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Molecular insights into 5-hydroxy-1-methoxyxanthone reactivity, stability and antidiabetic activity in green solvents

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Using combined pharmacological and computational methods, this study seeks to assess the therapeutic potential of 5-Hydroxy-1-Methoxyxanthone (5H1MX) while encouraging the use of green solvents. In order to verify molecule stability, intramolecular charge transfer, hyperconjugation, and stabilization energy were examined using Natural Bond Orbital (NBO) analysis. Density Functional Theory (DFT) techniques were used to examine the Mulliken charge distribution and Molecular Electrostatic Potential (MEP). Chemical reactivity was predicted and reactive spots were identified using Fukui functions and global descriptors. The C_{13}–C_{17} to C_{12}–C_{15} (π^*) interaction was found to have the highest stabilization energy of 472.42 kcal/mol. The gas phase had the largest band gap value (4.179 eV) among the environments under study. Using several green solvents, solvent effects were investigated, and the results showed a considerable impact on molecular characteristics and reactivity. The system's electrical behavior was further validated using ELF, LOL, and RDG investigations. In accordance with Lipinski's rule of five, positive pharmacological features were validated by drug-likeness measures and NMR analysis. Strong binding affinity for the target protein was shown by molecular docking data, indicating that 5H1MX is a viable option for antidiabetic applications.

Keywords: *Arenaria serpyllifolia* L., DFT, Fukui function, IEFPCM, Multiwave function

In contemporary chemical and medical research, a search for strong medicinal agents and ecologically safe solvents has grown in importance in contemporary chemical and medical research. In this regard, the incorporation of quantum mechanical techniques offers an effective method for deciphering the intricate interactions inside molecular systems and forecasting their behavior in different scenarios. This work is centered on a thorough investigation of Molecular Docking, Electrostatic, and Drug likeness, and molecular structure of various green solvents, as well as pharmacological studies of 5-Hydroxy-1-Methoxyxanthone ($C_{14}H_{10}O_4$), a compound of great interest because of its anti-diabetic properties. G. Don explained in the literature that a natural substance isolated from Mammea Africana and the synthetic 5- hydroxy-1-methoxy xanthone were similar (Found: C, 69.2; H, 4.2. C &1, 4 requires C, 69.4; H, 4.1%)[1]. As of a dichloromethane extract of the stem and roots of Hyperciumbrasiliense, four nove- γ-pyrone (hyperbrasilone), three known xanthones (1, 5-dihydroxy xanthone, 5-hydroxy-1-methoxyxanthone and 6-deoxyjacareubin) thereby betulinic acid were obtained. The xanthones and Hyperbrasilone exist in all antifungals against *Cladosporium cucumerinum*[2,3]. The bark of the Myanmar-native Kayeaassamica (Clusiaceae) was used to extract coumarin derivatives called theraphins (5-hydroxy-1-methoxyxanthone). Chemical and spectroscopic methods were utilized to establish their structures. Theraphin's only action against the KB cell line was minimal. The coumarins also showed a small amount of antimalarial activity. Two novel xanthones were extracted from the stem of Poeciloneuronpauciflorum. In addition to the two well-known xanthones (1, 5-dihydroxy- and 5-

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hydroxy-l-methoxyxanthone) and (-)-epicatechin, a novel xanthone (2, 7-dihydroxyxanthone) was recovered in the aerial portions (bark and stem) of Mammea acuminata which has biological uses[4,5].

Demand for novel antimalarial drugs is sparked by the evolution of antimalarial medication resistance. The medicinal herb Mammea siamensis, a member of the Calophyllaceae family, is utilized in several traditional Thai dishes. There are 13 chemicals in this plant, including the title compound, which has been proven to have strong antimalarial action. Therefore, the purpose of this work was to separate active substances from M. siamensis flowers and assess their potential for treating malaria[6]. 5-hydroxy-1-methoxyxanthone was extracted from *Arenaria serpyllifolia* L by solvent fractionation and subsequent separations with silica gel, ODS, Sephadex LH-20 and semi-preparative HPLC chromatography and their structures were characterized by spectroscopic investigation and identified[7]. A significant medicinal plant called *Arenaria serpyllifolia* L. grows in the subtropical and temperate Himalayan areas from Nepal to Kashmir. Traditional medicine makes use of plants to heal renal and bladder-related issues. Density functional theory (DFT) computations for the molecular structure and reactivity are performed, and topological studies are used to forecast the electron density distribution. A molecular Electrostatic Potential (MEP) investigation is carried out to reveal the molecular locations that are vulnerable to chemical assault. Particular target proteins are used for docking. Similar investigations conducted by other research groups demonstrated that these theoretical analyses offer an early understanding of the nature, reaction, and powerful therapeutic potential of organic substances in biological structures. Applying techniques based on deep learning to predict molecular characteristics like lipophilicity is another way to predict bioactivity and drug-like characteristics. These models are being demonstrated to provide accurate and reliable predictions[8,9]. Water, methanol, ethanol, and acetone were the solvents of choice for researching the influence of solvents on various physical as well as chemical properties. These substances were selected so that the gradation of their characteristics with increasing polarity could be seen. The use of green solvents is preferred since these molecules mostly interact favourably via hydrogen bonds. Since it serves as the surfactant of reaction and distribution in biological systems, water, the most used aqueous solvent, is the medium of most interest in the present work. Investigating the effects of the solvation is done using the continuous model, IEFPCM[10,11]. It is anticipated that the results will support the creation of chemical and pharmaceutical applications that are more efficient and sustainable, in line with current objectives of environmental stewardship and better health outcomes. A comprehensive investigation integrating quantum chemical analysis, solvent effects utilizing green media, and molecular docking for (5H1MX) is still lacking, despite several research highlighting the biological relevance of xanthone derivatives. Density Functional Theory (DFT), Natural Bond Orbital (NBO) analysis, Fukui function descriptors, and IEFPCM solvation models are all uniquely integrated in this work to assess the compound's reactivity and structure property connection. Additionally, the study focuses on ecologically safe solvents to comprehend their impact on biological and electrical characteristics. By offering fresh perspectives on the stability, reactivity, and antidiabetic potential of 5H1MX, this theoretical and pharmacological approach aids in the creation of long lasting and powerful medication candidates.

