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Computational Study of the Structural, Electronic, and Thermodynamic Properties of the Eugenol in The Gas Phase and Solvated Environments

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ABSTRACT

In this study, the structural and electronic properties of the eugenol molecule in the gas phase and in various solvent environments (n-octanol, acetone, ethanol, acetonitrile, DMF and water) were investigated theoretically. In accordance with the quantum chemical calculations performed at the MP2/6-311G(d,p) level, NLO (Nonlinear Optical) parameters of the eugenol molecule such as dipole moment, polarizability, anisotropy, hyperpolarizability, HOMO–LUMO energy difference and bond lengths were evaluated. The obtained results revealed that the solvent polarity affects the electronic distribution and bond characteristics of the molecule. Especially in polar solvents, a significant increase was observed in the dipole moment and hyperpolarizability values of eugenol; this increases the sensitivity and interaction capacity of the molecule in optoelectronic applications. In addition, small but systematic changes in the bond lengths support the effect of solvent–solute interactions on the molecule geometry. This study contributes to the understanding of the electronic and structural behaviors of eugenol depending on the solvent environment and sheds light on its usability in application areas such as pharmacological carrier systems and optical material design.

Keywords: Eugenol, Clove oil, Solvent-molecule interaction, HOMO–LUMO, Theoretical calculations quantum chemical calculations.

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Introduction

Eugenol (4-allyl-2-methoxyphenol, $C_{10}H_{12}O_2$) is an aromatic compound with a phenolic structure and is usually found naturally in the essential oils of plants belonging to the Lamiaceae, Lauraceae, Myrtaceae and Myristicaceae families. It is found in the highest amount in clove oil (Syzygium aromaticum). Eugenol was detected in the range of 9381.7–14650.0 mg per 100 grams in fresh material of S. aromaticum. This compound gives the clove plant its characteristic odor and is a clear or pale yellow, oily liquid [1]. Eugenol exhibits different solubility behaviors depending on the solvent medium. Due to its non-polar structure, it has very low solubility in water; however, it is well soluble in less polar environments such as 95% ethanol, while it shows limited solubility in 70% ethanol [2].

The log P value of approximately 2.20 reveals the lipophilic character of eugenol and shows that it shows high solubility in lipid-structured environments such as cell membranes [3]. Eugenol also shows high solubility in polar aprotic solvents such as acetonitrile and in highly polar environments such as dimethylformamide (DMF) [4]. In addition, thanks to its solubility in acetone, it can be used in various organic reactions; in this context, processes such as methylation of eugenol are used in the production of methyl eugenol, and this derivative compound is evaluated in the perfumery and flavor industry [5].

Although there are no specific studies on the direct reaction of eugenol in the gas phase with water vapor, it is thought that water vapor may be indirectly effective in atmospheric transformation processes due to its contribution to the production of OH radicals. This is considered to be an effective factor on the formation of secondary organic aerosols and the atmospheric fate of eugenol [6].

Eugenol is obtained by various extraction methods. These methods include solvent extraction, steam distillation, microwave-assisted extraction (MWAE), supercritical carbon dioxide extraction (SC-CO_2) and ultrasound-assisted extraction (UAE). Each method offers different advantages in terms of yield, environmental impact and target compound purity [7].

Quantum chemistry based DFT and HF calculations show that eugenol has higher free energy and hence higher reactivity compared to eugenol acetate due to its hydroxyl group. This reveals that eugenol is a more active compound in biological systems [8].

Eugenol has antimicrobial, anti-inflammatory, analgesic, antioxidant and anticancer activities. It is effective against bacteria, can prevent food spoilage and can be used as a local anesthetic. However, it has been reported that it can show toxic effects in high doses, causing DNA damage, liver failure and allergic reactions [9]. Eugenol, which is widely used in dentistry, can cause adverse effects such as tissue necrosis, contact allergy and hypersensitivity reactions in some individuals [10].

Microscopic studies have shown that eugenol is effective against bacteria such as Salmonella typhi by disrupting the cell membrane. As a result of this membrane disruption, vital molecules in the cell content leak and the bacteria die. In addition, its effectiveness increases even more in alkaline environments [11]. Eugenol has the strongest antiviral activity of seven compounds tested against the Ebola virus in the laboratory (EC_{50} = 1.3 µM). It has also been found to be effective against influenza and herpes viruses [12].

Eugenol and its derivatives inhibit tumor growth by inducing apoptosis in various cancer cells. It has anticancer effects in different tumor types such as melanoma, osteosarcoma, leukemia and gastric cancer [13]. It also induces apoptosis in difficult-to-treat tumors such as triple-negative breast cancer, while showing minimal toxicity in normal cells. These effects occur through the suppression of vital proteins such as E2F1 and survivin, and the inhibition of signaling pathways such as NF-κB and β-catenin [14].

Eugenol transported via polyurethane nanocapsules is more stable and effective than its free form and supports mitochondrial respiration. These systems are important for improving the pharmacokinetics of eugenol [15]. In addition, experimental studies in mouse aortas show that eugenol inhibits vascular contractions induced by KCl and PHE; it is thought that this effect may be on both voltage-dependent and receptor-mediated calcium channels [16].

Eugenol-loaded chitosan nanoparticles can be processed at high temperatures with thermoplastic flour and exhibit strong antioxidant effects. Therefore, it can be evaluated as a natural preservative agent in heat-processed food packaging [17]. However, its sensitivity to taste and smell limits its direct use. Therefore, microencapsulation techniques have been developed and a more stable eugenol has been used in food applications [18]. Studies on cataract treatment show that eugenol nanoencapsulated with chitosan is safe in human lens epithelial cells and can delay cataract development in in vivo models [19].

In this study, the structural and electronic properties of the eugenol molecule in the gas phase and in different solvent environments (n-octanol, acetone, ethanol, acetonitrile, DMF and water) were investigated. Quantum chemical calculations at the MP2/6-311G(d,p) level analyzed the nonlinear optical (NLO) parameters of the molecule such as dipole moment, polarizability, anisotropy, hyperpolarizability, HOMO–LUMO energy gap and bond lengths. The obtained data show that solvent polarity has significant effects on the electronic structure and bond characteristics of the molecule. Significant increases were detected in the dipole moment and hyperpolarizability values of eugenol, especially in highly polar solvents. This situation shows that the molecule can increase its sensitivity and interaction potential in optoelectronic systems. In addition, the regular and small changes observed in the bond lengths due to the solvent effect support that solvent–solute interactions are effective on the molecular geometry.

