

Molecular Docking, DFT, ADMET, and PASS-based Evaluations of Methyl β -D-Galactopyranoside Derivatives as Yellow Fever Virus Inhibitors

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Abstract. Carbohydrate-based scaffolds represent an attractive framework for the design of novel therapeutic agents because of their structural diversity, biocompatibility, and potential for selective biological interactions. Among them, galactopyranoside derivatives have drawn increasing attention owing to their pharmacological applications, particularly as antimicrobial and anticancer agents. In this study, an assortment of novel methyl β -D-galactopyranoside (**1**, MGalP) derivatives was evaluated for their thermodynamic stability, electronic properties, pharmacokinetics, and biological potential *via in silico* approaches. Density functional theory (DFT) calculations revealed that structural modifications enhanced molecular stability, polarizability, and reactivity. Molecular docking studies against yellow fever virus (YFV) (PDB ID: 6IW5) demonstrated favorable binding affinities (-5.5 to) compared with those of the parent compound. Compound **5** exhibited the greatest binding affinity of -7.0 kcal/mol. Strong interactions occurred with the amino acid residues TYR225 and TYR354, alongside PHE240, PHE339, LEU394, HIS227, ASP189, and GLY409. These findings suggest that aromatic and long-chain acyl modifications significantly improve binding properties. Pharmacokinetic profiling through ADMET prediction confirmed high intestinal absorption, good blood–brain barrier permeability, and acceptable solubility for most derivatives. PASS prediction further revealed promising antifungal and antiviral activities, suggesting the potential of these compounds as multifunctional drug candidates.

Keywords: Methyl β -D-galactopyranoside (MGalP); Molecular docking; Yellow fever virus activity; ADMET; PASS prediction.

1. Introduction

Carbohydrates are among the most abundant natural compounds. Structural components, energy sources, and facilitators of different biological processes have been identified [1]. In addition to their physiological roles, carbohydrate derivatives have gained increasing attention in medicinal chemistry owing to their structural flexibility [2], ability to engage in hydrogen bonding [3], and compatibility with biological systems [4]. Recently, modern methods have been employed for the separation of a wide variety of naturally occurring compounds derived from plants [5] and other components, among which carbohydrates are significant components [6]. The application of carbohydrate-derived therapeutics for treating infectious diseases has increased [7]. Glycans are carbohydrates composed of monosaccharide units linked by glycosidic bonds and are involved in cancer, inflammation, and microbial infections [8-10]. Their interactions with lectins are widely exploited in vaccines, antiviral agents, and immunotherapies, and they are key components of many natural products [11]. Owing to their ability to interact with microbial proteins and enzymes, carbohydrate derivatives are promising candidates for designing next-generation antiviral agents [12, 13]. Carbohydrate-based antiviral drugs, such as remdesivir, oseltamivir, and zanamivir, and vaccines are already being used to treat

viral diseases. These methods have shown promising results in treating HIV, COVID-19, herpes, hepatitis, and other viral diseases [14, 15].

Methyl β -D-galactopyranoside, a simple galactose derivative, also serves as a versatile lead structure [16]. It can be functionalized to improve its pharmacological properties. Structural modifications such as acylation, aromatic substitutions, and halogenation have been shown to increase binding affinities and biological activity [17]. In this study, six novel methyl β -D-galactopyranoside derivatives (**2-7**) were subjected to an integrated computational study. The thermodynamic stability, electronic properties, and reactivity of these materials were examined through density functional theory (DFT) calculations [18, 19]. Molecular docking was performed against yellow fever virus (YFV) (PDB ID: 6IW5) to assess its antiviral potential and identify its binding orientation, stability, and intermolecular forces. The arbovirus that causes yellow fever (YF) is a member of the genus *Flavivirus*, which includes positive single-stranded RNA viruses and the family *Flaviviridae*. Muscle soreness, headache, fever, jaundice, nausea, vomiting, and exhaustion are among the symptoms [20]. The clinical symptoms are so diverse that the diagnosis of yellow fever is challenging. Hemorrhagic fever may occur in people with severe infections and can result in death. In patients with severe symptoms, the incidence of fatalities is estimated to be between 20% and 50%

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[14]. Pharmacokinetic parameters and toxicity risks were analyzed through ADMET predictions, and PASS screening was conducted to estimate antimicrobial potential [21]. The combined results offer insights into the structure–activity relationships of these six derivatives, highlighting structural features that enhance antifungal activity.

Overall, this study highlights the potential of methyl β -D-galactopyranoside (MGalP) derivatives as

promising antiviral candidates [22]. All the derivatives displayed superior binding affinities, favorable reactivities, and acceptable pharmacokinetic properties, making them compelling leads for further in vitro and in vivo validation. This integrated computational approach facilitates the rational design of carbohydrate-based therapeutics and contributes to the broader development of novel antiviral strategies. The current research workflow is shown in Figure 1.