Computational details

Density Functional Theory (DFT) at the B3LYP/6-311++G(d,p) level of theory was used for all quantum chemistry computations[12,13]. The aforementioned source theory level was used for all additional computational, including MEP and FMOs in the gas phase and with selected solvents such as water, methanol, ethanol, and acetone. NBO investigations are being utilized to investigate whether atomic orbitals interact with isolated pairs, bonds, and anti-bonds[14,15]. Using the Swiss ADME online tool results on pharmacological characteristics and lipophilicity were obtained[16]. This work investigated the molecular docking interaction between the analyzed ligand molecule and the target protein using the Auto Dock 4.2.6 set and then assessed it by the Py MOL program[17].

Results and Discussion

GC-MS analysis

Gas chromatography–mass spectrometry (GC–MS) is a widely used technique for analyzing compounds in liquid, gaseous, and solid samples. The analysis begins with sample vaporization in the gas chromatograph, followed by separation using a capillary column. The chemical composition of Iranian propolis extracts that were collected in 2023 from two provinces in northern Iran: Ardabil and Polur from Mazandaran Province were measured through gas chromatography-mass spectrometry (GC-

MS) methods[18]. In addition, antimicrobial activity and cytotoxicity effects on HN5 and LNCaP cell lines were evaluated. The data were analyzed using one-way ANOVA and $P< 0.05$ was considered significant. The GC-MS analysis in Figure 1, identifies the presence of compounds that belong to different groups such as aromatics acids and their related esters, flavonoid and flavonoid derivatives and terpenes. Flavanone is the most dominant compound of flavonoids. The maximum growth inhibition is observed against S. aureus of ethanolic extract of propolis ($P< 0.05$). Moreover, cytotoxicity shows that ethanolic and dichloromethane extracts have more inhibitory effects on cell lines than the water extract.

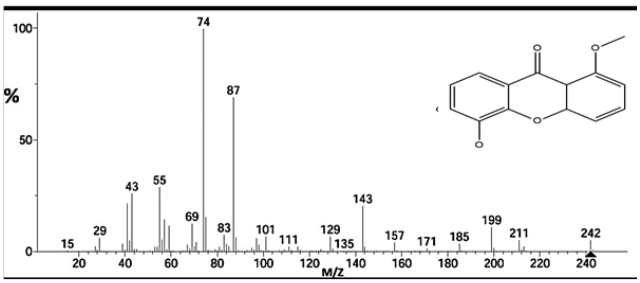

Fig. 1 — GC-MS Chromatogram of 5H1MX molecule

NBO analysis

NBO analysis is an effective tool for evaluating intermolecular and intramolecular interactions. This analysis is used to study the charge transport and conjugative interactions. The 2nd order Fock matrix approach is used to evaluate the links between donor and acceptor atoms in natural bonding analyses. It is feasible to determine the stabilization energies E (2) is connected to the de-localization of each donor (i) and acceptor (j). The NBO fraction that is off-diagonal is F (I,j). In the Fock matrix, the donor filling is represented by the principal diagonals of qi and Ei[19,20]. Table 1 displays the computed stabilized

Table 1 — Second-order perturbation theory analysis of Fock matrix in NBO basis for 5H1MX