Materials and Methods

Computational Methods

The structure of the eugenol molecule investigated in this study was modeled by GaussView program and transferred to Gaussian software for quantum chemical calculations. The geometry optimization of the molecule in the gas phase was performed using MP2 level and 6-311G(d,p) basis set. As a result of the calculations, the basic structural and electronic parameters of the molecule such as HOMO and LUMO orbital energies, electrostatic potential (ESP) maps, dipole moment values, total electronic energies, zero point corrections, thermal and free energy values, enthalpy calculations, Mulliken charge distributions and bond lengths were obtained. All calculations were performed on a high-performance computer infrastructure and the obtained results were supported by graphical analyzes in order to comparatively evaluate the effects of different solvent environments (gas, n-octanol, acetone, ethanol, acetonitrile, DMF and water) on the molecular properties. These analyzes provide comprehensive theoretical information about the solvent-dependent behavior of the eugenol molecule.

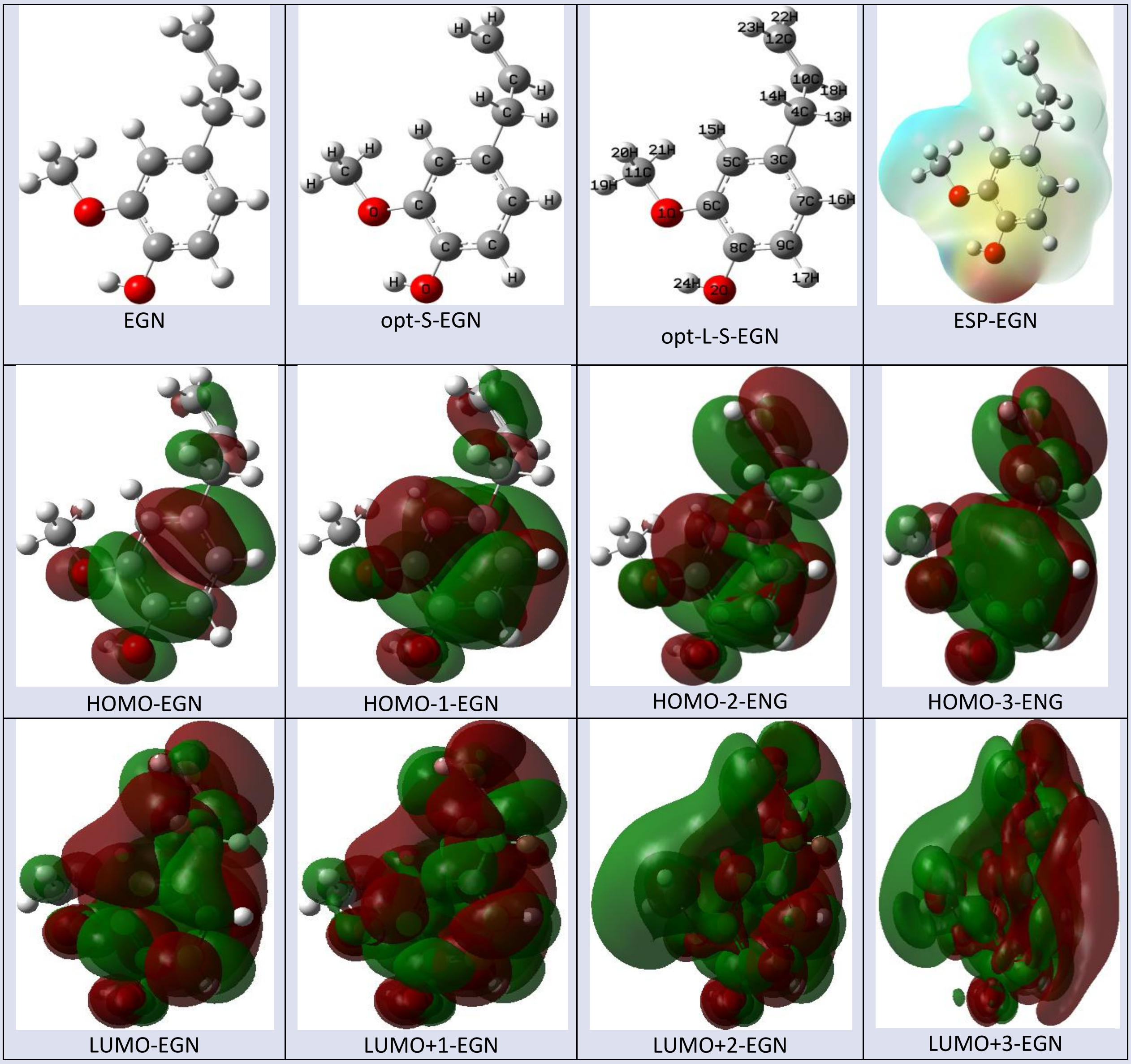

Figure 1. Optimization, HOMO, HOMO-1, HOMO-2, HOMO-3, LUMO, LUMO+1, LUMO+2, LUMO+3 and ESP form of EGN

Results and Discussion

Geometric Optimization of Eugenol Molecule in Gas Phase and Analysis of Electrostatic Potential Map with Frontier Molecular Orbitals (HOMO, LUMO, ESP)

The optimized structure of the eugenol molecule was obtained at MP2 level and using the 6-311G(d,p) basis set. The optimized structure of the eugenol molecule, HOMO, HOMO–1, HOMO–2, HOMO–3, LUMO, LUMO+1, LUMO+2, LUMO+3 orbitals and electrostatic potential (ESP) distribution are given in Figure 1.

Figure 1 shows the distribution of priority molecular orbitals (HOMO and LUMO) along with the electrostatic potential (ESP) surface of the eugenol molecule. It provides important information in terms of understanding the electronic structure of the molecule and possible reaction sites.

The ESP map represents the electron density on the surface of the molecule. The red regions indicate areas of high electron density (negative potential) generally concentrated around the hydroxyl group (-OH) and aromatic ring. These regions are important in terms of nucleophilic attack and have the potential to form hydrogen bonds. The blue regions represent areas of low electron density (positive potential) especially around the allyl side chain and hydrogen atoms and can be evaluated as electrophilic interaction sites.

The Highest Occupied Molecular Orbital (HOMO) is localized in electron-rich regions of the molecule, especially the aromatic ring and hydroxyl group. This indicates that these regions can play active roles in nucleophilic interactions. The HOMO-1 and HOMO-2 orbitals are also delocalized throughout the aromatic system, indicating resonance stabilization. HOMO-3 is lower energy and focused on internal bonds; although it contributes little to chemical reactivity, it provides information about the structural stability of the molecule.