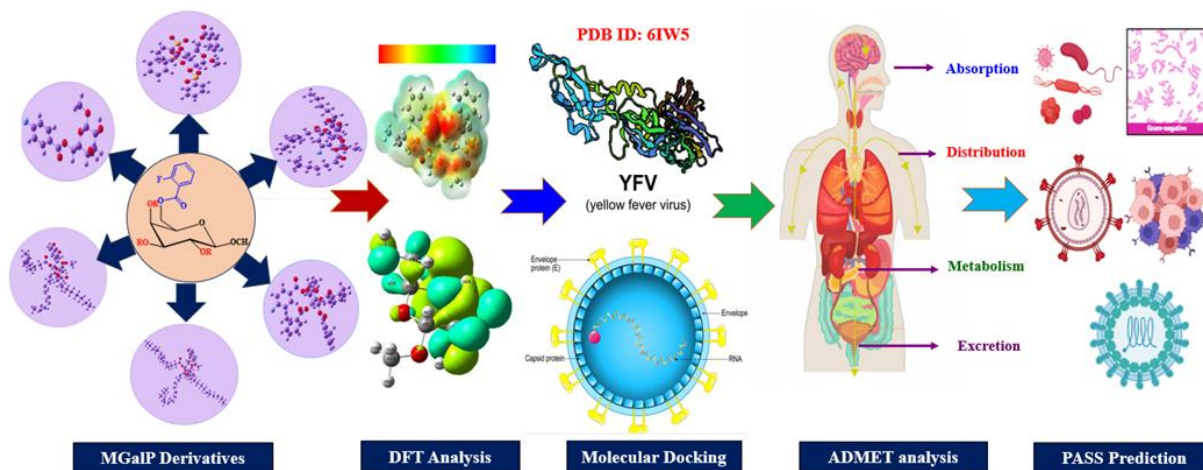


Figure 1. Workflow of the current research.

2. Computational Details

2.1. Designing and Optimization of MGaIP Derivatives

In regard to thermal, molecular orbital, and molecular electrostatic property calculations, computational chemists frequently turn to quantum mechanical approaches [23]. The results of the DFT method and the optimized chemical structures of the studied compounds are listed in Table 1. Using Gaussian 09 W (Revision D.01) software, we optimized the geometry and made further modifications to all of the synthesized derivatives. The thermodynamic and molecular orbital properties of the derivatives were optimized and examined via density functional theory (DFT) by employing the 6-31G++ basis set [24]. Essential metrics such as electronic energy, free energy, enthalpy, and dipole moment were computed for compounds 2–7. The border molecular orbitals, namely, the highest occupied molecular orbital (HOMO) and lowest unoccupied

molecular orbital (LUMO), were assessed and are shown in Table 2. Additional quantum chemical descriptors, including chemical potential (μ), electronegativity (χ), electrophilicity (ω), the HOMO–LUMO energy gap, hardness (η), and softness (S), were calculated via established methods [25].

$$\text{Gap } (\Delta E) = [\varepsilon_{\text{LUMO}} - \varepsilon_{\text{HOMO}}]$$

$$\eta = \frac{[\varepsilon_{\text{LUMO}} - \varepsilon_{\text{HOMO}}]}{2}$$

$$S = \frac{1}{2\eta}$$

$$\mu = \frac{[\varepsilon_{\text{LUMO}} + \varepsilon_{\text{HOMO}}]}{2}$$

$$\chi = -\frac{[\varepsilon_{\text{LUMO}} + \varepsilon_{\text{HOMO}}]}{2}$$

$$\omega = \frac{\mu^2}{2\eta}$$

Table 1. Structures of the synthesized MGaIP derivatives (2–7) with their smiles.

Entry	Structure	SMILES
1		<chem>[H][C@@](C(CO)O[C@@]([H])(OC)[C@@](O)1[H])(O)[C@@]1([H])O</chem>

Entry	Structure	SMILES
2		<chem>[H][C@@](C(COC(C2=CC=C(F)C=C2)=O)O[C@@]([H])(OC)[C@@](O)1[H])(O)[C@@]1([H])O</chem>
3		<chem>[H][C@@](C(COC(C5=CC=C(F)C=C5)=O)O[C@@]([H])(OC)[C@@](OS(C2=CC=CC=C2)(=O)=O)1[H])(OS(C3=CC=CC=C3)(=O)=O)[C@@]1([H])OS(C4=CC=CC=C4)(=O)=O</chem>
4		<chem>[H][C@@](C(COC(C2=CC=C(F)C=C2)=O)O[C@@]([H])(OC)(CCCCCCC=O)1[H])(OC(CCCCCC=O)[C@@]1([H])OC(CCCCCC=O)=O</chem>
5		<chem>FC1=CC=C(C(OC(C3=CC=C(C)C=CC=C3)=O)2[H])[C@@](OC(C3=C(C)C=CC=C3)=O)2[H])[C@@](OC(C5=C(C)C=CC=C5)=O)([H])[C@@]2([H])OC(C4=C(C)C=CC=C4)=O)C=C1</chem>

