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Research Article

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Theoretical Study of Carbamazepine Derivatives as a Possible Drugs by using Quantum Mechanics Methods

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ABSTRACT

The project concern with using of Quantum mechanics Calculation methods PM3 and AM1 methods by using the program Hyper chem. 8.08 to calculate the equilibrium geometrical structure of the drugs. Carbamazepine and its derivatives (R = -OH, -OCH_3, -F_2, -$OCOCH_2CL$, -Br) which are yet unused as a drugs. The physical properties of the drug and it's derivatives were calculate at their equilibrium geometrical structure as bond length, heat capacity, enthalpy, total energy, dipole moment, EHOMO, ELUMO, ionization energy, electron affinity and the IR, UV- Vis spectra. The theoretical results showed that energy of the derivatives (F2, Br) was similar to that of the drug and both have ionization energy similar to that of the drug, this result was improved by the similar polarity of both drug and derivatives.

Keywords: Carbamazepine; PM3 and AM1; Geometry optimization

INTRODUCTION

Carbamazepine is a drug used for epilepsy disease known by (CBZ), a drug effect on the nerves as the nerves pulses which cause the disease. The chemical formula is C15H12N2O and structure as shown in Figure 1 [1].

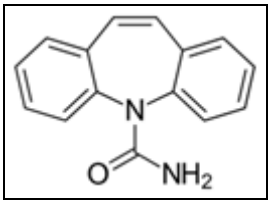


Figure 1: Structure of carbamazepine

The Carbamazepine use to increase the stability of the nerves membrane by the inhibition of release of the effected ion as (Na^+) by the closed of Na^+ channel [2]. Quantum Mechanic Calculation Semi – empirical method (PM3, AM1) was adduced to predict the physical properties of the Carbamazepine and it's derivatives to use these properties as correlations factors for qualification of possible drugs. Previous studies were reported that (AM1) method was used to calculate the equilibrium geometrical structure of derivative for (HIV-1) virus inhibitors and other physical properties to enhance the efficiency of the drugs [3]. Hyper chem. 8.08 program (AM1, PM3) methods were used to calculate the physical properties and the stability for Ampicillin drug and its derivatives [4].

EXPERIMENTAL SECTION

The program that used in the search: Hyper chem. It is a powerful software program that allows the construction of models of different organic compounds of these vehicles we will be able to measure the different molecular properties such as the corners of the bonds and the heat of formation etc. It allows for inferences about molecular stability and effectiveness molecular. This program is able to calculate the potential energy surfaces

that coats the particles, can this program to calculate the lowest energy molecular using different computational methods, it includes several copies of a Hyper chem. 6.2, Hyper chem. 7.2, Hyper chem. 8.0 [5]. The program that was used in this research Hyper chem. 8.08.

Computational Methods that were Used in the Search

Semi- empirical calculation method:

Term Semi –empirical it comes from empirical data. This method is based on the accounts Hartree – Fock links are faster than Ab initio and applied to large molecules and give accurate results. This method is useful in the study of the interactions of organic compounds [6] and it includes a number of modified models:

Austin model / version 1 (AM1): This method is considered the most sophisticated in the calculation ΔH_f and allow hydrogen as bond and calculate dipole moment m, electronic energy and the qualities of synthetic molecules and ionization energy determination as well as calculate the length and severity of the corner bond [7].

Parametric method / version 3 (PM3): This method is the upgraded version of the AM1 to overcome many of the disadvantages, and rely on approximation Neglect of Diatomic Differential Overlap (NDDO), the PM3 model is the development of the method of Semi- empirical, it uses organic molecules and many of the elements of the main aggregates [8]. It is the way in which it adopted in this research.

Types of Accounts by the way Semi – Empirical (PM3) (AM1)

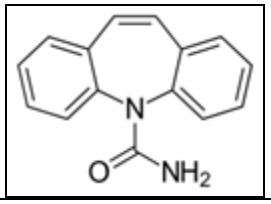
1. Single point Calculations to calculate the energy molecule and the properties of the geometric shape of the flexible given.
2. Geometry Optimization Calculations near give energy to determine the most stable from.
3. Vibrational Frequency Calculations find the natural vibrations of the ideal form of formula and show vibrational spectra and vibratory movements associated with animated transitions identified and mapped.
4. Transition state compositions stable matching set to transition situations using either eigenvector or synchronous transit methods and then calculates molecular properties.
5. Spectrum UV –Vis possible to calculate after creating overlapping structures to form the geometric ideal between HOMO (Highest Occupied Molecular Orbital) and LUMO (Lowest Unoccupied Molecular Orbital).
6. Electron density calculate.
7. Dipole moment calculate.
8. Electron charge calculate.
9. Vibrational frequencies account to absorb the infrared spectrum IR.
10. Ionization energy calculate which is defined as the energy required to remove an electron in a molecule is given by equation: [9] M + energy $\rightarrow$ $x^+ + e^-$.
11. Electron affinity calculate which is a recipe for measuring energy discharge when adding an electron to molecule to form a negatively charged ion, as follows: [10] $M + e^- \rightarrow M^-$ + energy.

