde edildi. Guanazole'nin konformasyonel yapıları gaz fazda incelendi ve nispi nüfus analizleri Boltzmann dağılımı kullanılarak elde edildi. Ayrıca, Guanazole'nin deneysel FT-IR spektrumu kaydedildi. Ek olarak titreşim frekansları ve şiddetler optimize yapılar kullanılarak her bir çözücü ortam için hesaplandı ve deneysel veriler ile kıyaslandı. Hesaplamamalarda Yoğunluk Fonksiyoneli Teorisi ve 6311++G(d, p) temel seti kullanıldı. Saf Guanazole'nin deneysel IR spektrumundan yola çıkılarak, Guanazole'nin katı fazda dimer yapıda olduğu belirlendi. Bu yüzden dimer yapı için detaylı incelemeler yapıldı.

Anahtar Kelimeler: Çözücü etkileri, guanazole, titreşim spektroskopisi, yoğunluk fonksiyoneli teorisi

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INTRODUCTION

3,5-diamino-1,2,4-triazole (Guanazole) molecule is given in $C_2H_5N_5$ closed formula and the molecular weight is about 99.09 g mol^{-1}. It is in solid phase at room temperature. Guanazole is an important biomolecule and it forms the basis of many studies published up to now because of its antitumor and anticancer effects on living tissues. Studies on the pharmacological and biological properties of the Guanazole molecule have gained a significant impetus in the 1970s and are still effective today [Vick et al., 1970; Dave et al., 1978; Suter and Romagna, 1990; Ho et al., 2003; Xin et al., 2012]. The identification of structural, physical and chemical properties of molecules with such important medicinal and pharmacological effects is also of great importance. Therefore, in the literature, there are many published papers on the structural and vibrational properties of Guanazole. In their articles published in 2005, Kumar et al. examined vibrational modes of Guanazole using infrared spectroscopy and Density Functional Theory (DFT) methods. Next, Guennoun et al. calculated the vibrational modes, energy and geometric parameters of free Guanazole using DFT and Hartree-Fock (HF) theories. In addition, for the molecule, studies on various metal complexes and different physical properties have also been published. [Aurkie et al., 2008; Penglei et al., 2015; Haixiang et al., 2016].

Although there are many published studies on the investigation of vibration mode modes of free Guanazole in solid phase, there is no published study of solvent effects on this molecule as far as we know. In order to fill this gap in the literature, the structural, vibrational and some physical properties of Guanazole in various solvent media have been investigated in detail. It is quite important to examine the behavior, physical and chemical properties of any molecule in a solvent environment because solvent media are physical factors that directly affect the absorption, transport and diffusion of a drug into the living organism. There are many methods and theories to study these effects. One of most popular methods for the research of solvent effects is Polarizable continuum model (PCM). When examining solvent interactions, PCM treats solvents as a continuous polarized environment rather than as individual molecules [S. Miertuš et al., 1981]. This allows the calculation costs to fall significantly, which is the biggest problem in ab initio calculations. In this study, DFT method were used for the calculations of many physical-chemical properties of Guanazole in solvent media. The optimized molecular structures of Guanazole in Benzene (C_6H_6-ε=2.27), Toluene (PhMe-ε=2.37), Chloroform ($CHCl_3$-ε=4.71), Dichloromethane (DCM-ε=8.93), Acetone (ACTN-ε=20.49), Ethanol (EtOH-ε=24.85), Methanol (MeOH-ε=32.61) and Acetonitrile (ACN-ε=35.69) solvents were obtained and they compared with the crystal structure parameters from the literature. Experimental FT-IR spectrum was recorded in solid phase. DFT calculated vibrational modes of Guanazole in vacuum and in solvent media were compared with the experimental FT-IR spectrum. Dimeric structure was also investigated based on the experimental spectrum. The energies and some thermochemical properties of the structures were also calculated using the same methods. The results obtained were discussed and the effects of solvent environments on Guanazole were elucidated in detail.

MATERIAL AND METHOD

A commercial sample of Guanazole was purchased from Aldrich and used without further purification. The infrared spectrum of the molecule was recorded between 3700-550 cm^{-1} by Perkin Elmer Spectrum 100 FT-IR spectrometer with ATR (Attenuated total reflection) equipment.

The calculations of energies, optimized molecular structures and vibrational frequencies of Guanazole have been performed by using Gaussian03 program with the help of Gaussview visualization program [Frisch et al., 2004; Dennington et al., 2008]. All calculations were made on personal computers. The calculated frequencies were scaled by 0.98 to correct the difference between the calculated and experimental vibrational frequencies. All calculations in vacuum and in solvent media were performed DFT method with 6-311++G(d,p) basis set. From the optimized structures, vibrational frequencies and intensities were calculated. The fundamental vibrational modes were characterized by their PED (potential energy distribution) obtained by using the VEDA4 program [Jamróz et al., 2004].