The Lowest Unoccupied Molecular Orbital (LUMO) is largely located on the allyl group and partially on the aromatic ring. These regions are advantageous in terms of electron acceptance and are important for possible electrophilic reactions. The LUMO+1 to LUMO+3 orbitals have higher energy levels and have a wider delocalization. These orbitals are especially important in terms of excited state transitions, charge transfer processes and photochemical behavior.

The orbital distribution and HOMO-LUMO energy difference are critical to understand the chemical reactivity of Eugenol, its interaction mechanisms and its potential in applications such as drug delivery systems or molecular electronics.

Table 1. Contributions of the highest energy filled atomic orbitals in the gas phase and different environments of the eugenol molecule HOMO, HOMO−1, HOMO−2, HOMO−3.

			HOMO				
Atoms	**Gas**	**n-octanol**	**Acetone**	**Ethanol**	**Acetonitrile**	**DMF**	**Water**
O1	4.79	5.29	5.34	10.85	5.36	5.36	5.37
O2	8.81	8.29	8.25	14.5	8.23	8.23	8.22
C3	23.62	22.9	22.84	17.83	22.81	22.81	22.79
C6	14.92	14.87	14.84	14.02	14.83	14.83	14.82
C7	13.78	15.41	15.55	13.48	15.61	15.61	15.65
C8	22.94	23.06	23.07	18.71	23.07	23.07	23.07
C9	5.59	4.64	4.56	4.6	4.53	4.53	4.5
			HOMO-1				
O1	4.62	4.73	4.75	8.84	4.76	4.76	4.76
C3	-	-	-	4.77	-	-	-
C5	32.45	32.51	32.46	32.17	32.44	32.44	32.43
C6	11.91	11.29	11.25	6.47	11.24	11.24	11.22
C7	14.77	12.75	12.56	9.75	12.48	12.47	12.42
C9	26.24	25.62	25.5	24.21	25.46	25.45	25.42
C12	-	-	-	4.07	-	-	-
			HOMO-2				
C10	39.88	39.29	39.19	37.37	39.15	39.15	39.12
C12	46.75	45.25	45.02	44.66	44.93	44.92	44.85
			HOMO-3				
O1	12.17	13.39	13.48	16.3	13.52	13.52	13.55
O2	7.95	6.79	6.68	6.47	6.64	6.64	6.61
C3	13.65	12.1	11.93	12.29	11.85	11.85	11.8
C4	4.42	5.02	5.09	4.8	5.12	5.12	5.14
C5	11.53	9.75	9.56	6.1	9.48	9.47	9.42
C7	-	17.27	17.2	20.77	17.17	17.17	17.15
C8	17.69	-	-	-	-	-	-
C9	-	13.21	13.26	13.11	13.27	13.27	13.29
C10	12.68	4.39	4.52	4.39	4.58	4.58	4.62

Table 2. LUMO LUMO+1 LUMO+2 LUMO+3 contributions of the lowest energy empty atomic orbitals in the gas phase and different environments of the eugenol molecule.

LUMO							
Atoms	**Gas**	**n-octanol**	**Acetone**	**Ethanol**	**Acetonitrile**	**DMF**	**Water**
C3	5.8	7.38	7.75	6	7.92	7.93	8.04
C5	26.05	27.9	28.04	28.25	28.09	28.09	28.12
C6	10.77	9.54	9.2	11.43	9.03	9.03	8.92
C7	5.82	5.21	4.95	7.61	4.82	4.82	4.74
C8	8.4	10.79	11.23	8.89	11.43	11.45	11.58
C9	26.24	27.8	27.79	29	27.77	27.77	27.76
H14	5.55	4.35	4.28	-	4.25	4.25	4.22
LUMO+1							
C3	15.54	15.95	15.7	15.08	15.57	15.57	15.48
C6	9.22	12.48	13.03	7.63	13.28	13.29	13.47
C7	17.11	20.5	21.05	14.37	21.31	21.32	21.49
C8	11.97	11.09	10.7	11.86	10.52	10.51	10.39
C10	15.89	14.03	13.79	19.44	13.68	13.67	13.58
C12	15.96	14.63	14.5	21.43	14.42	14.42	14.36
LUMO+2							
C3	-	-	-	11.14	-	-	-
C6	-	-	-	9.53	-	-	-
C7	-	-	-	11.7	-	-	-
C8	-	-	-	7.11	-	-	-
C10	-	-	-	25.65	-	-	-
C12	-	-	-	24.19	-	-	-
H13	-	-	-	-	4.07	4.08	4.17
H14	-	5.82	6.17	-	6.29	6.3	6.38
H15	20.02	25.9	26.35	-	26.49	26.49	26.57
H16	-	6.6	7.17	-	7.41	7.42	7.6
H18	-	5.96	6.17	-	6.28	6.29	6.37
H19	24.7	15.34	14.57	-	14.27	14.26	14.06
H20	28.79	21.99	21.15	-	20.81	20.79	20.55
H21	28.97	23.59	23.08	-	22.88	22.87	22.74
H22	6.61	8.92	8.97	-	9	9	9.02
H23	9.15	14.28	14.71		14.87	14.88	14.97
LUMO+3							
C10	-	4.28	4.39	-	4.45	4.45	4.5
C11	-	-	-	5.87	-	-	-
C12	2.39	6.63	6.79	-	6.86	6.86	6.92
H13	27.75	20.12	19.01	6.75	18.53	18.51	18.17
H14	-	-	-	6.23	-	-	-
H15	-	-	-	19.99	-	-	-
H16	40.92	39.7	39.25	14.15	39.02	39.01	38.83
H17	5.65	10.01	10.51	-	10.71	10.72	10.86
H18	11.12	8.93	9.33	-	9.51	9.53	9.65
H19	6.93	4.89	4.92	-	4.93	4.93	4.94
H20	5.62	5.81	5.93	5.5	5.97	5.98	6.01
H21	-	-	-	5.96	-	-	-
H22	5.12	-	-	4.19	-	-	-
H23	-	-	-	6.95	-	-	-
H24	-	-	4.39	23.94	-	-	-

Investigation of the Change in Atomic Contributions to Frontier Orbitals of Eugenol Molecule Depending on the Polarity of Various Solvents

Table 1 and Table 2 show the atomic orbitals of the highest occupied molecular orbitals (HOMO, HOMO−1, HOMO−2, HOMO−3) and lowest unoccupied molecular orbitals (LUMO, LUMO+1, LUMO+2, LUMO+3) of the eugenol molecule in different environments (Gas (ε = 0), n-octanol (ε = 9.8629), Acetone (ε = 20.493), Ethanol (ε = 24.852), acetonitrile (ε = 35.688), DMF (ε = 37.219), Water (ε = 78.3553)).

