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Investigation of a QM/MM study on interaction of a carbon nanotube with cytarabine drug in various solvents and temperatures

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Abstract

At the present time, usage of nanotubes in medicinal science and biology is further studied. Nanotubes can pass through cell walls, transfer, and liberate drugs in particular tissues. The goal of this article is to survey the interaction of a nanotube with an anticancer drug. In this study, transferring of an anticancer drug called cytarabine with zigzag (5, 0) carbon nanotube is studied. All computations are surveyed by quantum mechanics and molecular mechanics (MM)/Monte Carlo simulation (in various force fields such as MM+, assisted model building with energy refinement, and optimized potential for liquid simulations) in various temperatures, and their results are achieved in gas phase, water solvent, and methanol solvent, respectively.

Keywords: Solvent effect, Quantum mechanics, Cytarabine, Zigzag (5, 0) carbon nanotube, Force field

Background

Cytarabine is a chemotherapy agent utilized chiefly in the therapy of hematological malignancies like non-Hodgkin lymphoma and acute myeloid leukemia [1]. In addition, cytarabine has been known as Ara-C (arabinofuranosyl cytidine) [2]. In two randomized trials, the utilization of interferon and intermittent parenteral cytarabine has been estimated [3,4]. This combination raises the cytogenetic response rate further, and in one trial [3], it enhanced overall survival compared with interferon alone. However, subcutaneously administered cytarabine has some defects. Following parenteral administration by the ubiquitous enzyme deoxycytidine deaminase, which results in a comparatively short serum half-life, it quickly undergoes systemic deamination [5]. It needs daily subcutaneous injection to render the drug and is also associated with upper gastrointestinal symptomatology, particularly mucositis and nausea [3]. In addition, carbon nanotubes (CNTs) have attracted an uninterrupted interest in different areas since their discovery because of their unique structure and electrical/mechanical characteristics [6,7] which make them interesting for many potential usages in electronic devices, sensors, structural integrity [8], biomedical engineering [9-11], nanoinjectors [12], drug delivery [13], gene therapy [14], and in catalysis supports. We can categorize CNTs as single-wall carbon nanotubes (SWCNTs) and multiwall carbon nanotubes (MWCNTs) [15]. In fact, SWCNTs are grapheme cylinders with a wall thickness of 1 atomic layer and a diameter of around 1 nm. High aspect ratio, enormous surface, hollow geometry [6] are some their exciting characteristics. Other characteristics include high-current carrying capacity, superior thermal properties, fast response, and good reversibility [7,16]. SWCNTs have three configurations. It will be in the form of an armchair if the nanotubes $n = m$ and whenever $n = 0$ or $m = 0$, it will be in zigzag form with any other n and m, it will be in chiral variety. Each of these configurations has its own characteristics and properties [17,18]. MWCNTs are made of multiple rolled layers (concentric tubes) of graphite. Using two models, we can depict the configurations of multiwall nanotubes. In one of these models, the Russian model, sheets of graphite are set in concentric cylinders, e.g., (0, 8) SWCNTs are within a larger (0, 17) single-wall nanotube. In the second model, the parchment model, a single sheet of graphite is rolled around itself, just like a scroll of parchment or a rolled newspaper. In multiwall nanotubes, the interlayer distance is somehow equal to the distance between grapheme layers in graphite, which is nearly 3.4 Å. Two concentric cylindrical grapheme layers conform to double-wall carbon

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nanotubes. Accordingly, they blend with the interesting electronic characteristic of SWCNTs with the superior mechanical strength of MWCNTs [19].

This paper is concentrated on the interaction of a carbon nanotube with an anticancer drug named cytarabine. Nowadays, in the universe of new medicine, carbon nanotubes have experimentally showed their capacity in passing through the cell shell. Accordingly, scientists believe that they can apply them in releasing active drug molecules in the cell, particularly in the most sensitive and essential molecules for special diseases such as cancer, AIDS. The physical and chemical nature of these nanotubes has been studied by many scientists in order to prepare this material for such a significant task. Scientists pay special attention to carbon nanotubes consisting of fullerenes [20] because of their unequaled electrical, optical, and thermal characteristics. Scientists are very hopeful to develop and utilize carbon nanotubes in releasing vaccines by conducting basic and fundamental projects. Releasing drugs in cancer cells without harming healthy cells of tissues under study is very significant. After a number of research, we can understand that nanotubes can do this task correctly [21,22]. With the use of molecular mechanics (MM)/Monte Carlo (MC) simulation (in various force fields such as MM+, assisted model building with energy refinement (AMBER), and optimized potential for liquid simulations (OPLS)), the interaction of cytarabine with zigzag (5, 0) carbon nanotube was studied. Furthermore, we have studied the effects of solvents on their interaction by means of quantum mechanics (QM). We applied the self-consistent reaction field method (SCRF) for the simulation of solvent effects by QM method. Thus, it can be seen that we described the solvent effects on the thermodynamic values of this interaction using QM and MM methods.