RESULT AND DISCUSSIONS

Energetics and Thermochemical Properties

Guanazole has two tautomers due to its molecular structure. In this study, tautomeric structures were named Guanazole-1 and Guanazole-2. The optimized structures of both tautomers are given in Figure 1.

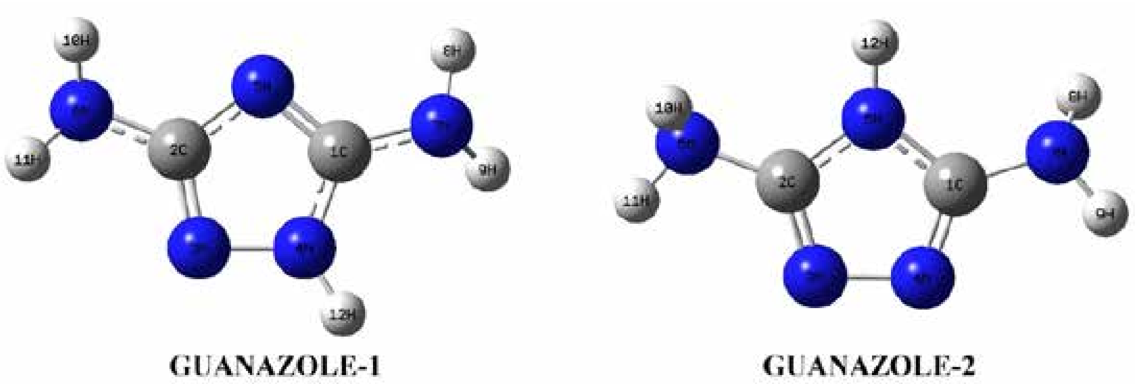

Figure 1. Optimized molecular structures of Guanazole-1 and Guanazole-2

The total energies of Guanazole-1 and Guanazole-2 were calculated as -353.084854 H and -353.069002 H, respectively, in the vacuum environment. This suggests that Guanazole-1 is more stable than Guanazole-2. The calculated energy difference between the tautomeric structures is 9.95 kcal mol^{-1}. This energy difference is quite large and according to Boltzmann relative population analysis, the probability of having Guanazole-1 is 100% due to this energy difference. The energy difference shows itself also the same in solvent environments, and the probability of the presence of Guanazole-2 is 0% in solvent environments. Therefore, all calculations and interpretations made in the rest of this paper apply to Guanazole-1.

Table 1. DFT calculated total energies and some important thermochemical parameters of Guanazole.

Parameters	**Vacuum**	**C_6H_6**	**PhMe**	**$CHCl_3$**	**DCM**
Dielectric constant	1.00	2.27	2.36	4.71	8.93
(Total Energy (Hartree	-353.08485	-353.09835	-353.09917	-353.10775	-353.11236
*(Energy Dif. (Kcal/Mol	0.00	8.47	8.99	14.37	17.26
(Dipole Moment (Debye	2.5984	3.2104	3.2372	3.6553	3.8646
(Z.P.V.E. (Kcal/Mol	58.399	57.808	57.759	57.334	57.075
(Entropy (cal/mol.K	78.323	78.280	78.365	78.234	78.181
(Heat Cap. (cal/mol.K	24.261	24.305	24.343	24.330	24.335
Parameters	**ACTN**	**EtOH**	**MeOH**	**ACN**	
Dielectric constant	20.49	24.85	32.61	35.69	
(Total Energy (Hartree	-353.11597	-353.11645	-353.11711	-353.11728	
*(Energy Dif. (Kcal/Mol	19.53	19.83	20.24	20.35	
(Dipole Moment (Debye	4.0316	4.0552	4.0856	4.0639	
(Z.P.V.E. (Kcal/Mol	56.865	56.836	56.795	56.786	
(Entropy (cal/mol.K	78.141	78.141	78.156	78.134	
(Heat Cap. (cal/mol.K	24.332	24.335	24.345	24.335	

* The energy differences indicate the changes of the energies in the solvent media relative to the vacuum

It can be seen from Table 1 that the dipole moment of Guanazole changes significantly from the vacuum to the solvent environment. Since the dipole moment is the measure of the polarity of a molecule, the polarizable continuous model approach included in the theoretical calculations reveals that the dipole moments show significant increases. For Guanazole, the entropy and heat capacity changes do not show a linear increase with increasing dielectric constant of the solvent medium. In some environments it showed an increase and in some environments it showed a decrease. This instability is thought to originate from the polarity of the changing solvent environment.

