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Theoretical investigation of Malva sylvestris L. in point of Nano Bio Technology

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ABSTRACT

Over the past decade, the chemical behavior of flavonoids as antioxidants has become the subject of intense experimental research. Plants represent a main source of natural antioxidants that might serve as leads for the development of novel drugs. Malva sylvestris L. known to have various medicinal properties since several decade ago, were evaluated for their antioxidant compounds ,Most of these bioactive properties correlated with antioxidant activity of phenolic compounds found in the plant ,11 phenolic composed were isolated from water leaf extract of Malva sylvestris L. ,the main phenolic acids identified in Malva sylvestris L. leave's are gallic , pyrogalllol ,vanillic , synergic , cinnamic and chrisin acid .antioxidant and antiprotozoic activities quercetin is the major flavonoid in the human diet and has been reported for their radical scavenging effect .They have been proved to have potential preventive and therapeutic effects in many diseases . This study involves substitution of the functional group of methyl in the active site of some terpenoids isolated from Malva sylvestris L. with other functional groups such as F,Cl,and Br and calculations by keywords Opt, NMR,and Freq for optimization and chemical shift calculations and drive thermodynamic parameters including Enthalpy ,Gibbs free energy respectively. The quantum mechanics (QM) calculations were carried out GAUSSIAN98 at NMR by using B3LYP methods with 6-31G basis set.

Keywords: Flavonoids; Antioxidant; Malva sylvestris L.; Nuclear magnetic resonance (NMR)

INTRODUCTION

Free radicals due to increases of technology, radiation, chemical pollutants, toxins, preservative drugs, deep fried fast foods as well as physical stress, including atherosclerosis, arthritis, ischemia and reperfusion injury of many tissues, central nervous system injury, gastritis, cancer and AIDS [1].currently, there is a world wide trend and interest towards the use of medicinal and aromatic plants as antioxidants in foods [2]. Besides, they are well known and have been traditionally used as natural drugs as antioxidants, anti inflammation and antiseptics to treat many ranges of illness. Therefore consuming antioxidants as free radical scavengers may be necessary [3].

In vascular plants, more than 4000 phenolic and polyphenolic compounds are the most antioxidants which have been identified, namely, phenolic acids, tannins, coumarins, anthraquinones, flavonoids,

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phenolic diterpens and anthocyanin [4]. Which have the ability to scavenge free radicals, donate hydrogen atoms or electrons, or chelate metal cations [5]. High correlation was reported between total flavonoids and phenolic phenolic compounds of plants with free radical scavenging activity, inhibition of hydrolytic and oxidative enzymes [1]. Phenolic compounds have antioxidant properties and can protect against degenerative diseases. All plants based-foods have phenols, which affect their appearance, odor, taste and oxidative stability. Phenolic antioxidants such as hydroxybenzoates and flavonoids are important classes of natural antioxidant .The antioxidant efficiency of the phenolic acids and flavonoids have been related to the number of hydroxyl groups in the molecule and also to their hydrogen radical donating abilities [6]. Phenolic acids present in plants are hydroxylated derivatives of benzoic and cinnamic acids. Flavonoids are low molecular weight compounds, consisting of fifteen carbon atoms, arranged in a C6-C3-C6 configuration .Essentially the structure consists of two aromatic rings A and B, joined by a 3-carbon bridge ,usually in the form of a heterocyclic ring ,C .The aromatic ring A is derived from the acetate/malonate pathway, while ring B is derived from phenylalanine through the shikimate pathway. Variations in substitution patterns to ring C result in the major flavonoid classes [7].

Oxidation is a natural process in organisms for the production of energy to fuel biological cycles. Conversely, the uninhibited production of oxygen-derived free radicals is involved in the onset of many diseases such as cancer as well as in many degenerative diseases related with aging [8]. Antioxidants are compounds that can delay or inhibit the oxidation of lipids or other molecules by inhibiting the initiation or propagation of oxidizing chain reactions [9]. Antioxidants are important components because they protect against free radicals, such as reactive oxygen species in the human body. Free radicals are known to be the major contributors to degenerative diseases of aging and are recognized as major factors causing cancer. The human can use antioxidants either as dietary, food supplements or as a medicine [10]. Malva sylvestris L. is a species of the Mallow genus Malva in the family of Malvaceae and is considered to be the type species for the genus.Known as common Mallow to English speaking Europeans.

