Prediction of the structural and spectral properties for *L,L*-ethylenedicysteine diethylester (EC) and its complex with Technetium-99m radionuclide

Mehdi Nabati*

Synthesis and Molecular Simulation Laboratory, Chemistry Department, Pars Isotope Company, P.O. Box: 1437663181, Tehran, Iran

ABSTRACT

The technetium-99m complex of the *L,L*-ethylenedicysteine diethylester (EC), of the brain imaging agent, was reported as a good choice for replacement of the renal nuclear medicines like OIH radiopharmaceutical. This present research work studies the structural, electronic and spectral properties of the EC compound and its complex with technetium-99m radionuclide from theoretical insight. All computations were done by Gaussian 03 package at B3LYP/6-31+G(d,p) level of theory. The frontier molecular orbital (FMO) computations show the stability of ^{99m}Tc-EC structure is lower than the EC molecule. In contrast, the highest reactivity is related to the ^{99m}Tc-EC complex. From the nuclear magnetic resonance (NMR) calculations, the comparison between chemical shifts of carbon atoms of ^{99m}Tc-EC to EC molecule shows the carbon atoms of technetium-99m-EC complex are more shielded. Also, the natural bond orbital (NBO) analysis shows more d orbitals of technetium atom and more p orbitals of sulfur, nitrogen and oxygen atoms are used for Tc-S, Tc-N and Tc-O molecular orbital hybrids.

Keywords: ^{99m}Tc-ethylenedicysteine; Density functional theory; Nuclear medicine; Radiopharmaceutical; Reactivity; Structural properties

INTRODUCTION

Radionuclide imaging techniques (single photon emission computed tomography [SPECT] and positron emission tomography [PET]) are used to monitor the concentration and location of radionuclide labeled molecules [1, 2]. Among all radionuclides, technetium-99m has been preferred to label nuclear medicines because of inexpensive isotope cost and favorable low energy (140 KeV versus 511 KeV for ^{18}F) [3]. In last years, several ^{99m}Tc labeled renal radiopharmaceuticals have been prepared and developed as potential alternatives to ^{131}I or ^{123}I orthoiodohippurate (OIH) nuclear medicine because of its undesirable physical properties [4]. In 1990, it was investigated the polar metabolite, ^{99m}Tc-*L,L*-ethylenedicysteine diethylester, of the brain imaging agent, was rapidly and efficiently excreted into the urine in mice [5]. This observation led them to pursue the evaluation of ^{99m}Tc-EC as a good renal nuclear medicine. To date, technetium 99m-ethylenedicysteine (EC) is the most successful radiopharmaceutical [6]. It is a successful example of a stable N2S2 chelate. Using a standard coupling method,

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*Corresponding author: mnabati@ymail.com

^{99m}Tc-EC-medicine conjugates have been developed to characterize tumors [5, 6]. ^{99m}Tc-EC has been extensively investigated and reported as a good choice for replacement of ^{131}I-orthoiodohippurate renal nuclear medicine. ^{99m}Tc-EC imaging agent provides a direct measurement of effective renal plasma flow [7].

Although the preparation and diagnostic activity of ^{99m}Tc-EC nuclear compound as a renal imaging agent were appeared several years ago, but the relationship between its chemical structure and activity still comes across serious difficulties. Moreover, it was understood that the chemical structure of [99m]Tc-*L*,*L*-ethylenedicysteine diethylester compound and its physical and chemical properties has significant influence on its both therapeutic and diagnostic activities [5-7]. Modern theoretical chemistry techniques, especially density functional theory (DFT) method, have been proven to be excellent tools for determining molecular structures [8-16]. The *L*,*L*-ethylenedicysteine diethylester (EC) compound is synthesized and its kit formulation is performed in Pars Isotope Company. In the present research work, the structural and spectral properties of this radiopharmaceutical are studied by the density functional theory (DFT) method.

COMPUTATIONAL METHOD
The geometry optimizations and single point calculations of the compounds in gas phase have been carried out using the density functional theory (DFT) method [17] with Becke, 3-parameter, Lee-Yang-Parr (B3LYP) exchange correlation corrected functional [18] and the 6-31+G(d,p) basis set using the GAUSSIAN 03 program [19]. The B3LYP/Lanl2DZ computational method was used to optimization of the technetium radionuclide. The imaginary frequencies were not shown in frequency computation analysis of the optimized molecules. The energies of the molecules were computed with a self-consistent field (SCF) convergence of 10^{-8} a.u. for the density matrix.

