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The Essential Oils of *Laurus nobilis* L. and Molecular-Spectroscopic Analysis for 1,8-Cineole

Omer ELKIRAN*[1], Mustafa KARAKAYA[2]

Abstract

In the present study, the chemical composition of the essential oils obtained from leaves of *Laurus nobilis* naturally grown in Turkey were evaluated using by GC and GC-MS and chemical differences were depated in means of chemotaxonomy. The leaves of the plant samples were hydro-distilled. Twenty components were identified representing 99.3% of the oils, The main compounds in the essential oils were; 1,8-cineole (%48.47), β-pinene (%14.45), linalool (%8.15) and α-pinene (%5.97). In addition, the complexation energies, chemical shifts of the carbon and hydrogen atoms in the 1,8-cineole structures were calculated by ab initio theoretical approaches. The performances of the B3LYP and M06 functionals were tested on carbon and hydrogen complexation energies of the investigated compound. The electronegativity effect of oxygen and solvent effect on complexation energy of the carbons and hydrogens were evaluated with the results obtained.

Keywords: *Laurus nobilis*, Essential oils, 1,8-cineole, GC-MS, Complexation energy, Density functional theory

1. INTRODUCTION

Essential oils are one of the important work areas of the pharmaceutical and cosmetic industry [1]. The *L. nobilis* is also plant that has cineolic essential oils content. 1,8-cineole is the chemical components present in high proportions in the essential oil content of this plant. The other names of the 1,8-cineole molecule are eucalyptol or 1,8-epoxy-*p*-menthane in literature [2]. This compound is used as food flavoring because it has a sharp aroma and as pharmaceutical chemical [3-6].

As a result of our detailed literature search, the following areas have been carried out in on the quantum computations of this molecule. The molecular orbital's, eigenvalues and symmetry for each orbital [7], vibration frequencies [8,9] have been reported for the 1,8-cineole by density functional theory (DFT) calculations. Molecular docking and binding energies have been computed β-cyclodextrin inclusion complex with five essential oil compounds (linalool, eugenol,

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methyl eugenol, estragole, and eucalyptol) modeled by DFT both in the gas phase and in the aqueous phase using polarizable continuum methods [10].

Theoretical IR Frequencies, shifting of bands, second order perturbation energies of hydrogen bonds and interactions for 1,8-cineole + o-, m- and p-cresol binary mixtures at 298.15 K analyzed by using (DFT) with B3LYP hybrid functional [11]. In addition, DFT and experimental studies on cycloaddition reactions of C.N-disubstituted nitrones [12], 2, 4, 6-trimethyl phenol [13] and nickel (II) complexes [14] are recently available in the literature. We wish to investigate the complexation energies, chemical shifts of the carbon and hydrogen_atoms in the 1, 8-cineole structures and to comment the results from approximation methods in this study. According to the literature, leaves of *L. nobilis* have not been the subject of any investigation for this region and this paper is the first such phytochemical study on this plant of Central Black Sea region.

2. EXPERIMENTAL

2.1. Plant materials

L. nobilis specimens were collected in June 2016 from Sinop. The specimens were studied Sinop University, SUBITAM, Sinop, Turkey.

2.2. Isolation of the essential oils

The leaves (100g) were subjected to hydro distillation using a Clevenger-type apparatus for 3 h to yield essential oil.

2.3. Gas chromatography (GC) analysis

The essential oil was analyzed using HP 6890 GC equipped with a FID detector and an HP-5 MS column (30m×0.25mm i.d., film thickness 0.25 μm) and the capillary column were used. The column and analysis conditions were the same as in GC-MS. The percentage composition of the essential oils was computed from GC–FID peak areas without correction factors.

2.4. Gas chromatography/mass spectrometry (GC-MS) analysis

The oil samples were analyzed by GC-MS, using a Hewlett Packard system. HP-Agilent 5973N GC-MS system with 6890 GC. HP-5 MS column (30m×0.25mmi. d., film thickness 0.25 μm) was used with helium as the carrier gas. Injector temperature was 250 ^{0}C, split flow was 1ml/min. The GC oven temperature was kept at 70^{0}C for 2 min and programmed to 150 ^{0}C at a rate of 10 ^{0}C / min and then kept constant at 150^{0}C for 15 min to 240 ^{0}C at a rate of 5 ^{0}C/min. Alkanes were used as reference points in the calculation of relative retention indices (RRI). MS were taken at 70 EV and at a mass range of 35–425. Component identification was carried out using spectrometries electronic libraries (WILEY, NIST). The components of the essential oils were in Table 1 and the chromatograms were shown in Figure 1.

