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AN *IN-SILICO* STUDY OF SOME NATURAL AND SYNTHETIC COMPOUNDS AS POTENTIAL INHIBITORS FOR FACTOR XA

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Recent research has demonstrated the significance of factor Xa and its inhibitors as a possible treatment approach. Since currently approved drugs have a wide variety of side effects, new anticoagulants must be developed. So, the goal of this in silico research is to find molecules that may act as factor Xa inhibitors.
The structure of factor Xa (2w26) was obtained from the Protein Data Bank database, while the structures of the organic compounds were obtained from the ZINC database or via other means. In order to verify the anti-factor Xa action of these chemical compounds, iGemDock program was used to perform molecular docking.
The compound (1) [5-hydroxy-2-(3-hydroxy-4-phenylmethoxyphenyl)-3,7-bis(phenylmethoxy)chromen-4-one] showed the best interaction value against the 2w26 enzyme, and the binding energy was (–167.702 kcal/ mol); whereas the reference rivaroxaban was (–149.661 kcal/mol). These results lead to suggest new organic compounds as factor Xa inhibitors and further in vitro studies are required to confirm.

Keywords: *factor Xa Inhibitors; iGemdock; Lipinski's rule; molecular docking.*

INTRODUCTION

Several recent studies have demonstrated the importance of factor Xa as a promising anticoagulant target, in addition to, the usage of many factor Xa inhibitors to prevent and treat a lot of thrombotic diseases[1–6]. The coagulation process involves proteins in coagulation reactions, which are called blood coagulation factors. Generally, they are present in the plasma in an inactive state but can be activated. Therefore, the coagulation process is a complex cascade of enzymatic reactions that can be activated via both intrinsic and extrinsic pathways[7]. The final step in coagulation is the formation of the fibrin clot from fibrinogen, by the action of thrombin, which acts as a serine protease, which is generated by prothrombin through factor Xa[8]. Therefore, factor X is considered the connecting point between the coagulation cascades. Recent investigations have established the relationship between thrombosis and Covid-19 [9] where Covid-19 causes vast inflammation-promoting cytokine. The Cytokines in turn increase the liver's production of clotting factors, as explained by Beverley Hunt, medical director of Thrombosis UK and a practicing clinician. Besides, there is a new study suggesting that there is a similarity among SARS-CoV-2 Mpro and coagulation factors thrombin and Factor Xa, which gives more importance to Factor Xa inhibitors[10,11]. Direct Factor Xa (FXa) inhibitors have anticoagulant, anti-inflammatory, and antiviral activities, and they probably hold a considerable promise in treating COVID-19[12].

FXa structurally belongs to the serine proteases of the trypsin-like family. The crystal structure of human factor Xa was deposited in May 1993 for the first time. The active site of factor Xa is divided into four sub-pockets as S1, S2, S3, and S4. The S1 sub-pocket determines the major segment of selectivity and binding. Factor Xa inhibitors usually bind with

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the active pocket in an L-shaped conformation[13].

The *in-silico* study is a technique that predicts the preferred location of small molecules (ligands) within the active site of the FXa (ID:2W26) in this research. This method applies a cavity detection algorithm for distinguishing invaginations in the protein as candidate active site regions [14].

This research which is part of a master's degree thesis attempts to survey some organic compounds (more than 1000 compounds) that have been included in some recent studies in recent years. The interaction of Factor Xa was investigated with derivatives of phenolic compounds [15] or phenolic acids compounds [16] including benzoic acid, cinnamic acid, naphthoic acid, salicylic acid, gallic acid, and chromen [17], in addition to some flavonoids with a various type. In this part of the research, the focus was on the compounds that fulfill Lipinski's rules. The chemical structures of the investigated compounds, along with some proven drugs, are compared with rivaroxaban (**Figure 1** illustrates its structure) as a reference in **Table 1**. These compounds and their inhibitory effect on FXa were investigated by molecular docking for visualizing the efficiency of their potential effect as factor Xa inhibitors, theoretically.

