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Theoretical Study of Some Chemical Kinetic and physical properties for ibuprofen by using density function theory (DFT) with B3LYP/6-31G

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Abstract:

In this theoretical study, mathematical calculations and density function theory (DFT) were used with B3LYP/6-31G on ibuprofen for the purpose of calculation the equilibrium geometries , energies of HOMO orbital , LUMO orbital , ionization energies , electronic densities , the vibrational modes . It is some application Quantum calculations have reached some physical properties (E_{HOMO} , E_{LUMO} , ΔE , IP), in addition to calculating thermodynamic functions (E^0 , H^0 , A^0 ,S^0 , C_V)

This study is considered important of ibuprofen to find out informationabout ibuprofen in order to compare it with information about derivatives in order to reach the substance with the least side effects on the body.

Keywords:; Ibuprofen , Theoretical Study , density function theory

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Introduction

The compound ibuprofen is considered one of the first compounds that were derived from propanoic acid in the year 1969 as the best drug in the group of drugs belonging to non-steroidal anti-inflammatory NSAIDS drugs [(1)], as these drugs work to slow the production of prostaglandins that the body secretes during illness or inflammation, which is responsible for the relaxation and contraction of muscles and blood vessels And inhibiting enzymes that cause inflammation cyclooxygenases , such as COX2 , COX1 . Some studies have also shown that it has a negative effect in that it causes stroke and heart attack if taken for a long period of time and stomach bleeding[(2)] . One of the chemical properties of ibuprofen is its weak solubility in water, while it dissolves easily in alcohol , It is given as a racemic mixture of R and S antagonists, where S is ibuprofen , R-ibuprofen, which is the reason for its pharmacological activity. 50-65% of it is converted to senantiomer through acyl-COA These progesterone conversions occur in the liver or in the digestive tract One of the chemical properties of ibuprofen is its weak solubility in water, while it dissolves easily in alcohol [(3)] , It is given as a racemic mixture of R and S antagonists, where S is ibuprofen , R-ibuprofen, which is the reason for its pharmacological activity. 50-65% of it is converted to senantiomer through acyl-COA These progesterone conversions occur in the liver or in the digestive tract [(4)] Taking ibuprofen for a long period may hinder the effectiveness of aspirin in thinning the blood . Ibuprofen is marketed under trade names (Advil , Nurofen , Brufen)[(5)] . It was developed in the research department of Boots Group[(6)] . In order to increase painkillers and antibiotics the activity and its implications have been completed new compounds by carboxyl group derivative Non-steroidal antioxidants with heterocyclic systems [(7)], Brufen monocarboxyl monocarboxyl group. A hydrogen atom at position 2 in propanoic acid has been replaced by a phenyl group (2-methylpropylphenyl) [(8)]. It is used as a pain reliever, not an anesthetic, as well as an antipyretic and an inhibitor of

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cyclooxygenase, which is responsible for the production of prostaglandins, which are substances that the body releases in response to illness, fever, or Inflammation[9]

Quantum Computational Chemistry

Quantum computing is a wide range of specializations encompassing many computer sciences, physics, and mathematics that uses quantum mechanical calculations to solve complex problems more quickly than classical computers [10] . In quantum computing, subatomic particles, such as electrons or photons, are used that allow particles to exist in more than one state (i.e. 1 and 0) at the same time [11]**.** Density Function Theory (DFT) is one of the most important methods used in theoretical chemistry and physics, through which we can determine the thermodynamic properties and some physical properties of a multi-particle system (density, total energy of the system, physical and optical parameters of the material.....) and it can be Applied to diverse and complex systems[12]) We apply DFT to complex substances, such as proteins and carbohydrates although DFT relies on approximations of reactive exchange potentials, which are very precise for HF theory **In** electronic .(primary and semi-empirical approximations[13] structure calculations based on the study of atomic nuclei of complex particles, the system is described by the time-independent Schrodenker wave function and using the Born-Oppenheimer approximation as follows[14]