Computer's properties which used in this study:

System: Windows 2010
Hard disk: 464 GB
CPU: 1.70 GH + 2.40 GH_Z
RAM: 4 GB

Carbamazepine Drug

In this research study some of the physical properties of a drug Carbamazepine and some of the products of other studied theoretically, using calculation methods (PM3, AM1). The preliminary structure of the geometric spatial molecule drug Carbamazepine, it was then reduced energy in order to calculate the equilibrium geometry. It was also calculate fundamental vibration and the intensity of the absorption of the infrared spectrum when the geometry of the equilibrium of these derivatives in addition to the limits of energy and other physical values. As well as calculate the dipole moment, ionization energy and higher energy electrons orbital occupied EHOMO, lower energy electrons orbital unoccupied ELUMO, and the energy difference between the two, using calculation methods (PM3, AM1), reliance on account program Hyper chem. 8.08. The preparation of a number of existing derivatives of this compound in the literature of publication Figure 2 and are as follows [11]:



Chemical Names:	Carbamazepine; Tegretol; 5H-Dibenzo[b,f]azepine-5-carboxamid
Molecular Formula:	C15H12N2O
Molecular Weight:	236.26858 g/mol

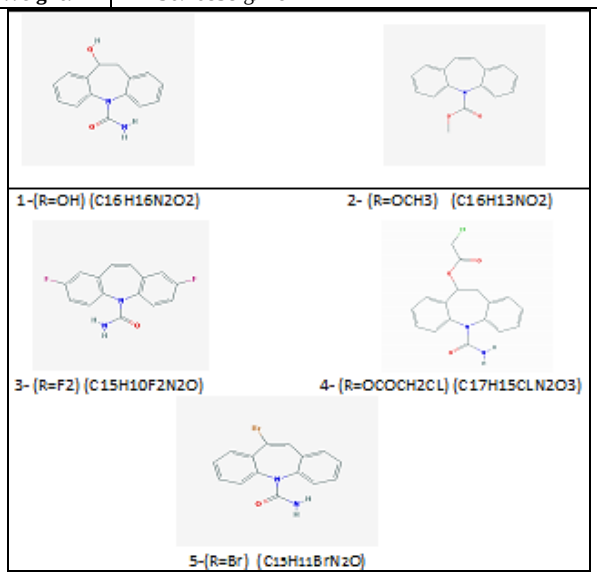


Figure 2: Forms of derivatives drug carbamazepine

RESULTS AND DISCUSSION

Theoretical Calculation of the Drug Carbamazepine and its Derivatives

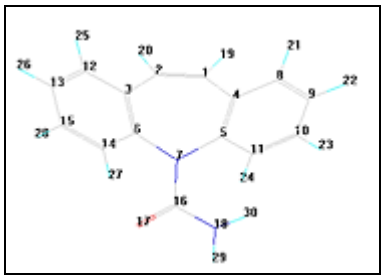


Figure 3: Spatial geometry of a drug carbamazepine

Equilibrium Geometry Shape Calculations

The initial image was painted to form geometric spatial molecule drug Carbamazepine using account program Hyper chem. 8.08, it was then reduced energy in order to calculate the equilibrium geometry the drug (Figure 3), with the extract entropy, in addition to the limits of energy and other physical values (Heat capacity) total energy, free energy using calculation methods semi – empirical (PM3, AM1) the drug Carbamazepine. The results for the two methods are relatively close, since the difference between the two methods is due to the difference in ways that account (Approximations used both ways). Negative values highly the different energies of a drug Carbamazepine and its derivatives show as high stability. Since the derivative (R=OCOCH2CL) stability is the most (-86153.8, -95262.2) other derivatives and medicine foundation. It was also the calculate dipole moment which is the sum of moments of molecular bonds, and the dipole moment is used to measure the polar molecule. It was calculated the dipole moment of drug Carbamazepine and a group of derivatives by using semi – empirical method (PM3, AM1) as in the Table 1. It came dipole moment between the two methods close torque values, and it found that most of the derivatives are less polarity of the foundation drug except for the last two derivatives and which contain halogen atoms (CL, Br) where increased polar molecule. The increase means more polar ionize molecule or decompose in the body, a recipe sometimes seem useful in the event that the period needed for decomposition is sufficient for the performance of his duty drug in the body and then disintegrates after that. The results of the two methods generally convergent and found that the most value

derived is more polar and therefore faster disintegration, most therefore be relatively derived asymptotic to the polarity of the drug in order to be possible to use it as a drug since the disintegration of the drug rapidly lead to the selection of him as property interest. The difference of the value of a bilateral torque pole between the methods (PM3, AM1) back to put the equilibrium geometry of the two methods as well as to the negligence some of the values on the way on the other account.

