Studying the interaction of calcium, potassium and sodium ions with 3 isomers of Docetaxel drug and the effect of these ions on physicochemical and thermodynamic properties: A DFT computation

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Abstract

In this study, the interaction of Ca^{2+}, K^+ and Na^+ ions along with 3 isomers of Docetaxel drug and their physical and thermodynamic properties have been computed and investigated using DFT method calculations. These calculations are based on B3LYP quantum chemical level and at 6-311G** basis orbital set. The proximity of ions has been studied in order to determine physical and thermodynamic properties. Approaching the ions to Docetaxel drug causes different events like changing angles between bonds, bond lengths, shape and orbital energy levels and other physicochemical characteristics. DOS graphs have been plotted to obtain some quantum chemical data. The results have shown that the HOMO orbitals, are localized around the C-C bonds, whereas the LUMO orbitals are more localized around the oxygen and nitrogen atoms of Docetaxel. The obtained results show that these metallic cations tend to stay in the suitable spatial situations to diminish their own density of electrical charge. When one of the ions approached the drug, the orbitals change in terms of shape and energy, and will fit to the new situation. Accordingly, the obtained results show that the absolute values of ΔE, ΔG and ΔH have the order of Drug-K^+<Drug-Na^+<Drug-Ca^{2+}, and the values of E_{HOMO}, E_{LUMO}, η, μ, ΔN_{max} and S have the order of $K^+ \approx Na^+ < Ca^{2+}$.

Keywords: Docetaxel isomers; DOS plots; spatial situation; intracellular; extracellular.

Introduction

About 55 to 60 percent of an adult's body is made of liquids. The liquids are divided into two intracellular and extracellular categories and two-thirds of them are intracellular. Organic materials and proteins are about 30 percent, while potassium and magnesium cations and hydrogen phosphate anion are also the important ions in the intracellular liquids [1]. Sodium, potassium, calcium, and magnesium cations and chlorine anion are the most important in extracellular liquids. The amount of extracellular organic matters is much less than the intracellular ones [2-5]. The structure of these ions changes due to the various environmental and biochemical factors, diseases etc. As an example, in the

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cancer patient's body, the amount of potassium reduces and sodium and chloride increases to an extent that the ratio of Na^+ to K^+ increases up to fivefold. These materials, certainly, affected the structure and the properties of other dissolved materials in the liquids. Therefore, studying these effects for a better understanding of substances, such as drugs, is very important. Docetaxel is an important drug in the Taxane family. The drug, which was synthesized from substances with an herbal origin [7], is effective in curing an extensive range of cancers such as breast, small and non-small cell lung, ovarian, prostate and urinary tract mucosa, head and neck, stomach and the bladder cancers [8-10]. Several computational studies have been led to a better understanding of the Taxane (a class of diterpenes) family [11-13].

Certain authors have studied the adsorption behavior of metformin drug on boron nitride fullerenes and have reported interesting results [14]. Furthermore, the density functional theory (DFT) study of O_2, N_2 adsorptions on H-capped (4,4) single-walled carbon nanotube was investigated [15]. The authors reported that the 13C chemical shielding isotropy and anisotropy values have varied remarkably, from CNT to the CNT-O2 and CNT-N2 systems, for adsorption sites [15]. The effects of Zn doping on the interaction of a single walled carbon nanotube with Penicillamine (PCA) drug using DFT method calculations were investigated [16]. The results of this study indicated that the interaction of PCA from its NH_2 group toward the surface of Zn-doped SWCNT shows an improved adsorption of the drug molecule with an appreciable binding energy in comparison with –OH and –C=O groups [16]. Also an Ab initio investigation of the SCN^- chemisorption of single-walled boron nitride nanotubes have been studied and the remarkable results of the interaction of SCN^- ion with single-walled boron nitride nanotubes were reported [17].

In this study, DFT calculations were carried out on the main, geometric and structural isomer of Docetaxel drug (Figure 1) to obtain physical and thermodynamic parameters, and electronic properties of interaction of Ca^{2+}, Na^+, and K^+ ions with Docetaxel drug in gaseous phase. The main objectives of this study are using DFT calculations to evaluate the accuracy and to help better understanding of the chemical reactivity of this drug.
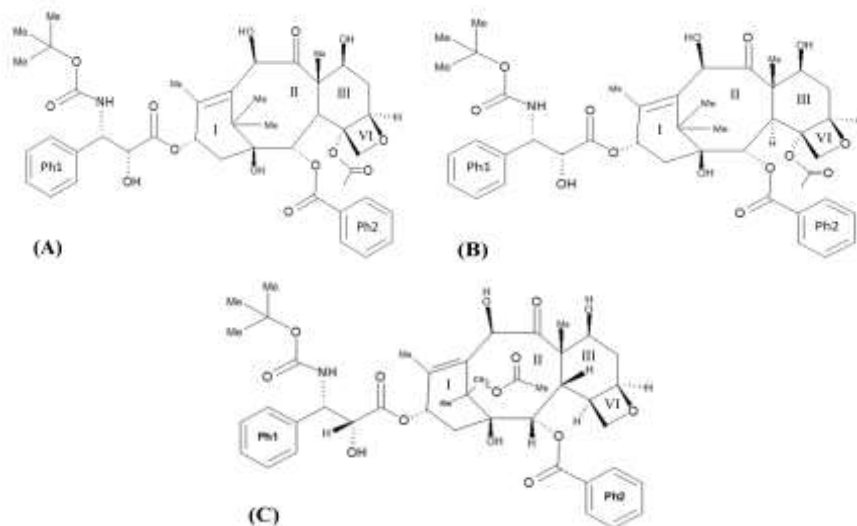
Figure 1. The optimized structures of Docetaxel isomers, **(A)**: main isomer, **(B)**: geometric isomer, **(C)**: structural isomer