$$\hat{H}\Psi = \left[\hat{T} + \hat{V} + \hat{U}\right]\Psi = \left[\sum_{i=1}^{N}\left(-\frac{\hbar^2}{2m_i}\nabla_i^2\right) + \sum_{i=1}^{N}V(\mathbf{r}_i) + \sum_{i<j}^{N}U(\mathbf{r}_i,\mathbf{r}_j)\right]\Psi = E\Psi,$$

where, for the *N*-electron system

Ĥ **Hamiltonian,**
E **total energy** ,
T̂ **kinetic energy,**

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$\hat{V}$ potential energy from the external field due to positively charged nuclei, $\hat{U}$ electron–electron interaction energy.

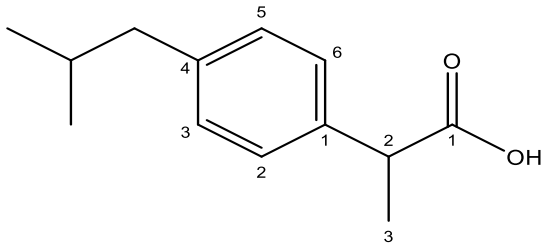
$\hat{T}$ and $\hat{U}$ universal operators [15], This complex equation for multiparticle bodies cannot be separated from single equations, as the wave function of the Schrödenker modifier has been expanded through the Slater determinants. However, the problem lies in the huge computational effort, which makes it impossible to apply it successfully to very large and complex systems [16] .

Calculation and Results

The geometric shape was calculated ((bond lengths and angels)) of Ibuprofen compound using DFT method According to the results calculated and recorded in the (**Fig 1 , table 1**)

Chemical formula : $C_{13}H_{18}O_2$

Molecular mass :206.29 g/mol



2-(4-isobutylphenyl)propanoic acid

Fig 1: (*RS*)- 2- (4- (2-Methylpropyl)phenyl) propanoic acid Ibuprofen:

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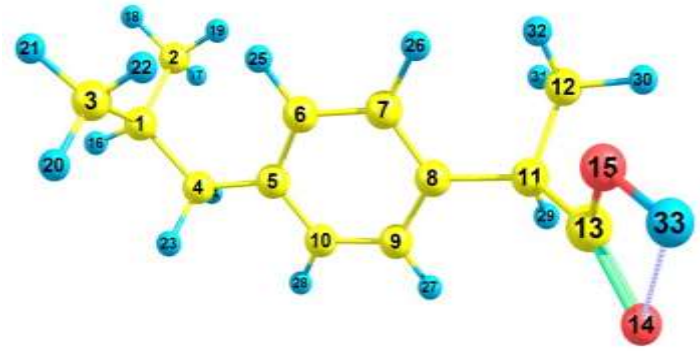


Fig 2 : Ibuprofen 3D Structure of Ibuprofen compound

carbon hydrogen oxygen

Table 1 : Geometric parameters bond lengths , angles in Angstrom unite for Ibuprofen

(bond lengths		*angles*	
R(1-2)	1.520	A(2-1-3)	110.6
R(1-3)	1.520	A(2-1-4)	112.5
R(1-4)	1.530	A(2-1-16)	107.5
R(1-16)	1.120	A(1-2-17)	111.6
R(2-17)	1.097	A(1-2-18)	111.2
R(2-18)	1.098	A(1-2-19)	111.1
R(2-19)	1.103	A(3-1-4)	112.5
R(3-20)	1.097	A(3-1-16)	107.5
R(3-21)	1.098	A(1-3-20)	111.6
R(3-22)	1.103	A(1-3-21)	111.2