Table 1: The physical properties of a drug carbamazepine and its derivatives when the equilibrium geometry and using methods (PM3, AM1)

		Total Energy (Kcal/mol)		Entropy (Kcal/mol/deg)		Free Energy (Kcal/mol/deg)		Heat Capacity (Kcal/mol/deg)		Dipole moment (debyes)	
		PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1
1	Carbamazepine	-59475.7	-64992.8	0.112	0.1127	-59475.7	-64862.7	0.054	0.0506	3.263	3.528
2	OH	-66251.4	-73036.6	0.1136	0.1142	-66251.4	-72889.1	0.048	0.0539	2.902	2.47
3	OCH3	-63613.2	-70876.4	0.117	0.118	-63613.2	-70736.8	0.064	0.0534	2.801	1.934
4	F2	-79070	-86734.3	0.1156	0.1167	-79070	-86614.6	0.049	0.0557	2.93	3.113
5	OCOCH2CL	-86153.8	-95262.2	0.1366	0.1435	-86153.8	-95101.1	0.057	0.0684	3.738	4.187
6	Br	-67269.7	-72821.6	0.1264	0.1136	-67151.4	-72821.6	0.0608	0.059	3.568	3.932

Calculate the Lengths of the Bonds of Drug Carbamazepine and Some of its Derivatives

It was extracted lengths bonds to the drug molecule Carbamazepine according to the methods of calculation Semi- empirical (PM3, AM1) respectively, and a groups of derivatives non studied theoretically when the geometry of the equilibrium as shown in the Table 2. He was found in general convergence bonds lengths of these derivatives with each other, it was to be a little shorter or a little longer, except for derivative (R=OH) found that bond (C1-C2) equal (1.542 -1.538) respectively, and derivative (R=OCOCH2CL) the length bond (C1-C2) equal (1.539-1.580), and the length of bond (C-CL) equal (1.766 – 1.740).

Table 2: The lengths of the bonds of a drug carbamazepine and its derivatives when the equilibrium geometry and using a calculation method semi – empirical (PM3, AM1)

Bond Length (A)													
	Description	R-		OH		OCH3		F2		OCOCH2CL		Br	
		PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1
1	C1=C2	1.339	1.34	1.542	1.538	1.337	1.341	1.337	1.341	1.539	1.58	1.331	1.345
2	C2-C3	1.456	1.45	1.509	1.496	1.457	1.451	1.458	1.451	1.508	1.497	1.444	1.455
3	C3=C4	1.403	1.416	1.402	1.415	1.404	1.415	1.406	1.417	1.408	1.416	1.407	1.416
4	C4-N7	1.452	1.421	1.458	1.422	1.451	1.42	1.454	1.416	1.46	1.42	1.456	1.423
5	N7-C6	1.453	1.416	1.456	1.413	1.455	1.425	1.451	1.42	1.46	1.424	1.456	1.418
6	C6=C5	1.403	1.415	1.403	1.415	1.402	1.414	1.405	1.414	1.407	1.414	1.493	1.415
7	C5-C1	1.455	1.45	1.496	1.486	1.456	1.45	1.458	1.45	1.495	1.488	1.455	1.448
8	C1-H19	1.1	1.106	1.111	1.123	1.1	1.107	1.102	1.107	1.112	1.125	1.098	1.108
9	C2-Br	…….	…….	.....	……	…….	……	……	……	…….	……	1.893	1.896
10	N7-C16	1.433	1.416	1.449	1.432	1.422	1.394	1.431	1.418	1.443	1.425	1.437	1.419
11	C16 =O17	1.228	1.252	1.226	1.252	1.224	1.243	1.228	1.253	1.231	1.254	1.225	1.254
12	C16-N18	1.428	1.391	1.427	1.384	…….	……	1.429	1.391	1.425	1.387	1.431	1.396
13	N18-H29	0.996	0.99	0.996	0.988	.....	……	0.996	0.988	0.995	0.991	0.995	0.99
14	C-F	0.997	……	0.995	……	.....	……	1.343	1.354	.....	…….	.....	…….
15	C5-C12	1.404	1.404	1.402	1.405	1.403	1.404	1.4	1.402	1.403	1.406	1.4	1.465
16	C12-H25	1.095	1.1	1.098	1.102	1.094	1.1	1.097	1.107	1.096	1.101	1.097	1.102
17	C12=C13	1.387	1.389	1.385	1.388	1.386	1.388	1.396	1.401	1.384	1.387	1.386	1.389
18	C13-H26	1.096	1.101	1.095	1.182	1.095	1.1	.....	……	1.094	1.098	1.096	1.1
19	C13-C15	1.392	1.395	1.392	1.394	1.392	1.395	1.402	1.408	1.391	1.394	1.39	1.394
20	C15-H28	1.096	1.1	1.093	1.101	1.093	1.099	1.095	1.099	1.095	1.099	1.094	1.101
21	C15=C14	1.388	1.389	1.386	1.388	1.386	1.388	1.385	1.385	1.385	1.387	1.398	1.389
22	C14-H27	1.096	1.101	1.093	1.104	1.897	1.1	1.097	1.102	1.111	1.101	1.099	1.102
23	C14-C6	1.404	1.414	1.404	1.419	1.401	1.411	1.402	1.413	1.407	1.417	1.401	1.413
24	C4-C11	1.401	1.412	1.397	1.411	1.402	1.412	1.402	1.412	1.4	1.41	1.399	1.413
25	C11-H24	1.097	1.101	1.096	1.1	1.097	1.1	1.096	1.102	0.995	1.1	1.096	1.104
26	C11=C10	1.388	1.389	1.39	1.391	1.388	1.389	1.386	1.386	1.392	1.391	1.388	1.388
27	C10-H23	1.095	1.101	1.096	1.101	1.094	1.1	1.097	1.098	1.094	1.1	1.096	1.101
28	C10-C9	1.39	1.395	1.389	1.395	1.392	1.395	1.402	1.406	1.389	1.392	1.392	1.393
29	C16-O	…….	…….	…….	…….	1.414	1.382	.....	……	…….	…….	.....	……
30	C2-O	……	……	1.407	1.415	.....	…….	.....	……	1.366	1.435	.....	…….
31	0-H	.....	…….	0.953	0.964	.....	…….	.....	……	……	…….	.....	…….
32	C-CL	.....	……..	.....	…….	.....	……	.....	…….	1.766	1.74	.....	…….