Donor	Type	ED/e(qi)	Acceptor	Type	ED/e(qj)	E(2) kcal/mol	E(j)-E(i) a.u.	F (I,j) a.u.
C 13 - C 17	π*	0.36202	C 12 - C 15	π*	0.31736	472.42	0.02	0.149
C 12 - H 20	σ	1.97716	C 13 - C 17	σ*	0.02326	462.19	0.33	0.347
O 2	LP (2)	1.90729	C 13 - C 17	σ*	0.02326	380.46	0.09	0.169
C 17 - H 24	σ	1.97813	C 13 - C 17	σ*	0.02326	380.26	0.38	0.34
O2	LP (1)	1.94188	C 13 - C 17	σ*	0.02326	322.9	0.11	0.171
C 12 - H 20	σ	1.97716	C 10 - C 14	π*	0.31675	320.95	0.19	0.238
C 12 - C 15	π	1.69592	C 18 - H 26	σ*	0.01948	300.5	0.65	0.425
C 12 - H 20	σ	1.97716	C 18 - H 26	σ*	0.01948	297.53	0.97	0.48
C 13 - C 17	π*	0.36202	C 11 - C 16	π*	0.28663	290.34	0.02	0.131
O 2 - C 10	σ	1.99052	C 10 - C 14	π*	0.31675	272.91	0.42	0.33
O 2 - C 18	σ	1.97799	C 18 - H 26	σ*	0.01948	263.63	1.09	0.479
C 14 - C 15	σ	1.97665	C 15 - H 22	σ*	0.01334	239.28	0.04	0.088
C 18 - H 27	σ	1.99551	C 18 - H 26	σ*	0.01948	239.15	0.83	0.399
O 2 - C 18	σ	1.97799	C 10 - C 14	π*	0.31675	233.87	0.31	0.26
O 2 - C 10	σ	1.99052	C 13 - C 17	σ*	0.02326	225.2	0.56	0.319
C 17 - H 24	σ	1.99551	C 10 - C 14	π*	0.31675	217.14	0.24	0.222
C 13 - C 17	π*	0.36202	C 18 - H 26	σ*	0.01948	215.29	0.52	0.683
O 3	LP (1)	1.97854	C 10 - C 14	π*	0.31675	165.01	0.22	0.185
C 11 - C 16	π*	0.28663	C 18 - H 26	σ*	0.01948	146.65	0.49	0.615
C 10 - C 14	σ	1.97793	C 10 - C 14	π*	0.31675	146.55	0.25	0.187
C 14 - H 21	σ	1.97677	C 18 - H 26	σ*	0.01948	133.5	0.87	0.304
C 12 - C 15	π*	0.31736	C 13 - C 17	π*	0.36202	128.34	0.13	0.117
C 5 - C 10	σ	1.97153	C 10 - C 14	π*	0.31675	118.61	0.24	0.164
C 18 - H 26	σ	1.99511	C 12 - H 20	σ*	0.01316	116.88	0.59	0.234
C 16 - H 23	σ	1.98074	C 13 - C 17	σ*	0.02326	115.7	0.2	0.137
C 10 - C 14	σ	1.97793	C 15 - H 22	σ*	0.01334	112.69	0.05	0.065
C 10 - C 14	π*	0.31675	C 18 - H 26	σ*	0.01948	108.61	0.78	0.634
C 18 - H 27	σ	1.99551	C 12 - H 20	σ*	0.01316	108.12	0.59	0.225
O 2 - C 18	σ	1.97799	C 12 - H 20	σ*	0.01316	107.03	0.85	0.27
C 12 - C 15	π*	0.31736	C 11 - C 16	π*	0.28663	106.06	0.15	0.115
C 12 - C 15	π*	0.31736	C 18 - H 26	σ*	0.01948	100.06	0.5	0.486
C 18 - H 26	σ	1.99511	C 12 - C 15	π*	0.31736	97.9	0.33	0.175
C 18 - H 27	σ	1.99551	C 12 - C 15	π*	0.31736	96.03	0.33	0.173
C 12 - H 20	σ	1.97716	C 12 - H 20	σ*	0.01316	91.58	0.73	0.231

energies between the 5H1MX's donor and acceptor pairs. The calculated stabilized energies between the donor and acceptor pairs of the 5H1MX are shown in (Table 1). Interaction C13-C17* to C12-C15* was determined to possess the highest stabilization energy which is 472.42 kcal/mol. An elevated E2 NBO analysis discloses a scheme with a high amount of recombination and an energetic interchange involving both donor and acceptor electrons. Other notable exchanges include C 12- H 20 to C 12- H20*, which has a lowermost stabilization energy of 91.58 kcal/mol[21,22].

Fukui functions

The population-based Fukui function provides quantitative information about the reactivity of individual atoms, including their nucleophilicity and electrophilicity[23,24]. Electron density differs with the number of electrons that are present at a certain region. The Fukui function involves adding or subtracting electrons from the molecule. Use this function to determine the reactivity of 5H1MX with various compounds. Fukui function, which determines local softness, may be utilized during biological studies to analyse ligand and protein docking. Exact charges of the Fukui function are derived via Mulliken population analysis[25,26]. The atom is being attacked electrophilically if f (r) is negative or nucleophilically if f(r) is positive. Each atom is included in Table 2 along with its Dual and function descriptions. The value of the atom 9C is the lowest (-0.124), and the value of the atom 14C is the greatest (+0.075). The dual descriptor ordering for positive values is 14C > 18C > 1O > 6C > 4O > 16C > 12C > 2O > 19H > 25H, 23H > 13C > 7C > 5C, and 21H > 20H. The negative f(r) is arranged in the following manner of 9°C, 3°C, >15°C, 10°C, 27°H, 26°H, 28°H, 22°H, and 11°C, 24°H.