Computational methods

In this study, the main isomer (Figure 1 (a)), geometric isomer (Figure 1 (b)), and structural isomer (Figure 1 (c)) of Docetaxel were designed and optimized using the Gaussian 03 software set [18]. Optimization and frequency calculations have been performed in order to obtain the physicochemical and quantum chemical properties using the B3LYP quantum chemical level and the 6-31G** basic orbital set [14,15]. Moreover, the ion effect, the effect of calcium, sodium and potassium ions presence near the ether rings (Figure 2 (a)), eight-member ring (Figure 2 (b)) and nitrogen (Figure 2 (c)) were investigated. The binding energy of ion to isomers (ΔE), enthalpy variations (ΔH), and Gibbs free energy (ΔG) variations were computed and determined. ΔE is defined as follows:

$$\Delta E = E_{iso+ion} - E_{iso} - E_{ion} \quad (1)$$

Considering the HOMO energy level as the energy of the Fermi level and LUMO energy as the first energy level of the conduction band, the chemical potential (μ), the hardness (η) and softness (S) were defined as follows:

$$\mu = -\chi = -\frac{I+A}{2} \quad (2)$$

$$\eta = \frac{I-A}{2} \quad (3)$$

$$S = \frac{1}{2\eta} \quad (4)$$

Where I (ionization potential) is the -E_{HOMO} (HOMO is the highest occupied molecular orbital), A (electron affinity) is the -E_{LUMO} (LUMO is the lowest unoccupied molecular orbital).

The best definition for global hardness is resistance to deformation in the presence of an electric field that can be increased with stability and can be decreased with the reactivity of the species.

Electrophilicity (ω) and the maximum amount of electronic charge, ΔN_{max} that the system may be accepted are defined as follows [16,17]:

$$\omega = \frac{\mu^2}{2\eta} \quad (5)$$

$$\Delta N_{max} = -\frac{\mu}{\eta} \quad (6)$$

Results and discussion

Firstly, the Docetaxel isomers 1 (A), 2 (B) and 3 (C) were optimized using B3LYP quantum chemical levels and the 6-31G** basic orbital set. Then Ca^{2+} ion was approached to the three isomers. After obtaining the results with Ca^{2+} ion, because of importance of interaction of isomers 2 and 3, K^+ and Na^+ ions were approached to these isomers. The positions of the ions were defined based on the molecular structure, orbitals and electrical charge of Docetaxel isomers and were optimized using B3LYP quantum chemical level and the 6-31G** basic orbital set. The obtained results are shown in Figures 2, 3 and 4
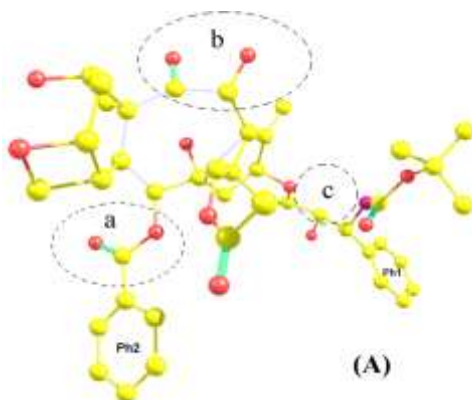
Figure 2. The 3 position **a**, **b** and **c** of Ca^{2+} ion located on Docetaxel isomers 1 (A)
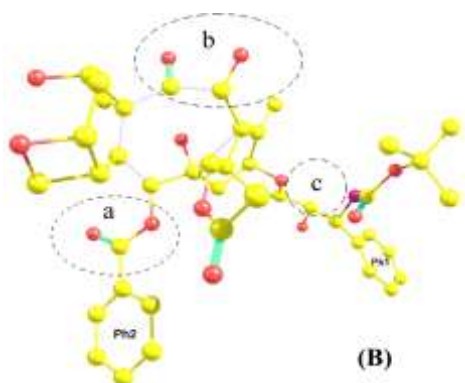
Figure 3. The 3 position **a**, **b** and **c** of Ca^{2+}, K^+ and Na^+ ions located on Docetaxel isomers 2 (B)
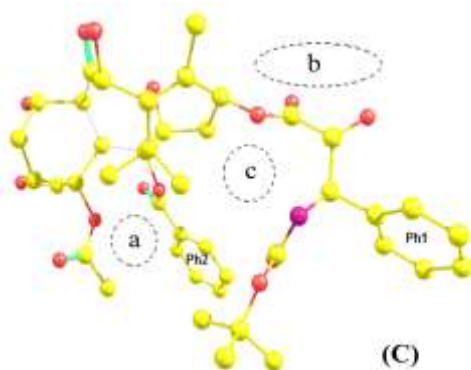
Figure 4. The 3 position **a**, **b** and **c** of Ca^{2+}, K^+ and Na^+ ions located on Docetaxel isomers 3 (C)

In **a** position, for all isomers, the ions were approached from outside to the ring IV. In this case, in isomers **(A)** and **(B)**, these ions are located between Ph2 ring and OAc branch, while in isomer **(C)** these ions are located between Ph2 and IV rings. In **b** position, for all isomers, the ions were approached from above the rings I and II, and are located between the nitrogen containing substitute and I and II rings. In **c** position, for all isomers, the ions were approached from a side other than **b** position and are located between the nitrogen containing substitute and I ring. The results of thermodynamical and physicochemical computations and calculations are shown in Tables 1 and 2. As seen in Table 1, thermodynamical values, in the case of each ion for the three isomers, approximately don't differ from each other. But the

differences of these values between interaction of Ca^{2+} ion and K^+ and Na^+ ions with Docetaxel isomers, in three positions **a**, **b** and **c**, are appreciable. This may be due to difference of charges of Ca^{2+} ion and K^+ and Na^+ ions.

These conditions are not seen in the physicochemical properties shown in Table 2. But the more appreciable differences are in relation with the dipole moments. This phenomenon, most probably, may be due to the position of displacement of charges in each case.

The density of state plots for Docetaxel isomers and their complexes with Ca^{2+}, Na^+, and K^+ ions, in three positions **a**, **b** and **c**, are shown in Figures 5 to 12.