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R(4-5)	1.497	A(1-3-22)	111.1
R(4-23)	1.110	A(4-1-16)	105.9
R(4-24)	1.110	A(1-4-5)	119.5
R(5-6)	1.394	A(1-4-23)	108.1
R(5-10)	1.401	A(1-4-24)	108.1
R(6-7)	1.389	A(17-2-18)	107.7
R(6-25)	1.105	A(17-2-19)	107.6
R(7-8)	1.394	A(18-2-19)	107.4
R(7-26)	1.101	A(20-3-21)	107.7
R(8-9)	1.397	A(20-3-22)	107.6
R(8-11)	1.504	A(21-3-22)	107.4
R(9-10)	1.387	(5-4-23)	107.2
R(9-27)	1.096	A(5-4-24)	107.2
R(10-28)	1.096	A(4-5-6)	124.2
R(11-12)	1.521	A(4-5-10)	117.2
R(11-13)	1.522	A(23-4-24)	105.8
R(11-29)	1.120	A(6-5-10)	118.6
R(12-30)	1.097	A(5-6-7)	120.7
R(12-31)	1.097	A(5-6-25)	119.2
R(12-32)	1.103	A(5-10-9)	120.9
R(13-14)	1.218	A(5-10-28)	119.6
R(13-15)	1.353	A(7-6-25)	120.1

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R(15-33)	0.952	A(6-7-8)	120.5
R(14-33)	2.200	A(6-7-26)	120.8
		A(8-7-26)	118.7
		A(7-8-9)	119.2
		A(7-8-11)	121.0
		A(9-8-11)	119.8
		A(8-9-10)	120.1
		A(8-9-27)	120.1
		A(8-11-12)	112.3
		A(8-11-13)	109.3
		A(8-11-29)	108.5
		A(10-9-27)	119.8
		A(9-10-28)	119.6
		(12-11-13)	111.2
		A(12-11-29)	108.4
		A(11-12-30)	111.6
		A(11-12-31)	110.7
		A(11-12-32)	111.2
		A(13-11-29)	106.9
		A(11-13-14)	127.6
		A(11-13-15)	117.1
		A(30-12-31)	107.7

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		A(30-12-32)	108.1
		A(31-12-32)	107.2
		A(14-13-15)	115.3
		A(13-14-33)	59.4
		A(13-15-33)	109.5
		A(15-33-14)	75.8
		A(30-12-32)	108.1
		A(31-12-32)	107.2
		A(14-13-15)	115.3
		A(13-14-33)	59.4
		A(13-15-33)	109.5
		A(15-33-14)	75.8
		A(30-12-32)	108.1
		A(31-12-32)	107.2
		A(14-13-15)	115.3
		A(13-14-33)	59.4
		A(13-15-33)	109.5
		A(15-33-14)	75.8

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Physical Properties

By applying quantum calculations and using the DFT method, some physical properties were identified of By applying quantum calculations and using the DFT method some physical properties were identified.

The low values of the HOMO orbital indicate that the molecule is a good electron donor, while the low value of the LUMO orbital indicates a good ability to transfer electrons. The negative value of the HOMO energy also indicates ease of ionization, and the difference between the orbitals, LUMO and HOMO, indicates the energy gap, which is the relative stability of the chemical activity compared to other analgesics **(table 2)**.

Table 3 : Some physical properties were identified of Ibuprofen

Comp.	E_{HOMO} (ev)	E_{LUMO} (ev)	E (LUMO - HOMO) (ev)	IP (ev)
	-9.4334	**0.0808**	**9.5142**	**9.4334**

Thermodynamics functions

In this theoretical study, a number of thermodynamic functions were reached that give us information about the effectiveness of the ibuprofen compound compared to other analgesics.

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Table 3 : Standard Thermodynamic Functions at 298.15 K of the Ibuprofen In KJ / mol

A^0 KJ / mol	S^0 J/ mol . K	E^0 KJ/mol	H^0 KJ/mol	G^0 KJ/mol	A^0 KJ/mol
Ibuprofen	**529.780**	**783.039**	**807.039**	**649.919**	**625.165**

Aim of Research

Ibuprofen is classified as a non-steroidal anti-inflammatory drug (NSAAID), and is used to treat pain, inflammation, and fever. Therefore, the aim of the theoretical study is

1- Identify some physical properties and compare them with experimental results for this drug

2.Identify the most important thermodynamic functions and compare them with the thermodynamic functions of profen derivatives to arrive at the compound that is characterized by the highest stability and stability.