RESULTS AND DISCUSSION
In this research work, I have presented the results of theoretical studying the *L*,*L*-ethylenedicysteine diethylester compound and its labeled structure with technetium-99m radionuclide. The studied structures are given in Scheme 1. All considered compounds are presented in the Table 1. DFT calculations were performed to shed light on how the technetium radionuclide influences the structural and spectral properties of the EC compound.
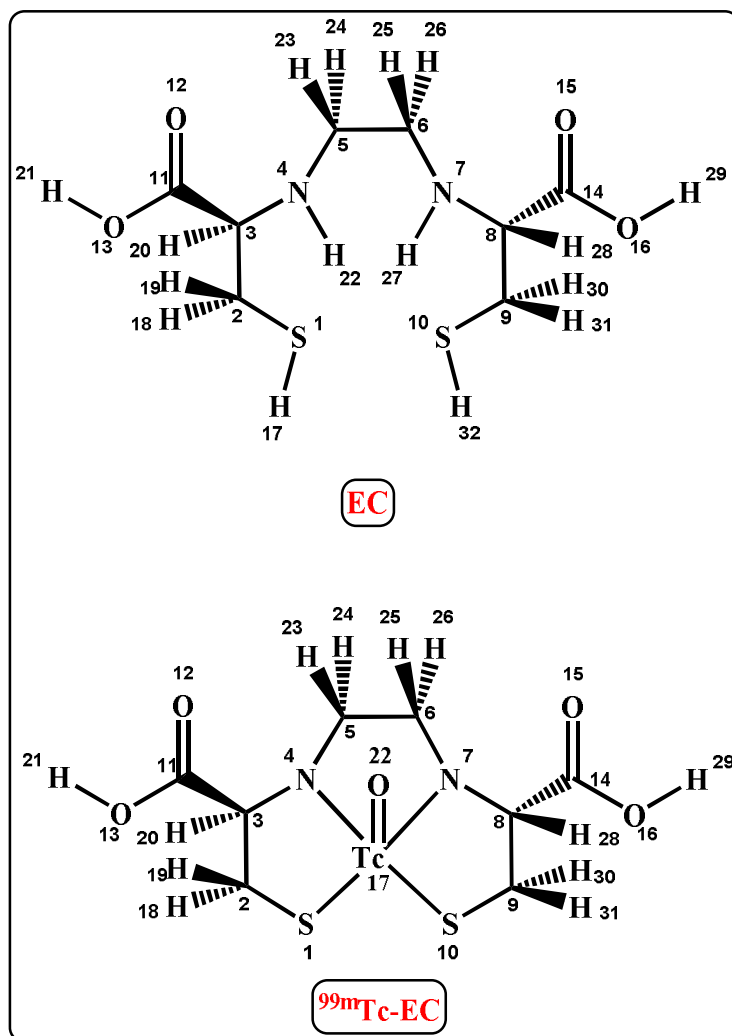
OPTIMIZED STRUCTURES
Table 1 indicates the bond lengths data of the optimized structures (Figure 1) of the studied molecules. From the data, we see the C-C bond lengths are not different from together in EC and ^{99m}Tc-EC structures, but the S-C and N-C bond lengths in EC structure are longer than same bonds in EC-99m-technetium structure. Also, it can be seen from the data that the C-O and C=O bonds in EC structure are smaller than the ^{99m}Tc-EC structure. Technetium-connected bonds length order in technetium-99m labeled structure of EC compound is Tc-S (single bond) > Tc-N (single bond) > Tc-O (double bond).

From the data of the Table 2, the C-N bonds of ^{99m}Tc-EC structure are stronger than EC structure, but the strongest C-C and C-S bonds are belonged to the EC compound. Also, the C=O bond order of carboxylic acid groups of EC structure (B.O. = 1.78) is more than technetium-99m-EC nuclear medicine (B.O. = 1.73). Adversely, the C-C, C-O and O-H bond

orders of COOH functional groups are 0.93, 1.04 and 0.70 for EC and 0.94, 1.05 and 0.71 for ^{99m}Tc-EC structure.

Natural bond orbital (NBO) population analysis describes the role of intermolecular orbital interaction in the chemical molecules, particularly charge transfer. This is performed by considering all possible interactions between filled donor and empty acceptor natural bond orbitals and estimating their energetic importance by second-order perturbation theory[20-25]. Table 3 shows the resulting natural bond orbitals population analysis

for ^{99m}Tc-EC structure. It can be seen from the data that the technetium atom participates about twenty percent in construction of Tc-S, Tc-N and Tc-O sigma bonds. In these bonds, more d orbitals of technetium atom and more p orbitals of sulfur, nitrogen and oxygen atoms are used for molecular orbital hybrids. The reason for more content of d orbital of technetium atom in spd hybrids of mentioned bonds is the high bond length of Tc-X sigma bonds (about 2 Angstrom). The electron occupancy order for these three sigma bonds is Tc-O > Tc-S = Tc-N.

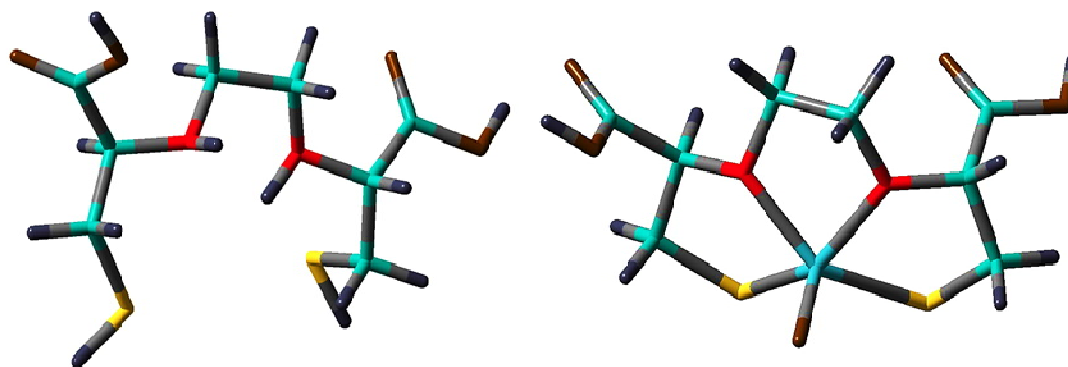**Scheme 1.** The studied structures with atomic numbering.

Fig. 1. The optimized structures of the studied molecules.