2.5. Computational details

Quantum calculations on the structural optimizations, the complexation energies and chemical shifts were performed using DFT [15], Becke's three-parameter (B3) exchange function [16] along with Lee-Yang-Parr correlational functional (LYP) [17] and M06-2X empirical exchange correlation functionals [18]. M05 and M06 functionals are taken into account for medium-range electron correlation, indirectly, to describe the dispersion interactions [19,20]. "6-311G" was selected as the basis set level with "*d,p*" polarization functions and "++" diffuse functions [21]. Inputs on the atomic coordinates of the 1,8-cineole compound were created by Gauss View program [22] and optimizations and the complexation energies and chemical shift data were obtained by using Gaussian 09W software database [23]. The complexation energies were computed by basis set superposition error (BSSE) and counterpoise (CP) corrections [24]. The water as a solvent, and polarizable continuum model (PCM) were selected for the calculations of solvent effects in CP approach. NMR chemical shifts computings were completed by the Gauge independent atomic orbitals (GIAO) method [25] with the chloroform solvent. Tetramethylsilane

(TMS) was used as a reference molecule in computing of the ^{1}H and ^{13}C isotropic magnetic shielding (IMS) of carbon or hydrogen atoms.

3. RESULTS and DISCUSSION

3.1. Essential Oil Composition

In this study, the chemical composition of the volatile metabolites of *L. nobilis* collected during the flowering period of Turkey. Essential oil of dried aerial parts of *L. nobilis* were evaluated by GC and GC-MS. The analysis results of essential oils of *L. nobilis* are shown in Table 1 and in Figure 1. 21 compounds were identified, representing 99.3% of the *L. nobilis*, essential oil (Figure 1.). At the end 1,8-cineole (48.47%), β-pinene (%14.45), linalool (%8.15) and α-pinene (%5.97) were also determined as the major compounds (Table 1).

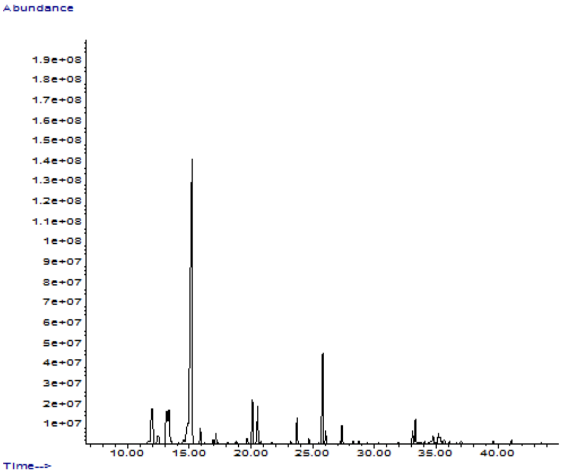

Figure 1 GC chromatogram of essentials oil of *L. nobilis*

Table 1 Chemical composition of essential oil of *L. nobilis*

	RT (min)	RRI	RRI*	Compounds	Peak area (%)
1	11.979	1112	1114^{a}	α-Pinene	5.97
2	12.470	1123	1122-1169^{b}	3-Carene	1.35
3	13.167	1138	1147^{a} 1085-1130^{b}	β-Pinene	14.45
4	14.531	1168	1154-1195^{b} 1188^{c}	α-Terpinene	0.61
5	15.207	1183	1186-1231^{b}	1,8-Cineole	48.47
6	15.890	1198	1261-1300^{b}	Terpinolene	1.25
7	17.156	1226	1148^{d} 1302^{a}	Linalool	0.66
8	20.115	1291	1209^{d}	4-Terpineol	3.81
9	20.538	1300	1215^{e}	α-Terpineol	3.31
10	23.721	1370	1259-1284^{b}	Bornyl acetate	1.97
11	24.677	1391	1391^{c}	(Z)-3-Hexenol	0.41
12	25.802	1416	1329-1358^{b}	α-Terpinyl acetate	8.15
13	26.049	1421	1411-1465^{b}	1-Octen-3-ol	1.06
14	27.365	1450	1394-1410^{b}	Methyl eugenol	1.44
15	33.093	1576	1562-1590^{b}	Spathulenol	1.22
16	33.322	1581	1563-1595^{b}	Caryophyllene oxide	2.06
17	34.054	1597	1532-1643^{b}	β-Guaiene, trans-	0.3
18	34.757	1613	1584^{e}	Ledene oxide	1.14
19	35.181	1622	1611-1655^{b}	β-Eudesmol	1.07
20	39.652	1720	1740^{f}	Cycloisolongifolene, 8,9-dehydro-9-formyl-	0.6
Oxygenated monoterpenes 72.10					
Sesquiterpenes hydrocarbons 20.81					
Oxygenated sesquiterpenes 6.39					
Total identified 99.30					