Recommendations

Future metabolic studies should focus on ibuprofen derivatives that are more effective and more stable for relieving pain, fever, and inflammation and that have fewer side effects on the body.

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References

1.Essentials of medical pharmacology , Tripathi K .D., (2003) **,** Non steroidal anti inflammatory drugs and anti pyretic analgesics. In **,** Jaypee Brothers, New Delhi .

2.Prog Lipid Res , Lloyd M.D., Yevglevskis M, Lee GL, Wood PJ, Threadgill MD, Woodman TJ , (2013) **,** α-Methylacyl-CoA racemase (AMACR): metabolic enzyme, drug metabolizer and cancer marker P504S**.** 52:220 –230

3.J Pharm Exp Ther, Rudy A.C., Knight PM, Brater D.C, Hall S.D. , (1991) **,** Stereoselective metabolism of ibuprofen in humans: administration of *R*-, *S*- and racemic ibuprofen 259:1133–1139.

4. J Clin Pharmacol Ther . Hall S.D., Rudy A.C., Knight PM, Brater D.C., (1995) **,** Lack of presystemic inversion of (R)- to (S)-ibuprofen in humans , 53:393–400

5. J Pharmacol Exp Ther. Rudy AC, Knight PM, Brater DC, Hall SD (1991). Stereoselective metabolism of ibuprofen in humans: administration of *R*-, *S*- and racemic ibuprofen **,** 259:1133–1139

6-J Pharm Sci , Jamali F, Mehvar R , Russell A.S ., Sattari S , Yakimets W.W., Koo J ., (1992) , Human pharmacokinetics of ibuprofen enantiomers following different doses and formulations: intestinal chiral inversion , 81:221–225.

7.Iraqi J Pharm Sci, Mayada R. and Tagreed N-A , (2019), Iraqi J Pharm Sci, Vol.28(1) 2019 Synthesis and anti-inflammatory study of new ibuprofen derivatives , 28(1)

8- Br J Cancer , li I.U, Luke B.T., Dean M., Greenwald P., (2005) Allellic variants in regulatory regions of cyclooxygenase-2: association with advanced colorectal adenoma **,** 93:953–959

ISSN print/ 2769-1926 ISSN online/ 2769-1934

9. Breast Cancer Res Treat. Brasky T.M, Bonner M.R ., Moysich K.B., Ochs-Balcom H.M., Marian C, Ambrosone CB, et al , (2011), Genetic variants in COX-2, non-steroidal anti-inflammatory drugs, and breast cancer risk: the Western New York Exposures and Breast Cancer (WEB) Study.. 126:157–165.10

10- J Pharm Pharm Sci , Rao P., Knaus E.E ., (2008), "Evolution of nonsteroidal anti-inflammatory drugs (NSAIDs): cyclooxygenase (COX) inhibition and beyond" .81 :2 *:* 11 100–110

11 Physical Review Letters , *Abrams . D. S , Lloyd S , (1999). "Quantum Algorithm Providing Exponential Speed Increase for Finding Eigenvalues and Eigenvectors"*. 83 (24): 5162–5165.

12. **Rev. Mod. Phys**, McArdle S. ; Endo, S. , (2020) , *"Quantum computational chemistry"*.. 92 (1) : 15-20

13. Rev. Mod. Phys , Kohn W . 1999. Nobel lecture: electronic structure of matter–wave functions and density functionals.. 71, 1253–1266.