Results and discussion

Here, the combination schema of cytarabine anticancer drug and zigzag (5, 0) carbon nanotube is shown in Figure 1. We have examined the thermodynamic values of the interaction of cytarabine with zigzag (5, 0) carbon nanotube in different dielectric constants.

In this work, we have done the said calculation by studying the following reaction:

$$\text{Cytarabine} + \text{SWCNT} \rightarrow \text{Cytarabine–SWCNT} \qquad (1)$$

Thus, in the first stage, we studied various force fields to estimate potential energy (kcal mol^{-1}) and other kinds of geometrical parameters on the interaction of cytarabine with the zigzag (5, 0) carbon nanotube. By utilizing three various force fields, the potential energy of molecules will not be similar. Thus, to compare the calculated potential energy of one specific molecule with a special force field and with the potential energy of another molecule computed in another force field is neither reasonable nor possible. In this examination, we revealed the differences in force fields by comparing the calculated potential energy utilizing different force fields such as MM+, AMBER, and OPLS that are show in (Figures 2, 3, and 4). Thus, it can be observed which water solvent has the lowest value of potential energy alterations. Also, it can be seen why OPLS is the best force field in the comparison of potential energy alterations in the water solvent (Figure 5, Table 1). Using different force fields, we can obtain the theoretical potential energy values; these are done by the joining of or attraction of the Van Der Waals force caused by dipole-dipole interactions and the experimental repelling forces caused by Pauli repulsion. In the opposite direction of the encircling medium, a dipole moment is made by the

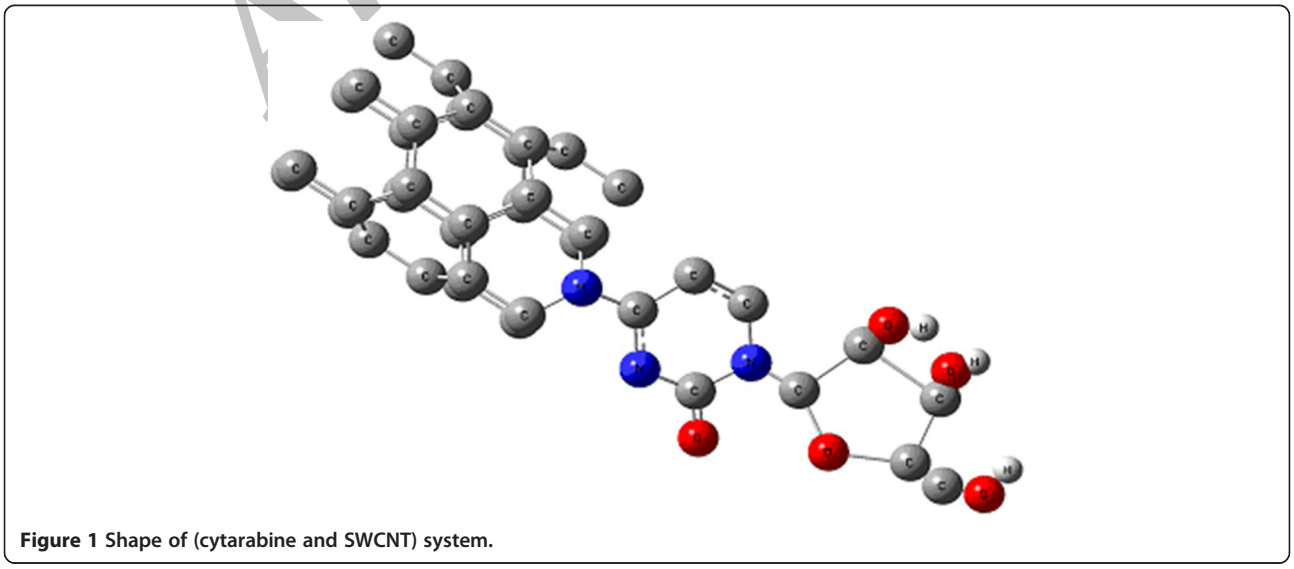

Figure 1 Shape of (cytarabine and SWCNT) system.