Molecular Parameters

The optimized molecular structure of Guanazole has been given previously in Figure 1. All calculated bond lengths and angles are also given in Table 2 along with experimental X-Ray diffraction data taken from the literature [Starova et al.; 1979].

When Table 2 is examined, it can be seen that the bond lengths and bond angles calculated in both the vacuum environment and the solvent environments are in good agreement with the experimental values. Deviations from the experimental values of all bond lengths calculated except for N-H bond lengths are less than 0.05 Å. Similarly, deviations from experimental values at all other angles, except for the bond angle at which hydrogen atoms are present, are less than 0.3°. It is known that in geometric parameters containing hydrogen atoms, there are errors that cannot be eliminated due to X-ray scattering factors. This can lead to large differences compared to those calculated in the molecular parameters such as X-H and X-X-H. As a result of this, significant differences also have seen in the comparison of calculated and observed vibrational modes.

Vibrational Modes and Assignments

Guanazole has 12 atoms and there are 30 vibration modes in total since there is no linear geometry. Vibration frequencies and relative intensities calculated in vacuum and solvent environments are given in Table 3 together with the experimental values. The recorded experimental IR spectrum is also given in Figure 2. Since the experimental data starts at 550 cm^{-1}, the vibrational modes are given after the eighth mode.

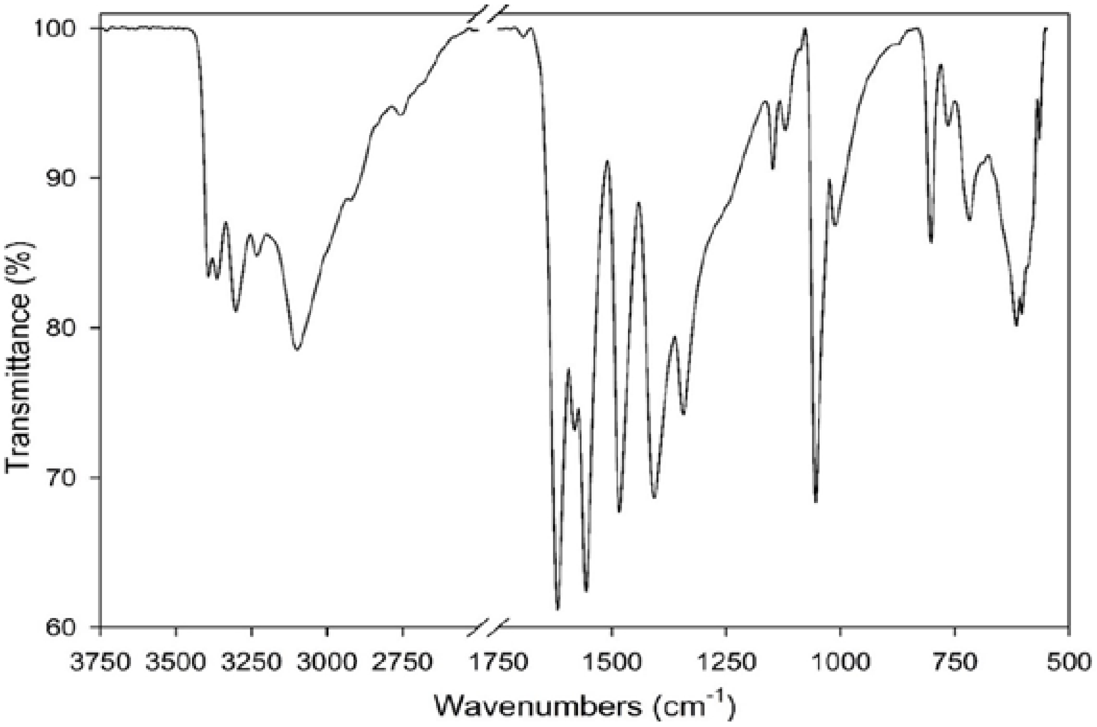

Figure 2. Recorded mid-IR spectrum of Guanazole.

Table 2. Calculated and measured molecular parameters of optimized Guanazole in solvent media.