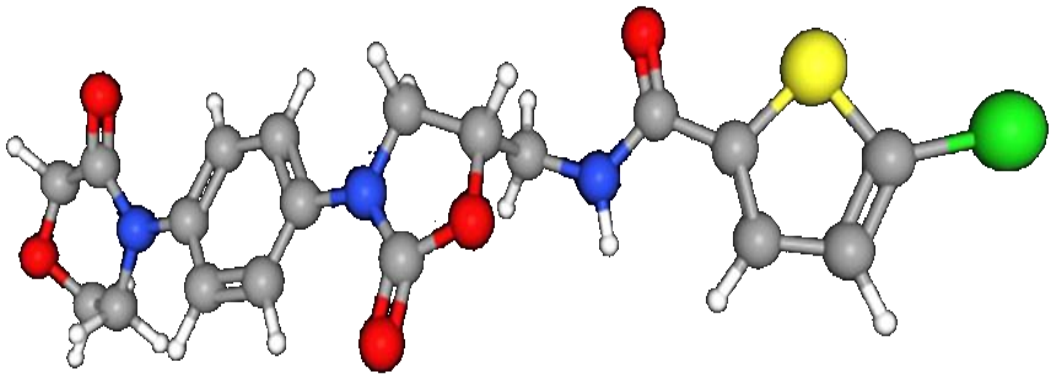


Fig. 1: The reference ligand (Rivaroxaban).

Table 1: Illustrates the structures and Lipinski's properties of the best 20 screened compounds used in this study that have been accepted by the "rule of five".

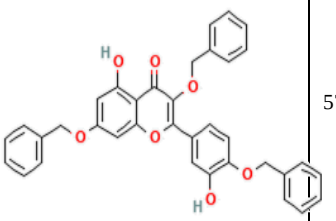
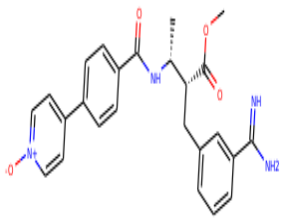
S. Num.	Common name	IUPAC Name	Compound structure	MW	#H-bond acceptors	#H-bond donors	LOG P	Lipinski #violations
1	5,3'-dihydroxy-3,7,4'-tribenzoxy flavone	5-hydroxy-2-(3-hydroxy-4-phenylmethoxyphenyl)-3,7-bis(phenylmethoxy) chromen-4-one		572.6	7	2	3.19	1
2	Otamixaban	methyl (2R,3R)-2-[(3-carbamimidoylphenyl)methyl]-3-[[4-(1-oxidopyridin-1-ium-4-yl)benzoyl]amino]butanoate		446.5	5	3	2.78	0

Table 1: Continued.