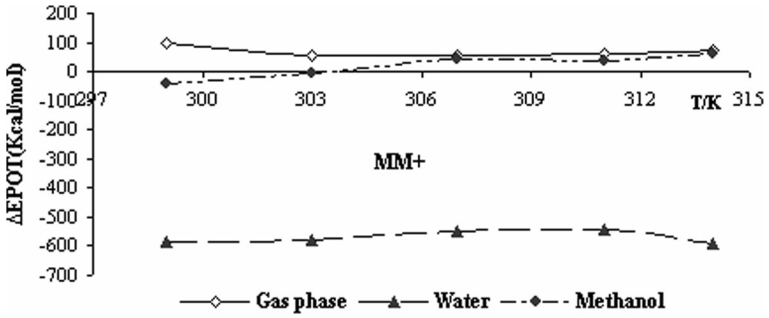

Figure 2 Potential energy alterations versus temperature in different solvents and MM+ force field for reaction 1.

thermodynamic values of solute dipole moment. Conversely, the medium polarizes the charge distribution in the solvent. The dipole moment values of cytarabine and zigzag (5, 0) carbon nanotube, (cytarabine/zigzag (5, 0) carbon nanotube) system in gas phase, and water and methanol at various temperatures have been related. It is revealed that dipole moment values in gas phase, water, and methanol increase with the increasing dielectric constant; we demonstrate these results in Table 2. A continuous dielectric constant signifies the presence of a solvent with a given dielectric constant in Onsager reaction field template. We must consider that the solute to be fixed into the cavity (usually with a spherical shape), with its radius in the molecule, and the electric field, which is related to the solute by the solvent dipole, will interact with the molecular dipole and will be directed to net stabilization. Now, it must be noted that salvation energy computed by SCRF method is the electrostatic distribution to the free energy of salvation. In this study, the cavity radii of cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system were calculated and were then substituted while efficiency was improving. We have also achieved the volumes of cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system. After computing the values of cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system, we came up with these outcomes: 8.70, 5.06, 5.73 Å, respectively. We have reached the point wherein, along the increasing solvent dielectric constant, the dipole moment for the anticancer drug, cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) Carbon nanotube) system in different ranges of temperatures (between 299 and 314 K) also increased, which is based on the dipole moment data in Table 2. After computing the values for the Onsager template, the fact that Gibbs free energy, energy, enthalpy, and entropy values of cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system are sensitive to the polarity of the encircling solvent. Thus, the Gibbs free energy, enthalpy, entropy, and energy values are revealed according to this approach in Table 3. All of these values have relationships with the dielectric constant. According to Table 3, everybody can understand that by increasing the temperature from 299 to 314K, the thermodynamic values of Gibbs free energy of cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system in gas phase, water, and methanol will decrease. We can get the lowest amount of Gibbs free energy at 314 K. The achieved Gibbs free energy values decrease, in all inspected temperature, if the solvent dielectric constant increases. For example, Gibbs free energy obtains the most negative value whenever cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system are released in water solvent. More or less, Table 3 shows the obtained Gibbs free energy, enthalpy, energy, and entropy values in different

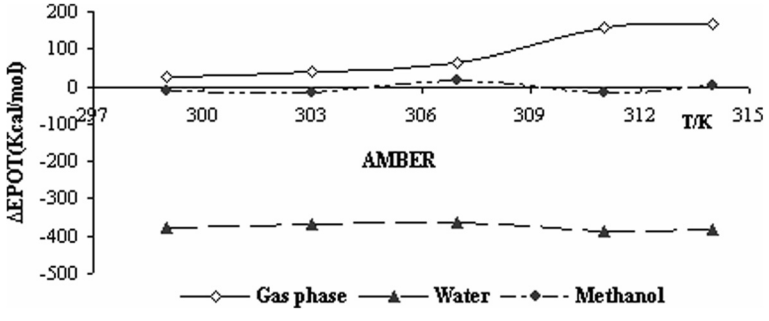

Figure 3 Potential energy alterations versus temperature in different solvents and AMBER force field for reaction 1.

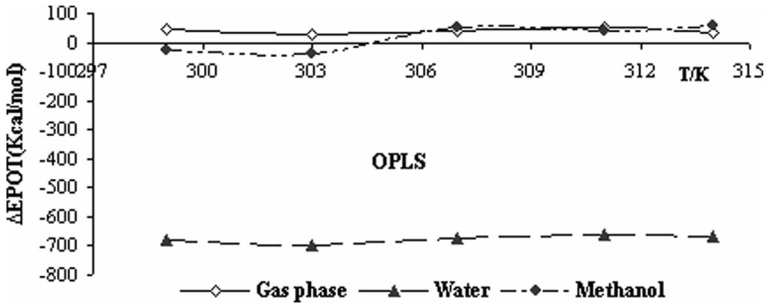

Figure 4 Potential energy alterations versus temperature in different solvents and OPLS field for reaction 1.

solvents. According to the temperature that changed between 299 and 314 K, the changes of energy, enthalpy, and entropy of cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system in gas phase, water, and methanol can be observed. Thus, we get to this point wherein the most positive value of energy, enthalpy, and entropy is 314 K if the temperature increases from 299 to 314 K. The other important point is that, after computing the values of energy, enthalpy, and entropy based on the solvent dielectric constant and increased values in temperature between 299 and 314 K, the value of energy and enthalpy becomes negative. The lowest values of energy and enthalpy and positive values of entropy can be obtained when cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system are in water solvent. In such cases, we can observe the most positive value of entropy.