Bond lengths (Å)										
Atoms	Vacuum	C_6H_6	PhMe	$CHCl_3$	DCM	ACTN	EtOH	MeOH	ACN	Exp.*
1C-4N	1.349	1.346	1.346	1.345	1.344	1.343	1.343	1.343	1.343	1.339
1C-5N	1.320	1.326	1.326	1.330	1.332	1.334	1.334	1.334	1.334	1.363
1C-7N	1.380	1.375	1.375	1.371	1.369	1.368	1.368	1.368	1.367	1.353
2C-3N	1.319	1.321	1.321	1.323	1.323	1.324	1.324	1.324	1.324	1.319
2C-5N	1.371	1.370	1.370	1.369	1.369	1.369	1.368	1.368	1.368	1.363
2C-6N	1.380	1.380	1.380	1.381	1.381	1.381	1.381	1.381	1.381	1.376
3N-4N	1.386	1.388	1.388	1.388	1.389	1.389	1.389	1.389	1.389	1.398
4N-12H	1.006	1.012	1.012	1.017	1.020	1.022	1.022	1.023	1.023	0.870
6N-10H	1.009	1.012	1.012	1.015	1.016	1.017	1.017	1.017	1.017	0.830
6N-11H	1.009	1.013	1.013	1.015	1.016	1.017	1.017	1.018	1.018	0.930
7N-8H	1.011	1.013	1.013	1.015	1.016	1.017	1.017	1.018	1.018	0.890
7N-9H	1.010	1.013	1.013	1.015	1.017	1.018	1.018	1.018	1.018	0.860
Bond angles (°)										
4N-1C-5N	110.4	110.2	110.2	110.1	110.1	110.1	110.0	110.0	110.0	110.4
4N-1C-7N	124.1	124.3	124.3	124.4	124.4	124.4	124.4	124.4	124.4	124.1
5N-1C-7N	125.5	125.4	125.4	125.4	125.4	125.4	125.4	125.4	125.5	125.4
3N-2C-5N	115.7	115.5	115.5	115.4	115.3	115.3	115.3	115.3	115.3	115.9
3N-2C-6N	123.1	123.1	123.1	123.1	123.2	123.2	123.2	123.2	123.2	122.9
5N-2C-6N	121.1	121.3	121.3	121.4	121.4	121.5	121.5	121.5	121.5	121.0
2C-3N-4N	101.4	101.5	101.5	101.6	101.7	101.7	101.7	101.7	101.7	101.5
1C-4N-3N	109.8	109.8	109.8	109.9	109.9	109.9	109.9	109.9	109.9	109.5
1C-4N-12H	129.6	129.7	129.7	129.5	129.4	129.3	129.3	129.3	129.2	132.5
3N-4N-12H	119.7	120.1	120.1	120.4	120.6	120.8	120.8	120.8	120.8	118.0
1C-5N-2C	102.8	102.9	102.9	103.0	103.0	103.0	103.1	103.1	103.1	102.7
2C-6N-10H	113.9	113.9	113.9	113.8	113.8	113.8	113.8	113.8	113.8	115.0
2C-6N-11H	114.5	114.4	114.4	114.3	114.3	114.3	114.3	114.2	114.3	114.0
10H-6N-11H	113.9	113.3	113.3	112.8	112.6	112.4	112.4	112.4	112.4	114.0
1C-7N-8H	112.2	113.2	113.2	113.9	114.2	114.4	114.4	114.5	114.5	115.0
1C-7N-9H	115.9	116.3	116.3	116.4	116.4	116.4	116.4	116.4	116.4	119.0
8H-7N-9H	112.5	112.9	112.9	113.2	113.4	113.4	113.5	113.5	113.5	115.0

*Data were taken from Ref.

Table 3. DFT calculated and experimental recorded vibrational modes of Guanazole.