Table 1. The bond lengths of the studied structures

Bonds	EC	EC-^{99m}Tc
S1-C2	1.848	1.840
C2-C3	1.539	1.536
C3-N4	1.452	1.452
N4-C5	1.469	1.463
C5-C6	1.527	1.527
C6-N7	1.461	1.458
N7-C8	1.448	1.439
C8-C9	1.537	1.536
C9-S10	1.852	1.846
N4-H22	1.018	-
N7-H27	1.018	-
S1-H17	1.349	-
S10-H32	1.349	-
N4-Tc17	-	2.009
N7-Tc17	-	1.982
S1-Tc17	-	2.383
S10-Tc17	-	2.383
O22-Tc17	-	1.697
C3-C11	1.538	1.531
C11-O12	1.212	1.220
C11-O13	1.358	1.358
O13-H21	0.973	0.972
C8-C14	1.533	1.544
C14-O15	1.209	1.211
C14-O16	1.360	1.372
O16-H29	0.972	0.972

Table 2. The bond orders (B.O.) of the studied structures

Bonds	EC	EC-^{99m}Tc
S1-C2	1.003	0.989
C2-C3	0.992	0.986
C3-N4	1.002	1.003
N4-C5	0.976	0.992
C5-C6	1.014	1.006
C6-N7	0.986	0.988
N7-C8	1.007	1.015
C8-C9	1.000	0.993
C9-S10	1.006	0.991
N4-H22	0.798	-
N7-H27	0.786	-
S1-H17	0.961	-
S10-H32	0.965	-
N4-Tc17	-	0.697
N7-Tc17	-	0.709
S1-Tc17	-	0.709
S10-Tc17	-	0.714
O22-Tc17	-	1.617
C3-C11	0.932	0.944
C11-O12	1.776	1.727
C11-O13	1.041	1.046
O13-H21	0.694	0.712
C8-C14	0.942	0.933
C14-O15	1.781	1.771
C14-O16	1.037	1.009
O16-H29	0.696	0.708

Table 3. The natural bond orbitals (NBOs) population analysis of the studied structures

Bonds	Occupancy	Population/Bond orbital/Hybrids
σ(S1-Tc17)	1.78908	77.63% S1 ($sp^{6.32}d^{0.01}$), 22.37% Tc17 ($sp^{0.45}d^{2.34}$)
σ(N4-Tc17)	1.78050	81.77% N4 ($sp^{3.96}$), 18.23% Tc17 ($sp^{0.50}d^{4.09}$)
σ(N7-Tc17)	1.80426	82.03% N8 ($sp^{2.61}$), 17.97% Tc17 ($sp^{0.46}d^{3.05}$)
σ(S10-Tc17)	1.80285	76.52% S10 ($sp^{6.32}d^{0.01}$), 23.48% Tc17 ($sp^{0.28}d^{2.21}$)
σ(Tc17-O22)	1.87499	25.81% Tc17 ($sp^{0.64}d^{13.02}$), 74.19% O22 ($sp^{10.01}d^{0.02}$)
π_1(Tc17-O22)	1.77025	15.20% Tc17 ($sp^{47.84}d^{99.99}$), 84.80% O22 ($sp^{99.99}d^{0.18}$)
π_2(Tc17-O22)	1.82746	20.07% Tc17 ($sp^{1.05}d^{15.22}$), 79.93% O22 ($sp^{10.08}d^{0.02}$)
σ(S1-C2)	1.97790	44.22% S1 ($sp^{6.07}d^{0.04}$), 55.78% C2 ($sp^{3.57}$)
σ(N4-C3)	1.98106	58.32% N4 ($sp^{2.14}$), 41.68% C3 ($sp^{2.98}$)
σ(N4-C5)	1.98364	59.73% N4 ($sp^{2.27}$), 40.27% C5 ($sp^{3.19}d^{0.01}$)
σ(C2-C3)	1.96645	48.62% C2 ($sp^{2.63}$), 51.38% C3 ($sp^{2.75}$)
σ(S10-C9)	1.98311	44.38% S10 ($sp^{6.13}d^{0.04}$), 55.62% C9 ($sp^{3.60}$)
σ(N7-C6)	1.98596	60.03% N7 ($sp^{2.02}$), 39.97% C6 ($sp^{3.24}d^{0.01}$)
σ(N7-C8)	1.98535	58.60% N7 ($sp^{1.87}$), 41.40% C8 ($sp^{2.94}$)
σ(C8-C9)	1.97285	51.72% C8 ($sp^{2.62}$), 48.28% C9 ($sp^{2.65}$)
σ(C5-C6)	1.98300	49.99% C5 ($sp^{2.64}$), 50.01% C6 ($sp^{2.64}$)

REACTIVITY AND STABILITY

In organic chemistry, frontier molecular orbitals (FMOs) give us more information about molecular structures and their reactivity and stability [26-28]. Figure 2 shows the frontier molecular orbitals (HOMO and LUMO) for EC compound and its complex with technetium-99m radionuclide. The HOMO and LUMO energies for EC molecule is -6.35 and -0.86 eV, respectively. Also, these FMOs in technetium-99m-EC complex indicate -2.11 and +1.93 eV, respectively. From these energies data, the HOMO/LUMO energies gap for EC and ^{99m}Tc-EC structures is 5.49 and 4.04 eV, respectively. So, the stability of ^{99m}Tc-EC structure is lower than the EC molecule. In contrast, the highest reactivity is related to the ^{99m}Tc-EC complex. From the density of states (DOS) graphs (Figure 3), we can see that the more HOMOs are participated in ^{99m}Tc-EC complex to the EC compound. This proves the more reactivity of the technetium-99m-EC complex.