Study the following reaction:

$$\text{Cytarabine} + \text{SWCNT} \rightarrow \text{Cytarabine–SWCNT}$$

In Table 4, we can observe the facts about the (cytarabine/zigzag (5, 0) carbon nanotube) system. If the solvent dielectric constant increases, the Gibbs free energy values of the interaction between solvent and solute molecules decrease. Noticeably, in Table 4, we can understand that the increase of solvent dielectric constant makes the enthalpy values of interaction between solvent and solute molecules move toward negative amounts. It reveals that the interaction between solvent and solute molecules is strong. According to Equation 1, the achieved entropy values are reasonable. In fact, the above reaction suggests that by coupling the anticancer drug of cytarabine with zigzag (5, 0) carbon nanotube, the entropy lessens. Now, we estimate and survey the data from another viewpoint on Equation 1:

We can see diagrams of $\Delta\mu_{\text{reaction}}$, $\Delta G_{\text{reaction}}$, $\Delta H_{\text{reaction}}$, and $\Delta S_{\text{reaction}}$ according to the temperature changes in Figures 6, 7, 8, and 9, respectively, in which the values of $\Delta\mu_{\text{reaction}}$, $\Delta G_{\text{reaction}}$, $\Delta H_{\text{reaction}}$, and $\Delta S_{\text{reaction}}$ are obtained on the basis of following function:

$$\Delta J = \Delta J_{\text{cytarabine–SWCNT}} - \left(\Delta J_{\text{cytarabine}} + \Delta J_{\text{SWCNT}}\right)$$

In this function, the J parameter is equal to the dipole moment values μ for Figure 6, Gibbs free energy values G for Figure 7, enthalpy values H for Figure 8, and entropy values for Figure 9. In Figure 6, we can recognize which of the values will change by the increasing solvent constant, $\Delta\mu_{\text{reaction}}$, in Figure 1 if the temperature is increased up to 314 K. Moreover, Figure 7 elaborates that the increase of temperature will also heighten the value

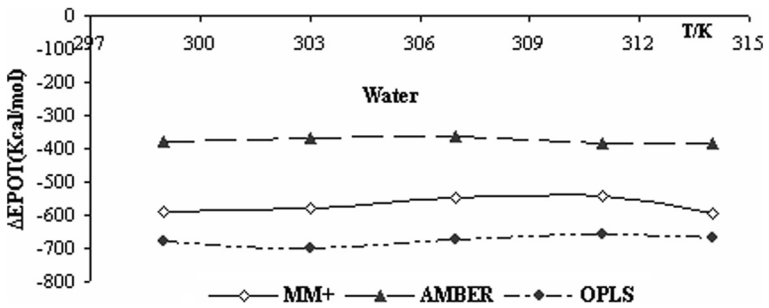

Figure 5 Potential energy alterations versus temperature for water solution in different force fields for reaction 1.

Table 1 Theoretical potential energy (kcal mol^{-1}) values in different solvents and same force fields

Media	Temperature (K)	$E_{Potential\ energy}$ (kcal mol^{-1})									$\Delta E_{Potential\ energy}$ (kcal mol^{-1})		
		Cytarabine			SWCNT			Cytarabine-SWCNT					
		MM+	AMBER	OPLS	MM+	AMBER	OPLS	MM+	AMBER	OPLS	MM+	AMBER	OPLS
Gas phase	299	44.73204	141.94	48.44767	213.1887	162.8669	213.1573	352.448	332.8886	306.8255	94.52726	28.0817	45.22053
	303	45.02634	171.42	66.91479	212.2316	136.945	224.6387	315.1821	346.3216	319.7139	57.92416	37.9566	28.16041
	307	32.37732	131.4695	54.23368	220.7707	167.3872	231.0695	309.8467	363.5419	326.0575	56.69868	64.6852	40.75432
	311	55.4327	44.88987	57.82224	218.8069	153.9778	214.3011	335.407	356.1648	323.0684	61.1674	157.29713	50.94506
	314	40.52354	43.73027	57.3092	218.3201	164.461	219.1929	332.468	374.97	308.1852	73.62436	166.77873	31.6831
Methanol	299	122.7491	96.822	94.18385	209.3418	182.3241	187.874	287.887	269.6387	255.4425	−44.2039	−9.5074	−26.6154
	303	97.2437	91.61169	133.0873	202.8216	188.161	193.7327	295.4447	262.1135	290.104	−4.6206	−17.65919	−36.716
	307	42.40936	99.70736	49.09336	206.8541	170.8445	195.9675	289.2411	288.5759	297.5085	39.97764	18.02404	52.44764
	311	43.54883	86.28603	40.9453	200.088	181.7183	189.4955	282.5071	251.2833	269.6509	38.87027	−16.72103	39.2101
	314	45.18951	93.74397	43.58532	205.6906	178.9124	180.3274	311.3402	274.331	280.4594	60.46009	1.67463	56.54668
Water	299	503.1399	274.194	526.6146	305.8046	268.0094	298.9091	220.7991	162.7351	146.6212	−588.145	−379.4683	−678.903
	303	503.894	272.4241	531.7231	304.791	244.0615	317.1772	228.5874	150.1159	150.7781	−580.098	−366.3697	−698.122
	307	500.529	275.7412	525.9601	291.5029	234.2437	295.3419	244.3345	144.6781	146.1943	−547.697	−365.3068	−675.108
	311	500.506	275.4447	526.4454	300.6973	273.7059	284.4701	257.0042	164.1786	151.0472	−544.1929	−384.972	−659.868
	314	501.2367	270.8107	531.7561	313.3305	262.9936	284.886	221.697	149.4395	147.7274	−592.870	−384.3648	−668.915