Mode	Vacuum		C_6H_6		PhMe		$CHCl_3$		DCM		ACTN		EtOH		MeOH		ACN		Exp.	PED (%)
	Freq.	I_{IR}	Freq.	I_{IR}	Freq.	I_{IR}	Freq.	I_{IR}	Freq.	I_{IR}	Freq.	I_{IR}	Freq.	I_{IR}	Freq.	I_{IR}	Freq.	I_{IR}		
8	577	60.56	573	80.65	571	81.57	546	92.18	534	93.20	527	94.54	525	94.01	523	93.60	524	94.12	566 w	$\Gamma_{HNCN}(80)+\delta_{HNH}(10)$
9	608	91.89	587	75.61	585	73.42	595	65.05	596	62.35	598	61.27	598	60.96	598	60.27	598	60.70	605 m	$\Gamma_{HNCN}(64)$
10	654	1.45	654	0.70	653	0.67	653	0.80	653	0.81	653	0.86	653	0.89	652	0.89	652	0.90	617 m	$\nu_{NC}(32)+\delta_{CNC}(29)$
11	703	4.63	698	1.46	698	1.40	698	2.05	698	2.38	698	2.66	698	2.71	698	2.76	698	2.77	722 w	$\Gamma_{NNNC}(54)+\Gamma_{CNCN}(23)$
12	754	11.72	755	9.97	755	9.76	756	9.73	756	9.40	756	9.34	756	9.37	756	9.34	756	9.37	767 vw	$\Gamma_{NNNC}(42)+\Gamma_{NCNC}(33)$
13	787	3.08	788	2.97	788	2.90	788	3.00	788	2.87	788	2.85	788	2.85	788	2.83	788	2.84	805 m	$\delta_{NCN}(57)+\nu_{NC}(26)$
14	997	1.61	1000	2.10	1000	2.10	1001	2.65	1001	2.89	1002	3.14	1002	3.17	1002	3.23	1002	3.23	1015 m	$\delta_{NCN}(44)+\nu_{NC}(32)+\delta_{CNC}(15)$
15	1042	10.83	1042	12.22	1042	12.04	1041	10.82	1039	10.72	1039	10.79	1039	10.69	1038	10.46	1038	10.69	1047 sh	$\delta_{HNC}(46)+\delta_{CNC}(31)$
16	1045	1.87	1044	0.75	1044	0.84	1044	2.15	1044	1.98	1044	1.82	1044	1.82	1044	1.91	1044	1.78	1056 s	$\nu_{NC}(44)+\delta_{HNC}(23)$
17	1111	1.38	1106	1.56	1106	1.54	1103	1.85	1101	1.98	1100	2.15	1100	2.15	1100	2.12	1100	2.18	1120 vw	$\nu_{NC}(59)+\delta_{HNC}(20)$
18	1145	0.10	1142	0.26	1142	0.28	1140	0.43	1139	0.52	1138	0.61	1137	0.62	1137	0.64	1137	0.64	1149 vw	$\delta_{HNC}(28)+\nu_{NC}(23)+\delta_{NCN}(10)$
19	1306	0.34	1306	0.42	1305	0.41	1304	0.53	1302	0.62	1301	0.70	1300	0.71	1300	0.71	1300	0.72	1345 m	$\delta_{HNN}(53)+\nu_{NC}(10)$
20	1403	35.57	1397	41.32	1397	41.26	1393	44.82	1391	45.81	1389	46.77	1389	46.82	1388	46.81	1388	47.01	1409 s	$\nu_{NC}(40)+\delta_{HNH}(14)$
21	1474	46.41	1467	46.23	1467	46.05	1463	45.90	1460	44.37	1458	43.73	1458	43.49	1457	43.12	1457	43.28	1486 s	$\nu_{NC}(53)$
22	1566	22.50	1559	41.82	1559	41.38	1549	45.81	1544	46.04	1540	47.21	1540	46.80	1539	46.00	1539	46.90	1558 vs	$\nu_{NC}(41)+\delta_{HNH}(13)$
23	1571	36.13	1561	20.67	1561	20.05	1556	17.29	1552	14.87	1549	13.14	1548	12.86	1547	12.47	1547	12.47	1582 s	$\delta_{HNH}(48)+\nu_{NC}(13)$
24	1618	100.0	1603	100.0	1602	100.0	1592	100.0	1586	100.0	1582	100.0	1581	100.0	1580	100.0	1580	100.0	1621 vs	$\delta_{HNH}(64)$
25	1632	24.59	1622	31.06	1621	30.90	1615	37.59	1611	40.22	1608	42.85	1608	43.07	1607	43.37	1607	43.65	1631 sh	$\nu_{NC}(35)+\delta_{HNH}(22)$
26	3493	9.45	3441	20.81	3439	21.30	3392	49.77	3338	63.68	3291	71.44	3286	72.17	3279	73.03	3275	73.97	3099 m	$\nu_{S[7N\text{-}8H+7N\text{-}9H]}(99)$
27	3505	7.32	3447	12.27	3446	12.59	3401	45.97	3375	37.54	3355	39.61	3352	39.88	3350	40.22	3348	40.43	3236 w	$\nu_{S[6N\text{-}11H+6N\text{-}10H]}(98)$
28	3588	11.47	3488	37.52	3485	38.40	3405	3.38	3382	11.81	3364	14.80	3362	14.91	3359	14.99	3358	15.47	3304 w	$\nu_{AS[7N\text{-}8H+7N\text{-}9H]}(100)$
29	3596	19.51	3535	16.48	3533	16.78	3491	22.17	3465	25.07	3444	27.75	3441	28.02	3438	28.35	3436	28.64	3361 w	$\nu_{4N\text{-}12H}(100)$
30	3608	10.17	3545	14.05	3543	14.28	3497	17.87	3472	19.72	3452	21.42	3449	21.56	3446	21.70	3444	21.95	3393 w	$\nu_{AS[6N\text{-}11H+6N\text{-}10H]}(100)$