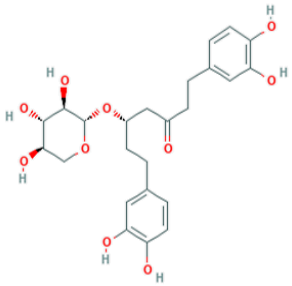
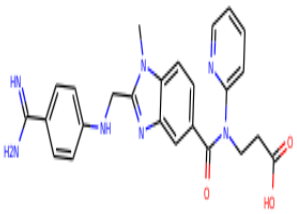
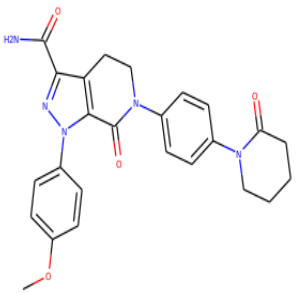
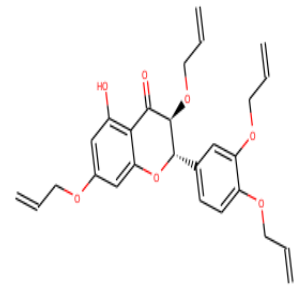
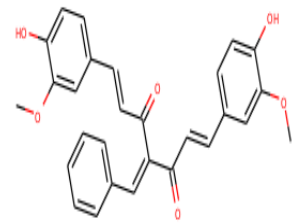
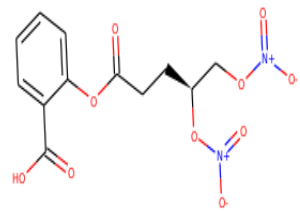
3	Oregonin	(5S)-1,7-bis(3,4-dihydroxyphenyl)-5-[(2S,3R,4S,5R)-3,4,5-trihydroxyoxan-2-yl]oxyheptan-3-one		478.49	10	7	-0.78	1
4	Dabigatran	3-[[2-[(4-carbamimidoylanilino)methyl]-1-methylbenzimidazole-5-carbonyl]-pyridin-2-ylamino]propanoic acid		471.51	6	4	1.89	0
5	Apixaban	1-(4-methoxyphenyl)-7-oxo-6-[4-(2-oxopiperidin-1-yl)phenyl]-4,5-dihydropyrazolo[3,4-c]pyridine-3-carboxamide		459.5	5	1	2.03	0
6	Quercetin Pentaallyl Ether	2-[3,4-bis(prop-2-enoxy)phenyl]-5-hydroxy-3,7-bis(prop-2-enoxy)-2,3-dihydrochromen-4-one		464.51	7	1	1.74	0
7	4-benzylidene curcumin	(1E,6E)-4-benzylidene-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione		456.49	6	2	2.65	0
8	2-{[4,5-Bis(Nitrooxy)Pentanoyl]Oxy}Benzoic Acid	2-(4,5-dinitrooxypentanoyloxy)benzoic acid		344.23	10	1	0.13	1

Table 1: Continued.

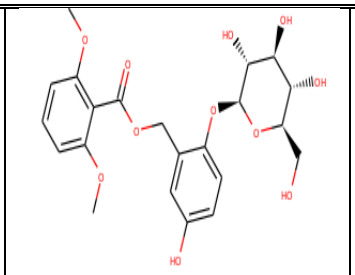
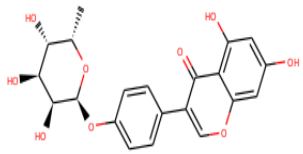
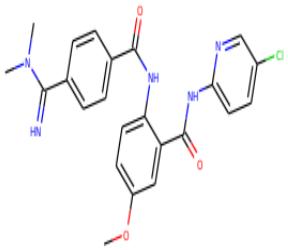
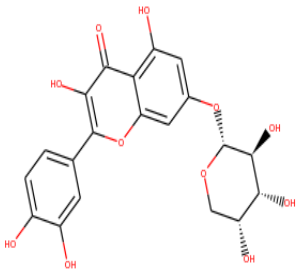
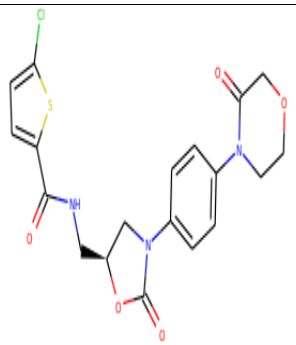
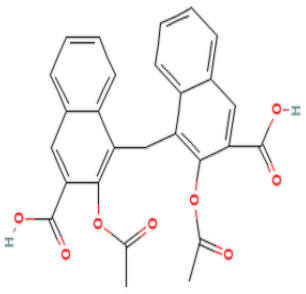
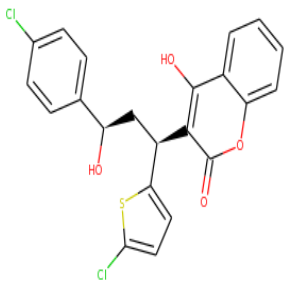
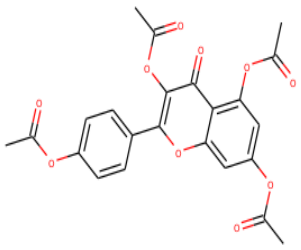
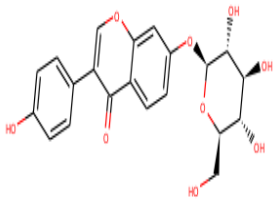
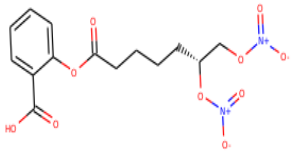
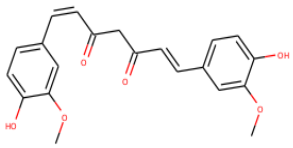
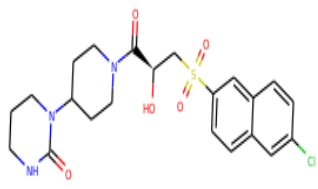
9	Curculigoside A	[5-hydroxy-2-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]methyl 2,6-dimethoxybenzoate		466.44	11	5	-0.88	1
10	Genistein 4'-Rhamnoside	5,7-dihydroxy-3-[4-(3,4,5-trihydroxy-6-methyloxan-2-yl)oxyphenyl]chromen-4-one		416.38	9	5	-0.84	0
11	Betrixaban	N-(5-chloropyridin-2-yl)-2-[[4-(N,N-dimethylcarbamimidoyl)benzoyl]amino]-5-methoxybenzamide		451.91	5	3	2.56	0
12	Quercetin 7-Xyloside	2-(3,4-dihydroxyphenyl)-3,5-dihydroxy-7-[(2S,4S,5R)-3,4,5-trihydroxyoxan-2-yl]oxychromen-4-one		434.35	11	7	-2.06	0
13	Rivaroxaban	5-chloro-N-[[(5S)-2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]-1,3-oxazolidin-5-yl]methyl]thiophene-2-carboxamide		435.88	5	1	1.41	0
14	4,4'-Methylene bis(3-acetoxy-2-naphthoic acid)	3-acetyloxy-4-[(2-acetyloxy-3-carboxynaphthalen-1-yl)methyl]naphthalene-2-carboxylic acid		472.44	8	2	4.04	0