$\Delta E_{Potential\ energy}$ (kcal mol^{-1}) = Difference of energy for (cytarabine-SWCNT) system + Sum of cytarabine and SWCNT for reaction 1 in different dielectric constants.

Table 2 Theoretical dipole moment μ (Debye) and $\Delta\mu$ (Debye) values in various temperatures for three phases

Temperature (K)	μ (Debye)			$\Delta\mu$ (Debye)	μ (Debye)			$\Delta\mu$ (Debye)	μ (Debye)			$\Delta\mu$ (Debye)
	Cytarabine	SWCNT	Cytarabine-SWCNT		Cytarabine	SWCNT	Cytarabine-SWCNT		Cytarabine	SWCNT	Cytarabine-SWCNT	
	Gas phase				Water				Methanol			
299	9.0282	0.0035	1454.3548	1445.3231	9.2747	0.0049	3048.6991	3039.4195	9.2579	0.0045	2876.4738	2867.2114
303	9.0279	0.0039	1454.3541	1445.3223	9.2756	0.0049	3048.6995	3039.419	9.2585	0.0042	2876.4735	2867.2108
307	9.0293	0.0036	1454.3549	1445.322	9. 2746	0.0047	3048.6989	3039.4196	9.2578	0.0040	2876.4737	2867.2119
311	9.0284	0.0037	1454.3551	1445.323	9. 2761	0.0048	3048.6993	3039.4184	9.2687	0.0041	2876.4732	2867.2004
314	9.0297	0.0039	1454.3546	1445.321	9. 2763	0.0046	3048.6990	3039.4181	9.2683	0.0045	2876.4735	2867.2007

$\Delta\mu$ (Debye) = Difference of dipole moment for (cytarabine-SWCNT) system + Sum of cytarabine and SWCNT for reaction 1 in different temperatures and three phases.

Table 3 Theoretical thermodynamic parameters in various temperatures for three phases at HF/3-21G level of theory

System	Media	Quantities	Temperature (K)				
			299	303	307	311	314
			Theoretical thermodynamic values				
Cytarabine	Gas phase	*G*	−548150.9401	−548150.9481	−548151.1686	−548151.296	−548151.4095
		H	−548119.9476	−548119.4974	−548119.2811	−548118.9685	−548118.7193
		E	−548120.0178	−548119.8632	−548119.5651	−548119.1063	−548118.8972
		S	0.103654	0.103794	0.103868	0.103947	0.104109
	Water	*G*	−548151.7088	−548151.9786	−548152.0916	−548152.3529	−548152.5122
		H	−548120.5483	−548120.2354	−548119.8861	−548119.6926	−548119.4326
		E	−548120.8651	−548120.4968	−548120.1091	−548119.8125	−548119.6061
		S	0.104599	0.104763	0.104904	0.105017	0.105318
	Methanol	*G*	−548151.6849	−548151.7821	−548151.8596	−548152.0382	−548152.5035
		H	−548120.5451	−548120.0847	−548119.6799	−548119.386	−548119.3087
		E	−548120.7163	−548120.4109	−548120.0616	−548119.6959	−548119.501
		S	0.104496	0.104612	0.104820	0.104991	0.105079
SWCNT	Gas phase	*G*	−707511.0458	−707511.5212	−707511.887	−707512.6031	−707512.9225
		H	−707476.036	−707475.791	−707475.433	−707475.299	−707475.175
		E	−707476.565	−707476.283	−707475.927	−707475.792	−707475.669
		S	0.117088	0.117918	0.118736	0.119948	0.120213
	Water	*G*	−707511.4476	−707511.9512	−707512.3825	−707512.7784	−707513.275
		H	−707476.1402	−707475.816	−707475.625	−707475.368	−707475.268
		E	−707476.7112	−707476.391	−707476.198	−707475.94	−707475.843
		S	0.118084	0.119256	0.11973	0.120451	0.121035
	Methanol	*G*	−707511.3785	−707511.8259	−707512.246	−707512.7319	−707513.0681
		H	−707476.101	−707475.805	−707475.601	−707475.3026	−707475.197
		E	−707476.658	−707476.312	−707476.155	−707475.853	−707475.751
		S	0.117984	0.11888	0.119364	0.120350	0.120608
Cytarabine - SWCNT	Gas phase	*G*	−710372.6617	−710372.8408	−710373.0034	−710373.1847	−710373.3096
		H	−710347.9077	−710347.9296	−710347.411	−710347.2389	−710347.084
		E	−710348.1863	−710347.8016	−710347.654	−710347.437	−710347.229
		S	0.083067	0.083205	0.083363	0.083427	0.083509
	Water	*G*	−806458.3497	−806458.3631	−806458.5791	−806458.7369	−806458.9894
		H	−806431.3989	−806431.0059	−806430.8517	−806430.6162	−806430.5546
		E	−806431.5072	−806431.217	−806430.9681	−806430.7761	−806430.6375
		S	0.090135	0.090287	0.090316	0.090420	0.0.90555
	Methanol	*G*	−806300.2457	−806300.3181	−806300.5183	−806300.8488	−806301.0853
		H	−806273.5288	−806273.3328	−806272.9297	−806272.8613	−806272.7854
		E	−806273.7822	−806273.5086	−806273.0515	−806272.9147	−806272.8582
		S	0.089654	0.089721	0.089865	0..089992	0.090127