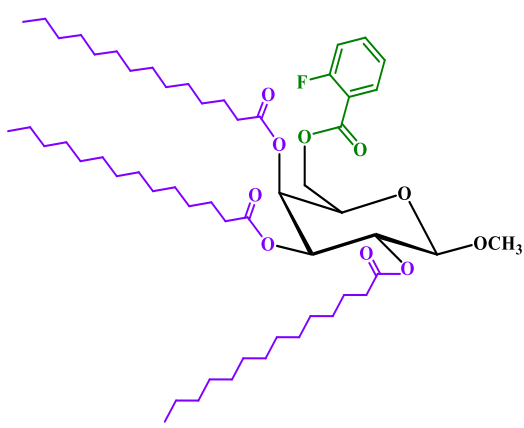
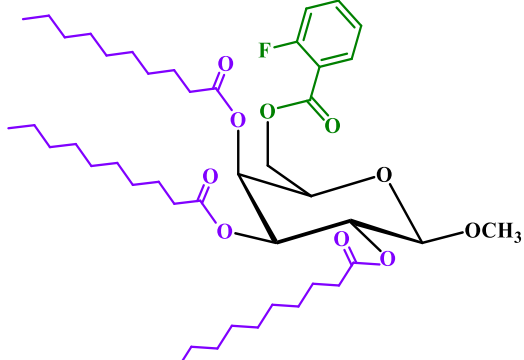
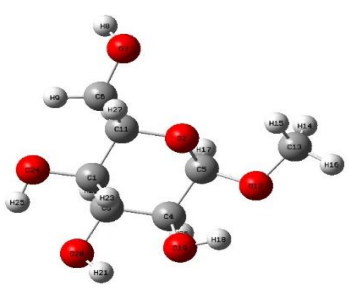
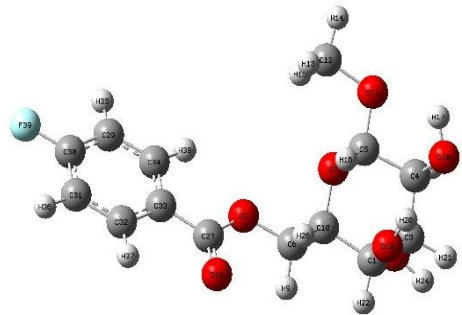
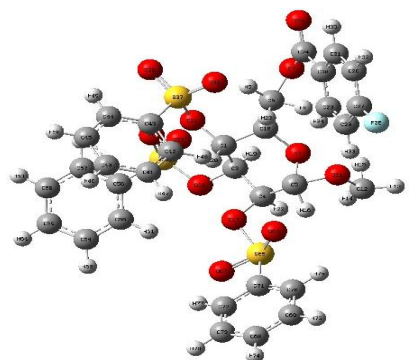
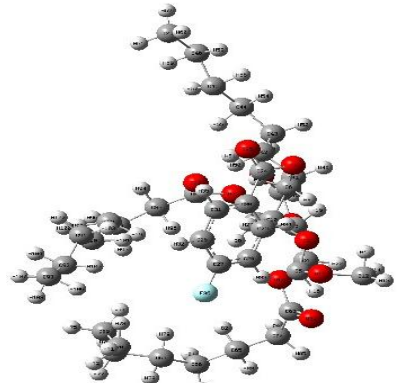
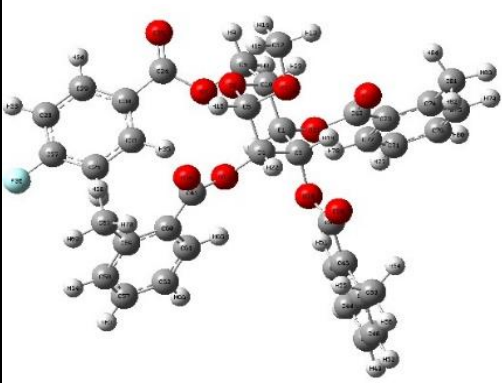
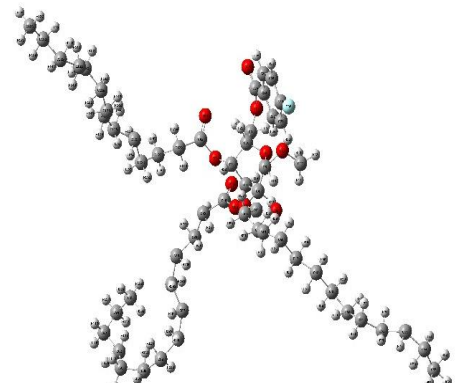
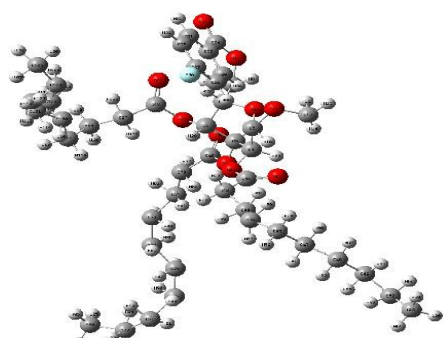
Entry	Structure	SMILES
6		<chem>FC1=CC=C(C(COCC(O[C@@]([H])(OC)[C@@](OC(C3=C(C)C=CC=C3)=O)2[H])[C@@](OC(C5=C(C)C=CC=C5)=O)([H])[C@@]2([H])OC(C4=C(C)C=CC=C4)=O)=O)C=C1</chem>
7		<chem>FC1=CC=C(C(COCC(O[C@@]([H])(OC)[C@]([H])2C2OC(C3=C(C)C=CC=C3)=O)[C@@](OC(C5=C(C)C=CC=C5)=O)([H])[C@@]2([H])OC(C4=C(C)C=CC=C4)=O)=O)C=C1</chem>

Table 2. 3D energy-minimized structures of MGalP (1) and its derivatives (2–7).

Entry	Optimized structure	Entry	Optimized structure
1		2	
3		4	

Entry	Optimized structure	Entry	Optimized structure
5		6	
7			

2.2. Molecular Docking Analysis

We used molecular docking to examine the interactions of the MGalP derivatives with the viral protein 6IW5. For this protein, the RCSB protein data database was used [26]. To conduct the docking analysis, we utilized AutoDock Vina. To import proteins and ligands, we converted pdb files to pdbqt format using AutoDock Tools (ADT) [27].