The increase in the length of these bonds because of the presence of groups of high electron density resulting in the further spread of electrons in larger size and this leads to increased stability of the relatively molecule. It had to change the lengths of these bonds the opposite effect it has led to a decline in the value of a binary determination of the pole in the derivative (R=OH) and increase torque dipole in derivative ($R=OCOCH_2CL$) relatively.

Infrared (IR) Spectra Calculation

The vibration frequencies and calculate the intensity of the absorption infrared spectroscopy of a drug Carbamazepine and a group of derivatives non studied theoretically using account program Hyper chem. 8.08 according to the method of calculation semi – empirical (PM3, AM1), It was the inclusion of the most important belonging to this drug that contains a number of main groups affiliated with the unit cm^{-1} give some spectral characteristics of other such intensity of each style patterns, the results were a very practical approach to the results for the two methods Tables 3-8.

Table 3: Comparison between experimental and theoretical values of the patterns of seismic movements frequencies drug Carbamazepine when the geometry of the equilibrium on according to method of calculation (PM3, AM1)

	Experimental [12]	PM3	Intensity km/mol	AM1	Intensity km/mol
N-H	3340	3211.48	18.6	3292.85	43.04
C-H aromatic	3023	3025.84	9.46	3404.7	7.19
C=O	1677	1632.63	16.22	1690.89	47.91
C=C	1594	1490.46	115.03	1569.65	187.91
C-N	1307	1357.63	41.9	1326.38	39.58
C-C	537	562.89	23.15	532.98	21.16

Table 4: Comparison between experimental and theoretical values of the patterns of seismic movements frequencies derivative drug Carbamazepine (R=OH) when the geometry of the equilibrium on according to method of calculation (PM3, AM1)

	Experimental [12]	PM3	Intensity km/mol	AM1	Intensity km/mol
O-H	3466	3425.69	2.88	3490.77	21.87
N-H	3340	3283	28.6	3292.85	23.04
C-H aromatic	3023	3069.57	13.88	3095.77	11.17
C=O	1677	1658.57	8.29	1667.2	5.7
C=C	1594	1548.77	7.53	1587.94	5.64
C-N	1307	1311.62	21.13	1316.92	18.32
C-C	537	537.73	8.08	548.67	6.54

Table 5: Comparison between experimental and theoretical values of the patterns of seismic movements frequencies derivative drug Carbamazepine (R=OCH3) when the geometry of the equilibrium on according to method of calculation (PM3, AM1)