Table 1. Thermodynamic properties of Docetaxel isomers and their complexes with Ca^{2+}, Na^+, and K^+ ions in three positions **a**, **b** and **c**.

		Thermal Energy	Cv	ZPE	S	ΔH	H	ΔG	G	ΔE	E
		kJ.mol⁻¹	J.mol⁻¹K⁻¹	kJ.mol⁻¹	J.mol⁻¹K⁻¹	kJ.mol⁻¹	Ha	kJ.mol⁻¹	Ha	kJ.mol⁻¹	Ha
Isomer 1		2570.41	913.92	2420.55	1303.03	-	-2777.25	-	-2777.40	-	-2777.25
Ion	**Position**										
Ca²⁺	a	2568.11	939.83	2418.38	1319.66	-698.36	-3453.40	-748.24	-3454.55	-743.03	-3454.40
	b	2567.40	934.31	2416.92	1319.50	-706.27	-3454.39	-687.84	-3454.53	-706.27	-3454.39
	c	2568.69	940.00	2418.72	1319.66	-658.99	-3454.37	-619.63	-3454.52	-658.99	-3454.37
Isomer 2		2565.60	915.04	2419.43	1307.59	-	-2777.23	-	-2777.38	-	-2777.23
Ion	**Position**										
Ca²⁺	a	2570.20	941.67	2420.47	1307.59	-858.53	-3454.42	-811.25	-3454.57	-858.53	-3454.43
	b	2570.03	936.19	2421.35	1316.03	-826.98	-3454.41	-788.09	-3454.56	-826.98	-3454.41
	c	2570.16	939.37	2420.43	1331.08	-789.93	-3454.40	-753.55	-3454.55	-789.93	-3454.40
K⁺¹	a	2571.54	942.17	2419.77	1067.57	-186.41	-3377.03	-152.25	-3377.18	-183.81	-3377.03
	b	2571.91	939.58	2420.93	1348.05	-196.93	-3377.03	-162.77	-3377.18	-194.32	-3377.03
	c	2572.33	940.42	2420.68	1349.22	-199.53	-3377.03	-165.37	-3377.18	-196.93	-3377.03
Na⁺¹	a	2573.08	940.50	2422.56	1324.18	-280.87	-2939.42	-238.90	-2939.57	-278.26	-2939.42
	b	2572.03	939.29	2421.35	1340.86	-280.87	-2939.42	-244.20	-2939.57	-275.66	-2939.42
	c	2572.91	938.58	2422.48	1341.07	-283.57	-2939.42	-246.81	-2939.57	-278.26	-2939.42
Isomer 3		2567.94	980.56	2422.48	1318.92	-	-2777.39	-	-2777.24	-	-2777.24
Ion	**Position**										
Ca²⁺	a	2572.79	940.21	2422.10	1327.36	-645.87	-3454.52	-687.84	-3454.36	-687.84	-3454.37
	b	2572.75	931.22	2423.94	1327.69	-763.97	-3454.56	-808.64	-3454.41	-808.64	-3454.41
	c	2572.00	935.48	2421.64	1355.11	-743.03	-3454.55	-779.79	-3454.40	-777.09	-3454.40
K⁺¹	a	2573.96	938.41	2421.56	1366.61	-120.80	-3377.17	-152.25	-3377.01	-149.65	-3377.02
	b	2575.01	935.48	2423.19	1363.64	-154.86	-3377.19	-186.41	-3377.03	-183.81	-3377.03
	c	2574.84	936.19	2423.02	1365.36	-149.65	-3377.19	-183.81	-3377.03	-181.20	-3377.03
Na⁺¹	a	2573.88	938.58	2421.43	1384.79	-186.41	-2939.55	-212.65	-2939.40	-210.05	-2939.40
	b	2575.84	933.77	2425.11	1348.84	-233.69	-2939.57	-270.45	-2939.42	-267.84	-2939.42
	c	2574.00	938.28	2421.39	1374.43	-215.26	-2939.57	-241.50	-2939.41	-238.90	-2939.41

Table 2. Physicochemical properties of Docetaxel isomers and their complexes with Ca^{2+}, Na^+, and K^+ ions in three positions **a**, **b** and **c**.

		ΔN$_{max}$	ω	S	η	μ	<R²>*	E$_{HOMO}$	E$_{LUMO}$	E$_{gap}$	Dipole moment			
											Total	Z	Y	X
				a.u.			a_0^2		a.u.			Debye		
Isomer 1		1.58	0.0009	5.62	0.09	-0.141	40339	-0.230	-0.052	0.178	7.616	0.90	4.821	-5.130
Ion	Pos.													
Ca²⁺	a	5.25	0.0035	7.87	0.06	-0.334	40280	-0.397	-0.270	0.128	18.316	0.49	15.289	-7.719
	b	7.00	0.0029	10.20	0.05	-0.343	48058	-0.392	-0.294	0.098	19.352	0.66	-9.469	-15.896
	c	6.59	0.0030	9.71	0.05	-0.340	44590	-0.391	-0.288	0.103	21.207	0.12	9.146	-19.100
Isomer 2		1.61	0.0009	5.62	0.09	-0.143	40032	-0.232	-0.054	0.178	7.069	0.27	4.050	-5.330
Ion	Pos.													
Ca²⁺	a	4.93	0.0036	7.46	0.07	-0.330	39795	-0.397	-0.263	0.134	13.889	0.52	11.679	-5.098
	b	5.16	0.0035	7.81	0.06	-0.330	47177	-0.394	-0.266	0.128	21.801	4.21	-1.819	-21.312
	c	5.97	0.0032	8.85	0.06	-0.338	50074	-0.394	-0.281	0.113	25.267	0.50	4.282	-23.017
K⁺	a	2.72	0.0021	6.02	0.08	-0.226	41069	-0.309	-0.143	0,165	10.932	0.88	7.637	-5.159
	b	2.34	0.0025	5.15	0.10	-0.227	49449	-0.324	-0.130	0.194	12.085	1.62	1.311	-11.902
	c	2.33	0.0023	5.32	0.09	-0.219	50868	-0.313	-0.125	0.188	17.772	0.37	4.832	-15.435