Finally, PyRx software (version 0.8) was used to conduct molecular docking simulations, with the protein functioning as the macromolecular receptor, whereas the drugs were modeled as the ligand [28]. All the bonds that were previously rotatable were made nonrotatable as part of this analysis's stiff docking. As a metric for the negative score, the affinity of the ligand toward the target was measured in kcal/mole. Discovery Studio Visualizer v20.1.0 was employed for the purpose of calculating and visualizing nonbonding interactions.

2.3. Pharmacokinetic Parameter Study

The pharmacokinetic behavior of MGalP derivatives, including absorption, metabolism, and toxicity, was analyzed using the admetSAR online database [29]. AdmetSAR employs structural comparison search techniques to predict the most current and comprehensive data for a diverse array of substances with documented ADME/T profiles, which have been meticulously validated. The admetSAR tool was employed for ADMET analysis. The database comprises nearly one million distinct compounds and 45 categories of ADMET-related proteins, species, or animals and has been rigorously curated from a wide array of literature.

2.4. PASS Prediction

A software product known as PASS (Prediction of Activity Spectra for Substances) is intended to assess the

overall biological potential of an organic drug-like molecule. The potential biological activities of a molecule were assessed with PASS software, which deduces activity on the basis of its molecular structure [30, 31]. More than 4000 biological activities may be predicted by the current PASS version. Its accuracy rate is 95% [32]. Probable activity (Pa) and probable inactivity (Pi) are the probabilities used to forecast the activity. The range of values is 0.000-1.000 [33]. The activity of a chemical compound is considered only when its Pa value exceeds its Pi value.

3. Results and Discussion

3.1. Thermodynamic Properties

Thermal and molecular orbital parameters are significantly affected by typical modifications to the molecular structure. The spontaneous character of a chemical reaction and the product stability can be inferred from the free energy and enthalpy data [34]. It is more appropriate to use values that are highly negative for thermal stability. The dipole moment also influences the formation of hydrogen bonds and nonbonded interactions in the formulation of drugs. The binding property can be enhanced by increasing the dipole moment [35]. MGalP has the lowest electronic energy (-722.4609 Hartree) and polarizability (86.6510 a.u.). This indicates relatively lower electronic flexibility. As the molecular size increased from 2 to 7, both the electronic energy and polarizability steadily increased, indicating improved stability and flexibility of the electronic cloud. The maximum electronic energy recorded for 7 is -2930.4752 Hartrees, whereas the largest dipole moment for 7 is 10.2680 Debye. Derivative 5 has the highest polarizability value of

388.0266 a.u., which is indicative of the potential for an increase in polarizability due to the presence of a bulky

acylating group. These thermodynamic parameters are listed in Table 3.

Table 3. Thermodynamic properties of MGalP derivatives (2-7).

Compound no.	Stoichiometry	Electronic energy (Hartree)	Entropy (Hartree)	Dipole moment (Debye)	Polarizability (a.u.)
1	C ₉ H ₂₀ O ₆	-722.4609	114.346	2.6868	86.6510
2	C ₁₉ H ₃₀ FO ₇	-1163.6833	153.154	1.4677	153.3600
3	C ₄₂ H ₅₈ O ₁₃ FS ₃	-2146.0920	-2145.1474	5.3017	297.6397
4	C ₄₇ H ₈₃ O ₁₀ F	-2263.3707	-2262.3361	4.8676	285.4970
5	C ₄₇ H ₆₄ O ₁₀ F	-2308.5441	-2379.5638	3.9558	388.0266
6	C ₆₇ H ₁₂₈ O ₁₀ F	-2462.2893	-2461.0490	3.9850	334.1340
7	C ₅₆ H ₁₀₇ O ₁₀ F	-2930.4752	-3429.8125	10.2680	357.9087

3.2. Attribution of frontier molecular orbitals

The chemical interaction and kinetic equilibrium within a molecule are defined by the frontier molecular orbitals, which are the most critical at the molecular level [36]. Frontier molecular orbitals are typically referred to as the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The measurements of orbital energies, hardness and softness, which are considered to be the two global chemical descriptors, are presented in Table 4. These values are also calculated for the primary compound and its

derivatives. The HOMO–LUMO energy gap varied from 4.3919 eV (127) to 5.6424 eV (615). The compound with the greatest softness was noted to be 5. In addition, compared with the other derivatives, compound 5 exhibited the lowest HOMO–LUMO gap and hardness, implying that the compound has a higher reactivity. The electron density was predominantly located on the upper portion of the galactopyranose ring in the LUMO plot of compound 5, as shown in Figure 2. Conversely, the electron was localized exclusively at the modified acylating group regions in the HOMO plot.

Table 4. Frontier molecular orbitals of MGalP derivatives.