Theoretical thermodynamic parameters *G*, *H*, *E* (kcal mol^{-1}), and *S* (kcal mol^{-1} K^{-1}) for cytarabine, SWCNT, and (cytarabine-SWCNT) system.

of $\Delta G_{reaction}$. Thus, $\Delta G_{reaction}$ has the lowest value at 299 K, and we then can reach to the point where the highest resistance for Equation 1 will occur. Also, Figure 9 reveals that the value of $\Delta S_{reaction}$ declines with increasing temperature. The most positive value, $\Delta S_{reaction}$, in Equation 1 can be observed, and it is the more resistant rate. In Table 4, we must notice that the alteration of $\Delta G_{reaction}$, $\Delta H_{reaction}$, and $\Delta S_{reaction}$, in terms of solvent dielectric constant, will decline the value of the noted $\Delta G_{reaction}$ in as much as the negative value of $\Delta G_{reaction}$ is

Table 4 Theoretical thermodynamic parameter alterations in various temperatures for three phases at HF/3-21G level of theory

Media	Quantities	Temperature(K)				
		299	303	307	311	314
		Theoretical thermodynamic values				
Gas phase	ΔG	545289.3242	545289.6285	545290.0522	545290.7144	545291.0224
	ΔH	545248.0759	545247.3588	545247.3031	545247.0286	545246.8103
	ΔE	545248.3965	545248.3446	545247.8381	545247.4613	545247.3372
	ΔS	−0.137675	−0.138507	−0.139241	−0.140468	−0.140813
Water	ΔG	449204.8067	449205.5667	449205.895	449206.3944	449206.7978
	ΔH	449165.2896	449165.0455	449164.6594	449164.4444	449164.146
	ΔE	449166.0691	449165.6708	449165.339	449164.9764	449164.8116
	ΔS	−0.132548	−0.133732	−0.134318	−0.135048	−0.135798
Methanol	ΔG	449362.8177	449363.2899	449363.5873	449363.9213	449364.4863
	ΔH	449323.1173	449323.2143	449322.3512	449321.8273	449321.7203
	ΔE	449323.5921	449322.9755	449322.1651	449322.6342	449322.3938
	ΔS	−0.132826	−0.133771	−0.134319	−0.135349	−0.13556

Theoretical thermodynamic parameter alterations ΔG, ΔH, ΔE (in kcal mol^{-1}), and ΔS (kcal mol^{-1} K^{-1}) for interaction of cytarabine with and zigzag (5, 0) carbon nanotube. Parameter alterations Δ (kcal mol^{-1}) = Difference of energy for (cytarabine-SWCNT) system + Sum of cytarabine and SWCNT for reaction 1 in three phases.

for water solvent; the water solvent is the best environment for Equation 1. According to Table 4, $\Delta H_{\text{reaction}}$ and $\Delta S_{\text{reaction}}$ values are reduced by the increase of solvent dielectric constant in temperature between 299 and 314 K. If Table 4 is considered, the fact that $\Delta S_{\text{reaction}}$ at 299 K gains the most positive value is attained; thus, the temperature 299 K will be the choice for Figure 1.

Conclusions

In this article, cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system were studied by two methods, quantum mechanics and molecular mechanic/MC simulation. Diagrams were showed that ΔE_{POT} and thermodynamic values of the reaction were dependent to the solvent dielectric constant. The calculated ΔE_{POT} values for the reaction in water are more stable because the potential energy alterations become lower. The computed values of ΔE_{POT} from force fields MM+, AMBER, and OPLS in water solvent were compared, and they showed that the OPLS force field is the best force field for the study of Equation 1. In the next calculation, we investigated the obtained results by the HF/3-21G and Gaussian 98 showing that water is the best solvent when cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system are placed in it because they have the most negative Gibbs free energy and the most positive entropy in this solvent.