The active components of the Malvaceae species are found in the leaves, flowers, seed and roots. Several studies document the mucilaginous polysaccharide content in the plant, the primary components are composed of rhamnose, galactose, galacturonic acid and glucuronic acid [11]. Flavonoids, phenolic acids, tannins and volatile oils have also been studied [12]. Malonated anthycyanins have been isolated from the flowers [13] Genotype and plant part were important sources of variability in proximate composition, mineral content ,anti-nutritive compounds, fatty acids and antioxidant activities [10]. Malva sylvestris L. had relatively high antioxidant capacity.Four major fatty acids (Linolenic, Linoleic, Palmitic and Oleic acids) measured more than 82% of total fatty acids in leaves and petioles [10].

METHODS

The main effective molecules in Malva sylvestris L. are desoxyhemigossypol (A), ancistroquinone (B), (+)-δ-cadinene (C). (Fig. 1) have methyl functional group in their active sites.

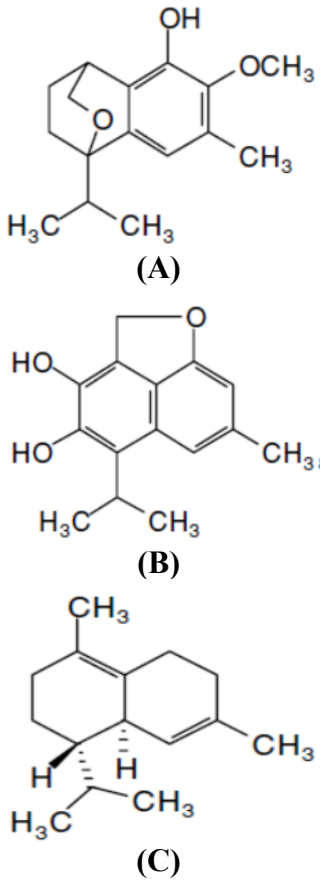


Fig. 1. Malva sylvestrisL. Effective molecules. Desoxyhemigossypol (A), ancistroquinone (B), (+)-δ-cadinene (C).

By using the Chem draw software, it is possible to show the chemical structure of the molecules that have main role in the anti cancer effect of Malva sylvestris L.the chemical structure saved in cdx file, then cdx file change to gjc file in Chem3d software, this process is continued until a set of low energy conformers has been generated.Energy, NMR, Opt, Freq computational studies was done using Gaussian 98 program at Hartree-Fock Theory. In computational physics and chemistry.The Hartree-Fock method is an approximate method for the determination of the ground –state wave function and ground –state energy of a quantum many-body system. the study involves the substitution of functional groups in the active site of effective molecules and calculations by keywords Opt and NMR Freq for optimization and chemical shift, Gibbs free energy and Enthalpy respectively.Typically it is only necessary to report the six principal compounds σ11, σ22, σ33 when discussing the magnitude of the shielding tensor, these tensors can also be described by three additional parameters:the isotropic value ,σiso non symmetric shielding tensor, Δσ, and shielding tensor anisotropy, Ω. In present work, we have calculated the lowest energy each locally geometrically stable structure, thermodynamic properties and NMR parameters in various replacement of electronegative elements. the electronic structure of the complex is treated at DFT/B3LYP treatment at 6-31G basis set for each locally geometrically stable structure we investigate the possibility of forming. The band gap of mentioned system as the relative differences in the energy of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) have been calculated.

RESULTS AND DISCUSSION

In this study, we have investigated NMR parameters, thermodynamic properties, stability energy and atomic charge in different replacement of halogen atoms (Table1). The electronic structure of complexes has optimized at DFT/B3LYP/6-31G* level for each replaced structure.

With σisotropic and σanisotropic and chemical shielding interaction parameters (σ11, σ22, σ33) and with using mathematical terms between them, chemical shift anisotropy (Δσ), asymmetry parameter (η) and shielding tensor anisotropy (Ω) were calculated for these effective molecules in different replacement of halogen atoms in their active sites (Table1).