Figure 4 shows the molecular electrostatic potential (MEP) graphs of the studied molecules. The blue and red loops indicate positive and negative potentials, respectively. The carboxylic acid functional groups of EC compound have more electrons than other segments of molecule because of their electronegative property. In contrast, all segments of 99mTc-EC complex show red color, but the Tc=O bond has more electron than other segments. So, we can simply see the more reactivity of technetium-99m-Tc complex compound by the MEP graph.

SPECTRAL STUDIES

In chemistry, the identification of chemical molecules is done by spectroscopy methods [29-31]. Here, the various spectral properties of the studied molecules are investigated and discussed.

Circular dichroism (CD) is dichroism involving circularly polarized such as the differential absorption of left- and right-handed light [32]. The Circular dichroism spectra of the studied molecules are shown in Figure 5. The CD spectra indicate that the carbon centers connected to the –COOH functional groups in EC compound show the left-handed property in dealing with the polarized light. The interaction of

these carbon centers with the polarized light is happened at wavelength 254.9996 nm with energy 39215.754 cm^{-1} and R (length) 14.0865. The absorption of left-handed light is done by carbon centers connected to the –COOH functional groups in technetium-99m-EC complex at wavelength 388.5407 nm with energy 25737.3296 cm^{-1} and R (length) 47.0818. The nitrogen atoms of ^{99m}Tc-EC complex are rigid and absorb the right-handed polarized light at wavelengths 431.9375 (with energy 23151.4982 cm^{-1} and R (length) -26.2145) and 432.1935 nm (with energy 23137.7867 cm^{-1} and R (length) -49.3805).

EC (HOMO)

EC (LUMO)

^{99m}Tc-EC (HOMO)

^{99m}Tc-EC (LUMO)
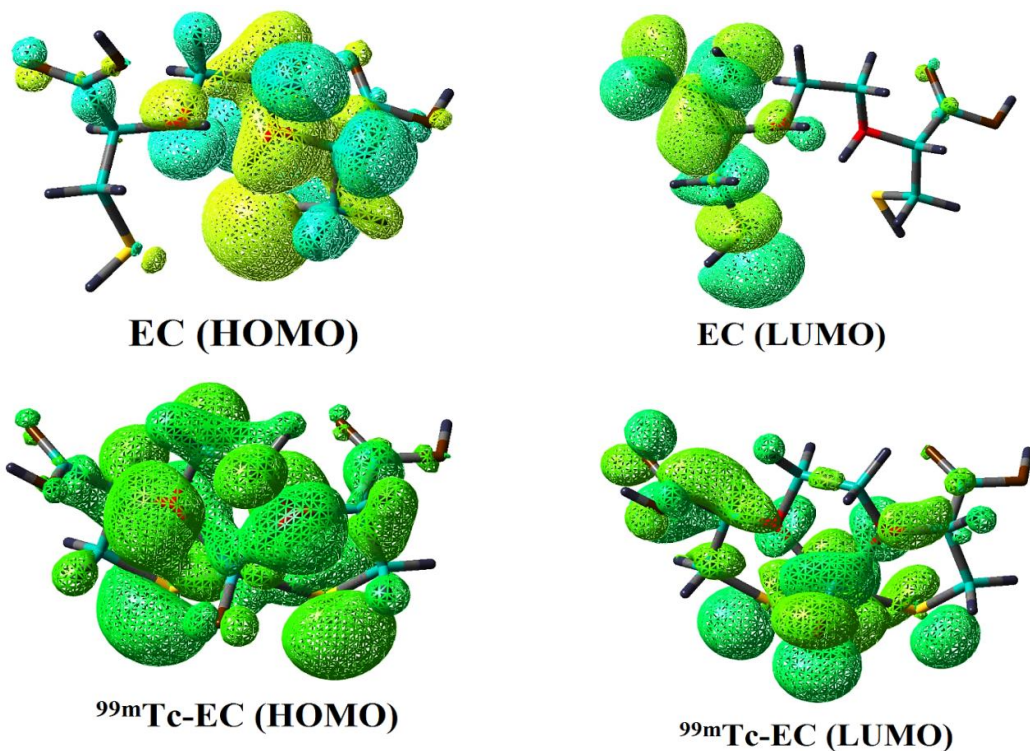
Fig. 2. The frontier molecular orbitals of the studied molecules.
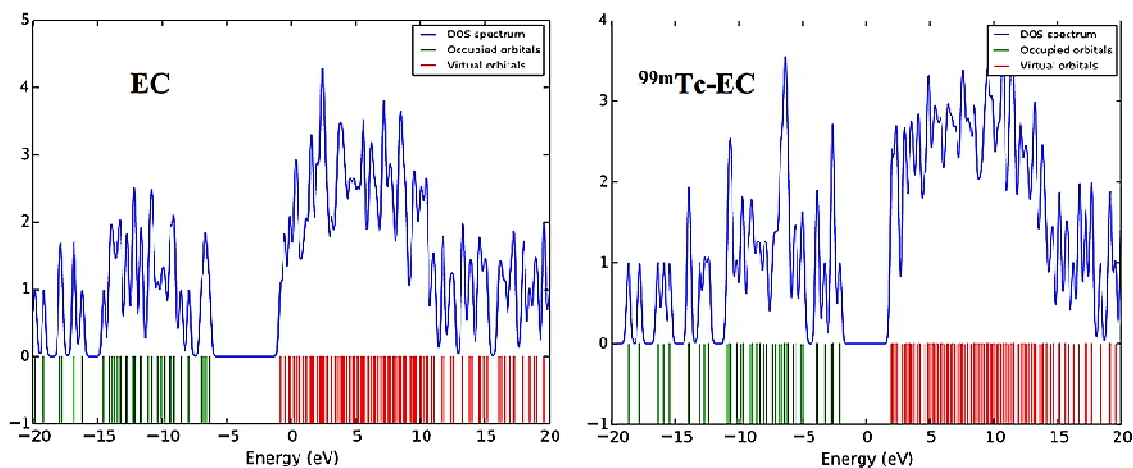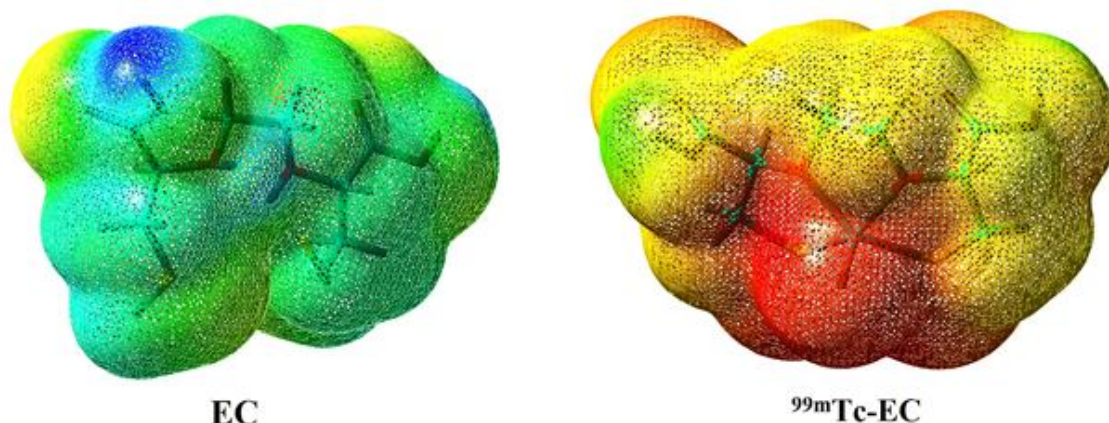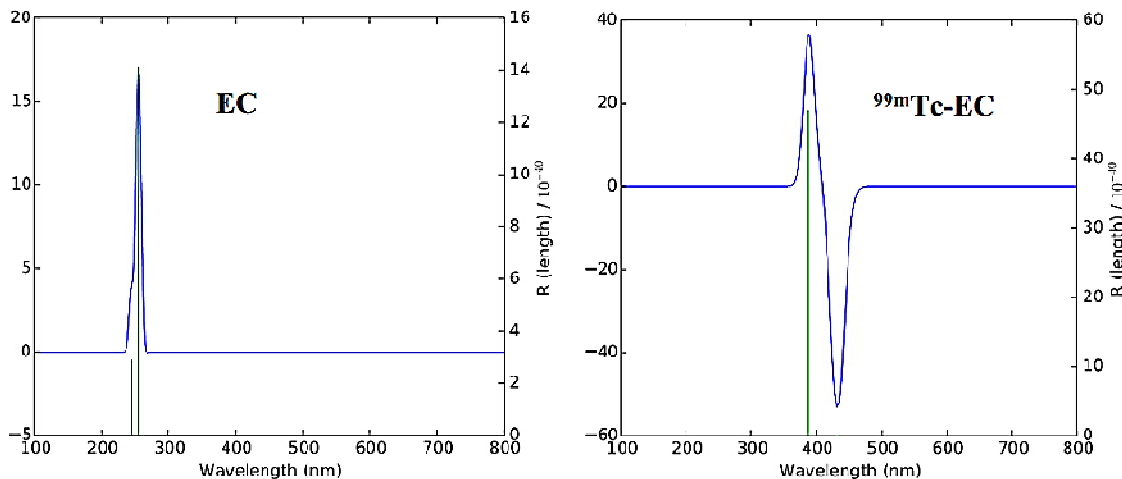