RT: Retention time, RRI: Relative retention index, RRI*: RRI from literature (a (26); b (27); c (28) d (29); e (30); f (31))

In the literature as 1.8-cineole, terpineol, β-pinene, α-pinene, p-cymene, β-caryophyllene as the main constituents of the essential oil of *L. nobilis* leaves are referred to. The acyclic monoterpenes (linalool and myrcenol) may also be present, as well as, dimethyl styrene, eugenol, methyl eugenol and carvacrol [32-36]. In our study, the first major compound is 1,8-cineole similar to other studies in Karadeniz region and different countries [37-40]. Also, another studies using *L. nobilis* essential oils from Brazil isoeugenol (53.5-57.0%) as first major compounds [32, 41]. In addition, our study major compounds of *L. nobilis* essential oils are show similarity and diversity with other studies. There are lots of factors affecting the production of secondary metabolites in plants. It can be explained as an environmental, geographical, physiological, genetic, political and social factors [37, 42].

3.2. Density Functional Theory Analysis

We have optimized the 1,8-cineole molecule with B3LYP hybrid functional, M06 functional approaches and Møller–Plesset second-order perturbation theory (MP2) to reveal the minimum energy structure. Optimized structure of the 1,8-cineole and relative energy diagram between the ab initio theoretical approaches is given in Figure 2. Total SCF energy is equal –467.263 a.u. in DFT/ restricted-B3LYP calculation method, 6-311++G (d,p) level. Relative energy of M06-2X functional approach (5.78 eV) is fairly smaller than MP2 method (38.49 eV). We are focused on the complexation energy calculation (for the carbons and hydrogens) between the B3LYP and M06-2X functional approaches. 1,8-cineole has cyclohexyl ring. The direction, position and dipole interaction of the dipole moment for the 1,8-cineole with Cs symmetry are reported in a previous DFT study [8]. We have calculated the dipole moment (field-independent basis) with the values of 1.5520 (RB3LYP), 1.5448 (RM06-2X), 2.3382 (RM06-2X solvent=water), 1.6882 Debye (RMP2-FC) by the 6-311++G (d,p) basis set.

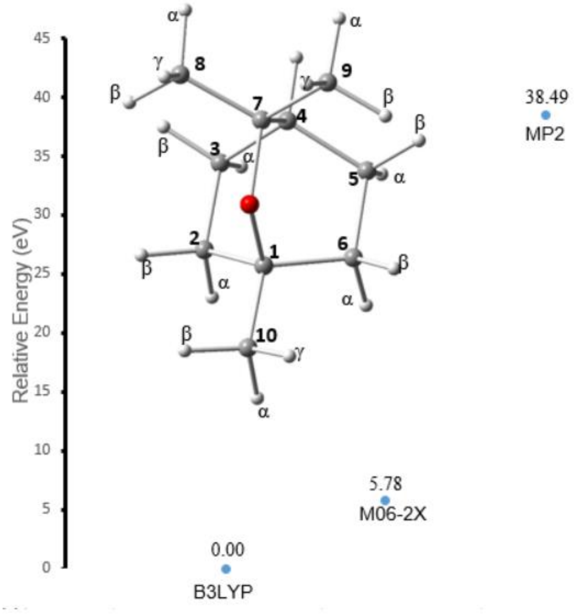

Figure 2 Optimized structure of the 1,8-cineole and relative energy diagram between the ab initio theoretical approaches

Table 2 shows to us the raw and corrected complexation energies with the BSSE energies of the total carbon and hydrogen atoms. The performances of the B3LYP and M06 functionals are tested in Table 2 for the carbon and hydrogen complexation energies of the investigated compound. Uncorrected and CP corrected energy are lower in the calculations of the B3LYP hybrid functional. However, the complexation energies of the total carbon and hydrogen are also lower at M06 functionals. When comparing the complexation energies of hydrogen and carbons in the same methods and basis sets, the hydrogens have of course weaker complexation energies. The atomic radius of hydrogen is much smaller. Because of the electronegativity effect of oxygen, the complexation energies of the carbons bonded to oxygen can be stronger than the others. The complexation energy (corrected) of the carbons are − 1996.94 (in gas phase) and − 1996.71 kcal/mol (in water solvent using PCM method) at M06-2X approach, B3LYP/6-311G (d, p) levels. The corrected complexation energy of the hydrogens are −1906.90 (in gas phase) and − 1906.13 kcal/mol (in water solvent using PCM method) at M06-2X approach, B3LYP/6-311G (d, p) levels. It can be said that the solvent effect weakens the binding energy of the carbons and hydrogens and intramolecular interaction. Binding energies of inclusion complexes with eucalyptol are − 2.86 (in water using PCM methods,−2.01 (as corrected in gas phase) and − 5.45 kcal/mol (as uncorrected in gas phase) at DFT/B3LYP/6-31G (d) levels in another study [11].