Table 1. Calculated parameters of Gibbs free energy, enthalpy, stability energy, Dipole moment and Δ(HOMO-LUMO) LUMO-HOMO band gap for desoxyhemigossypol structure(A) and different replacement of1-9 atoms of (a) F, (b) Cl and (c) Br at DFT/B3LYP/6-31G*level

COMPOUND	Dipole moment (Debye)	Energy relative (kcal/mol)	Enthalpy (kcal/mol)	Gibbs Free Energy (kcal/mol)	(HOMO-LUMO) (kcal/mol)
Desoxyhemigossypol (structureA)	0.614344398	0	186.478438	148.1986959	-0.16605
1F	1.162122795	-62×10^{-3}	182.4404379	142.4758421	-0.16708
9F	3.505048264	56×10^{-4}-	146.6449913	98.10803744	-0.16268
1Cl	3.17851908	-28×10^{-4}	181.8336397	141.2340079	-0.16054
9 Cl	4.06460316	-26×10^{-5}	138.0952234	83.83729826	-0.1486
1Br	3.173356805	-16×10^{-5}	181.5801273	140.4471155	-0.15744
9 Br	3.629681767	-15×10^{-6}	136.0200614	74.75289535	-0.12569

Table 2. Some of NMR parameters for each atoms of desoxyhemigossypol structure (A) DFT/B3LYP/ 6-31G*level

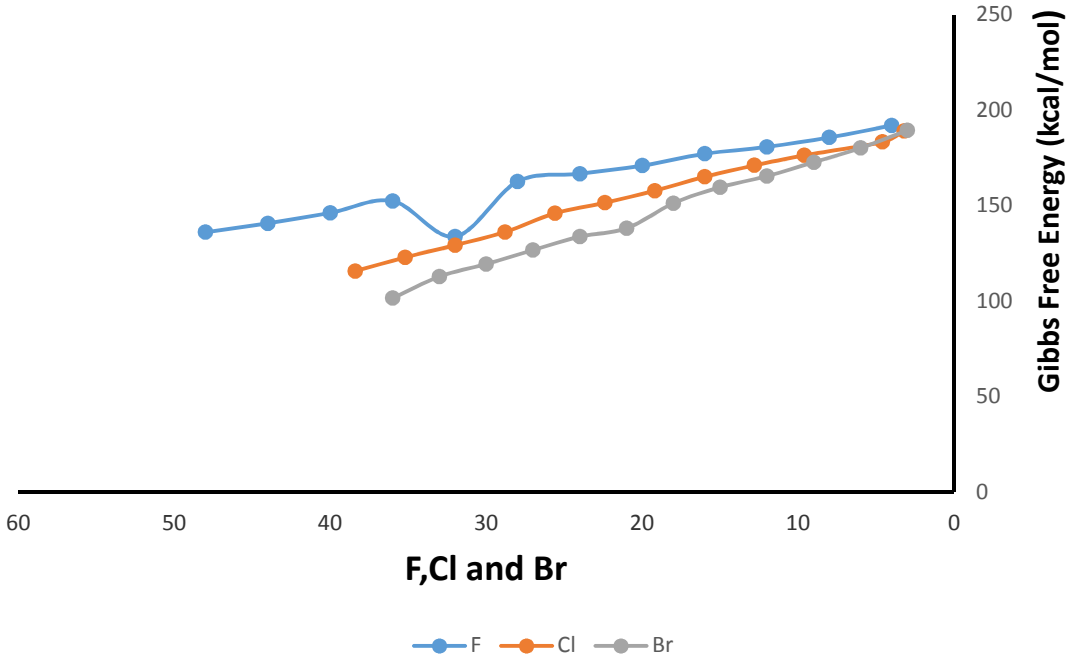
Number of Atom	charge	σIsotropic	σAnisotropic	η	Δσ	Ω
27 H	0.413105	28.0234	13.2161	0.658688	-15.9356	-10.6237
26 H	0.407337	29.0619	13.7382	0.93713	-14.1841	-9.456
4 C	0.334725	36.0243	94.8683	0.851704	-102.466	-68.3106
7 C	0.227193	50.9318	110.6324	0.618551	101.8761	73.7549
6 C	0.207719	58.6766	99.8304	0.65411	103.4635	66.5535
11 C	0.182123	58.7478	168.3051	0.549869	140.1027	112.2035
19 H	0.164387	26.8942	7.2276	0.645168	-8.7865	-5.8577
20 H	0.164359	26.8943	7.2272	0.645094	-8.78635	-5.8576
31 H	0.161251	29.9892	6.7621	0.489058	-9.0823	-6.0549
34 H	0.161251	29.9892	6.7621	0.489058	-9.0824	-6.0549
25 H	0.159744	29.6894	8.4976	0.626397	33.5802	5.6651
23 H	0.159743	29.6894	8.4977	0.626414	33.58015	5.6651
24 H	0.151881	30.3277	6.634	0.637079	-8.1046	-5.4031
30 H	0.151744	30.9533	8.3172	0.492732	35.13205	5.5448
33 H	0.151741	30.9534	8.317	0.492705	35.13215	5.5447
9 C	0.146227	71.1423	170.6665	0.047353	182.2262	113.7777
29 H	0.14096	30.8747	9.7394	0.11163	37.0052	6.4929
32 H	0.14096	30.8747	9.7394	0.11166	37.0051	6.4929
22 H	0.126219	26.0927	6.1987	0.681382	-7.3734	-4.9156
21 H	0.116343	25.2658	11.6231	0.611367	30.64585	7.7487
28 H	0.095961	29.5157	7.716	0.836139	32.50915	5.144
8 C	0.057128	74.3342	128.1311	0.277103	147.9198	85.4207
2 C	0.040528	77.8205	99.1856	0.748641	119.1928	66.1238
3 C	-0.00643	73.9576	144.0256	0.218388	159.4902	96.0171
1 C	-0.0954	118.7654	69.9996	0.531907	153.0207	46.6664
16 C	-0.17098	157.0927	10.3304	0.721105	-12.0045	-8.003
12 C	-0.25203	93.9964	111.8997	0.612689	145.743	74.5998
10 C	-0.30587	81.3173	114.1921	0.986879	119.8808	76.1281
18 C	-0.44092	167.1866	29.4063	0.685409	180.0724	19.6042
17 C	-0.44092	167.1877	29.4053	0.685505	180.0721	19.6035
13 C	-0.53222	165.7585	37.3865	0.723251	181.6696	24.9244
5 O	-0.5479	205.6306	95.4421	0.909155	240.3348	63.6281
14 O	-0.63388	226.2139	51.341	0.975787	-51.9703	-34.6468
15 O	-0.63609	228.9292	94.9359	0.816257	266.3891	63.2906