Fig. 3. The density of states (DOS) graphs of the studied molecules.

Fig. 4. The molecular electrostatic potential (MEP) graphs of the studied molecules.

Fig. 5. The CD spectra of the studied molecules.

The UV-Vis spectra of the studied molecules are indicated in Figure 6. In the UV-Vis spectrum of EC compound, the peaks at wavelengths 244.876, 254.999 and 261.640 nm with energies 40836.939, 39215.754 and 38220.459 cm^{-1} are related to the (HOMO→LUMO (40%), HOMO-2→LUMO (41%), HOMO-1→LUMO (4%) and HOMO→LUMO+1 (5%)), (HOMO→LUMO+1 (75%), HOMO-2→LUMO (3%), HOMO-1→LUMO (2%), HOMO→LUMO (2%) and HOMO→LUMO+2 (8%)) and (HOMO-3→LUMO (15%), HOMO-2→LUMO (17%), HOMO-1→LUMO (20%), HOMO→LUMO (40%) and HOMO-5→LUMO (2%)) transitions, respectively. In contrast, the electronic transitions of ^{99m}Tc-EC complex are happened at high wavelengths and low energies. The transitions (HOMO-2→LUMO (15%), HOMO→LUMO (65%), HOMO-3→LUMO (4%) and HOMO-1→LUMO (3%)), (HOMO-2→LUMO (28%), HOMO-1→LUMO (23%), HOMO→LUMO (21%), HOMO-2→LUMO+1 (4%) and HOMO-1→LUMO+1 (3%)) and (HOMO-

2→LUMO+1 (31%), HOMO-1→LUMO+1 (27%), HOMO→LUMO+1 (15%), HOMO-3→LUMO+1 (5%), HOMO-2→LUMO (3%) and HOMO-1→LUMO (5%)) take place at wavelengths 388.541, 431.937 and 432.193 nm with energies 25737.330, 23151.498 and 23137.787 cm^{-1}, respectively.