Table 2 — Condensed Fukui function, local softness, and dual descriptor of 5H1MX

Atom	Mulliken atomic charges			Fukui functions			dual des	local softness		
	0, 1 (N)	N +1 (-1, 2)	N-1 (1,2)	f_r^+	f_r^-	f_r^0	delta fr	sr+ f_r^+	sr-f_r^-	sr0 f_r^0
1 O	-0.0069	0.082079	-0.05563	0.089	0.049	0.069	0.04	0.019	0.011	0.015
2 O	-0.1151	-0.075285	-0.1378	0.04	0.023	0.031	0.017	0.009	0.005	0.007
3 O	-0.2626	-0.202601	-0.39386	0.06	0.131	0.096	-0.071	0.013	0.029	0.021
4 O	-0.2254	-0.158691	-0.2551	0.067	0.03	0.048	0.037	0.015	0.006	0.011
5 C	1.05287	1.094466	1.013845	0.042	0.039	0.04	0.003	0.009	0.009	0.009
6 C	1.17317	1.224589	1.160879	0.051	0.012	0.032	0.039	0.011	0.003	0.007
7 C	-0.8394	-0.869292	-0.80553	-0.03	-0.034	-0.032	0.004	0.007	-0.007	-0.007
8 C	-1.483	-1.516936	-1.40535	-0.034	-0.078	-0.056	0.044	0.007	-0.017	-0.012
9 C	-0.1403	-0.129837	-0.27454	0.01	0.134	0.072	-0.124	0.002	0.029	0.016
10 C	-0.0957	-0.051684	-0.1709	0.044	0.075	0.06	-0.031	0.01	0.016	0.013
11 C	0.56656	0.64548	0.483074	0.079	0.083	0.081	-0.005	0.017	0.018	0.018
12 C	-0.5945	-0.558113	-0.60593	0.036	0.011	0.024	0.025	0.008	0.002	0.005
13 C	-0.2908	-0.280771	-0.29602	0.01	0.005	0.008	0.005	0.002	0.001	0.002
14 C	0.23134	0.311801	0.225593	0.08	0.006	0.043	0.075	0.018	0.001	0.009
15 C	-0.2159	-0.240353	-0.26168	-0.024	0.046	0.011	-0.07	0.005	0.01	0.002
16 C	-0.2492	-0.211045	-0.25298	0.038	0.004	0.021	0.034	0.008	0.001	0.005
17 C	0.00298	0.02115	-0.07959	0.018	0.083	0.05	-0.064	0.004	0.018	0.011
18 C	-0.292	-0.301411	-0.23114	-0.009	-0.061	-0.035	0.051	0.002	-0.013	-0.008
19 H	0.18962	0.23553	0.158778	0.046	0.031	0.038	0.015	0.01	0.007	0.008
20 H	0.18689	0.238623	0.135418	0.052	0.051	0.052	0	0.011	0.011	0.011
21 H	0.19287	0.252586	0.136302	0.06	0.057	0.058	0.003	0.013	0.012	0.013
22 H	0.17991	0.233593	0.119124	0.054	0.061	0.057	-0.007	0.012	0.013	0.012
23 H	0.17612	0.239542	0.120675	0.063	0.055	0.059	0.008	0.014	0.012	0.013
24 H	0.13466	0.19052	0.077096	0.056	0.058	0.057	-0.002	0.012	0.013	0.012
25 H	0.26704	0.297947	0.244507	0.031	0.023	0.027	0.008	0.007	0.005	0.006
26 H	0.17469	0.18101	0.15848	0.006	0.016	0.011	-0.01	0.001	0.004	0.002
27 H	0.11955	0.144706	0.077014	0.025	0.043	0.034	-0.017	0.005	0.009	0.007
28 H	0.16267	0.202397	0.115267	0.04	0.047	0.044	-0.008	0.009	0.01	0.009