When Table 3 and Figure 2 are examined, it can easily be seen that the strongest vibrational mode is the H-N-H bending mode, which is calculated at 1618 cm^{-1} and is shown at 1621 vs in the experimental spectrum. This mode, which is originated by the angle bending movement between atoms 8H-7N-9H and 10H-6N-11H is assigned as H-N-H bending mode by Kumar et al. 8H-7N-9H and 10H-6N-11H atoms. In addition, the mode was very severely affected by varying solvent environments because it was outside the Triazole ring. The vibrational frequencies are shifted by 15, 16, 26, 32, 36, 37, 38 and 38 cm^{-1} in solution phases, respectively. The N-C stretching modes are calculated at 1632, 1566, 1474, 1403, 1111, 1045 and 654 cm^{-1}. All of these modes, except the one calculated at 1474 cm^{-1} are also combinations of H-N-H and H-N-C bending vibrations, too. It was found that the N-C vibrations in the plane of the Triazole ring were more severely affected by the changing solvent environment. For example, at the mode number 25 which is caused by the stretching vibrations between atoms 1C-7N and 2C-6N, the frequencies shifted about 25 cm^{-1} from gas phase to solution phases. However, mode 20 which is combination of the stretching vibrations between 2C-5N and 1C-5N atoms shows a shift of 15 cm^{-1}.

The most serious changes that occur in vibrational modes are those in the functional group region. Guanazole has five N-H stretching modes computed at 3608, 3596, 3588, 3505, and 3493 cm^{-1} which are significantly affected from the changing media. In each of the N-H stretching vibrations, 164, 160, 230, 157 and 218 cm^{-1} shifts were occurred passing from gas phase to solution phases.

There is an important situation in investigation of vibrational modes in the functional group region. Five bands were seen as expected in the 3000-3500 cm^{-1} region of the experimental spectrum. From these bands, 3393-3361 and 3304-3236 cm^{-1} are similar, while 3099 cm^{-1} is different from the other. We think that bands observed at 3393-3361 and 3304-3236 cm^{-1} originated from N-H$_2$ vibrations and at 3099 cm^{-1} originated from N-H vibration. However, when Table 3 is examined it will be seen that the stretching vibration between 4N-12H atoms for Guanazole T1 structure is calculated at 3596 cm^{-1}. Namely, according the theoretical calculations, the N-H stretching mode was calculated at frequencies greater than N-H$_2$ stretching modes. There are also inconsistencies in the calculated and observed vibration intensities. In the functional group region, the strongest band calculated is mode 29, while the most intense band observed is 3099 m. All these conditions indicate that the structure is in the dimeric phase, not the monomer. Therefore, in this study, the dimeric phase calculations of Guanazole were also investigated.

Dimerization of Guanazole

Dimer structures usually form in the end result of bonding two monomers with hydrogen bonds. Previous studies have shown that dimerization seriously affects vibrational frequencies [Bilkan et al, 2017]. In this study, it was thought that solid Guanazole was in dimeric structure due to the reasons mentioned above. In this case, many possible dimer structures for Guanazole can be mentioned, but the most likely structure that will provide the dominance of the N-H stretching vibration is the structure given in Figure 3. The calculated and observed vibrational modes of this structure for the functional group region were given in Table 4 in detail.

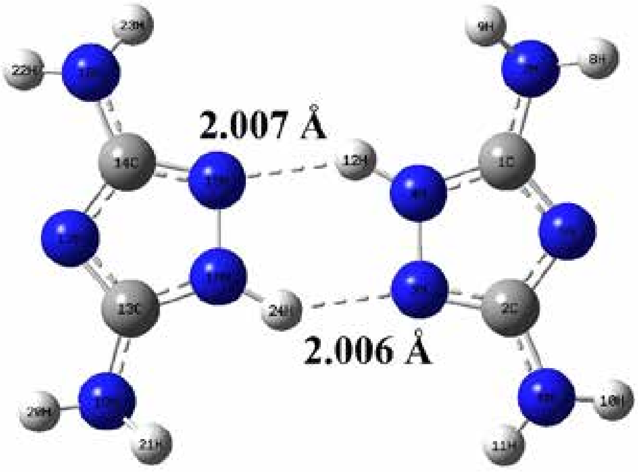

Figure 3. Dimeric structure of Guanazole.

Table 4. Calculated and observed N-H stretching modes of Guanazole dimer.