14. **Physical Review** , Kohn, W.; Sham, L. J. (1965). "Self-consistent equations including exchange and correlation effects".140 (4A): A1133–A1138

15. **Int J Quant Chem** , Burke, K and Wagner. L. O. , (2013). "DFT in a nutshell ". 113 (2) : 96

16. J Appl Phy , Assadi, M. H. N.; et al . (2013). "Theoretical study on copper's energetics and magnetism in TiO_2 polymorphs". 113 (23): 233913, Synthesis, Characterization and Preliminary Study of the Anti-Inflammatory Activity of New Pyrazoline Containing Ibuprofen
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7. Iraqi J Pharm Sci, Mayada R. and Tagreed N-A , (2019), Iraqi J Pharm Sci, Vol.28(1) 2019 Synthesis and anti-inflammatory study of new ibuprofen derivatives , 28(1)

8- Br J Cancer , li I.U, Luke B.T., Dean M., Greenwald P., (2005) Allellic variants in regulatory regions of cyclooxygenase-2: association with advanced colorectal adenoma **,** 93:953–959

9. Breast Cancer Res Treat. Brasky T.M, Bonner M.R ., Moysich K.B., Ochs-Balcom H.M., Marian C, Ambrosone CB, et al , (2011), Genetic variants in COX-2, non-steroidal anti-inflammatory drugs, and breast cancer risk: the Western New York Exposures and Breast Cancer (WEB) Study.. 126:157–165.10

10- J Pharm Pharm Sci , Rao P., Knaus E.E ., (2008), "Evolution of nonsteroidal anti-inflammatory drugs (NSAIDs): cyclooxygenase (COX) inhibition and beyond" .81 :2 *:* 11 100–110

11 Physical Review Letters , *Abrams . D. S , Lloyd S , (1999). "Quantum Algorithm Providing Exponential Speed Increase for Finding Eigenvalues and Eigenvectors".* 83 (24): 5162–5165.

12. Rev. Mod. Phys, McArdle S. ; Endo, S. , (2020) , *"Quantum computational chemistry"*.. 92 (1) : 15-20

13. Rev. Mod. Phys , Kohn W . (1999). Nobel lecture: electronic structure of matter–wave functions and density functionals.. 71, 1253–1266.

14. **Physical Review** , Kohn, W.; Sham, L. J. (1965). "Self-consistent equations including exchange and correlation effects".140 (4A): A1133–A1138

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15. **Int J Quant Chem** , Burke, K and Wagner. L. O. , (2013). "DFT in a nutshell ". 113 (2) : 96

16. J Appl Phy , Assadi, M. H. N.; et al . (2013). "Theoretical study on copper's energetics and magnetism in TiO_2 polymorphs". 113 (23): 233913, Synthesis, Characterization and Preliminary Study of the Anti-Inflammatory Activity of New Pyrazoline Containing Ibuprofen
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دراسة نظرية لبعض الخواص الكيميائية الحركية والفيزيائية للأيبوبروفين باستخدام نظرية دالة الكثافة (B3LYP/6– 31G) DFT

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الملخص

في هذه الدراسة النظرية، تم استخدام الحسابات الرياضية ونظرية دالة الكثافة (DFT) مع B3LYP/6-31G على الإيبوبروفين لغرض حساب هندسة التوازن، طاقات مدار HOMO ، مدار LUMO، طاقات التأين، الكثافات الإلكترونية، أنماط الاهتزاز. . ومن بعض التطبيقات التي توصلت إليها الحسابات الكمية بعض الخواص الفيزيائية (E_{HOMO}، E_{LUMO} ، ΔE ، IP)، بالإضافة إلى حساب الدوال الديناميكية الحرارية (E^0، H^0 ، A0 ، S^0 ، C_V). تعتبر هذه الدراسة مهمة بالنسبة للإيبوبروفين لمعرفة المعلومات عن الإيبوبروفين ومقارنتها بالمعلومات المتعلقة بمشتقاته للوصول إلى المادة ذات الآثار الجانبية الأقل على الجسم.

الكلمات الافتتاحية : ايبوبروفين، دراسة نظرية , نظرية دالة الكثافة