Compound No.	ϵ HOMO (eV)	ϵ LUMO (eV)	Gap, ΔE (eV)	Hardness, η (eV)	Softness, S (eV ⁻¹)	Chemical potential, μ (eV)	Electro-negativity, χ (eV)	Electro-philicity, ω (eV)
1	-6.4267	-2.0354	4.3919	2.1956	0.4554	-4.2310	2.6326	0.9357
2	-6.4871	-1.2381	5.2990	2.6445	0.3810	-3.8626	4.0342	3.3068
3	-6.8378	-1.3154	5.5224	2.7612	0.3622	-4.0766	4.0766	3.0094
4	-6.5869	-0.9445	5.6424	2.8212	0.3545	-3.7657	3.7657	2.5132
5	-6.7402	-1.4558	5.2844	2.6222	0.3984	-4.0980	3.7758	2.5100
6	-6.5491	-1.0226	5.5265	2.7632	0.3619	-3.7859	3.7859	2.5935
7	-6.8139	-1.6618	5.4520	2.7760	0.3882	-4.2379	4.2379	3.4859

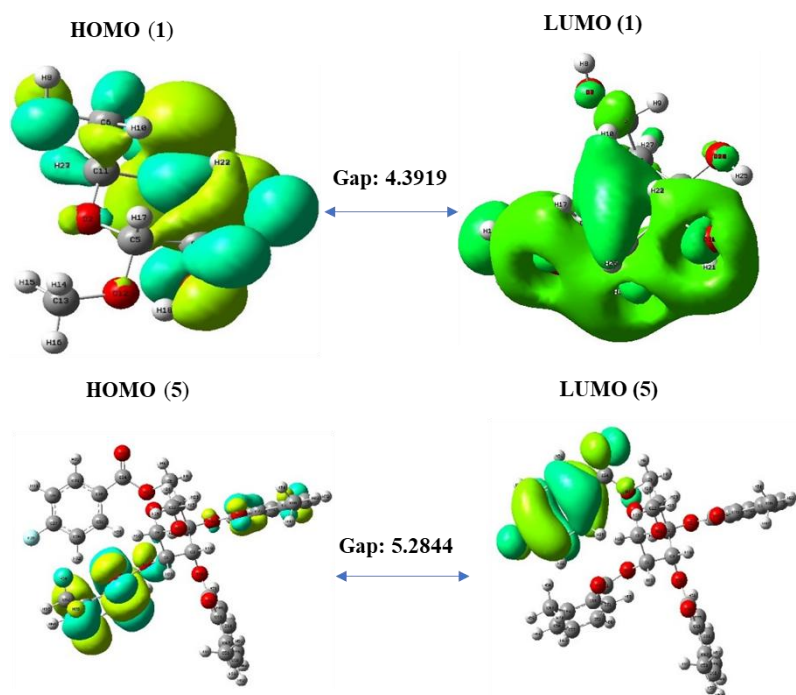


Figure 2. HOMO and LUMO molecular orbital distribution plots for MGalP derivatives (1) and (5).

3.3. Molecular Electrostatic Potential

The molecular electrostatic potential (MEP) is a well-known reactivity map that illustrates the locations of organic molecules that are most likely to be attacked by charged reagents, which can be either electrophilic or nucleophilic. With its assistance, one may gain a better understanding of the mechanisms of biological recognition and the interactions between hydrogen bonds [36]. The MEP counter map is an easy instrument that can be used to predict the potential interactions that may occur between different geometries [37]. In Figure 3, the optimized results of the density functional theory (DFT) model with a basis set of 6-31G++ are presented for the MGalP derivatives ranging from compounds 2-

7. One of the primary reasons why molecular electron microscopy is useful for correlating molecular structure with physicochemical characteristics lies in its ability to depict molecular geometry along with positive, negative, and neutral electrostatic region areas all at the same time through the use of color grading. The MEP was utilized to predict the reactive regions that are responsible for electrophilic and nucleophilic assaults on the optimized structure of MGalP derivatives, namely, from 2–7. The areas shown in red are favorable for electrophilic interactions, whereas the blue areas are most favorable for nucleophilic interactions. Green indicates regions with neutral electrostatic potentials.