Table 3. Some of NMR parameters for each atoms of desoxyhemigossypol structure (A) and replacement with 9 Br at DFT/B3LYP/6-31G*level

Number of Atom	charge	σIsotropic	σAnisotropic	η	Δσ	Ω
1 C	-0.09603	118.3874	70.1649	0.559593	70.16495	46.7767
2 C	0.049557	74.0923	104.7673	0.664424	104.7674	69.8449
3 C	-0.00765	71.9588	140.4885	0.196042	140.4886	93.659
4 C	0.335117	37.3859	90.4637	0.855979	-97.4837	-64.9891
5 O	-0.54261	203.7139	95.0789	0.958451	95.07885	63.3859
6 C	0.211004	55.0032	103.9946	0.62915	103.9946	69.3297
7 C	0.300995	44.6021	120.144	0.511777	120.144	80.096
8 C	0.019807	75.8105	111.2692	0.356445	111.2692	74.1795
9 C	0.174123	69.815	167.053	0.069962	167.053	111.3686
10 C	-0.28961	82.4282	127.732	0.495113	127.732	85.1547
11 C	0.168295	47.1945	144.1477	0.371858	144.1477	96.0984
12 C	-0.21663	92.4578	117.7359	0.445973	117.7359	78.4906
13 O	-0.62356	220.7988	64.2625	0.852756	64.26255	42.8417
14 O	-0.64108	189.9253	120.8761	0.308401	120.8761	80.5841
15 C	-0.2353	109.6426	29.9493	0.173338	29.94935	19.9662
16 C	-0.04861	62.6503	15.961	0.190701	-26.8095	-17.873
17 C	-0.14849	60.5906	34.724	0.139568	34.72395	23.1493
19 C	-0.07186	61.2072	28.1328	0.945772	-28.917	-19.2779
28 H	0.174215	26.8476	7.6139	0.660245	-9.172	-6.1147
29 H	0.17605	26.835	7.6283	0.691828	-9.0179	-6.0119
30 H	0.176649	24.6711	17.1758	0.368513	17.17585	11.4506
31 H	0.166583	25.2296	10.1726	0.670009	10.1726	6.7817
32 H	0.413089	28.7588	14.8997	0.949734	14.89975	9.9332
33 H	0.429089	26.0564	17.067	0.392421	17.0671	11.3781
34 H	0.24001	26.5996	7.934	0.779971	7.93395	5.2893

We have found that effective molecules, structure with most number of halogen denoted has maximal shift in theoretical level. Also we have seen that by increasing charge transfer, value of chemical shift and chemical anisotropy has been increased (Fig. 4).