Mode	Freq.	I_{IR}	Exp.	PED (%)
57	3307	0.04	3099 m	$\nu_{AS[4N-12H+16N-24H]}(86)$
58	3328	100.00		$\nu_{S[4N-12H+16N-24H]}(80)$
59	3501	0.69	3236 w	$\nu_{S[19N-20H+19N-21H]}(59)+\nu_{S[7N-8H+7N-9H]}(33)$
60	3501	3.28		$\nu_{S[7N-8H+7N-9H]}(68)+\nu_{S[19N-20H+19N-21H]}(13)$
61	3504	1.68	3304w	$\nu_{S[6N-11H+6N-10H]}(77)+\nu_{S[18N-22H+18N-23H]}(18)$
62	3504	0.61		$\nu_{S[18N-22H+18N-23H]}(71)+\nu_{S[6N-11H+6N-10H]}(13)$
63	3599	0.70	3361 w	$\nu_{AS[7N-8H+7N-9H]}(76)+\nu_{AS[19N-20H+19N-21H]}(14)$
64	3599	3.61		$\nu_{AS[19N-20H+19N-21H]}(72)+\nu_{AS[7N-8H+7N-9H]}(22)$
65	3605	1.47	3393 w	$\nu_{AS[6N-11H+6N-10H]}(84)+\nu_{AS[18N-22H+18N-23H]}(16)$
66	3605	1.91		$\nu_{AS[18N-22H+18N-23H]}(88)+\nu_{AS[6N-11H+6N-10H]}(12)$

Table 4 also shows in detail which atoms the vibrational modes originate from. The vibration frequencies calculated for dimer structures were usually calculated in pairs since they originate from the same two structures. For example, when examining Table 4, it can be seen that the complete calculated modes except for modes 57 and 58 is calculated in pairs. The strongest mode in the functional group region according to Table 4 is the vibrations between atoms 4N-12H and 16N-24H, which is quite consistent with the situation observed in the experimental spectrum.

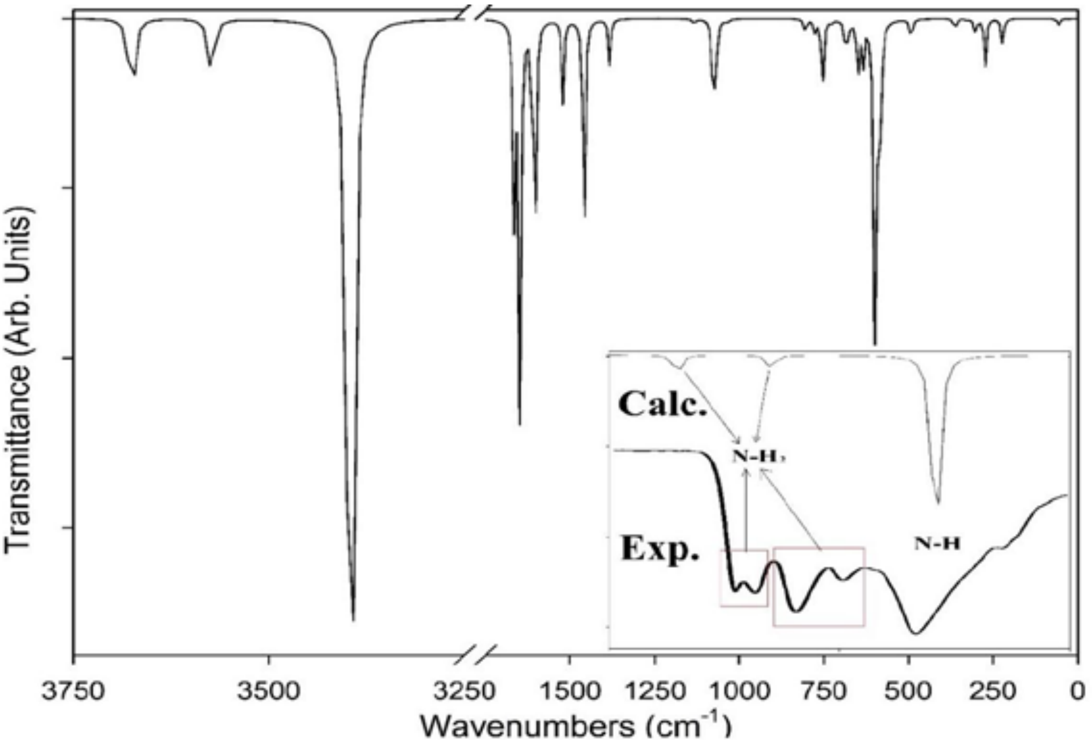

Figure 4. Calculated IR spectrum of dimer structure of Guanazole.