Figure 7 indicates the IR spectrum of the studied molecules. EC compound: IR [Harmonic frequencies (cm^{-1}), intensities (KM/Mole)]: 19.5465 (0.5698), 23.8772 (0.0631), 26.1998 (0.3497), 38.1673 (2.9445), 58.4883 (0.0495), 66.5062 (0.6668), 82.7025 (2.8216), 101.3611 (3.6974), 107.9383 (0.8370), 113.7209 (0.4087), 158.9812 (3.2123), 173.2771 (17.0914), 189.0493 (16.2812), 199.4765 (7.2790), 228.5890 (0.9851), 252.9751 (0.7837), 274.9494 (0.9398), 287.2346 (0.6649), 304.5606 (0.7639), 343.7736 (0.6832), 403.9636 (3.3625), 452.8206 (9.6937), 485.2098 (4.6105), 534.3203 (8.9924), 570.1424 (25.3316), 584.4213 (44.4079), 599.7066 (69.8478), 614.4000 (84.4045), 620.3777 (15.7822), 681.5393 (3.6578), 695.1584 (51.0492), 722.4545 (84.9249), 740.3206 (62.3954), 770.2656 (28.1643), 796.2198 (13.3283), 829.8306 (15.7025), 845.3313 (19.7333), 877.5720 (10.8663), 898.7478 (17.0379), 928.3772 (20.1992), 930.7621 (4.2405), 970.2777 (7.5521), 981.1827 (5.2965), 1018.7177 (3.7115), 1040.2926 (8.6225), 1081.9950 (7.0666), 1109.0141 (70.8761), 1121.6811 (36.8804), 1140.6335 (351.0011), 1160.3434 (31.5249), 1161.3723 (190.3365), 1176.6216 (24.0730), 1203.0480 (12.3758), 1241.1723 (4.3304), 1259.7865 (22.4362), 1265.6947 (11.3810), 1283.9357 (5.4251), 1300.4624 (14.8277), 1310.3639 (8.1920), 1330.5581 (24.4640), 1334.2158 (49.3094), 1345.0962 (23.8581), 1357.8075 (15.9301), 1391.0192 (0.1187), 1399.2323 (6.2262), 1412.3563 (2.9517), 1480.6607

(28.8794), 1483.5318 (19.1250), 1502.5502 (0.4740), 1510.2115 (20.4279), 1525.0079 (61.6248), 1528.4715 (10.9787), 1813.8929 (318.1083), 1829.7757 (261.9656), 2678.4418 (18.1484), 2679.5416 (23.1530), 2885.3040 (53.4383), 2899.2572 (105.2571), 2985.9536 (71.1016), 3067.3001 (15.0267), 3074.4052 (20.3057), 3084.4854 (13.4616), 3094.6942 (5.6341), 3111.4197 (11.0553), 3138.5554 (4.0737), 3157.1731 (2.5583), 3520.2597 (22.7031), 3521.3439 (13.9894), 3750.9818 (80.4570), and 3760.6289 (79.7792).

Technetium-99m-EC complex: IR [Harmonic frequencies (cm^{-1}), intensities (KM/Mole)]: 33.0255 (0.5375), 43.1882 (0.8017), 45.0956 (1.3629), 55.5627 (0.6947), 92.2873 (1.0014), 105.2596 (1.6724), 120.8338 (1.4838), 145.2760 (1.0330), 157.1708 (1.5909), 190.7648 (1.3505), 195.0099 (1.3021), 217.0753 (1.3885), 236.1832 (1.1531), 260.9935 (3.0470), 286.5366 (7.5590), 289.4750 (0.9017), 298.9065 (3.7956), 320.9685 (4.1056), 345.9309 (7.7376), 352.9864 (17.8836), 373.3584 (35.0350), 377.1138 (6.5681), 404.8036 (34.2216), 485.8356 (6.3874), 516.2202 (4.5454), 544.1973 (11.3641), 580.7238 (25.0776), 598.6675 (79.0016), 612.6199 (33.5267), 626.3047 (52.8941), 634.4831 (12.1394), 651.3336 (50.2681), 683.3335 (4.7591), 710.1946 (35.6880), 736.3522 (43.2685), 788.2417 (9.9447), 809.8022 (23.6295), 847.2438 (27.0664), 887.2411 (13.8418), 919.8543 (12.9679), 944.4382 (6.1206), 969.4730 (73.9608), 973.9682 (192.6937), 1008.4297 (6.6623), 1022.3464 (3.2803), 1075.2176 (71.1848), 1081.3326 (178.0167), 1101.6403 (5.2088), 1114.3190 (280.4612), 1148.8282 (51.2413), 1166.3807 (182.7832), 1179.8025 (14.3193), 1197.6537 (36.9000), 1216.8931 (18.2210), 1231.4759 (3.4077), 1249.4344 (6.7695),

1254.5497 (14.2398), 1284.5901 (6.0976), 1292.3356 (22.0167), 1306.0539 (15.3409), 1320.8026 (3.2697), 1341.5768 (52.9005), 1349.8905 (0.3502), 1351.4236 (28.4353), 1370.7464 (1.4649), 1398.4071 (18.7265), 1477.1038 (1.5537), 1479.1586 (3.6055), 1491.4978 (0.2724), 1503.1832 (4.3073), 1772.2037 (398.6407), 1811.5243 (200.1037), 2915.2350 (78.6917), 2942.3446 (65.4707), 2943.7175 (98.5920), 2953.8111 (88.5072), 2975.2719 (134.5202), 3029.4862 (74.5300), 3052.3582 (47.0893), 3061.4805 (55.4334), 3106.0666 (14.5688), 3122.3194 (11.8124), 3752.8764 (29.2401), and 3753.8233 (39.8245).