As a result, it has been shown that by increasing F, Cl and Br atoms, the Gibbs free energy and Enthalpy and stability energy have been decreased and the system has been stabilized (Fig. 2). The result indicate that electronegative atoms enlarges the dipole moment by, which for molecule corresponds to an increase with regard to the number of F, Cl and Br atoms (Fig. 2). It seems that, for these effective molecules with different replacement of halogen atoms in their active sites the highest Δ (HOMO-LUMO) values and then highest stability has been occurred by increasing the number of halogen (X=F, Cl, Br).


250
200
150
100
50
0
Gibbs Free Energy (kcal/mol)
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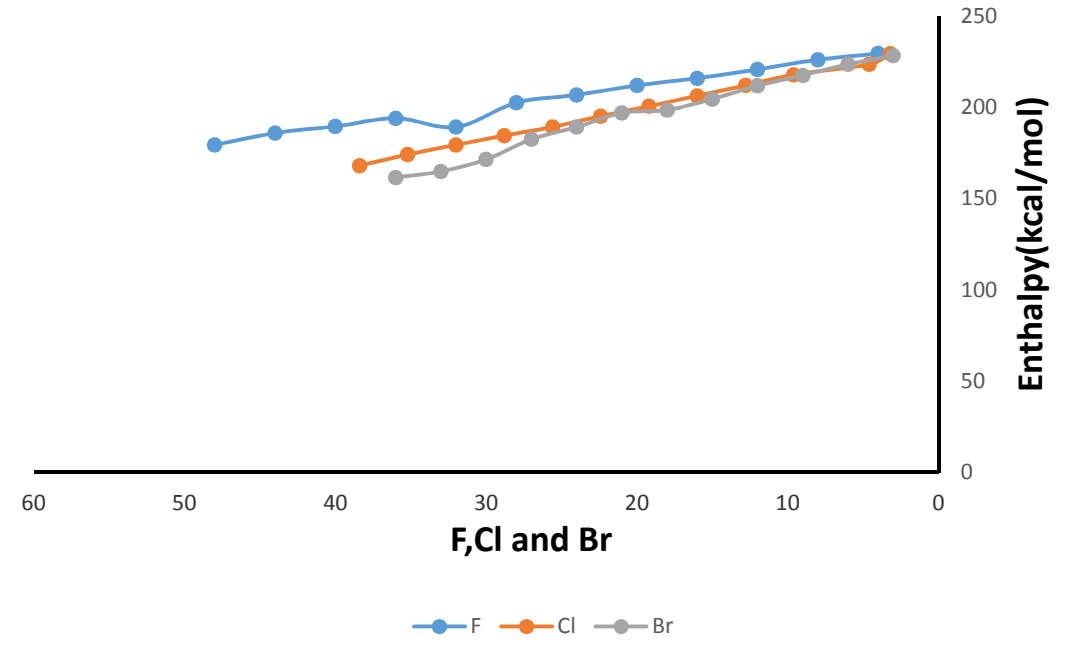
50
40
30
20
10
0
F,Cl and Br
F
Cl
Br

(a)


250
200
150
100
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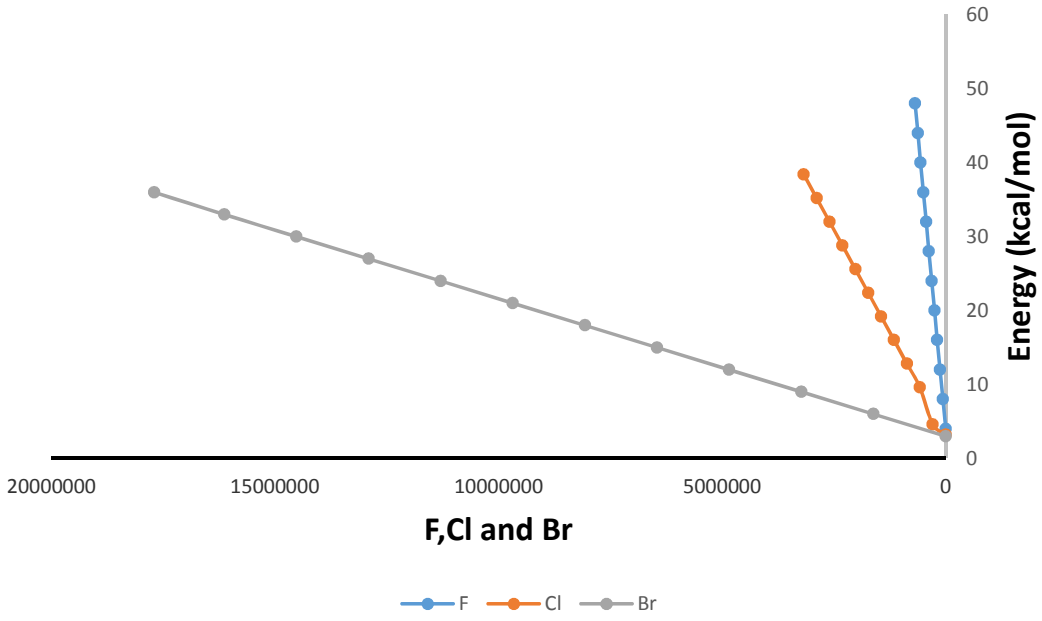
Enthalpy(kcal/mol)
60
50
40
30
20
10
0
F,Cl and Br
F
Cl
Br