Data for the HOMO orbital indicate high electron density, especially concentrated on O1, O2 and aromatic ring carbons (C3, C6, C7, C8). This distribution shows that especially the hydroxyl group (O1) and the aromatic system are nucleophilic. It was observed that the contribution on O1 and O2 increased as the solvent polarity increased; this supports the importance of the hydroxyl group in terms of hydrogen bonding and electron donation.

Similarly, density is observed on atoms such as C5, C6, C7, C9 in the HOMO−1 and HOMO−2 orbitals; it is understood that these orbitals contribute to the aromatic resonance system and affect the stability of the molecule. HOMO−2 contributions are directed more towards aliphatic side chain atoms (C10, C12), which is valuable in terms of alternative interaction paths.

HOMO−3 is a lower energy orbital located in more internal bonds and is contributed by O1, O2 and some aromatic carbons. This orbital may contribute to the structural integrity and photophysical behavior of the molecule.

The LUMO and LUMO+1 orbitals generally represent regions where electrophilic interactions can occur. LUMO densities are concentrated on atoms such as C3, C5, C6, C7 and C9, indicating that these regions have electron acceptor potential. LUMO+1 is more widespread on atoms such as C6, C7, C10 and C12, providing information about higher energy excited states.

The LUMO+2 and LUMO+3 orbitals are related to transition states and advanced electron transition processes after photoexcitation. The contributions of these orbitals are mostly concentrated on hydrogen atoms (H13–H24) and some side chain carbons (C10–C12). It has been observed that these contributions increase in polar solvents, emphasizing the decisive role of the solvent effect on photophysical processes.

In general, it has been observed that increasing solvent polarity has significant effects on electron distribution, especially in solvents that can form hydrogen bonds (such as ethanol and water). This change shows the sensitivity of the molecule to environmental conditions in terms of both bond structure and reactivity. In addition, the concentration of HOMO-LUMO contributions in certain atoms indicates that these regions may be the priority targets for chemical interactions.

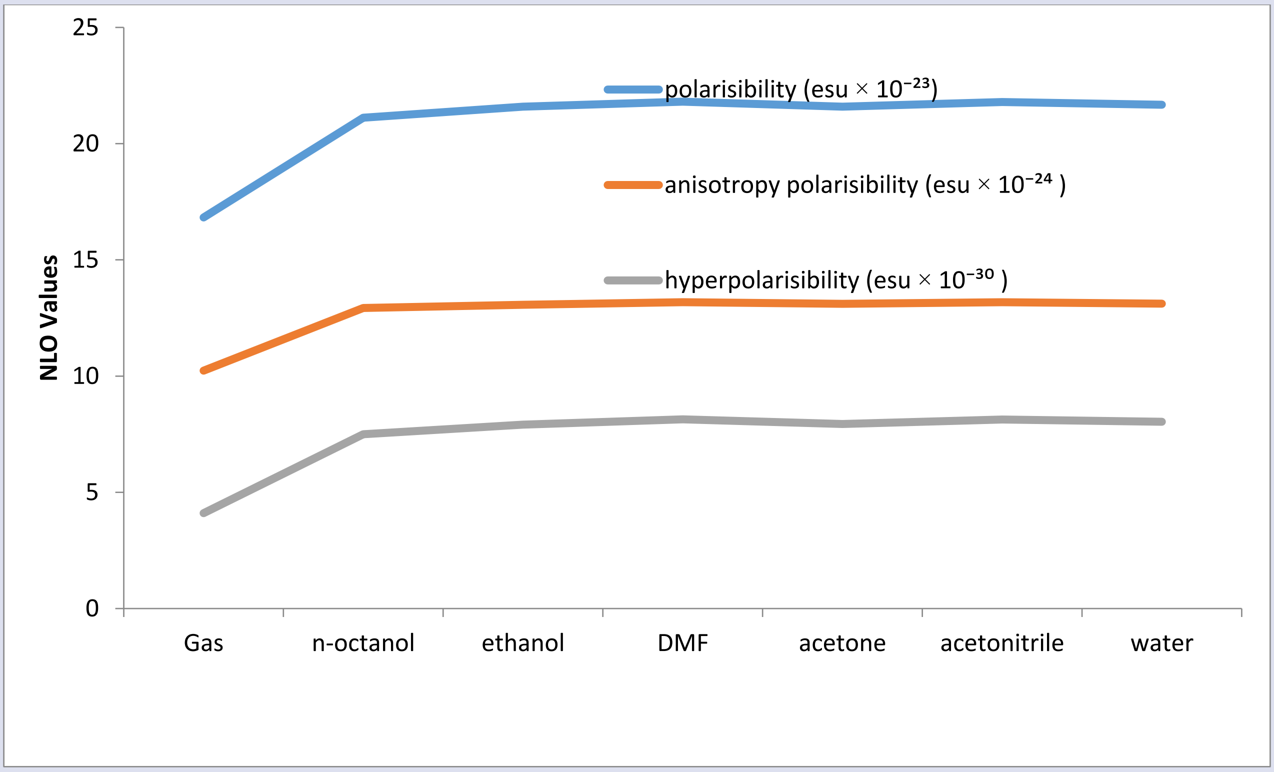

Figure 2. NLO values of the eugenol molecule in the gas phase and in different solvent environments (n-octanol, acetone, ethanol, acetonitrile, water).

Evaluation of Polarizability and Nonlinear Optical (NLO) Properties of Eugenol Molecule in Different Solvents

Figure 2 compares three important electrical properties of eugenol molecule in different solvent media (gas, n-octanol, acetone, ethanol, acetonitrile, DMF, water). Polarizability, anisotropic polarizability, and hyperpolarizability. These three parameters are critical to understanding how molecules respond to external electric fields and how these properties change under the influence of the medium.

Figure 2 shows the electronic properties of the eugenol molecule in different solvents. The lowest value in terms of polarizability was observed in the gas medium with 16.82; this is the medium in which the molecule is least responsive to the electric field. The highest polarizability value was recorded in the DMF solution with 21.81. When the anisotropy polarizability values were examined, the lowest value was observed in the gas medium (10.23), while the highest value was obtained in DMF (13.18). This situation shows that the directional electrical effects of DMF on the eugenol molecule are most pronounced. In terms of Hhyperpolarizability, the lowest value was measured in the gas medium with 4.10, and the highest value was measured in DMF with 8.14. Polar solvents such as water (8.03), acetonitrile (8.13) and ethanol (7.91) also exhibited high Hhyperpolarizability values. In general, a significant increase in the polarizability, anisotropy and hyperpolarizability values of the eugenol molecule was observed in polar solvents (especially DMF, acetonitrile and water).