The NMR technique is a good method for identification of the structure of the organic compounds [33]. The ^{1}H and ^{13}C chemical shifts of the studied molecules are listed in Table 4. The theoretical chemical shifts data is compared to the experimental values. The Figures 8 and 9 indicate the comparison between the theoretical and experimental ^{1}H and ^{13}C
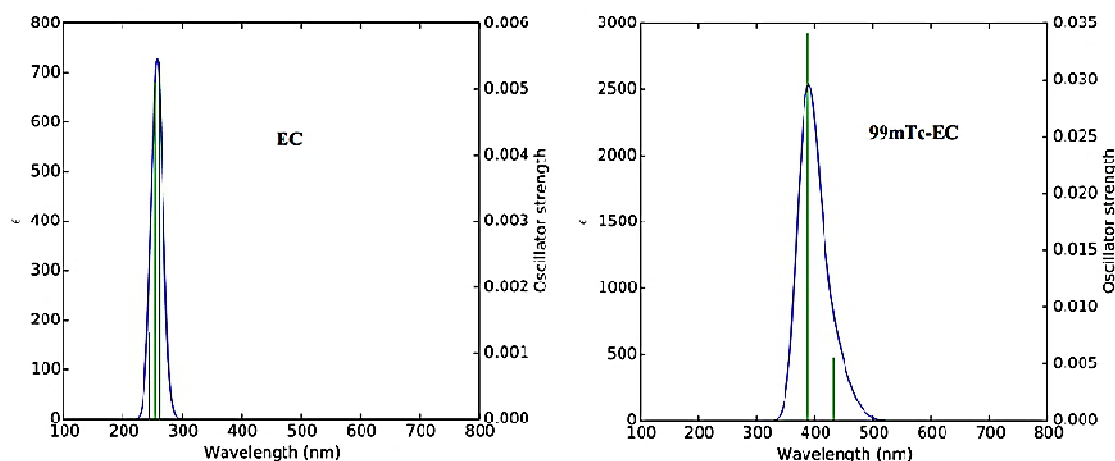

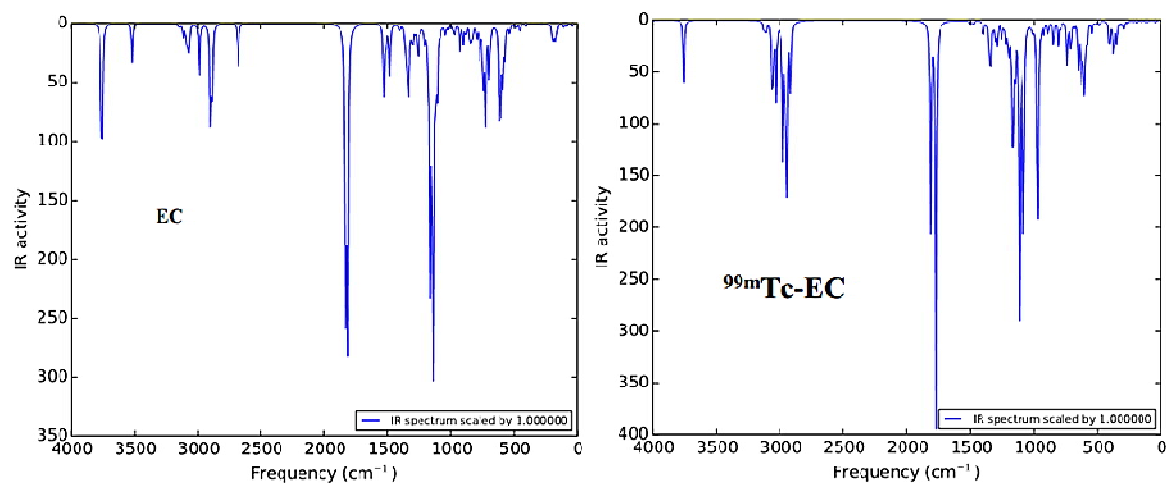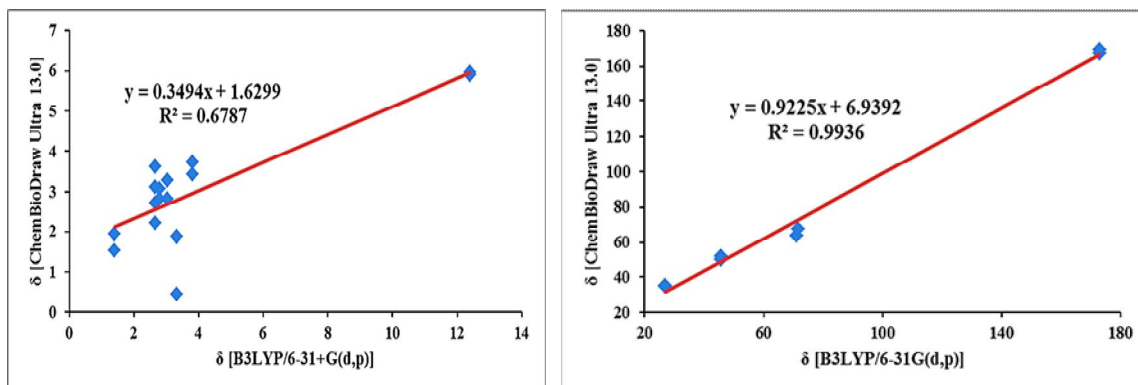**Fig. 6.** The UV-Vis spectra of the studied molecules.