Methods

Computational method

We conducted all computations by quantum mechanics and molecular mechanics/Monte Carlo simulation (in

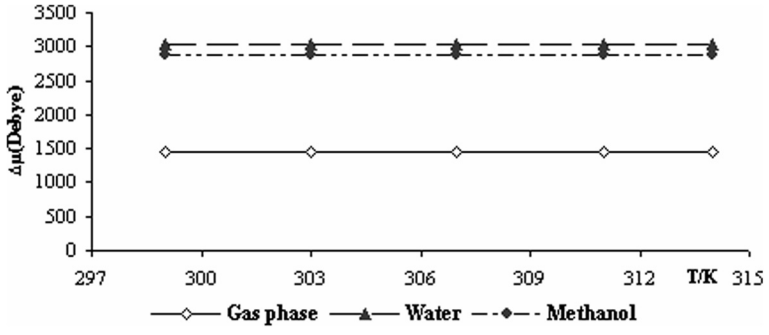

Figure 6 Dipole moment alterations calculated versus temperature for reaction 1.

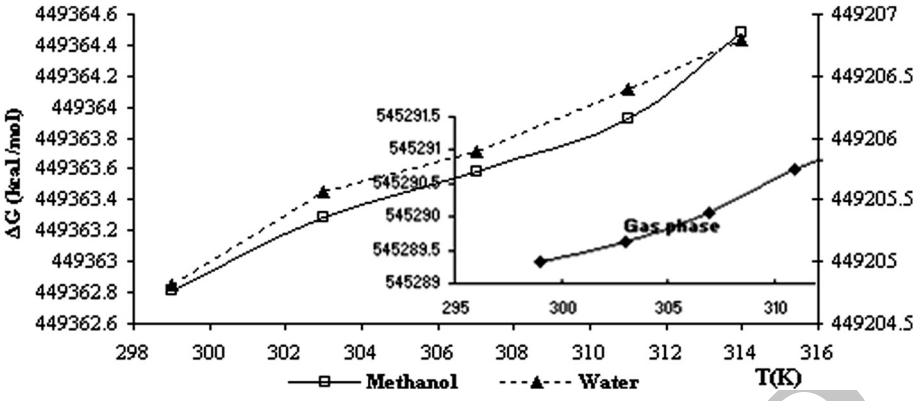

Figure 7 Gibbs free energy alterations (kcal mol^{-1}) calculated versus temperature for reaction 1 for three phases.

various force fields such as MM+, AMBER, and OPLS) in various temperatures. At first level, we carried out all calculations using the program HYPER CHEM (Hypercube, Inc., Gainesville, FL, USA). In this study, different force fields were used to determine the potential energy. Thus, we can observe the difference in force field by comparing the computed potential energy with the applied force fields namely MM+, AMBER and OPLS. At the next level, using the Hartree-Fock (HF) method, we conducted calculations of the theoretical level. It is important to choose a level which is well matched with the molecular system being studied. Accurate geometry coordinates and energy parameters control conformational interconversions; in molecular systems, they are particularly important. Low-energy structures found on each surface were closed and exposed to unlimited quantum mechanical minimization using HF/3-21G SCRF [23]. To determine thermodynamic values of cytarabine, zigzag (5, 0) carbon nanotube, and (cytarabine/zigzag (5, 0) carbon nanotube) system, we performed a theoretical analysis at the HF/3-21 level. By means of the Onsager method as implemented in the Gaussian 98 program [24], we modeled the solvent effects. The geometries of the cytarabine and single-wall carbon nanotube and the interaction of a nanotube with an anticancer drug in various solvents were optimized using the Onsager model at the Hartree-Fock level of theory. We investigated the cytarabine single-wall carbon nanotube and interaction of a nanotube with an anticancer drug in gas phase ($\varepsilon = 1$) and various solvent media and dielectric constants: water ($\varepsilon = 78.39$) and methanol ($\varepsilon = 32.63$), at various temperatures.

Theoretical background

SCRF method

In using the SCRF model in the quantum chemical theory, the form and volume of the solute molecule needs to be determined specifically for any set of compounds; we know some of the approaches to calculate these properties, but no nonempirical method for their study had been developed. However, we can conclude from