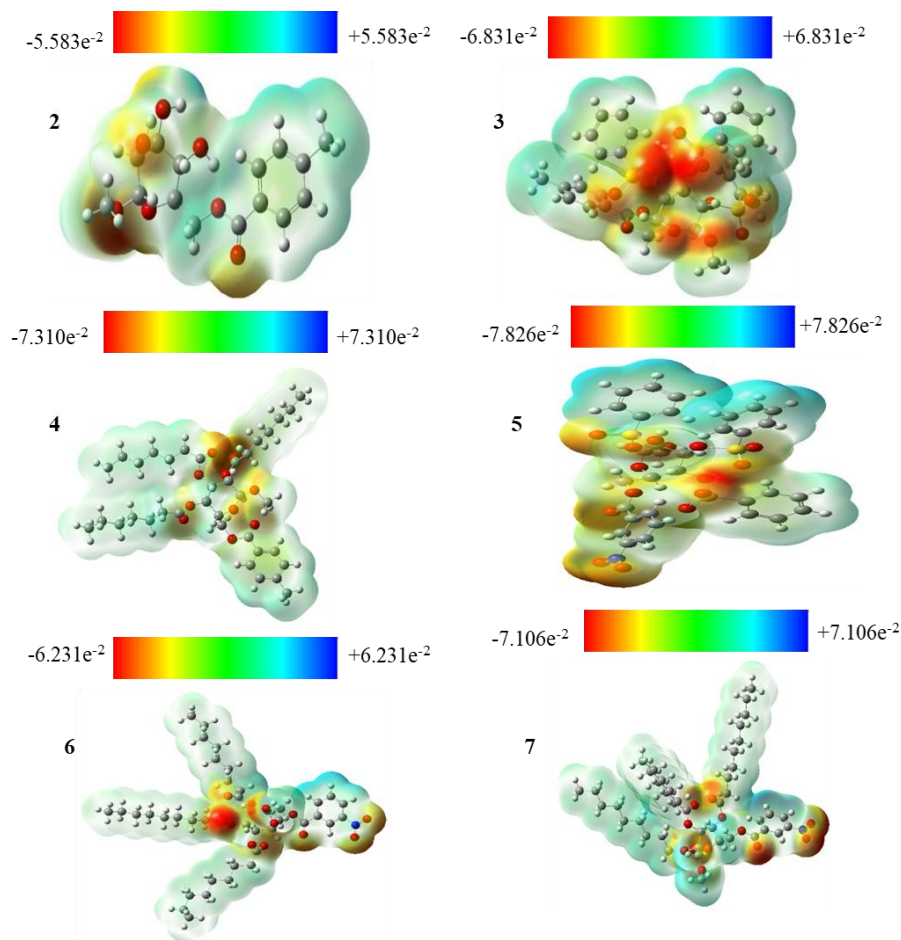


Figure 3. Molecular electrostatic potential map of MGalP derivatives (2-7).

3.4. Exploration of Molecular Docking

As a method in molecular modeling, molecular docking is used to find the ideal orientation with respect to a target receptor and to study the interactions between the two in great detail [38, 39]. Indeed, we docked MGalP ligands to yellow fever virus (YFV) (PDB: 6IW5) to determine their antiviral capabilities. For this work, the crystal structure of yellow fever virus (YFV) was obtained directly from the Protein Data Bank. The results revealed that the viral protein bound to MGalP (1) with an affinity of -5.0 kcal/mol and that its derivatives (2-7) had binding affinities for 6IW5

ranging from -5.5 to -7.00 kcal/mol, as shown in Table 5. This investigation also revealed that the ligands (2-7) primarily engaged with the amino acid residues TYR225 and TYR354, which served as significant binding hotspots. Further stabilizing interactions were noted with PHE240, PHE339, LEU394, HIS227, ASP189, and GLY409. Despite the fact that all of the compounds have the potential to be antiviral agents, the calculated binding energies reveal that derivative 5, which has the highest negative binding energy value of -7.00 kcal/mol of all the analyzed compounds, may be the most effective inhibitor of YFV.

Table 5. Binding affinities (kcal/mol) of MGalP derivatives.

Compound	Binding affinity	No. of hydrogen bonds	No. of hydrophobic bonds	Interaction type
1	-5.0	6	-	H, C
2	-5.5	5	1	H, H, C, C, C, PA
3	-6.1	3	3	H, PS, PPS, PPT, PA
4	-5.1	5	13	H, C, PS, A, PA
5	-7.0	6	11	H, H, H, PS, PPS, PPT, A, PA,
6	-6.0	6	5	H, C, PS, PPS, PA
7	-5.6	6	7	H, C, A, PPS, PA

The interaction types are indicated as follows: **H** = conventional hydrogen bond; **C** = carbon–hydrogen bond; **A** = alkyl; **PA** = π -alkyl; **PPS** = π - π stacked; **PS** = π - σ ; and **PPT** = π - π T-shaped.

As shown in Table 5, when tested against the viral protein 6IW5, derivative **5** had the highest binding scores when measured. The highest electron density, indicated by the maximum binding score, was observed in compound **5**, which featured *o*-toluoyl chloride and fluorobenzoyl chloride aromatic substituents. The structures of **3** and **6** contain sulfonyl groups and myristoyl chlorides, respectively. The incorporation of heteroatoms (Cl, F) resulted in slight variations in binding affinities, whereas replacement with a halogenated aromatic ring increased the affinity. Moreover, modifying the –OH group in conjunction

with a lengthy aliphatic chain or aromatic ring improved binding. Predictions of molecular structure and behavior are frequently based on nonbonding interactions.

In protein–ligand docking, CH/O contact is the most frequently detected nonbonding interaction among all of the following interactions: CH/O, CH/ π , NH/ π , OH/ π , and CH/N. Table 6 and Figure 4 display the nonbonding interactions, whereas an extended view of the protein–ligand interactions of derivative **5**, the docked pose, hydrogen bonds, and hydrophobicity are presented in Figure 4 derivatives.

Table 6. Selected binding affinities (kcal/mol) and nonbonding interactions of MGalP and its derivatives.

Drugs	Hydrogen Bond		Hydrophobic Bond	
	Residues	Distance (Å)	Residues	Distance (Å)
1	VAL145	2.51986		
	ASP361	2.25061		
	VAL145	2.39824		
2	ILE355	2.78119	VAL145	4.63493
	SER357	2.27841		
	SER357	2.99423		
	SER357	2.78482		
	THR173	2.71367		
3	TYR225	2.74916	ASP110	3.50741
	HIS227	3.08753	LEU394	3.86084
	TYR354	2.21982	PHE240	4.62261
	ASN392	2.51220	PHE339	5.17081
	UNK0	2.19992	UNK0	4.11601
	TYR335	3.66672	PHE115	5.03268
	TYR225	2.74916	HIS227	5.12795
	HIS227	3.08753	VAL449	3.84919
4	TYR107	2.67035	TYR225	3.96961
	LEU177	2.28158	PHE115	3.66941
	GLY213	2.9095	LEU394	3.98047
	TYR354	2.26566	TYR225	5.26254
	LEU451	3.33204	TYR225	4.09365
			PHE240	5.29267