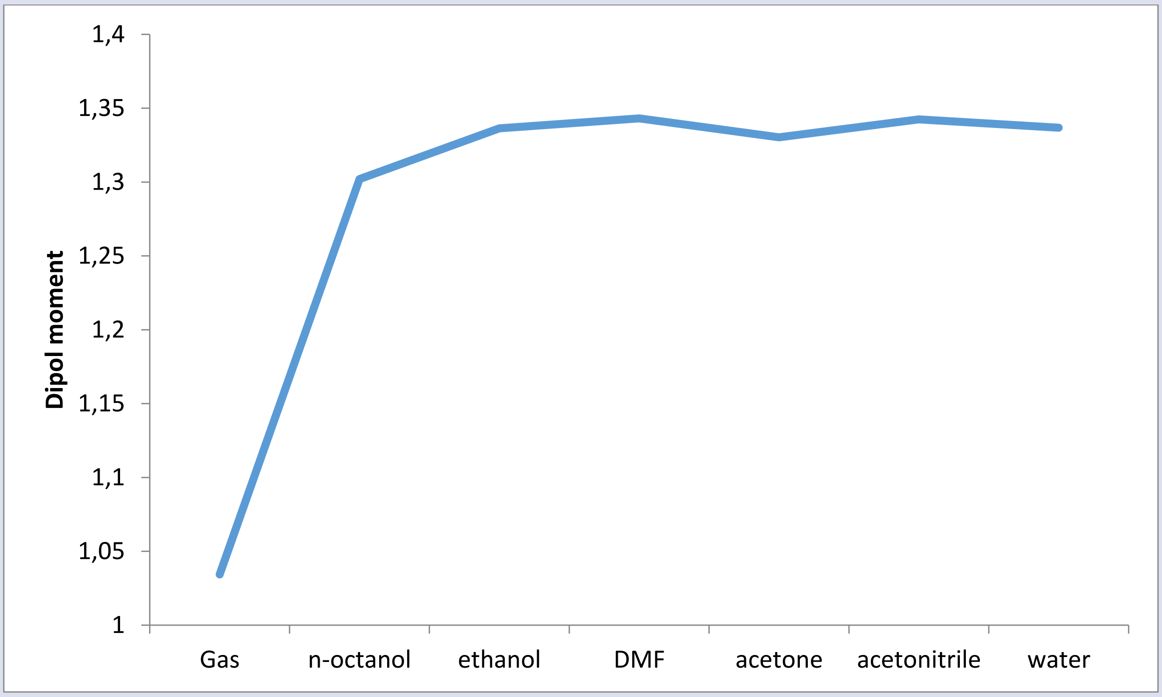

Figure 3. Dipol Moment of eugenol molecule

Investigation of the Effect of Different Solvent Environments on the Dipole Moment of the Eugenol Molecule

Figure 3 shows the dipole moment (in Debye) values of eugenol measured in different solvent environments comparatively.

As seen in Figure 3, the lowest dipole moment value was measured in the gas phase and this value is 1.0343 D. This is due to the fact that there are almost no interactions between molecules in the gas environment. Since there is no solvent effect in this environment, the molecule exhibits its natural (intrinsic) polarity.

A significant increase in the dipole moment value is observed when polar solvents are used. For example, while the dipole moment is 1.3020 D in the n-octanol environment, this value increases to 1.3364 D in a more polar solvent such as ethanol. Similar values obtained in solvents such as acetone (1.3303 D), DMF (1.3431 D) and acetonitrile (1.3424 D) show that these solvents have similar polar properties and affect the polarization of the molecule in a similar way. The highest dipole moment value was observed in the DMF (1.3431 D) environment. This shows that DMF is a highly polar solvent and strongly affects intermolecular interactions. Acetonitrile (1.3424 D) is also among the solvents that provide a similarly high dipole moment. Water, as a solvent that can form strong hydrogen bonds and has a high dielectric constant, provides a very high dipole moment of 1.3368 D. This shows that water can significantly affect the electronic distribution of the molecule. Generally speaking, as the polarity of the solvent increases, the dipole moment value of the molecule also tends to increase. These data reveal how critical the solvent selection plays in determining molecular structure and interactions.

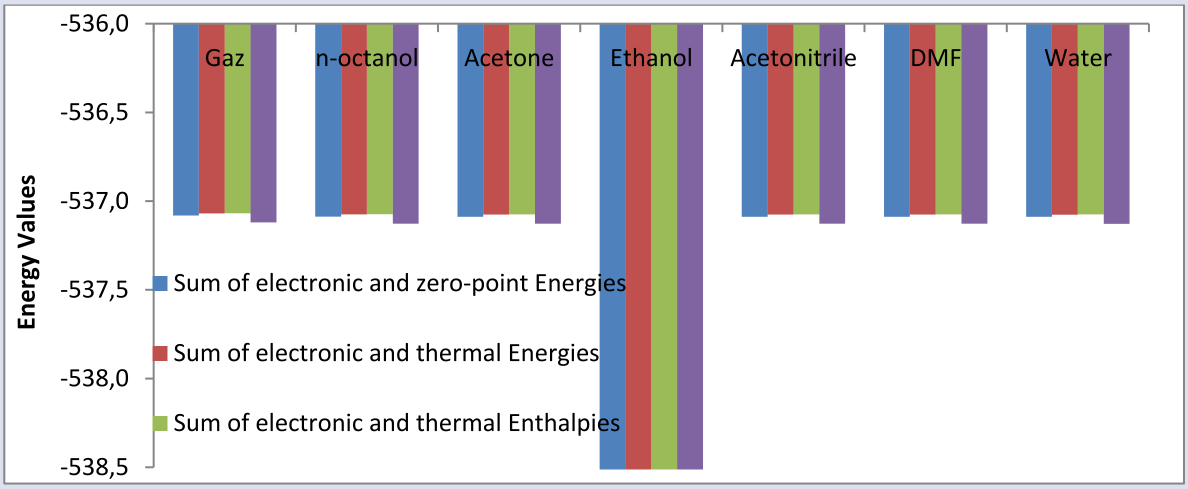

Figure 4. The sum of electronic and zero-point energy, sum of electronic and thermal energy, sum of electronic and thermal enthalpy and sum of electronic and thermal free energy of the eugenol molecule (in au units).

Investigation of the Effect of Polarity of Different Solvents on Electronic and Thermodynamic Energy Parameters of Eugenol Molecule

Figure 4 presents the data of thermodynamic parameters of the eugenol molecule calculated in different environments (gas phase and various solvents). These data consist of the sum of electronic and zero-point energy, sum of electronic and thermal energy, sum of electronic and thermal enthalpy and sum of electronic and thermal free energy values obtained using density functional theory (DFT).