	Experimental [12]	PM3	Intensity km/mol	AM1	Intensity km/mol
C-H	3162	3196.95	29.95	3149.22	0.59
N-H	3340	3241.87	16.65	3237.83	13.75
C-H aromatic	3023	3043	3.12	3066.53	0.72
C=O	1677	1634.56	14.44	1629.62	10.75
C=C	1594	1538.1	10.14	1572.52	7.37
C-N	1307	1345.67	0.11	1303.45	34.77
C-C	537	523.08	0.67	533.58	0.5

Table 6: Comparison between experimental and theoretical values of the patterns of seismic movements frequencies derivative drug Carbamazepine (R=F2) when the geometry of the equilibrium on according to method of calculation (PM3, AM1)

	Experimental [12]	PM3	Intensity km/mol	AM1	Intensity km/mol
N-H	3340	3410.37	3.12	3477.98	51.5
C-H aromatic	3023	3017.45	11.3	3061.33	7.65
C=O	1677	1659.23	78.22	1611.82	94.31
C=C	1594	1578.23	0.23	1569.68	2.05
C-N	1307	1379.94	0.11	1317.84	0.65
C-C	537	535.66	16.75	576.06	0.59
C-F	1000-1300	1224.48	0.1	1219.72	0.3

Theoretical Atomic Charge Calculation

Analysis in computational chemistry depends on the atomic charge in the study of molecules as Figure 4. The atomic charge distribution has a significant impact on the (Electrostatic potential, Dipole moment and Theoretical absorption spectra), Table 9 it shows the charge distribution of each atom in the molecule drug Carbamazepine and a group of non – studied theoretically derivatives, using the program Hyper chem. 8.08 according to the method Semi – empirical (PM3, AM1), it found that all the hydrogen atoms carry a positive charge and most of the carbon atoms are negatively charged, except (C16) carry a positive charge in molecular

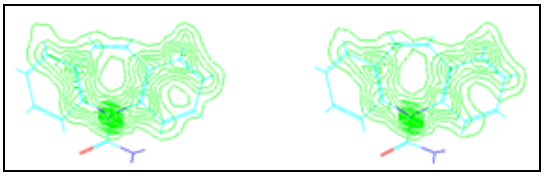
drug and its derivatives in order to contact with the atom (O) negative, nitrogen also carries a negative charge and the halogens (CL, F, Br) are negatively charged and negatively charged oxygen is also. The results of the two methods are close or identical to calculate the atomic charge, the atomic charge vehicles account generally affects the extent of the effectiveness of the compound and the active sites in the compound as the increased charge of atomic negative or positive value indicates increase the effectiveness of this atom. The results for two methods were identical atoms, the results indicate that the higher the effectiveness is in the atoms (N18, O17, O20) of most derivatives except derived (R=OCOCH2CL) effectiveness of atom N18 go down in a clear and unique atom effectiveness O17 this derivative and it is expected to decrease the effectiveness of this derivative as property. The density of the atomic charge of drug Carbamazepine according typical (PM3, AM1).

Table 7: Comparison between experimental and theoretical values of the patterns of seismic movements frequencies derivative drug Carbamazepine (R=OCOCH2CL) when the geometry of the equilibrium on according to method of calculation (PM3, AM1)

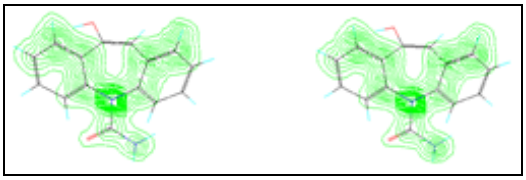
	Experimental [12]	PM3	Intensity km/mol	AM1	Intensity km/mol
N-H	3340	3413.61	3.61	3516.11	78.18
C-H aromatic	3023	3075.66	22.48	3010.45	13.4
C=O	1775-1660	1789.53	15.3	1713.56	40.42
C=C	1594	1559.12	10.87	1562.84	29.05
C-N	1307	1384.2	17.33	1296.02	18.09
C-O-C	1163-1258	1164.52	1.08	1163.64	2.16
C-C	537	572.94	3.65	504.96	2.66
C-CL	800-850	811.17	0.7	826.83	12.86

Table 8: Comparison between experimental and theoretical values of the patterns of seismic movements frequencies derivative drug Carbamazepine (R=Br) when the geometry of the equilibrium on according to method of calculation (PM3, AM1)

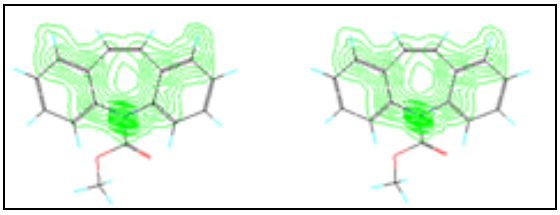
	Experimental [12]	PM3	Intensity km/mol	AM1	Intensity km/mol
N-H	3340	3516.49	3.37	3513.88	44.34
C-H aromatic	3023	3073.25	21.35	3025.06	28.25
C=O	1775-1660	1637.47	16.12	1683.23	50.13
C=C	1594	1590.09	118.9	1562.55	240.86
C-N	1307	1275.81	13.32	1262.35	18.22
C-C	537	582.37	37.16	509.43	30.31
C-Br	800-850	852.37	90.59	821.04	36.7