| Ion	Pos.												
Na⁺	a	2.78	0.0022	6.06	0.08	- 0.230	39446	- 0.312	- 0.147	0.165	9.160	0.10	6.265	- 4.313
	b	2.43	0.0026	5.24	0.10	- 0.233	46566	- 0.328	- 0.137	0.190	11.778	2.68	2.824	- 11.116
	c	2.34	0.0023	5.29	0.09	- 0.222	49726	- 0.316	- 0.127	0.189	17.330	0.85	5.713	- 15.277
Isomer 3		1.48	0.0010	5.21	0.10	- 0.142	42598	- 0.238	- 0.046	0.192	6.187	0.15	- 1.973	- 4941
Ion	Pos.												
Ca²⁺	a	12.96	0.0013	20.00	0.03	- 0.324	43475	- 0.349	- 0.299	0.050	26.567	0.79	11.567	22.610
	b	6.07	0.0028	9.35	0.05	- 0.325	45620	- 0.378	- 0.271	0.107	22.012	2.40	- 6.327	- 20.945
	c	6.94	0.0027	10.24	0.05	- 0.333	49096	- 0.381	- 0.285	0.096	24.248	0.22	- 0.043	- 21984
K⁺	a	3.41	0.0017	7.52	0.07	- 0.227	44460	- 0.293	- 0.160	0.133	16.252	0.52	6.162	12.386
	b	2.53	0.0023	5.59	0.09	- 0.227	48857	- 0.316	- 0.137	0.179	12.967	0.60	- 2.271	- 11.908
	c	2.57	0.0022	5.68	0.09	- 0.226	50085	- 0.314	- 0.138	0.176	18.301	0.22	0.361	- 15.779
Na⁺	a	3.10	0.0018	6.99	0.07	- 0.222	43426	- 0.293	- 0.150	0.143	16.485	0.58	1.447	12.551
	b	2.69	0.0023	5.81	0.08	- 0.231	46740	- 0.317	- 0.145	0.172	11.703	0.29	- 1.552	- 11.370
	c	2.82	0.0023	6.02	0.09	- 0.234	48057	- 0.317	- 0.151	0.166	16.346	0.32	0.820	- 15.743
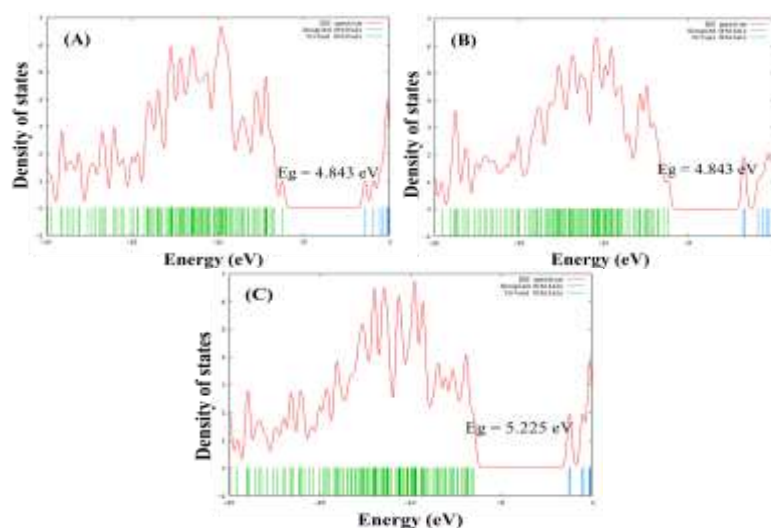
Figure 5. DOS plots of Docetaxel pristine isomers (A), (B) and (C)
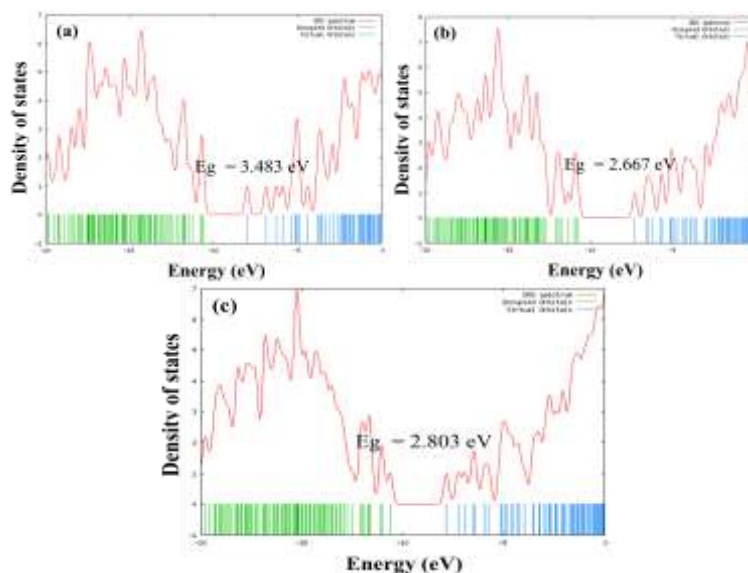