(b)


60
50
40
30
20
10
0
Energy (kcal/mol)
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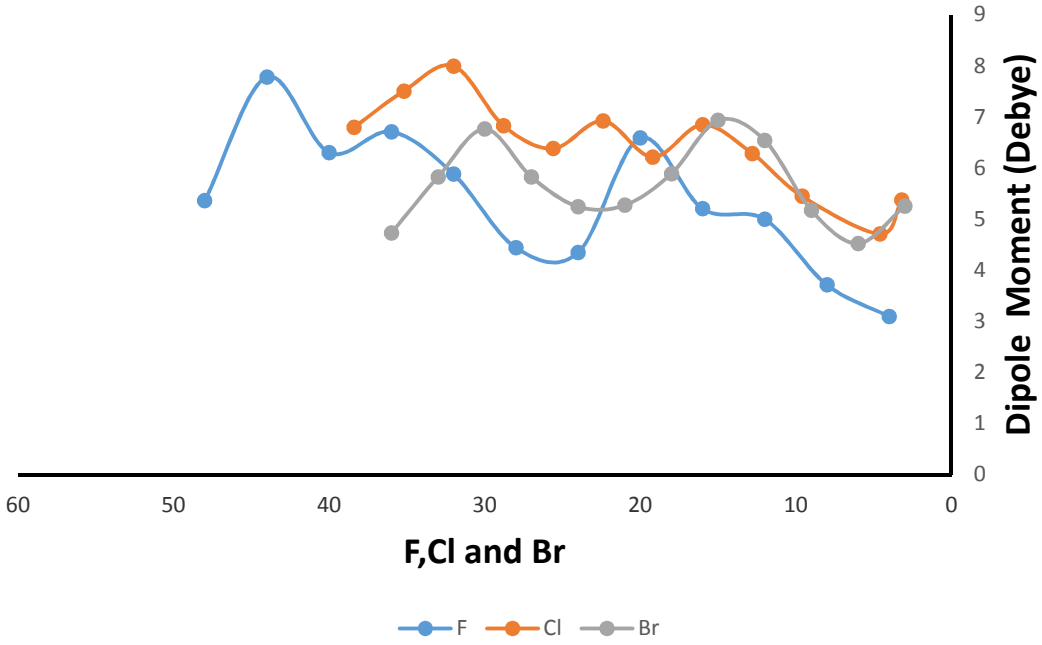
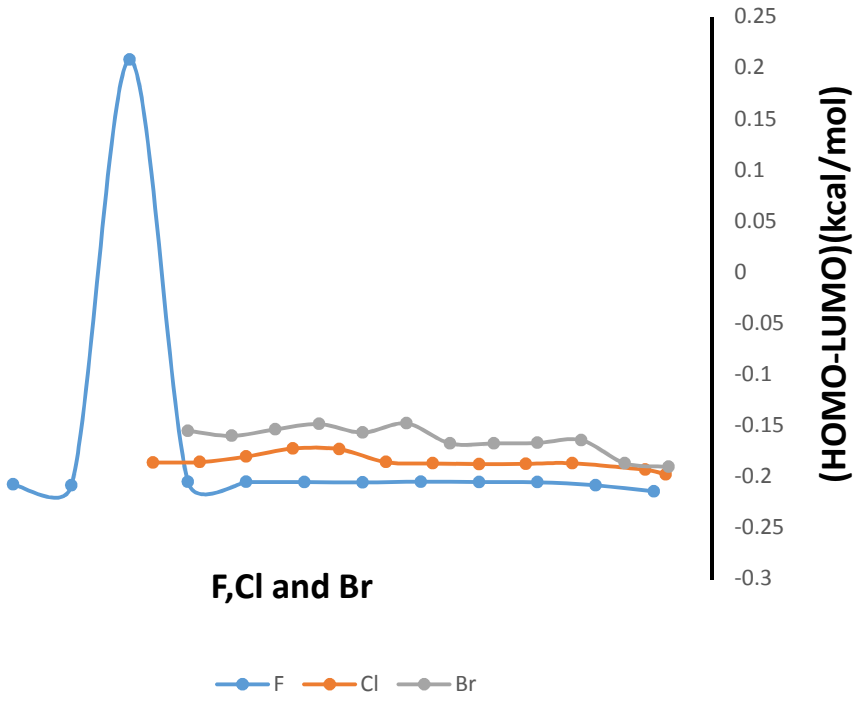
15000000
10000000
5000000
0
F,Cl and Br
F
Cl
Br