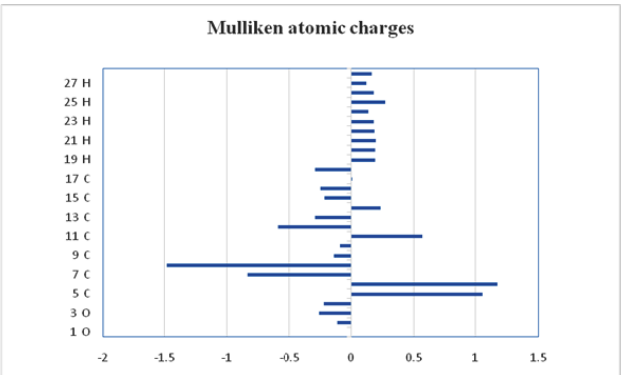

Fig. 2 — Mulliken atomic charges of 5H1MX

Table 3 — Mulliken atomic charges of 5H1MX

Atom	Mulliken atomic charges	Atom	Mulliken atomic charges
1 O	-0.007	15 C	-0.216
2 O	-0.115	16 C	-0.249
3 O	-0.263	17 C	0.003
4 O	-0.225	18 C	-0.292
5 C	1.053	19 H	0.190
6 C	1.173	20 H	0.187
7 C	-0.839	21 H	0.193
8 C	-1.483	22 H	0.180
9 C	-0.140	23 H	0.176
10 C	-0.096	24 H	0.135
11 C	0.567	25 H	0.267
12 C	-0.595	26 H	0.175
13 C	-0.291	27 H	0.120
14 C	0.231	28 H	0.163

Mulliken charge studies

The estimation of Mulliken charge distribution for 5H1MX was carried out and (Fig. 2) shows the graphical representation. The Mulliken charge distribution reveals significant variation in charge among the 28 atoms of 5H1MX. 6C carries the highest positive charge of 1.173167. Carbon has a higher local electronegative charge than any other atom, giving 5C the second-highest positive charge (1.052874). Positive charges are present on all other carbon atoms (0.231344, 0.002982). It has been established that hydrogen molecules only possess positive charges and that oxygen molecules possess just negative charges shown in (Table 3).

MEP analysis

The MEP calculation of the 5H1MX molecule is displayed in (Fig. 3) along with the colour-graded maps. The MEP analysis, which depends on many factors like dipole moment and the density of electrons, indicates the type of chemical attack that may occur at all the different reactive sites inside the molecule under investigation[27]. The developed

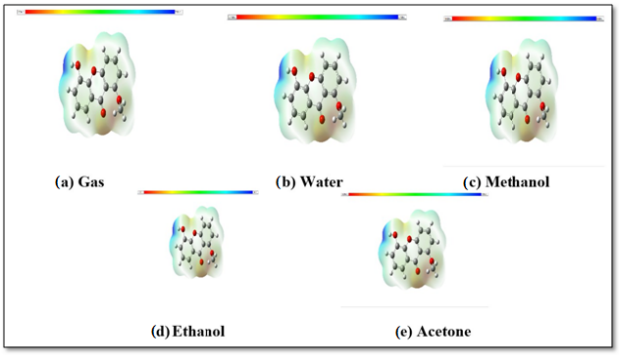

Fig. 3 — MEP maps of the 5H1MX compound in gas and green solvent

electrostatic potential is calculated over a surface having a uniform electron density on which the Mep map is built[28]. According to this system of color grading, nucleophiles prefer blue regions while electrophilic reagents are most likely to attack red sections. Upon solvation, there is no discernible change in color gradation. However, the medium's polarity increases during solvation and the electrostatic potential range expands significantly. As a result, the potential range expands from - 7.000 10^{-2} a.u. to 7.000 10^{-2} a.u. (atomic unit is referred to as a.u.) in the gaseous phase, 8.472 10^{-2} a.u. to 8.472 10^{-2} a.u. in water, 8.425 10^{-2} a.u. to 8.425 10^{-2} a.u. in methanol, 8.401 10^{-2} a.u. and 8.401 10^{-2} a.u. in ethanol and -8.380 10^{-2} a.u. to 8.380 10^{-2} in acetone. Finally, it demonstrates that the water solvent's polarity gradient is higher. Therefore, when the polarity of the solvents rises, the molecules exhibit a larger potential range, suggesting that they would interact with solvation in a more polar (charged) manner and a compound's bioactivity may be anticipated based on the MEP map[29]. The intermolecular interactions controlling the stability and reactivity of the 5H1MX molecule are better understood thanks to the electronic characteristics derived from NBO, MEP, and Fukui function investigations. Strong donor-acceptor interactions, which greatly enhance molecule stability, are indicated by the high stabilization energy found in NBO analysis. Electron-rich and electron-deficient areas that are vulnerable to electrophilic and nucleophilic assaults, respectively, are further identified by the MEP surface. Additionally, RDG–NCI analysis verifies that the molecular framework contains weak non-covalent interactions such steric repulsions and van der Waals forces. These interactions affect the molecule's binding affinity toward biological targets and are essential in