In Figure 4, the calculated IR spectrum for the dimer structure is given. When the 3000-3500 cm^{-1} region is examined, it is seen that the intensities of observed and calculated vibrational modes are in harmony with each other. This proves that Guanazole exhibits dimerization in the solid phase. The differences between the frequencies calculated and observed for this region are due to the fact that the molecules adjacent to the dimer structure in the solid phase affect the stretching vibrations of 18N-22H, 19N-20H, 7N-8H and 6N-10H. The hydrogen bonded dimer structure of Guanazole is in binary connected and the binding is of type N-H···N. The intermolecular hydrogen bond distances were calculated to be 2.006-2.007 Å.

CONCLUSIONS

In this study, we have performed the experimental and theoretical studies on vibrational, structural and some chemical properties of Guanazole anti-tumor agent. Molecular structure optimizations were performed in gas and solution phases. From the optimized results, two stable tautomeric structures were found. Moreover, the relative energy differences of these conformations are not very close to each other. Thus, relative population distributions show that Guanazole is 100% available in Guanazole-1. The calculated frequencies are compared with the experimental spectrum and each fundamental vibrational mode is described in detail. Based on the experimental spectrum, dimeric structure was determined and investigated in detail. Hydrogen bond lengths and relative energy differences of the dimer structure was calculated. The results of this study showed that Guanazole was severely affected by the changing solvent environment.

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REFERENCES

Aurkie R, Mitra S, Rosair GM, 2008. A novel hydroxo-bridged cyclic tetranuclear copper (II) complex using the guanazole ligand: Synthesis, crystal structure and thermal analysis, Inorganic Chemistry Communications 11: 1256-1259.

Bilkan MT, 2017. Structural and spectroscopic studies on dimerization and solvent-ligand complexes of Theobromine, Journal of Molecular Liquids, 238: 523-532.

Dave C, Paul MA, Rustum YM, 1978. Studies on the selective toxicity of guanazole in mice, European Journal of Cancer, 14: 33-40.

Dennington RD, Keith TA, Millam JM, 2008. GaussView 5, Gaussian, Inc.

Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Montgomery JA, Jr., Vreven T, Kudin KN, Burant JC, et all, 2004. Gaussian, Inc., Gaussian 03, Revision D.01, Wallingford CT.

Jamróz MH, 2004. Vibrational Energy Distribution Analysis VEDA 4, Warsaw.

Guennoun L, Jastimi JE, Guédira F, Marakchi K, Kabbaj OK, Hajji AE, Zaydoun S, 2011. Molecular geometry and vibrational studies of 3, 5-diamino-1, 2, 4-triazole using quantum chemical calculations and FT-IR and FT-Raman spectroscopies, Spectrochimica Acta Part A, 78: 347-353.

Haixiang Z, Dong Y, Liu H, 2016. Two new luminescent Zn (II) compounds constructed from guanazole and aromatic polycarboxylate ligands, Journal of Molecular Structure, 1105: 112-117.

Ho JA, Pickens CV, Gamscik MP, Colvin OM, Ware RE, 2003. In vitro induction of fetal hemoglobin in human erythroid progenitor cells, Experimental hematology, 31: 586-591.

Kumar VK, Keresztury G, Sundius T, Xavier RJ, 2005. Hydrogen bonding and molecular vibrations of 3, 5-diamino-1, 2, 4-triazole, Spectrochimica Acta Part A, 61: 261-267.

Miertuš S, Scrocco E, Tomasi J, 1981. Electrostatic interaction of a solute with a continuum. A direct utilizaion of AB initio molecular potentials for the prevision of solvent effects, Chemical Physics, 55: 117-124.

Penglei C, Li X, 2015. Construction of two new Zn (II)-guanazole frameworks via varying organic carboxylate ligands, Journal of Molecular Structure, 1081: 182-186.

Starova GL, Frank-Kamanetskaya OV., Shibanova EF, Lopyrev VA, Voronkov MG, Makarskii VV, 1979. X-ray diffraction examination of the molecular structure of guanazole (3,5-diamino-ih-i,2,4-triazole), Khimiya Geterotsiklicheskikh Soedinenii, 10: 1422-1423.

Suter W, Romagna F, 1990. DNA repair induced by various mutagens in rat hepatocyte primary cultures measured in the presence of hydroxyurea, guanazole or aphidicolin, Mutation Research/ Fundamental and Molecular Mechanisms of Mutagenesis, 231: 251-264.

Xin Z, Jie Y, Rosenberg MR, Wan J, Zeng S, Cui W, Xiao Y, Li Z, Tu Z, Casarotto MG, Hu W, 2012. Design and synthesis of pinanamine derivatives as anti-influenza A M2 ion channel inhibitors, Antiviral research, 96:91-99.

Vick JA, Herman EH, 1970. Cardiovascular effects of Guanazole, Toxicology and applied pharmacology, 16:108-119.