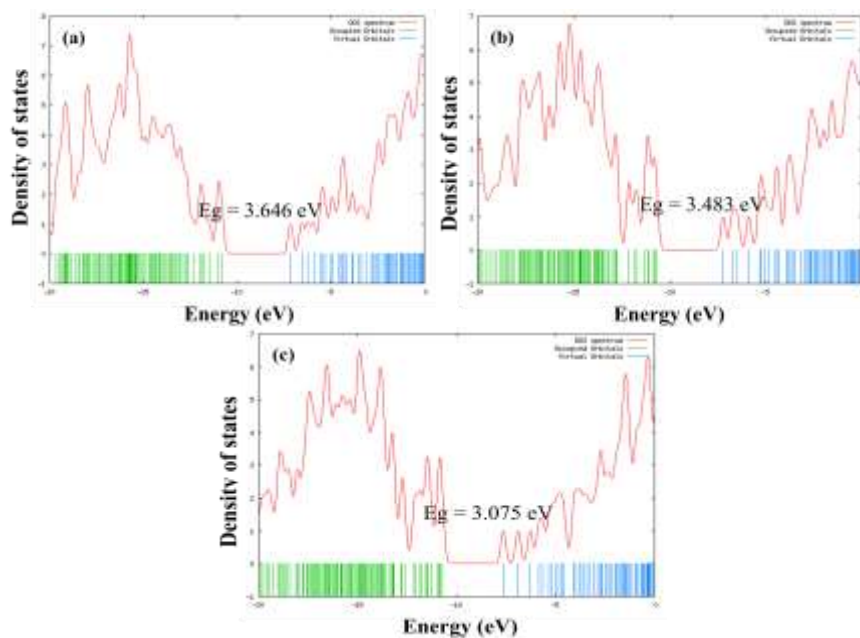**Figure 6**. DOS plots of Docetaxel isomer 1, complex with Ca²⁺ in **(a)**, **(b)** and **(c)** positions

Figure 7. DOS plots of Docetaxel isomer 2, complex with Ca^{2+} in **(a)**, **(b)** and **(c)** positions
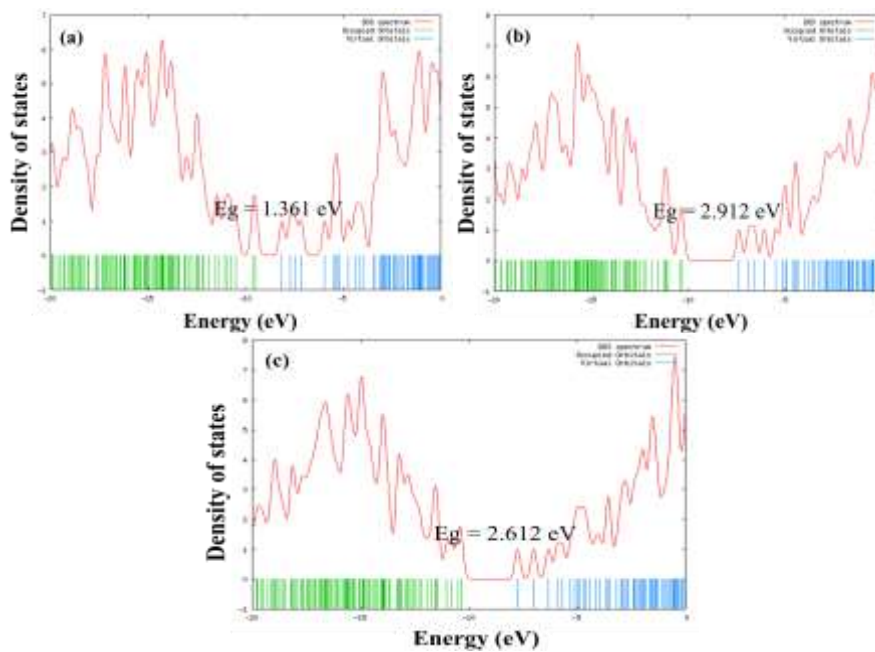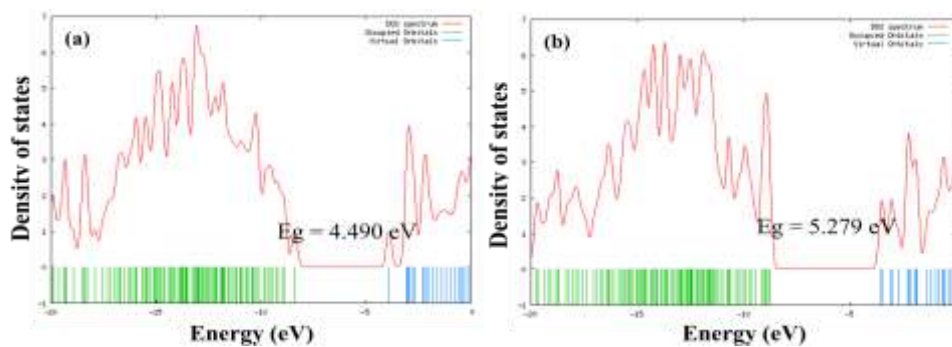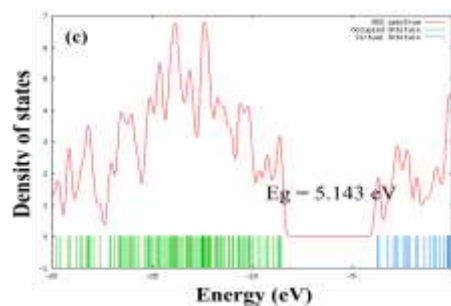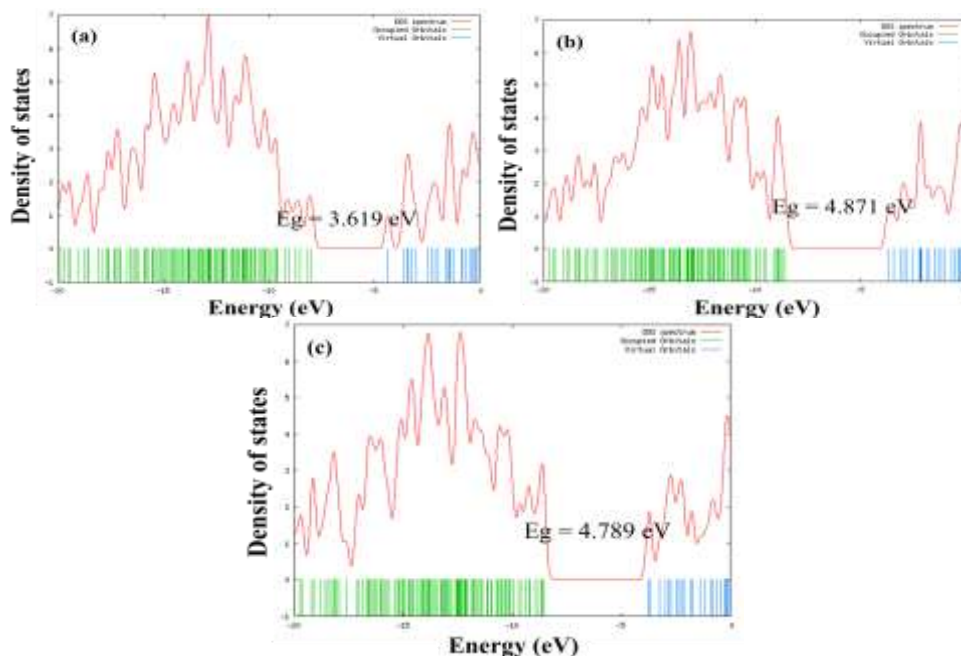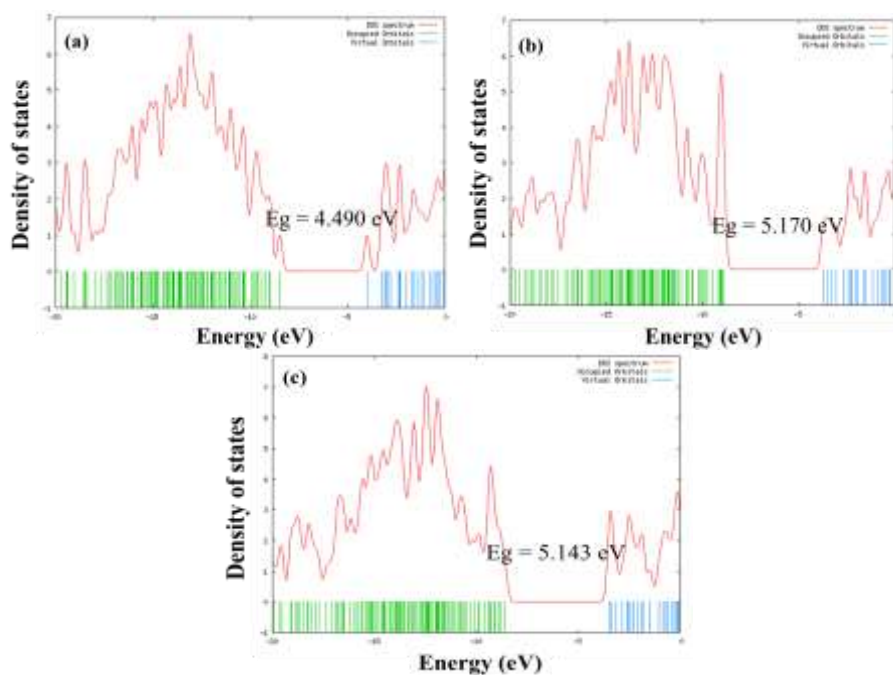