Fig. 7. The IR spectra of the studied molecules.

chemical shifts of the molecular structures at studied computational method. The correlation coefficients 0.68 and 0.77 for hydrogen nucleus of EC compound and ^{99m}Tc-EC complex, respectively, show the the computational method can't simulate the chemical shifts of hydrogen atoms. In contrast, the large correlation coefficients (0.99 and 1 for carbon nucleus of EC compound and ^{99m}Tc-EC complex, respectively) show the accuracy of the computations for prediction of carbon atoms. From the data of the Table 4, the comparison between chemical shifts of carbon atoms of ^{99m}Tc-EC to EC molecule shows the carbon atoms of technetium-99m-EC complex are more shielded. It is happened because of the labeling of EC structure with technetium-99m radionuclide.

Table 4. The ^{1}H-NMR and ^{13}C-NMR chemical shifts data of the studied structures

Nucleus	Chemical Shift (ppm)			
	EC		^{99m}Tc-EC	
	Theoretical chemical shifts ($\delta = \delta_{TMS} - \delta'$)	δ (Chemical shifts from ChemBioDraw Ultra 13.0)	Theoretical chemical shifts ($\delta = \delta_{TMS} - \delta'$)	δ (Chemical shifts from ChemBioDraw Ultra 13.0)
H-17	1.551	1.400	-	-
H-18	3.078	2.790	3.450	2.790
H-19	3.278	3.040	3.371	3.040
H-20	3.727	3.810	4.468	3.770
H-21	5.953	12.390	5.229	12.390
H-22	1.885	3.320	-	-
H-23	3.617	2.670	3.228	2.670
H-24	2.219	2.670	4.173	2.670
H-25	2.716	2.670	3.304	2.670
H-26	3.117	2.670	3.335	2.670
H-27	0.447	3.320	-	-
H-28	3.417	3.810	3.585	3.770
H-29	5.904	12.390	5.285	12.390
H-30	2.829	2.790	3.335	2.790
H-31	2.824	3.040	3.004	3.040
H-32	1.938	1.400	-	-
C-2	34.797	26.900	44.429	13.000
C-3	63.876	71.000	76.879	59.000
C-5	51.823	45.800	62.305	35.000
C-6	49.959	45.800	66.354	35.000
C-8	67.675	71.500	82.770	59.000
C-9	35.355	26.900	46.562	13.000
C-11	167.104	172.800	173.914	174.700
C-14	169.343	172.800	177.743	174.700

Fig. 8. The relationship between theoretical and experimental ^{1}H and ^{13}C chemical shifts of the EC molecule.
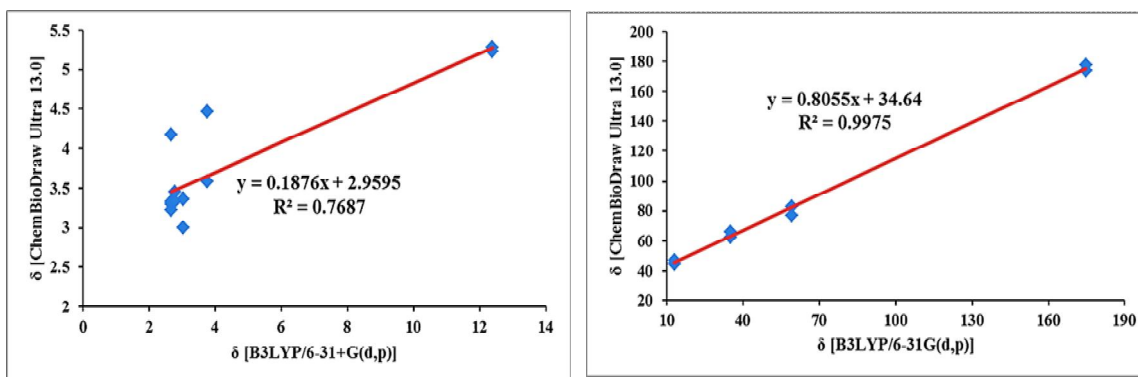
Fig. 9. The relationship between theoretical and experimental ^{1}H and ^{13}C chemical shifts of the ^{99m}Tc-EC structure.

CONCLUSIONS

In summary the present research work was focused to investigation of the the structural, electronic and spectral properties of *L,L*-ethylenedicysteine diethylester compound and its complex with technetium-99m radionuclide using B3LYP/6-31+G(d,p) level of theory. The B3LYP/Lanl2DZ computational method was used to optimization of the technetium radionuclide. The main of this work was to study the structural properties (bond lengths, bond angles, dihedral angles and bond orders), natural bond orbitals (NBOs) population analysis, reactivity (frontier molecular orbitals analysis) and spectral analysis (CD, UV-Vis, IR and NMR spectroscopy techniques) of the studied molecular structures. In first step, the molecules were optimized at mentioned level of theory. Then, the other computations were done on the structures. The structural and spectral analysis data shows the computational method has a good accuracy to the experimental data. From the FMO computations, the stability of ^{99m}Tc-EC structure is lower than the EC molecule. In contrast, the highest reactivity is related to the ^{99m}Tc-EC complex. Also, the comparison between chemical shifts of carbon atoms of ^{99m}Tc-EC to EC molecule shows the carbon atoms of technetium-99m-EC complex are more shielded.

CONFLICT OF INTERESTS

The author declares that there is no conflict of interests regarding the publication of this paper.

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