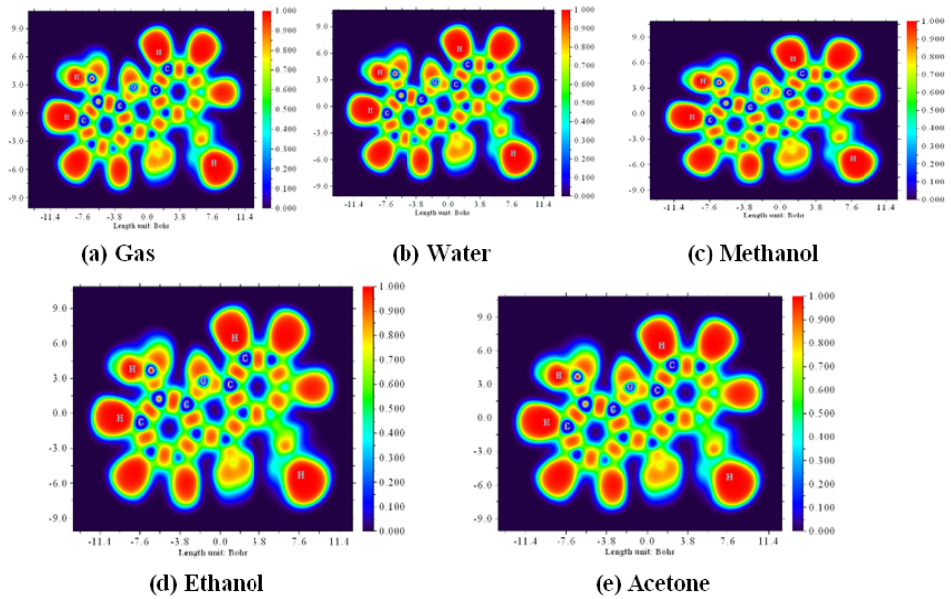

Fig. 4 — ELF colour-filled maps of the 5H1MX molecule in gas and different solvents

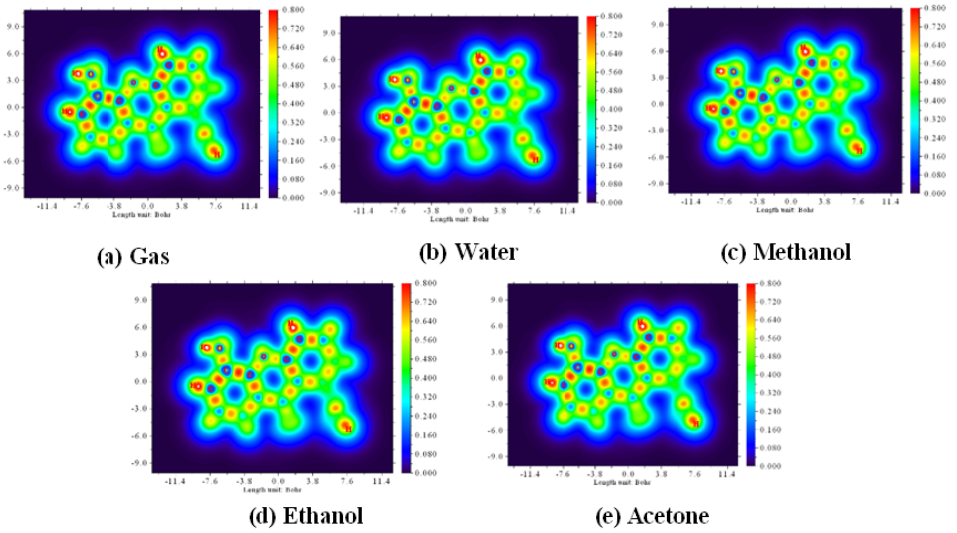

Fig. 5 — LOL colour-filled maps of the 5H1MX molecule in gas and different solvents

determining the overall structural stability. Thus, a clear connection between molecule structure, stability, and biological activity is established by combining the interpretation of electronic descriptors with interaction analysis.

ELF and LOL analysis

The strength of Pauli repulsion between molecular orbitals is predicted by the Electron Localised Function analysis (ELF). Illustrations of the ELF emission in gas and solvents are shown in (Fig. 4)[30]**.** Hydrogen 1s orbitals are extremely tiny, and molecular aromatic hydrogens have an abundance of red regions, which means that substantial Pauli repulsion is occurring there. The bluish regions are the higher 2s and 3s orbitals of oxygen and aromatic carbons that are concentrated since there is less Pauli repulsion in these locations. However, Pauli repulsion increases as orbital electrons become closer as well as suffer repulsion on engagement such that reddish patches can be detected in the bonded orbital overlay around aromatic carbons. In various solvent media, Pauli repulsion does not appear to fluctuate[31].

The depth of pi-orbital delocalization over a complete biological system is shown by the Localised Orbital Locator (LOL) research. The LOL output photos in various media are shown in (Fig. 5). As the

density of electrons overflows the top edge and the core of the hydrogen atom has a higher LOL value in the covalent region, it indicates red. The position of electron reduction via valence to its inner shell is indicated through a bluish circle.