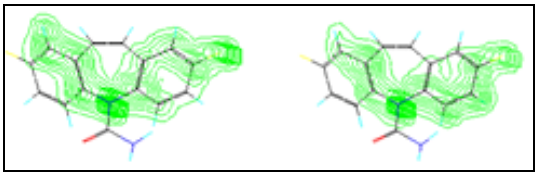
AM1 PM3



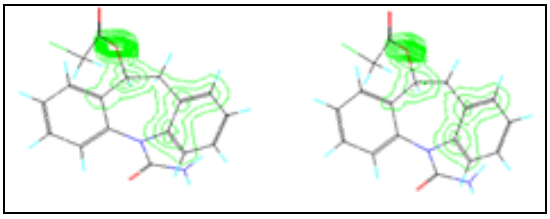
AM1 (R=OH) PM3 (R=OH)



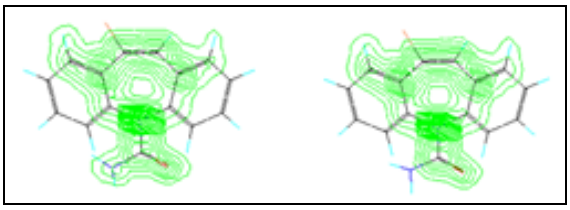
AM1 (R=OCH3) PM3 (R=OCH3)



AM1 (R=F2) PM3 (R=F2)



AM1 (R=OCOCH2CL) PM3 (R=OCOCH2CL)



AM1 (R=Br) PM3 (R=Br)

Figure 4: The density of the atomic charge of drug Carbamazepine and derivatives according typical (PM3, AM1)

Table 9: Atomic charge calculate of a drug Carbamazepine and its derivatives when the equilibrium geometry and using methods (PM3, AM1)

Atoms charge													
	Atoms	Carbamazepine		OH		OCH3		F2		OCOCH2CL		Br	
		PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1
1	C1	-0.101	-0.128	0.122-	-0.122	-0.076	-0.113	-0.061	-0.09	-0.071	-0.125	-0.08	-0.094
2	C2	-0.065	-0.029	-0.082	0.082	-0.089	-0.108	-0.101	-0.126	0.126	0.075	-0.054	-0.115
3	C3	-0.048	-0.065	-0.117	-0.117	-0.034	-0.042	-0.004	-0.015	-0.125	-0.117	-0.116	-0.048
4	C4	-0.028	0.1	-0.105	0.105	-0.034	-0.083	-0.077	0.05	-0.045	0.054	-0.015	0.099
5	C5	-0.025	-0.04	-0.075	-0.075	-0.038	-0.114	-0.023	-0.032	-0.071	-0.056	-0.081	-0.066
6	C6	-0.053	0.066	-0.047	0.047	-0.044	-0.13	-0.042	0.085	-0.069	0.054	-0.084	-0.267
7	N7	0.063	-0.274	-0.201	-0.261	0.117	-0.117	0.088	-0.272	0.086	-0.134	0.086	-0.267
8	C8	-0.088	-0.113	-0.12	-0.12	-0.09	-0.115	-0.124	-0.145	-0.082	-0.106	-0.078	-0.106
9	C9	-0.102	-0.135	-0.138	-0.138	-0.1	-0.119	0.07	0.09	-0.092	-0.125	-0.104	-0.134
10	C10	-0.09	-0.114	-0.113	-0.113	-0.091	-0.124	-0.124	-0.157	-0.09	-0.11	-0.078	-0.109
11	C11	-0.082	-0.115	-0.125	-0.125	-0.099	-0.118	-0.085	-0.124	-0.069	-0.133	-0.091	-0.12
12	C12	-0.086	-0.115	-0.119	-0.119	-0.089	-0.132	-0.12	-0.151	-0.098	-0.139	-0.091	-0.107
13	C13	-0.099	-0.133	-0.129	-0.129	-0.1	-0.126	0.066	0.068	-0.099	-0.105	-0.091	-0.135
14	C14	-0.092	-0.122	-0.128	-0.128	-0.087	-0.114	-0.116	-0.149	-0.093	-0.179	-0.101	-0.114
15	C15	-0.121	-0.134	-0.139	-0.136	-0.089	-0.115	-0.062	-0.091	-0.115	-0.049	-0.06	-0.152
16	C16	0.21	0.409	0.398	0.398	0.352	0.401	0.208	0.405	0.2	-0.018	0.201	0.394
17	O17	-0.399	-0.391	-0.399	-0.391	-0.414	-0.384	-0.397	-0.382	-0.401	-0.254	-0.392	-0.379
18	N18	-0.003	-0.432	-0.004	-0.443	……	…..	-0.003	-0.399	-0.005	-0.054	-0.002	-0.394
19	H19	0.103	0.128	0.108	0.108	0.101	0.139	0.104	0.135	0.081	0.12	0.081	0.143
20	H20	0.101	0.129	……	…….	0.101	0.13	0.105	0.133	0.059	……..	0.093	…….
21	H21	0.105	0.133	0.121	0.121	0.107	0.136	0.129	0.155	0.1	0.156	0.117	0.146
22	H22	0.105	0.134	0.134	0.134	0.106	0.135	……..	…….	0.108	0.143	0.108	0.138
23	H23	0.105	0.136	0.138	0.138	0.105	0.138	0.127	0.155	0.108	0.143	0.106	0.138
24	H24	0.118	0.15	0.157	0.157	0.114	0.147	0.125	0.155	0.117	0.154	0.12	0.154
25	H25	0.112	0.148	0.151	0.151	0.116	0.114	0.123	0.156	0.125	0.228	0.123	0.152
26	H26	0.107	0.137	0.138	0.138	0.106	0.135	0.125	0.154	0.109	0.143	0.0109	0.139
27	H27	0.107	0.137	0.138	0.138	0.105	0.136	……	…….	0.109	0.143	0.108	0.14
28	H28	0.109	0.137	0.14	0.14	0.106	0.136	0.125	0.151	0.111	0.142	0.113	0.14
29	H29	0.064	0.238	0.233	0.233	0.044	0.109	0.05	0.239	0.066	…….	0.052	0.23
30	H30	0.049	0.226	0.22	0.22	0.035	0.092	0.067	0.225	0.052	…….	0.054	0.216
31	F	…….	.....	…….	……	……	…..	-0.091	-0.104	.....	…….	…….	……
32	Br	.....	.....	…….	…….	……..	……	…….	.....	……..	…….	-0.149	0.038
33	cl	…….	…….	…….	…….	…….	……	…….	…….	0.017	-0.048	…….	……
34	O20	……..	…….	-0.324	-0.324	.....	……	……..	…….	.....	-0.256	.....	…….
35	H31	.....	…….	…….	.....	…….	……	.....	……..	…….	…….	.....	…….
36	O17	…….	…….	.....	.....	-0.254	-0.265	.....	.....	.....	.....	.....	.....