According to Figure 4, when the free energy values of eugenol in all environments are compared, it is seen that the environments with the lowest free energy values are water, DMF and acetonitrile (approximately -537.128 Hartree each). This situation shows that eugenol enters into more stable interactions with these solvents and its solubility may be high in these environments. When compared to the gas phase (-537.120 Hartree), it can be said that the presence of solvents increases the thermodynamic stability of eugenol.

Especially in ethanol medium, the free energy value is quite low compared to other solvents (–538.694 Hartree), but this difference may indicate that the ethanol solution is based on a different basic structure (probably solvate complex), because the initial energy is also significantly lower than the others (–538.655 Hartree). The free energy of eugenol is at similar levels in solvents such as n-octanol, acetone and DMF, and it is seen that it presents a stable solubility profile in these solvents. As a result, the fact that eugenol has a lower free energy especially in polar aprotic solvents (acetonitrile, DMF) and polar protic solvents (water, ethanol) reveals that its solubility and chemical stability are high in these environments. This situation is important in terms of choosing the appropriate solvent in drug delivery systems or pharmaceutical formulations.

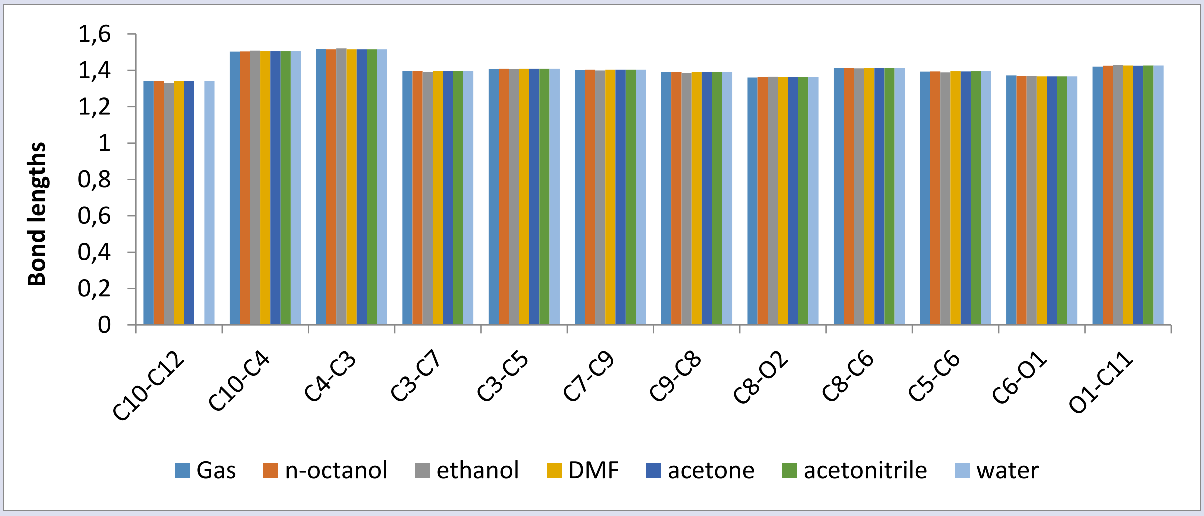

Figure 5. Bond lengths (Å) between the basic atom pairs in the eugenol molecule in the gas phase and in various solvent environments (n-octanol, ethanol, DMF, acetone, acetonitrile and water).

Investigation of Bond Lengths of Eugenol Molecule in Gas Phase and Various Solvents

Figure 5 shows how the bond lengths between the basic atom pairs in the eugenol molecule change in the gas phase and in various solvent environments (n-octanol, ethanol, DMF, acetone, acetonitrile and water). According to the results obtained, small changes occurred in the bond lengths depending on the polarity of the solvent environments.

Particularly, minor changes were observed in bonds such as C10–C4, C4–C3, and O1–C11 due to the effect of the solvent. For example, while the O1–C11 bond length is 1.41994 Å in the gas phase, it extends to 1.42822 Å in the ethanol medium. This situation shows that the solvent molecules redistribute the electron density and cause the molecular structure to be rearranged. In addition, the shortening observed in some solvents in the C6–O1 bond may be due to specific solvent-molecule interactions such as hydrogen bonds and dipole interactions. In general, polar solvents (e.g. DMF, water) have a more pronounced effect on bond lengths. These changes provide important clues regarding the chemical reactivity and biological interaction potential of eugenol.

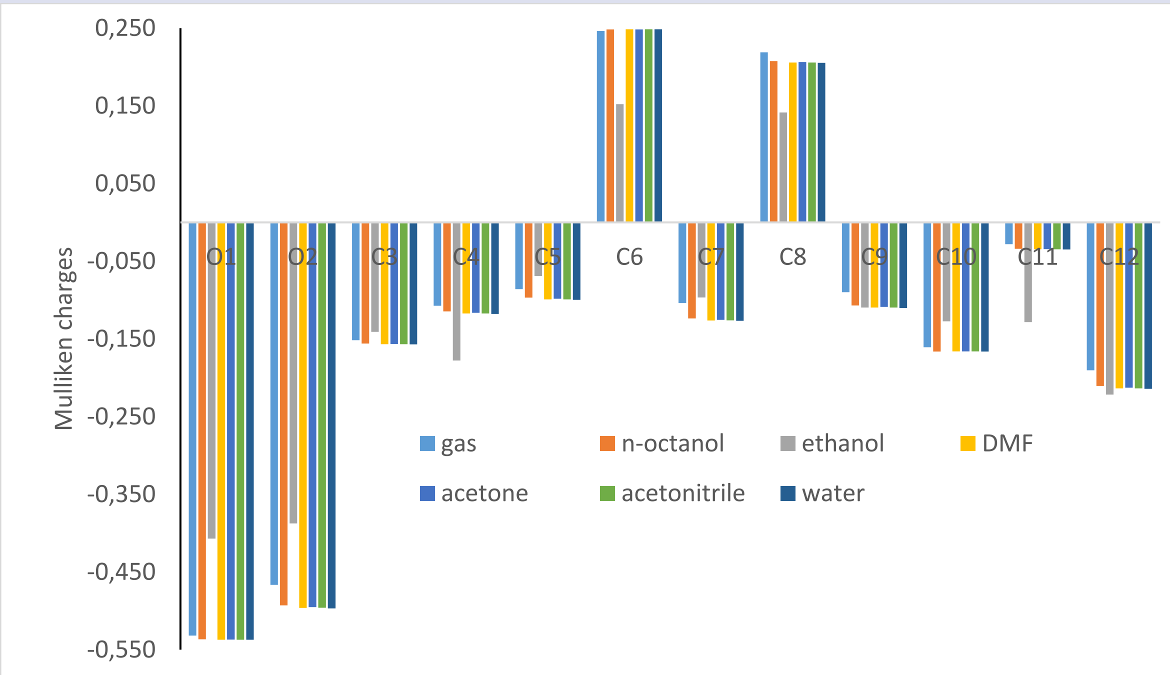

Figure 6. Mulliken charge (ē) changes of atoms in the eugenol molecule in the gas phase and in different solvents (n-octanol, ethanol, DMF, acetone, acetonitrile and water).