Table 2 Energy values of the 1,8-cineole by ab initio calculations and 6-311++G(d,p) level

	Total carbon atoms		Total hydrogen atoms	
Energies	B3LYP	M06-2X	B3LYP	M06-2X
Uncorrected energy (a.u)	-467.2629	-467.0505	-467.2629	-467.0505
CP corrected energy (a.u.)	-467.2489	-467.0323	-467.2510	-467.0334
BSSE energy (a.u)	0.0141	0.0182	0.0120	0.0172
Raw complexation energy (kcal/mol)	-1884.77	-2008.39	-1801.62	-1917.68
Corrected complexation energy (kcal/mol)	-1875.94	-1996.94	-1794.12	-1906.90

The computed ^{1}H and ^{13}C NMR chemical shifts of 1,8-cineole are listed in Table 3. The computed data are compared with the experimental ones [43] obtained from the literature. Mean absolute errors (MAE) are narrow and indicate that the calculations are consistent with the experimental results. The carbon and hydrogen atoms in the table are numbered and symbolized according to the model in Figure 2. The chemical shifts of the carbons are calculated to be 76.735 ppm (B3LYP), 72.618 ppm (M062X) in **1** and 81.141 ppm (B3LYP), 76.903 ppm (M062X) in **7**. When compared to the others, these values are the highest values. The chemical shifts are also lowest in **3** and **5**. There is a deshielding effect of oxygen due to electronegativity. Due to the electronegative effect, carbons close to the oxygen atom have higher chemical shifts. We can conclude that the deshielding effect is higher on the carbon **1** and **7**. The previous studies have emphasized that the electron-withdrawing groups made smaller the shielding [44, 45].

Table 3 Computed ^{13}C and ^{1}H NMR Chemical Shifts (δ) of 1,8-cineole by ab initio calculations

Labeled Atoms	$\delta^{*}_{calculated}$ (ppm) (B3LYP approach)	$\delta^{*}_{calculated}$ (ppm) (M06-2X approach)	$\delta^{**}_{experimental}$ (ppm)
C1	76.735	72.618	73.62
C2	35.937	35.662	31.57
C3	28.711	28.052	22.90
C4	38.407	34.916	33.00
C5	28.714	28.037	22.90
C6	35.937	35.685	31.57
C7	81.141	76.903	69.77
C8	30.544	33.203	28.92
C9	30.544	33.226	28.92
C10	30.167	33.575	27.61
H2(α)	1.555	1.4255	1.50
H2(β)	1.605	1.6303	1.661
H3(α)	1.493	1.5396	1.50
H3(β)	2.066	2.0485	2.022
H4	1.302	1.0695	1.41
H5(α)	1.492	1.5394	1.50
H5(β)	2.066	2.0484	2.022
H6(α)	1.555	1.4292	1.500
H6(β)	1.605	1.6302	1.661
H8(α)	0.944	0.9411	1.239
H8(β)	1.505	1.4163	1.239
H8(γ)	1.154	1.1994	1.239
H9(α)	0.944	0.943	1.239
H9(β)	1.506	1.4157	1.239
H9(γ)	1.154	1.2004	1.239
H10(α)	0.859	0.8823	1.050
H10(β)	1.056	1.1848	1.050
H10(γ)	1.056	1.1829	1.050
MAE	*1.71378571*	*1.615775*	

*solvent=chloroform and Polarizable Continuum Model.

**Taken from Ref. [23]

4. CONCLUSION

The findings showed that the *L. nobilis* had a low-level variation in essential oil composition and this study demonstrates the occurrence of 1,8-cineole (eucalyptol) chemotype of *L. nobilis* in Central Black Sea region of Turkey. In general, the essential oil composition of *L. nobilis* patterns from the different region showed that, the species has sabinene, myrcene, camphene were the major and predominant compounds.

The complexation energies, chemical shifts of the carbon and hydrogen_atoms in the 1,8-cineole structures are computed by B3LYP hybrid functional and M06 functional approaches in our theoretical work. The calculations by M062X functional approach have provided the effective results to us for the raw and corrected complexation energies. The solvent effect weakens the complexation energy of the carbons and hydrogens and intramolecular interaction. The complexation energies of the carbons bonded to oxygen are strong due to the electronegativity effect of oxygen. The calculated ^{1}H and ^{13}C NMR chemical shifts of 1,8-cineole are consistent with the experimental results. Due to the electronegative effect, carbons close to the oxygen atom have higher chemical shifts.

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The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by the authors.

Authors' Contribution

All authors have contributed in experimental study and writing of the manuscript equally.

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