Drugs	Hydrogen Bond		Hydrophobic Bond	
			PHE240	4.22225
			PHE339	4.6841
			PHE339	5.19947
			TYR354	5.11959
			TYR354	5.04967
			VAL108	4.77021
			LEU177	5.24195
5	ASP189	2.27916	MET262	2.82696
	ASP189	2.75304	TRP209	5.06605
	ASP189	3.02198	TRP209	4.7066
	ILE204	3.05221	ALA261	3.89684
	UNK0	2.19992	ALA187	5.1788
	ASP206	3.06667	VAL188	5.23392
			VAL205	5.12795
6			ALA261	3.84919
	TYR256	1.95554	LYS407	3.89323
	GLY409	2.85243	TYR256	5.53241
	SER410	2.27099	UNK0	4.04004
	PRO229	3.64078	PRO244	4.60907
	GLY409	3.62895	LYS404	5.39476
7			GLY409	3.55391
	ASP191	2.55578	ALA365	5.67321
	LEU247	4.15223	VAL244	4.44232
	SER416	3.35697	TRP312	4.21042
	TYR234	3.21156	TYR256	3.72416
	ILE356	2.43467	LYS178	3.48923
	ASP451	4.25341	TYR352	5.11584

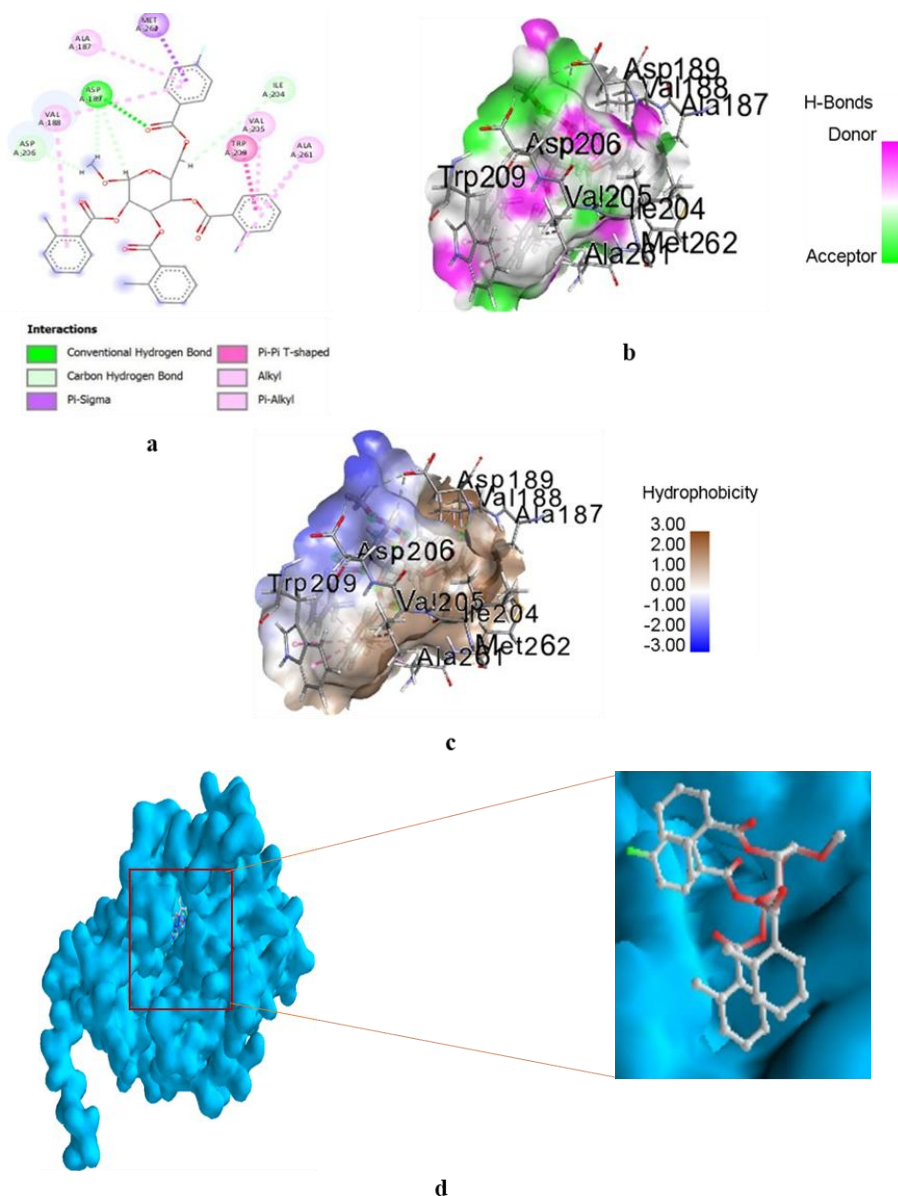


Figure 4. (a) Docked pose of **5** with 6IW5; (b) hydrogen bonding; (c) hydrophobicity determined via Discovery Studio; (d) expanded view of protein–ligand interactions.