(c)


9
8
7
6
5
4
3
2
1
0
Dipole Moment (Debye)
60
50
40
30
20
10
0
F,Cl and Br
F
Cl
Br

(d)



(e)

Fig. 2. Plotted of (a) Gibbs free energy (b) Enthalpy (c) Stability energy (d) Dipole moment and (e) (HOMO-LUMO) band gap for ancistroquinone (structure B) and different replacement of 1-9 atoms of F, Cl and Br (X).

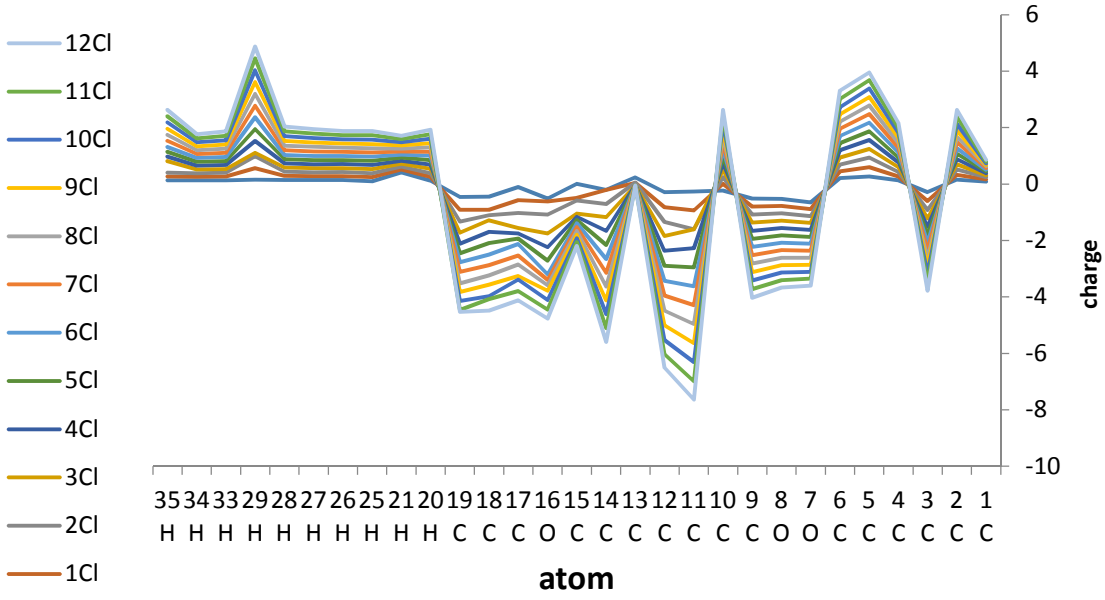


Fig. 3. Calculated atomic charge each atoms of via ancistroquinone (structure B) and replacement Cl electronegative atoms at DFT/B3LYP/6-31G* level.