Figure 8. DOS plots of Docetaxel isomer 3, complex with Ca^{2+} in **(a)**, **(b)** and **(c)** positions
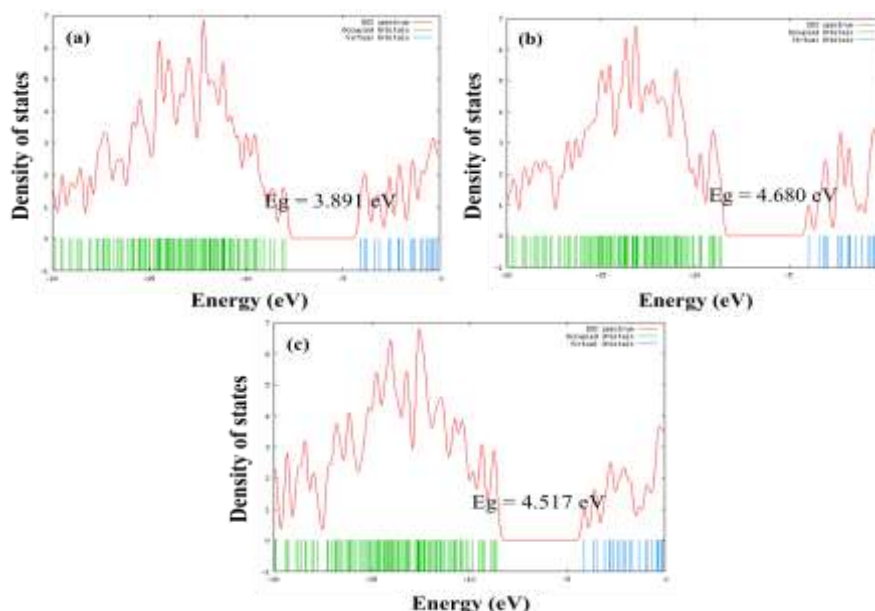
Figure 9. DOS plots of Docetaxel isomer 2, complex with K$^+$ in **(a)**, **(b)** and **(c)** positions

Figure 10. DOS plots of Docetaxel isomer 3, complex with K$^+$ in **(a)**, **(b)** and **(c)** positions

Figure 11. DOS plots of Docetaxel isomer 2, complex with Na$^+$ in **(a)**, **(b)** and **(c)** positions

**Figure 12**. DOS plots of Docetaxel isomer 3, complex with Na^+ in **(a)**, **(b)** and **(c)** positions

As seen in the above figures, the general shape of the graphs is very similar to each other; however, this is highly dependent on the type of ion and its position. Thus, gap energies of Docetaxel complexes with K^+ and Na^+ ions shown in Table 2 and Figures 9 to 12, are approximately close to each other and more or less are in the same range. Whereas, gap energies of Docetaxel complexes with Ca^{2+} ion shown in Table 2 and Figures 6 to 8, are different from the above mentioned gap energies. These differences, more probably, may be due to the difference of ions charges. In some cases, one or more points can be seen on the plots with zero density. When calcium ions approach isomer 3 from different positions, this event is more visible (Figure 4). Furthermore, the plots show that the maximum DOS of real orbitals, for complexes with Ca^{2+}, has a lower energy level compared to the other ones. This may be attributed to higher electric charge of Ca^{2+}.