3.5. ADMET Analysis

The AdmetSAR server was used to determine whether the derivatives (**2-7**) caused any toxicity or changes in the pharmacokinetic profile. The AdmetSAR platform uses an *in silico* technique to predict ADME data and construct a library of drugs with similar properties [40]. The following pharmacokinetic and pharmacodynamic factors are considered: gastrointestinal absorption in humans, the blood–brain barrier, cytochrome P450 inhibition, acute toxicity in rats, and the suppression of hERG channel activity [41, 42]. A summary of the

findings is provided in Table 7. According to the data in Table 5, all substances had a high probability of having a positive value (a value above the stipulated threshold indicating excellent permeability) in the case of the blood–brain barrier and human intestine absorption. In addition, an inhibitor of P-glycoprotein was produced via modifications to MGaIP. Compared with the parent compound MGaIP, compounds **2**, **3**, **6**, and **7** showed no carcinogenicity. Additional research on this topic is necessary since the inhibitory nature of hERG might cause long QT syndrome [43, 44].

Table 7. Selected pharmacokinetic parameters of the MGaIP derivatives.

Compound no.	BBB (log BB)	CYP2C19 inhibitor (Yes/No)	Intestinal absorption (Human) (% absorbed)	P-glyco protein inhibitor (Yes/No)	Water solubility (mg/L)	Carcinogenicity (Rat)	hERG inhibitor (Yes/NO)
1	0.11525	No	35.5749	No	85718	negative	low risk
2	0.02794	Yes	73.0121	No	3516.94	negative	medium risk
3	0.13580	Yes	99.6618	Yes	0.11128	negative	low risk
4	0.25896	Yes	99.7882	Yes	11.2605	positive	low risk

Compound no.	BBB (log BB)	CYP2C19 inhibitor (Yes/No)	Intestinal absorption (Human) (%) absorbed	P-glyco protein inhibitor (Yes/No)	Water solubility (mg/L)	Carcinogenicity (Rat)	hERG inhibitor (Yes/NO)
5	2.7192	Yes	99.2651	Yes	0.00067	positive	low risk
6	10.2288	Yes	96.2761	Yes	4.59492	negative	medium risk
7	7.8538	Yes	98.7389	Yes	3.6497	negative	medium risk

3.6. PASS Prediction

Prior to the introduction of virtual molecules into the biological testing process, the probable biological activity of these compounds can be evaluated through PASS [45]. It is possible to assess the likelihood that the chemical under study is a member of Pa (probability of being active), which defines the chance of a compound falling within the active subclass, whereas Pi (probability of being inactive) reflects the likelihood of it being inactive [46]. The varying pharmacological potential of the studied compounds was reflected by the

PASS prediction (Table 8). Compounds **4** and **6** ($P_a = 0.509$) demonstrated the greatest potential antibacterial action, whereas compound **3** ($P_a = 0.315$) demonstrated the lowest probability. The strongest anticarcinogenic activity was **1** ($P_a = 0.562$), followed by **2** ($P_a = 0.501$); **4** and **6** had the strongest antiviral activity ($P_a = 0.655$), while **2** ($P_a = 0.618$) was also noteworthy. All of the compounds had mild anti-inflammatory effects. However, the most effective values were **2** ($P_a = 0.631$) and **1** ($P_a = 0.620$).

Table 8. Prediction of the antiviral, antimicrobial, and anticarcinogenic activity of MGaP (**1**) and its derivatives (**2-7**)

Compound No.	Antibacterial		Anticarcinogenic		Antiviral		Anti-inflammatory	
	P_a	P_i	P_a	P_i	P_a	P_i	P_a	P_i
1	0.490	0.017	0.562	0.015	0.569	0.022	0.620	0.028
2	0.486	0.018	0.501	0.019	0.618	0.017	0.631	0.026
3	0.315	0.055	0.496	0.020	0.277	0.091	0.554	0.042
4	0.509	0.016	0.383	0.034	0.655	0.013	0.614	0.029
5	0.464	0.020	0.359	0.039	0.583	0.020	0.608	0.030
6	0.509	0.016	0.383	0.034	0.655	0.013	0.614	0.029
7	0.464	0.020	0.359	0.039	0.583	0.020	0.608	0.030

4. Conclusions

In this work, a comprehensive computational evaluation, was conducted on MGaP derivatives, with a particular emphasis on their pharmacological, molecular docking, and thermodynamic characteristics. Molecular docking revealed that derivatives (**2-7**) presented greater binding affinities and more extensive nonbonding interactions with the 6IW5 protein than did the original drug (**1**). Thermodynamic and FMO experiments suggested favorable stability and electronic properties over the course of the research. By revealing the creation of H-bonds and hydrophobic and other chemical interactions, research has provided insights into the possible inhibitory effects that these compounds may have. This investigation contributes to a more thorough understanding of the possible antiviral activity of novel compounds through the use of an integrated strategy. On the basis of the ADMET projections, it was determined that all of the medicines had high intestinal absorption values, which indicates that oral bioavailability was favorable. The vast majority of the derivatives showed beneficial permeability at the blood–brain barrier. In addition, the ADMET analysis revealed that compared with the original medication, the modified derivatives had more favorable pharmacokinetic profiles and exhibited lower levels of toxicity. These compounds were shown to be more effective against viral pathogens, microbial pathogens, and carcinogenic pathogens, according to the findings of the pass prediction. These findings provide the groundwork for further experimental research and the optimization of

compounds that have been discovered as possible inhibitors, with the ultimate goal of developing efficacious antiviral treatments.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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