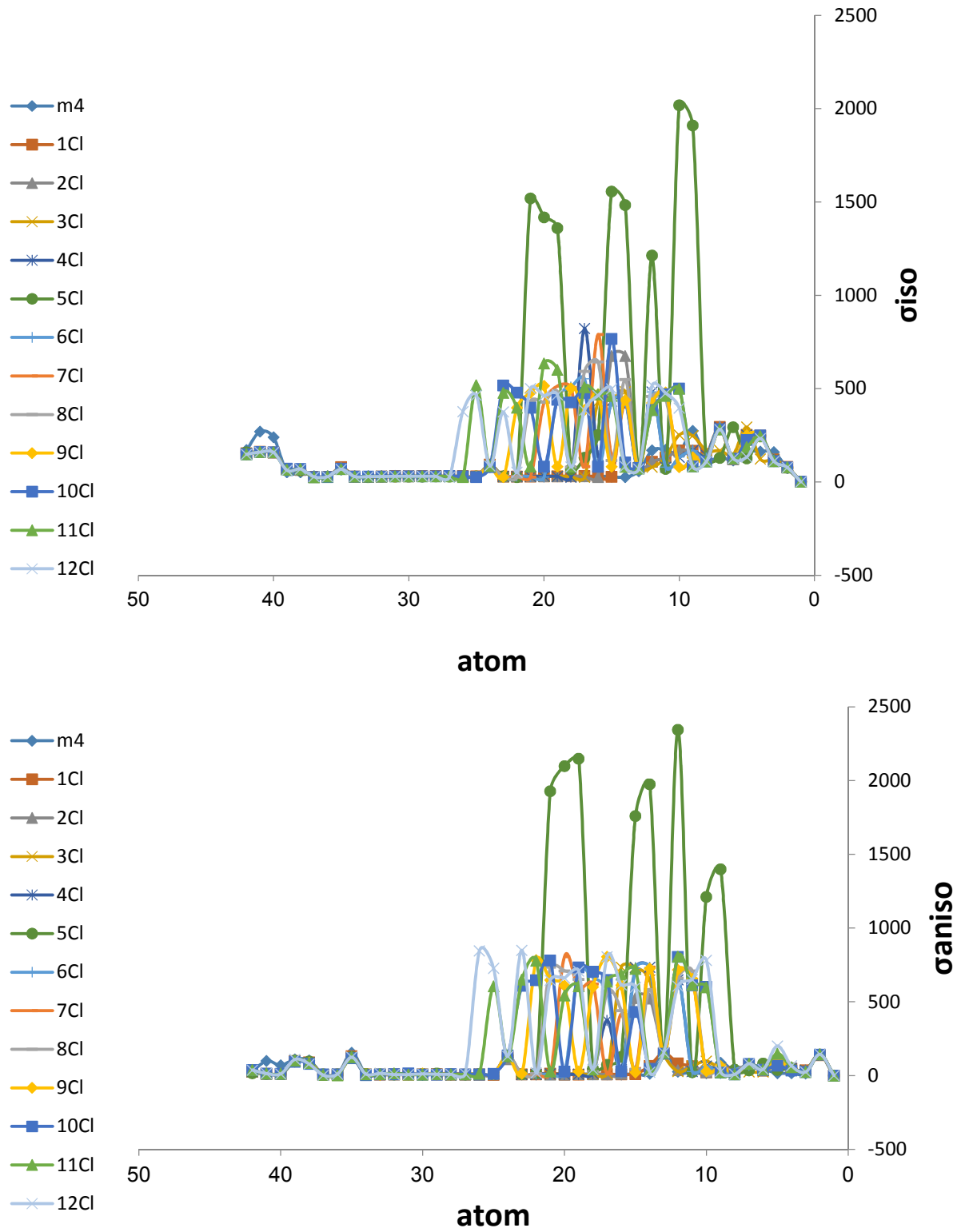


Fig. 4. calculated NMR parameters of isotropic chemical shielding (σisotropic) and anisotropic chemical shielding (σanisotropic)(ppm) foe each atoms of ancistroquinone structure(B) and different replacement of F electronegative atoms at DFT/B3LYP/6-31G* level.

CONCLUSION

In this paper we have been calculated NMR parameters, thermodynamic properties, HOMO-LUMO gap, stability energy, atomic charge and dipole moment with different replacement of halogen atoms in the main effective molecules in Malva sylvestris L., desoxyhemigossypol (A), ancistroquinone (B), (+)-δ-cadinene (c) (Fig. 1). The result shows that stability of terpenoids isolated from Malva sylvestris L increase with increasing number of halogen and by increasing the electronegative atoms of F, Cl and Br to mentioned structure, changes of each pick has been increased and also we have seen the same behavior for halogens in this replacement and system with most halogen (F, Cl and Br) replacement showed highly effects in DFT theoretical level with demonstrated some high comparable peaks. Also, complexes correlated strongly with the total electron charge transfer and electronegative effect. Mentioned molecule have effective role in anticancer characteristic of Malva sylvestris L. were selected.

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