According to the obtained data, different orders can be seen for the orbitals and energy levels. Based on these data, the energy order of Ca^{2+}-drug> Na^+-drug > K^+-drug for the studied orbitals and the energy order of Na^+-drug > K^+-drug > Ca^{2+}-drug for the difference between virtual and real energies were obtained for isomers 2 and 3.
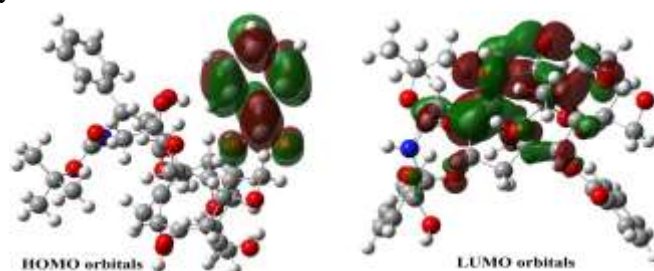
Figure 13. Distribution of HOMO and LUMO orbitals in Docetaxel drug
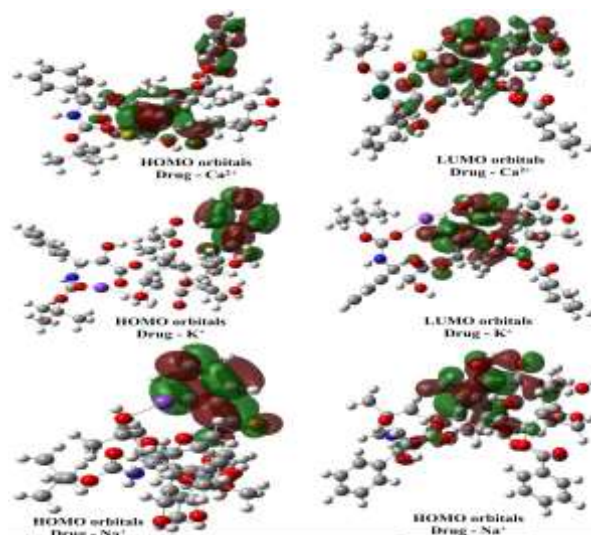
Figure 14. Distribution of HOMO and LUMO orbitals in Docetaxel drug – ion

The comparison of different positions of ions' approaching to the drug shows more and various energy orders. For example, the energy order of **a**> **c**≥ **b** for LUMO level, the energy order of **b**> **c** ≥ **a** for HOMO level and the energy order of b>**c**>**a** for the difference between virtual and real orbitals can be observed in isomer 2. Also, the energy order of c> **a** ≥ b for HOMO level, and the energy order of **b**>**c**>**a** can be seen in isomer 3 for the difference between the real and virtual levels. Nevertheless, all these energy orders can be attributed to the effect of the size and the charge of ions.

Distribution of HOMO and LUMO orbitals in Docetaxel and its complexes Ca^{2+}, Na^+, and K^+ ions are shown in Figures 13 and 14. As shown in these figures, the HOMO orbitals are localized around the C-C bonds, whereas the LUMO orbitals are more localized around the oxygen and nitrogen atoms of Docetaxel. This can be attributed to the presence of electrons in HOMO orbitals and the absence of electrons in the LUMO orbitals as electron donor and acceptor, respectively.

When the calcium ion approaches isomers 1 or 2 in position **a**, the metal-ligand binding energy (ΔE), ΔG and ΔH will achieve the most negative value. In the same position, the E_{HOMO} will also show the most negative value and the energy gap and hardness reaches to the maximum values. However, the binding energy (ΔE), ΔG and ΔH haven't any considerable difference for sodium and potassium ions in all three positions of isomer 2 (Table 1 and Figure 15). The obtained results reveal that the binding energy increases for Drug-Ca^{2+} comparing with Drug-K^+ and Drug-Na^+ (Table 1). The cause of these phenomena may be interpreted by the higher charge of Ca^{2+}.

The most negative values of E_{HOMO} and chemical potential (μ), and the maximum of bond gap, hardness (η) and electrophilicity (ω), for all cases, can be observed in position **b**. Considering isomer 3, the most negative values of E_{HOMO}, ΔE, ΔG, ΔH and the maximum of band gap and electrophilicity for all cations, can be seen in the position **b**. Furthermore, considering isomers 1 and 2 in the cases of K+ and Na+, position **a** has the maximum value of ΔN_{max} and S.

Eventually, from the obtained results, it can be concluded that the absolute values of ΔE, ΔG and ΔH have the order of Drug-K^+<Drug-Na^+<Drug-Ca^{2+}, and

the values of E_{HOMO}, E_{LUMO}, η, μ, ΔN_{max} and S have the order of $K^+ \approx Na^+ < Ca^{2+}$.