Potential Molecular Electrostatic (PEM)

We've been finding the energy values of the orbits of the occupied orbital's and unoccupied orbital's electrons, and through the program Hyper chem. 8.08 using method semi- empirical (PM3, AM1) as shown in the Table 10. After obtaining the best position of the molecule when it has less energy total and be more stable (when

developing poise) after drawn by the program we get the molecular orbitals and the energy value of each orbit, it represents the highest HOMO over the busy molecular electrons and the amount of energy =EHOMO, the LUMO lowest unoccupied round electrons and the amount of energy =ELUMO. These orbits were sacrificed after the (2D) program Hyper chem. 8.08, as well as the energy gap between the levels account HOMO, LUMO in accordance with the relationship: ΔE=EHOMO – ELUMO The increase in lines indicate increasing energy orbitals and therefore increasing the effectiveness of this orbital. Increasing the energy difference between two orbitals (HOMO, LUMO) can be concluded by increasing the energy needed to move on to the busy is busy orbital. You can use this energy for the purpose of comparison between the derivatives there was the necessary basic medication – powered teams could not rule out this derivative but differences emerged for all derivatives are relatively close.

Table 10: The difference between the higher energy orbit and lower energy orbit of the drug Carbamazepine and its derivatives over when the equilibrium geometry and using method (PM3, AM1)

		E Homo (ev)		E LUMO (ev)		ELUMO – E HOMO	
		PM3	AM1	PM3	AM1	PM3	AM1
1	Carbamazepine	-8.692503	-9.326069	-0.66807	0.06603671	8.024433	9.3921057
2	OH	-8.565202	-9.526613	-0.68668	0.1691592	7.878522	9.3574538
3	OCH3	-8.410507	-8.559913	-0.54157	0.1898681	7.868937	8.7497811
4	F2	-8.380852	-9.562009	-1.06553	-0.3615452	7.315322	9.2004638
5	OCOCH2CL	-9.288295	-9.652782	-0.33308	-0.2664759	8.955215	9.3863061
6	Br	-8.483474	-9.402239	-0.390274	-0.0779501	9.0932	9.3242889

Ionization Energy Calculate

The ionization energy associated with a relationship with a higher energy orbital full of electrons, as follows: [10]. IE=-EHOMO The high value in energy of ionization mean high stability of the molecule and on the other hand, the low ionization energy means high effectiveness of the molecule. And increase the efficiency of the molecule relative to its low ionization energy. The ionization energy calculate of the drug Carbamazepine and its derivatives non studied theoretically by using program Hyper chem. 8.08 according to the method of calculation semi – empirical (PM3,AM1) as in the Table 11. Found that a derivative (OCOCH2CL) of the highest ionization energy for this less efficiency relative to the ionization energy high by his method of calculation PM3and are more calculate than the method of calculation AM1.