RDG -NCI analysis

A distinctive technique for predicting and illustrating the strongest molecular connections is the Reduced Density Gradient which can be calculated using Atomistica online tool and VMD software[32]. A hydrogen bond forms such that green denotes a Wander-Waals interaction and red denotes steric repellent interactions as shown in (Fig. 6). For weak connection projections, sign $(\lambda_2)\rho$ (a.u.) ranging from -0.04 to 0.04 in RDG maps have been obtained in many solvents including gas, water, methanol, ethanol, and acetone. The elliptical red plate at the aromatic ring hub is connected to phenyl rings and has a significant steric impact because of strong repellent forces[33,34]. Red-green spotted flaky zone from 0.00 to 0.01 a.u. displays the C-H connections denoting a weak Vander Waals force of contact, and a low electron density. There are no significant NCI or H-bonds between the phenyl rings, according to RDG evaluation, because there are no blue spikes between 0.01 and 0.04 a.u. In addition, a blue-ringed area that is scattered across the picture indicates the presence of an H-bond inside the molecular structure. Due to the effects of the solvent, 5H1MX does not significantly change in the case of RDG.

Drug likeness

The compound 5-Hydroxy-1-Methoxyxanthone ($C_{14}H_{10}O_4$) has attracted interest because of its possible anti-diabetic properties. The assessment of the drug's safety profile, mechanism of action, and efficacy is part of the pharmacological inquiry. Criteria for drug-likeness activity can be predicted by the Lipinski rule of five[35], if it will have strong drug-like qualities and be an excellent option for a drug. In the current investigation, the overall score value of a drug's likeness is calculated. The criteria measuring the compound's drug-likeness are compiled in (Table 4). The Swiss ADME program may be used in this way to carry out a range of tasks[36,37]. The set of criteria put forward by Lipinski[38] is in favour of this result. It is assured to adhere to the drug rules, therefore there are no violations. The molecular weight is 242.23 g/mol, with HBD (Donor) =1, and HBA (Acceptor) = 4. Lipophilicity is a vital physical–chemical factor for defining drug similarity.

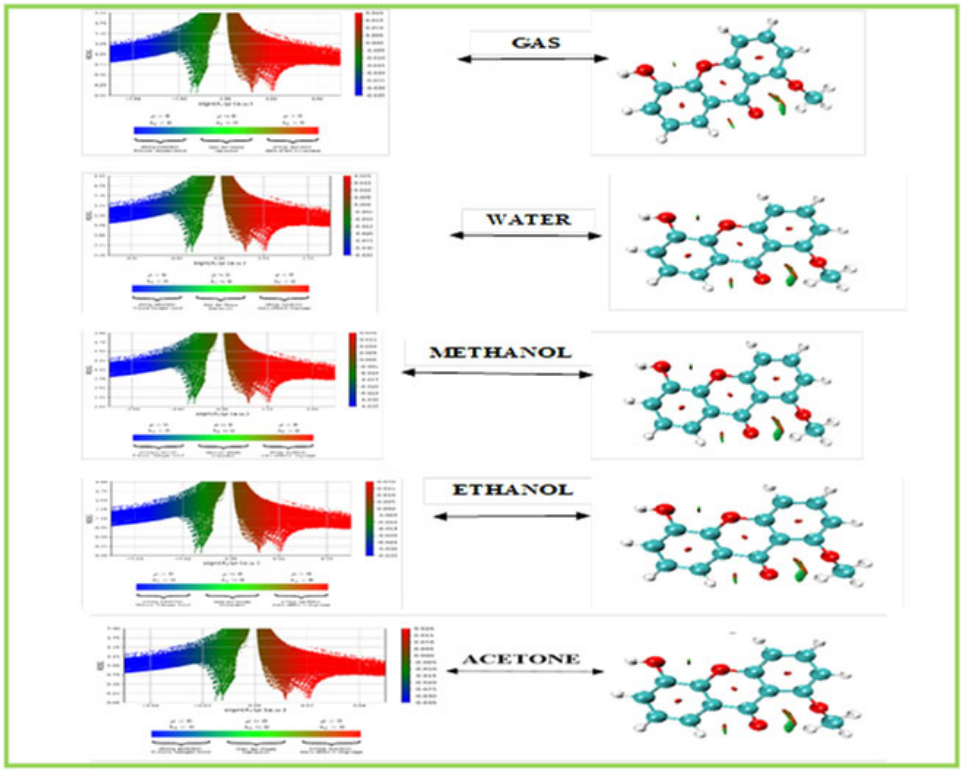

Fig. 6 — RDG and NCL analysis of the 5H1MX molecule in gas and different solvents

Table 4 — Drug discovery parameters for 5H1MX

Descriptor	Value
Physiochemical properties	
Hydrogen Bond Donor (HBD)	1
Hydrogen Bond Acceptor (HBA)	4
AlogP	0
Topological polar surface area (TPSA)	59.67 Å²
Molar refractivity	68.51
Number of atoms	28
Number of rotatable bonds	1
Lipophilicity	
iLOGP	2.14
XLOGP	2.58
WLOGP	2.66
MLOGP	1.13
SILICOS-IT	2.98
Consensus LOGP	2.30
Water Solubility	
LogS(ESOL)	-3.48
Pharmacokinetics	
GI absorption	High
Log Kp (skin permeation)	-5.95 cm/s
Druglikeness	
Lipinski	Yes, 0 violation
Veber	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
Leadlikeness	No;1 violation: MW<250
Synthetic accessibility	2.95

Therefore, it is evident that the title compound accurately describes the characteristics necessary for the chemical to function as a drug. It is obvious from this that the chemical's name appropriately captures the qualities necessary for the drug to serve as a treatment. These findings demonstrate that the chemical is bioactive[39].