The effect of K^+, Na^+ and Ca^{2+} ions on the variation ΔE, ΔG, ΔH and S of three Docetaxel isomers in the a, b, and c positions has shown in Figure 15.
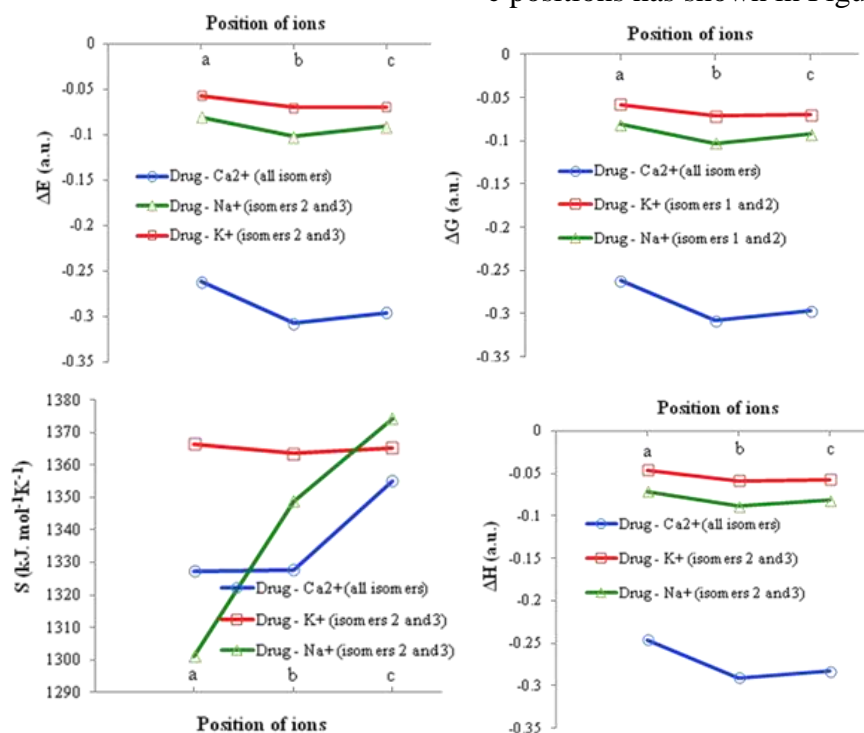
Figure 15. The variation of average values of ΔE, ΔG, ΔH and S in **a**, **b**, and **c** positions of three Docetaxel isomers

As shown in Figure 15, the variation of ΔE, ΔG and ΔH are approximately identical and any significant difference haven't been observed. But the variation of Entropy S for Drug-Na^+ complex is different from the two other complexes. It means that the interaction of Na^+ follows the order of **c>b>a**. This phenomenon may be more probably, related to size of Na^+ and electron donor potential of these positions.

Finally, the changes in the number and type of hydrogen bonds in different structures of Docetaxel isomers and their complexes with cations have investigated using ChemCraft software. The results are shown in Table 3.

Hydrogen bonds are very important in terms of their effect on the structure and physicochemical properties of Docetaxel drug. Before comparing the positions and ions in various isomers, it is necessary to study Table 3. The process of change in the number of hydrogen bonds in different orders is not entirely regular and does not follow a simple pattern. The highest number of hydrogen bonds has been observed in isomer 3, especially when K+ and Na+ approach the drug. Except for the position **a** for both potassium and sodium ions, in other conditions, three hydrogen bonds are not observed on an oxygen.

Table 3. The number and type of hydrogen bonds in different structures of Docetaxel isomers and their complexes

Docetaxel isomer I	Cation	Position	Total number of H bonds	2 H bonds on one H	2 H bonds on one O	3 H bonds on one O

		Pristine	11	1	3	0
	Ca^{2+}	a	9	1	1	0
		b	11	0	1	0
		c	12	0	3	0
		Pristine	12	0	2	0
	Ca^{2+}	a	11	1	2	0
		b	10	0	1	0
		c	10	0	1	0
Docetaxel isomer II	K^{+}	a	10	1	1	1
		b	10	0	2	0
		c	8	0	1	0
	Na^{+}	a	11	1	1	1
		b	10	0	2	0
		c	8	0	1	0
		Pristine	13	2	2	0
	Ca^{2+}	a	12	1	4	0
		b	11	1	2	0
		c	11	1	2	0
Docetaxel isomer III	K^{+}	a	15	2	3	1
		b	11	1	3	0
		c	14	2	1	0
	Na^{+}	a	14	2	2	1
		b	12	1	2	0
		c	14	2	1	0

As seen in Table 3, the total number of H bonds in isomer III of Docetaxel drug and its complexes with cations increased comparing to the two other isomers. Certainly, this increase in H bonds will affect the behavior of physicochemical properties that shown in Tables 1 and 2.

The calculations show that most of the hydrogen bonds (H---O) have an electrical charge of more than 0.4, and those bonded to oxygen having a sp3 hybridation have an electrical charge of more than 0.5. There are 9 similar hydrogen bonds between isomers 1 and 2; isomers 2 and 3 also have also 9 similar hydrogen bonds.

Conclusion

Approaching the ions to Docetaxel drug have been caused different events like changing angles between bonds, bond lengths, shape and orbital energy levels and other physicochemical characteristics. When an ion is approached to each isomer from position a, makes Ph2 to approach towards ring IV and creates deformations in the rings III and IV.

Approaching of the ions from position **b** (the upper part of ring II) will place them in the position between rings I, II and substituted nitrogen. In position **c**, the position related to nitrogen, the ions enter from outside of molecule towards nitrogen and are placed between ring I and the first part of substituted nitrogen. Approaching the ion from position **b** shows the greatest effect on the ring II, and hence changes in hydrogen bonds in this position are more limited than position **a**.

Approaching the ions to Docetaxel drug causes different events like changing angles between bonds, bond lengths, shape and orbital energy levels and other physicochemical characteristics. DOS graphs have been plotted to obtain some quantum chemical data. The results have been shown show that the HOMO orbitals, are localized around the C-C bonds, whereas the LUMO orbitals are more localized around the oxygen and nitrogen atoms of Docetaxel.

The obtained results show that the absolute values of ΔE, ΔG and ΔH have the order of Drug-K^{+}<Drug-Na^{+}<Drug-Ca^{2+}, and the values of E_{HOMO}, E_{LUMO}, η, μ, ΔN_{max} and S have had the order of K$^{+}\approx$ Na^{+}<Ca^{2+}.

Overall, Ca^{2+}, Na$^+$, and K$^+$ ions approach from different positions towards Docetaxel drug and create the different complexes. The investigations show that the interactions of ions have significant effects on thermodynamical and physicochemical properties of Docetaxel drug.

Acknowledgments

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