Changes in the Mulliken charge distribution of atoms in the eugenol molecule in the gas phase and various solvents (n-octanol, ethanol, DMF, acetone, acetonitrile and water)

The Mulliken charge changes of atoms in the gas phase and different solvents at the MP2/6-311G(d,p) level were analyzed in detail and are given in Figure 6. The obtained data reveal the sensitivity of atoms to solvent interactions and possible changes in the electronic structure.

The charge of the O1 atom is at its lowest value in ethanol with -0.407 ē, while it carries a more negative charge of -0.537 ē in all other solvents. This shows that the O1 atom is generally not affected by solvent effects, but is less negatively charged in the ethanol environment. The charge of the O2 atom is -0.387 ē in ethanol and reaches -0.497 ē in the water environment. This shows that O2 interacts more strongly with some solvents and its charge becomes more negative in these environments. The charge of the C3 atom is constant around -0.157 ē in all solvents, while it was observed as -0.141 only in ethanol. This small difference reveals that C3 generally has a stable charge distribution, but shows a weaker interaction with ethanol. The C4 atom carries the most negative charge with -0.178 ē in the ethanol environment, while the charge varies between -0.107 ē and -0.118 ē in other solvents. This difference suggests that ethanol has a more pronounced effect on the C4 atom.

The C5 atom is also sensitive to solvent changes; the charge, which is -0.069 ē in ethanol, increases to -0.100 ē in the water environment. This shows that C5 has varying interactions with different solvents. The C6 atom carries a lower positive charge with a value of 0.152 ē in ethanol, while it has higher positive values such as 0.248 ē in other environments. This shows that the interaction of ethanol with C6 is lower than in other solvents.

The charge of the C7 atom is -0.097 ē in ethanol, while it reaches a value of -0.127 ē in the water environment. This indicates that its charge increases and the interaction becomes stronger in more polar solvents. C8 has a lower positive charge with a value of 0.141 ē in the ethanol environment, and this value is approximately between 0.206–0.219 ē in other solvents. This shows that C8 is sensitive to solvent polarity.

C9, C10 and C11 atoms also respond to solvent effects in a similar way. Especially C11 has a significantly more negative charge of -0.128 ē in ethanol environment, while this value is around -0.035 ē in other solvents. This shows that the effect of ethanol on C11 is stronger. Finally, C12 atom reaches the highest negative charge of -0.222 ē in ethanol, while its charge varies between -0.190 ē and -0.214 ē in other environments. This shows that C12 interacts strongly with ethanol.

These findings reveal the analysis of the atoms' responses to the solvent environment based on the data obtained from Mulliken charges in Figure 6 and show how the electronic distribution in the solution changes depending on the solvent.

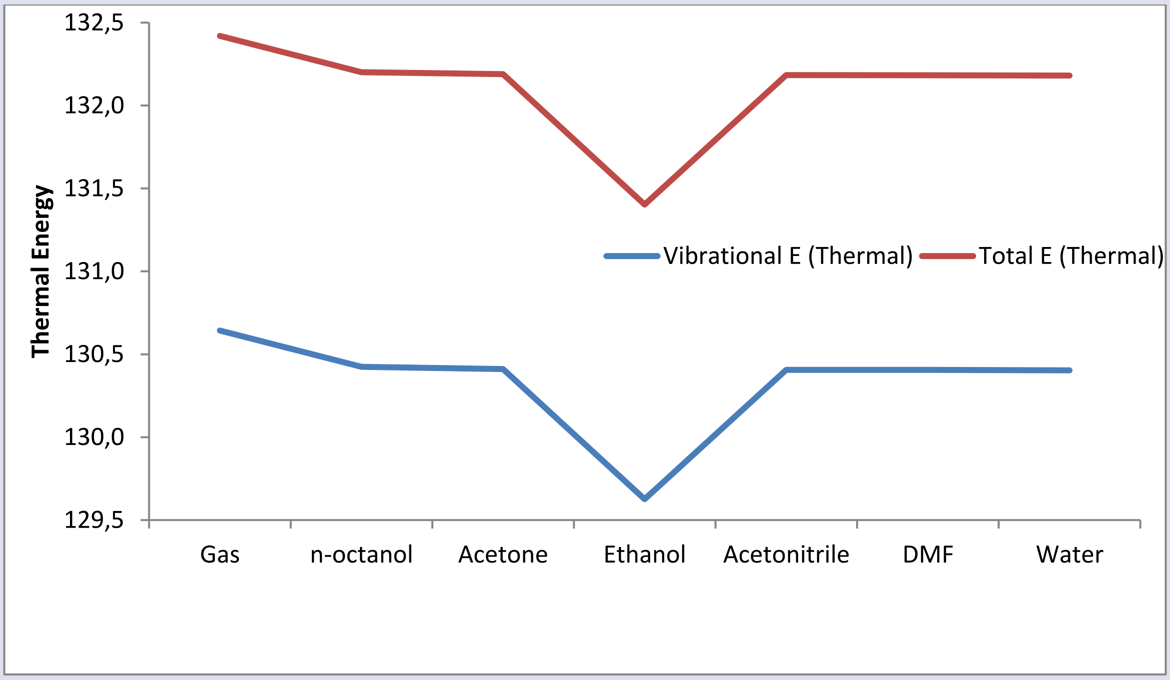

Figure 7. Comparison between thermal vibrational energies and total thermal energies calculated for eugenol compound in different solvents.

Comparative Study of Thermal Vibrational and Total Thermal Energy Parameters of Eugenol Molecule in Different Solvent Environments

Figure 7 shows the thermal vibrational energies (Vibrational E) and total thermal energies (Total E) of eugenol compound in gas phase and different solvents (n-octanol, acetone, ethanol, acetonitrile, DMF and water) in kcal/mol.

According to the data, vibrational energy of eugenol in gas phase has the highest values with 130.643 kcal/mol and total thermal energy with 132.420 kcal/mol. This situation shows that the molecule has more energy in gas environment where it can move freely independent of solvent effect.