Table 11: The ionization to drug Carbamazepine and its derivatives

	Ionization Potential (ev)	
	PM3	AM1
Carbamazepine	8.692503	9.326069
OH	8.565202	9.5266113
OCH3	8.410507	8.559913
F2	8.380852	8.562009
OCOCH2CL	9.288295	9.652782
Br	8.483474	9.402239

Electron Affinity Calculate

The energy of electron affinity is given by equation: [10] EA= -E LUMO [10]. The high value of the energy of electronic affinity means less stabilizing and thus lead to higher efficiency of the molecule to link, the low energy electronic affinity means high efficiency and stability of a few. The energy of electronic affinity of a drug Carbamazepine and its derivatives account non studied theoretically by using program Hyper chem. 8.08 according to the method calculation semi – empirical (PM3, AM1) as shown in the Table 12. Found that less energy is derived (OCOCH2CL) his electronic affinity any high stability of small and efficient as the method of calculation PM3 and are more accurate than the method of calculation AM1.

Table 12: Electronic affinity of a drug carbamazepine and its derivatives

	Electron affinity (ev)	
	PM3	AM1
Carbamazepine	0.66807	0.0660367
OH	0.68668	0.1691592
OCH3	0.54157	0.1898681
F2	1.06553	0.3615452
OCOCH2CL	0.33308	0.2664759
Br	0.390274	0.0779501

Correlations

For the purpose of comparison between the theoretical results of a drug Carbamazepine and its derivatives sum up the results that affect effectively as derived in the Table 13.

Table 13: A summary of the results of the theory of a drug Carbamazepine and its derivatives

	Molecular Formula	Total Energy (Kcal/mol)		E LUMO – E HOMO		Heat Capacity (Kcal/mol/deg)		Dipole moment (debyes)	
		PM3	AM1	PM3	AM1	PM3	AM1	PM3	AM1
Carbamazepine	C15H12N2O	-59475.7	-64992.8	8.024433	9.392105	0.054	0.0506	3.263	3.528
OH	C16H16N2O2	-66251.4	-73036.6	7.878522	9.357453	0.048	0.0539	2.902	2.47
OCH3	C16H13NO2	-63613.2	-70876.4	7.868937	8.749781	0.064	0.0534	2.801	1.934
F2	C15H10F2N2O	-79070	-86734.3	7.315322	9.200463	0.049	0.0557	2.93	3.113
OCOCH2CL	C17H15CLN2O3	-86153.8	-95262.2	8.955215	9.386306	0.057	0.0684	3.738	4.187
Br	C15H11BrN2O	-67269.7	-72821.6	8.6932	9.324288	0.0608	0.059	3.568	3.932

The results in the Table 13 show that the original property Carbamazepine is less stable than the derivatives in general, as it has a higher energy and that way AM1 has given the results of energy higher than the PM3 and the way this is due to the spatial form you choose the way. On the other hand, the value of (EA) to the drug and its derivatives have been relatively few shows that a high stability of the effectiveness of a few and this is supported by high (IE) values to the drug and its derivatives a relatively few effective. The two derivatives who were getting closer to the original drug gap energy by way of AM1 are derived (R=F2) and (R=Br) derivative and this is supported by the results dipole moment values as it was derivatives themselves are close to the original values of the drug and approaching the polarity of the original drug.

CONCLUSION

Results demonstrated that there is an excellent possibility to use quantum mechanics calculations to choose one of the drugs used to treat some chronic diseases and studied theoretically by using program Hyper chem. 8.08 according to the method of calculation semi – empirical (PM3, AM1) and a number of its derivatives as drugs have not tested yet. And studied theoretically compare the results with the original property to determine the validity of using them as a promising future. The results showed the following: For the drug Carbamazepine and its derivatives theoretical study proved that he has a higher energy than any derivatives be less stable than derivatives. And two derivatives who approaching original drug gap energy and the determination of the values of the dipole moment they (R=F2) (R=Br) as close to the original as close to the original values of this drug can be used as drugs possible. And derivative (R=OCOCH2CL) the original drug dose not match the theoretical calculations for this can't be used as a drug.

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