Table 1: Continued.

15	Tioclomarol	3-[3-(4-chlorophenyl)-1-(5-chlorothiophen-2-yl)-3-hydroxypropyl]-4-hydroxychromen-2-one		447.33	4	2	4.04	0
16	Kaempferol Tetraacetate	[4-(3,5,7-triacetyloxy-4-oxochromen-2-yl)phenyl] acetate		454.38	10	0	1.65	0
17	Daidzin	3-(4-hydroxyphenyl)-7-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxychromen-4-one		416.38	9	5	-1.11	0
18	2-{[6,7-Bis(Nitrooxy) Heptanoyl]Oxy}Benzoic Acid	2-(6,7-dinitrooxyheptanoyloxy)benzoic acid		372.28	10	1	0.66	1
19	Curcumin	(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione		368.38	6	2	1.47	0
20	Letaxaban	1-[1-[(2S)-3-(6-chloronaphthalen-2-yl)sulfonyl-2-hydroxypropanoyl] piperidin-4-yl]-1,3-diazinan-2-one		479.98	5	2	1.86	0

MATERIALS AND METHODS

Protein Preparation

The receptor protein related to human Factor Xa, and required for the docking study has been retrieved from the Protein Data Bank (PDB) [18,19] which is the main source in sites of structural biology, and it is a major repository for 3D structure data of giant molecules. The protein (PDB ID:2w26) had a resolution factor of 2.08 A°. The enzyme was downloaded, then saved in PDB file format. **Figure 2** shows the active site of (2w26) and binding ligand Rivaroxaban (RIV).