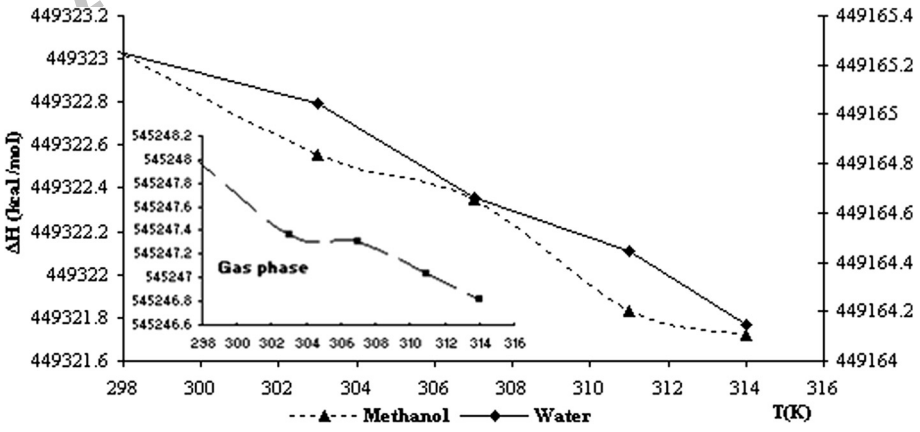

Figure 8 Enthalpy alterations (kcal mol^{-1}) calculated versus temperature for reaction 1 for three phases.

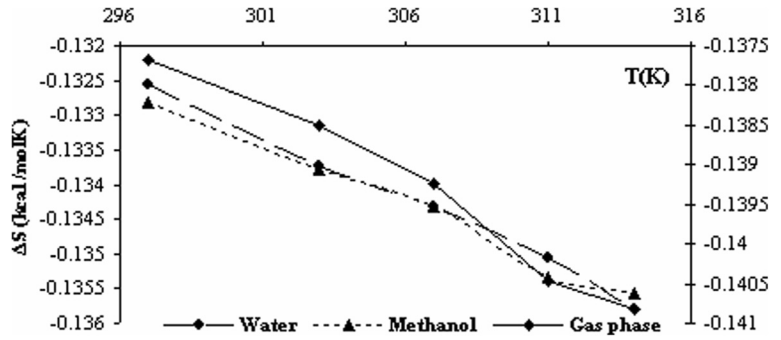

Figure 9 Entropy alterations (kcal mol^{-1} K^{-1}) calculated versus temperature for reaction 1 for three phases.

the results of the model calculations that the simple model that assumed a spherical or an ellipsoidal shape of the cavity for the solute molecule is likely satisfactory for comparatively tiny and strong molecules. We then selected this method in our computations [25]. In the past years, the Onsager-SCRF code elaborated by Wiberg and co-workers [26,27] for the Gaussian computational code has been famous. The Onsager model describes the system as a molecule with a multipole moment inside a spherical cavity surrounded by a continuous dielectric. In some programs, only the dipole moment is used, and therefore, we cannot apply them for molecules with zero dipole moment. Qualitatively, the results from using the Onsager model and HF calculations are correct rules.

Molecular mechanics (Monte Carlo simulation)

By performing statistical sampling experiments, the Monte Carlo method provides approximate solutions to a variety of mathematical problems. Where statistical simulation is defined in quite general terms as a method that utilizes sequences of random numbers to conduct the simulation, we can loosely determine them as a statistical simulation method. We then can declare that the Monte Carlo method is a collection of various methods and unique processes. This process includes performing many simulations using random numbers and probabilities to get approximations of the answer to the problem. Our notion about defining the characteristic of the Monte Carlo method is its use of random numbers in its simulation. We apply the metropolis algorithm more than any other algorithm because of its simplicity in the Monte Carlo method [28]. By random displacement, we can determine the accuracy of the algorithm in small displacement; all moves are acceptable, but in huge cases, only the small moves are accepted. In this study, by comparing the computed potential energy using the force field MM+, AMBER, and OPLS in the Monte Carlo simulation, we illustrate the chemical calculation. Scientists use the HyperChem professional 7.1 in this investigation. Using this software, geometry optimization and Monte Carlo simulation have been performed. They have performed the quantum chemical calculations on the interaction of cytarabine with open-end SWCNT by means of the Gaussian 98 program package [29] using the standard 3-21G basis set. We apply a simple approximation in the Hartree-Fock level and in the Gaussian program, and in order to calculate the radius of cavity which forms the hypothetical surface of the molecule [30,31]. We also utilize the volume of the solute. Both the solute and solvent are placed in the same cavity. How the SCRF approaches define the cavity and reaction field differ with each other. We take into account and consider the effect of the solvent in accordance with the self-consistent reaction field method. This method is based on the Onsager reaction field theory of electrostatic solvations. We consider the solvent as a uniform dielectric with a given dielectric constant, especially in this model. We then investigate solvent effects on the values of Gibbs free energy, enthalpy, entropy, energy, dipole moment of water, and methanol surrounding cytarabine open-end of the (SWCNT) system within the Onsager self-consistent reaction field model using the Hartree-Fock method as well as the various temperature effects on cytarabine open-end of SWCNT. We can compare the obtained thermodynamic values of cytarabine open-end of SWCNT in gas phase and in various solvents such as water and methanol.

Competing interests

The author declares that she has no competing interests.

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