In n-octanol and acetone environments, vibrational and total thermal energies are 130.424 / 132.201 and 130.411 / 132.189 kcal/mol, respectively. These values are slightly lower compared to gas phase, but still remain high compared to other solvents. This shows that eugenol mobility in these solvents is still high.

A significant decrease is observed in ethanol environment. The vibrational energy is 129.626 kcal/mol, and the total thermal energy is 131.403 kcal/mol. This decrease suggests that stronger interactions with ethanol (e.g. hydrogen bonds) limit the free vibration of eugenol, thus reducing the energy of the system. In acetonitrile, DMF and water solvents, the vibrational energies of eugenol are quite close, 130.406, 130.406 and 130.403 kcal/mol, respectively. Their total thermal energies are also very similar, 132.184, 132.183 and 132.181 kcal/mol. This similarity shows that the interactions of eugenol with these solvents are of similar intensity and that the energy levels remain stable.

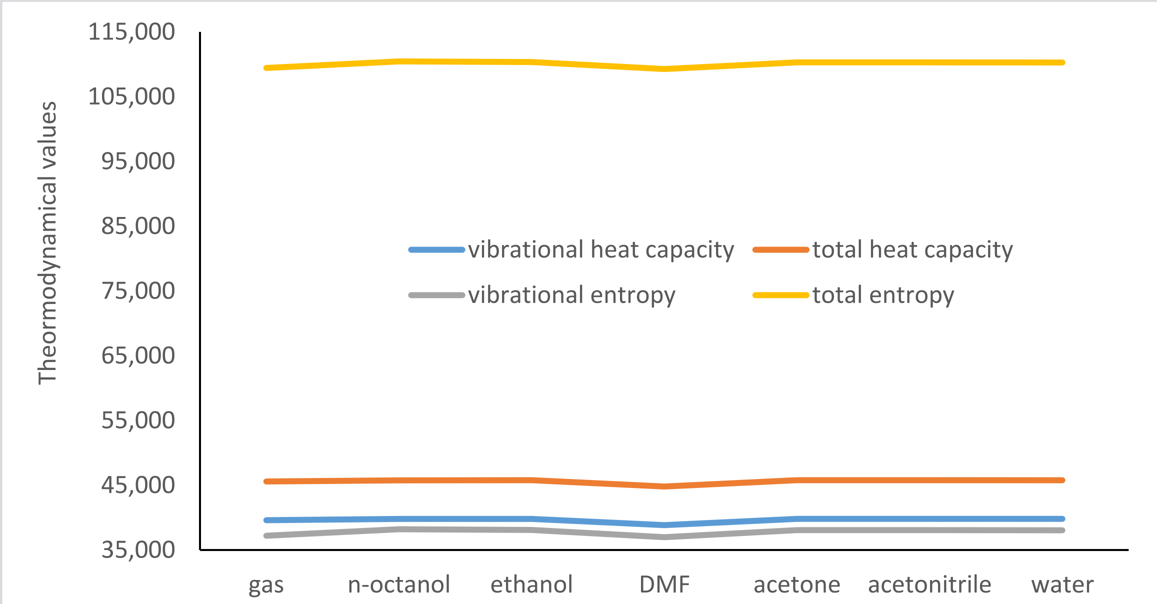

Figure 8. Vibrational and total specific heat capacity (Cv) and entropy (S) values of eugenol molecule in different solvents

Evaluation of thermal total and vibrational specific heat capacity and entropy values of eugenol molecule under the effect of different solvents

According to the data presented in Figure 8, the vibrational and total heat capacities (Cal/molK) and entropy values of eugenol molecule in different environments were compared. In terms of vibrational heat capacity, the values are quite similar and vary between 38.84 (ethanol) and 39.81 (acetonenitrile, DMF, water). The lowest vibrational heat capacity was observed in ethanol (38.845), while the highest value was recorded in acetonenitrile, DMF and water (39.812). In terms of total heat capacity, all environments have similar values and are around 45.77.

When the entropy values are examined, the lowest vibrational entropy value was measured in ethanol with 36.982, and the highest was measured in n-octanol with 38.209. The total entropy varies between 109.26 (ethanol) and 110.45 (n-octanol), with the n-octanol medium having the highest total entropy. These differences show the effect of the solvent medium on the degrees of freedom and vibration modes of the molecule. In general, the thermodynamic properties of eugenol are related to the solvent polarity and hydrogen bonding capacity. In particular, environments such as n-octanol and acetonitrile increase the entropic arrangement and vibrational movements of the molecule, which is reflected in the total entropy and heat capacity. These results provide important clues in understanding the sensitivity of eugenol to environmental conditions and its molecular interactions with the solvent medium.

Conclusion

In this study, the structural, electronic and thermodynamic properties of the eugenol molecule in different solvent environments (n-octanol, acetone, ethanol, acetonitrile, DMF and water) together with the gas phase were analyzed theoretically in detail. The calculations were performed at the MP2/6-311G(d,p) level and the obtained data provided a basic reference in understanding the effects of solvent polarity on molecular properties.

The frontier orbital (HOMO and LUMO) analyses performed for the eugenol molecule clearly revealed how different solvents affect the electron density distribution. The increase in electronic density observed especially around the –OH group indicates that this region is a dominant center in terms of reactivity. The decrease in the HOMO-LUMO energy difference with the increase in solvent polarity indicates a potential increase in the chemical reactivity of the molecule.

Changes in dipole moment and polarizability values revealed that eugenol showed higher electrical reactivity in polar environments, and this made it possible to evaluate the molecule in terms of nonlinear optical (NLO) properties. It was observed that hyperpolarizability values increased significantly, especially in highly polar solvents such as water and DMF. These results support the usability of eugenol in optoelectronic devices or electro-optic materials.

Electrostatic potential distributions showed that the electrophilic and nucleophilic regions of the molecule were reshaped depending on the solvent. It is thought that the molecule showed a more pronounced polarization tendency, especially in solvents with high dielectric constants such as water, and this situation may affect target-specific interactions in biological systems.

When evaluated in terms of thermodynamic parameters, it was determined that there were visible differences in enthalpy, free energy and total energy values due to the effect of different solvents, but the general structure stability was preserved. This shows that the chemical structure of eugenol is relatively resistant to solvent environments and can maintain its effectiveness in various biological environments.

Overall, this study provides a detailed theoretical profiling of the properties of the eugenol molecule that vary depending on the solvent environment and provides important contributions to understanding the potential of this molecule in pharmaceutical, biosensor and nanotechnological applications. Understanding the molecule-solvent interactions is critical to predict the behavior of eugenol under environmental conditions.

Conflicts of interest

The authors declare that there is no conflict of interest.

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