Molecular docking

The molecular docking method is now often employed in biological research for the creation of new drugs. The 5H1MX molecule has a strong anti-diabetic effect, the target protein (PDB ID: 3CV7) associated with diabetes was obtained from the Protein Data Bank (RCSB)[40]. This work attempts to evaluate the binding affinity of 5-Hydroxy-1-Methoxyxanthone to target proteins and its possible effect on glucose metabolism by combining computational predictions with experimental data. It is anticipated that the outcomes of these investigations will offer significant perspectives on the medicinal possibilities of this substance and its function in the control of diabetes. To acquire the rank one value at

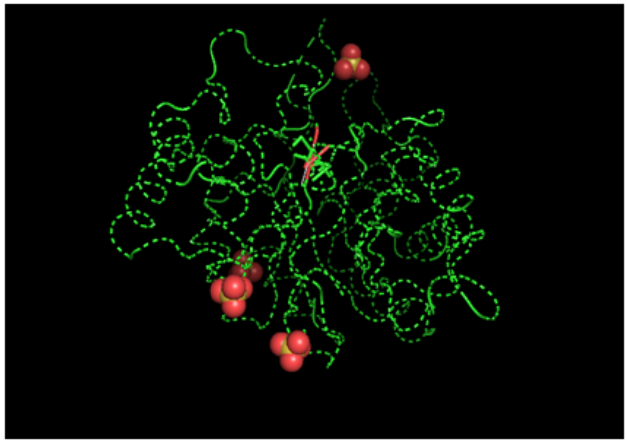

Fig. 7 — Molecular docking with 3cv7 protein

Fig. 8 — 3D diagram of Molecular docking with 3cv7 protein

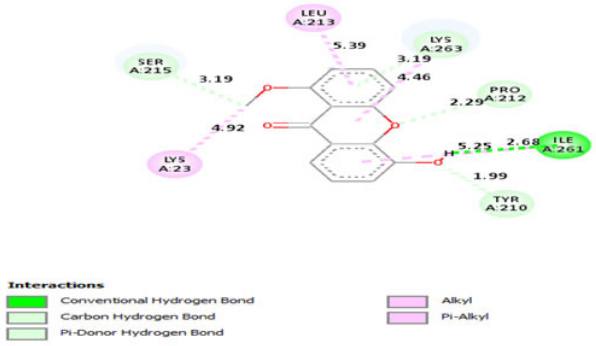

Fig. 9 — 2D diagram of Molecular docking with 3cv7 protein

the lowest feasible cost, as shown in (Fig. 7), the 5H1MX molecule was docked into the active site of the target protein. Molecular docking binding energies (kcal/mol), bond lengths, and the number of residues is provided in (Table 5). Figure 8 shows a 3D depiction of the docked position of 3cv7. The two-dimensional model is shown In (Fig. 9). The low binding energy of the protein 3cv7, which is -7.14

Table 5 Molecular docking with antidiabetic's protein of 5H1MX

Protein (PDB ID)	Residue	Type of Interactions	Bond dist. (Å)	Binding energy (Kcal/ mol)	Estimated inhibition constant (micromolar)	Inter molecular energy (Kcal/mol)	vdW + H bond + dissolve Energy (kcal/mol)	Reference RMSD (Å)
3cv7	LEU A-213	Alkyl	5.39	-7.14	5.88	-7.73	-7.65	27.95
	LYS A-23	Pi- Alkyl	4.92					
	SER A-215	Carbon H- Bond	3.19					
	LYS A-263	Carbon H- Bond	3.19					
	PRO A- 212	Pi-Donor H- Bond	2.29					
	TYR A-210	Pi-Donor H- Bond	1.99					

kcal/mol, makes it suitable for biological activity[41,42]. This chemical is recommended as a possible diabetes treatment since it has strong protein binding with 3cv7 and a low binding energy value[43].

Conclusion

The current work verifies the structural and electronic characteristics of 5H1MX using a combination of experimental and theoretical methodologies. Strong donor-acceptor contacts with high stabilization energy were found by NBO analysis, suggesting molecular stability. While ELF, LOL, and RDG investigations shed light on electron localization and intermolecular interactions, MEP and Fukui analysis indicated important reactive sites. The chemical demonstrated significant binding affinity (−7.14 kcal/mol) for the target protein and excellent drug-likeness characteristics. These results imply that 5H1MX is a good option for the development of antidiabetic medications.

Conflict of interest

All authors declare no conflict of interest.

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