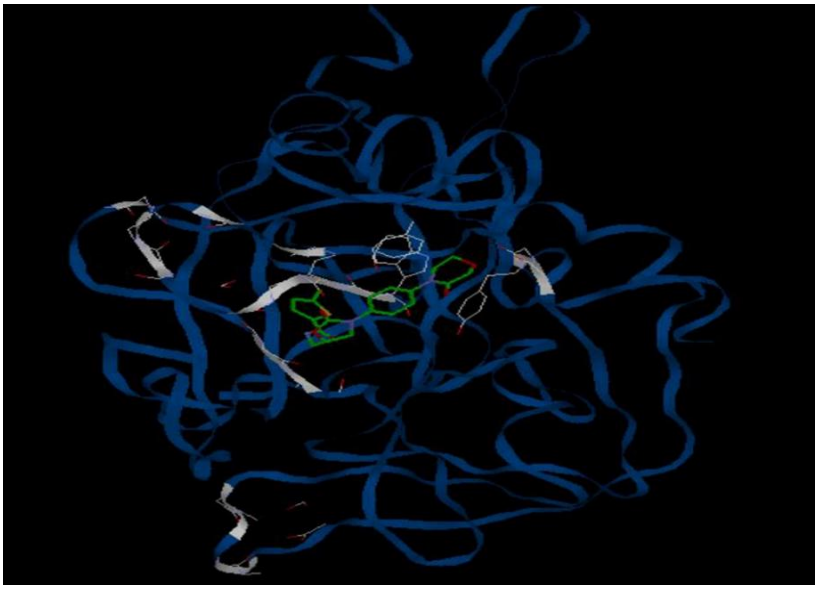


Fig. 2: 3D Binding site of 2w26 in blue color with reference inhibitor (RIV) whose color is green.

Ligands preparation

The organic compounds that we reported here had been chosen after a study of the

literature. Indeed, more than 1000 compounds that are derivatives of phenolic compounds or Phenolic acid were chosen. Some of which were drawn in the two-dimensional (2D) structures using ACD chem sketch software[20]. Some other chemical structures were reclaimed from the Pubchem database[21–23] or were retrieved from the ZINC database[24]. Afterward, the compounds were saved in Sdf or mol format and converted to mol2 format using the OPEN BABEL software[25].

Afterward, a total of 100 high binding energy compounds resulting from the *in-silico* study were made to follow the previous rules. Data of the compounds were obtained from the SwissADME website[26].

However, despite the importance of the aforementioned rules, there have been critical opinions that relied on the fact that 6% of oral medications don't fulfill the Lipinski's rule, such as azithromycin, cyclosporine, digoxin, and many anti-tumors and viruses, in addition to the fact that several drugs for oral use have been licensed by the Food and Drug Administration in recent years although they didn't fulfill to previous bioavailability rules. Some recent studies have also shown the biological effectiveness of compounds of natural origin, despite exceeding the limits of these rules[27–32].

Protein-ligand docking

After a literature review to collect compounds[33], iGemdock v2.1 was used to perform the docking study for the enzyme (2w26) that interacts with the selected phenolic or Phenolic acid compounds, natural compounds such as aglycones and their derivatives, vitamins, and some approved drugs by the FDA. It is available for free and was used in previous research[34–38].

iGemdock v2. 1

IGemdock is an integrated virtual screening (VS) environment for preparations through post-screening analysis with pharmacological interactions. The docking software iGemdock was used as a molecular docking tool to dock the protein of the enzyme (2w26) with our selected compound. iGemdock provides interactive interfaces to prepare the screening compounds' library and the binding site of the targeted enzyme. Then, using the in-house docking tool iGemdock, each compound in the library was docked into the binding site. Afterward, iGemdock inferred protein-compound interaction and then clustered the screening compounds for the post-screening analysis based on profiles of hydrogen-bonding (H), electrostatic (E), and Van der Waal's (V) interactions. Furthermore, based on compound structures, iGemdock inferred the pharmacological interactions. Finally, iGemdock ranks and visualizes the screening compounds by combining the pharmacological interactions and energy-based

scoring functions made available by iGemdock. the protocol “accurate docking” was used by setting a population size of 800 with 80 generations and 10 solutions.

After the docking, the software performed the post-docking analysis to find the docking pose and its energy values. The empirical scoring function of iGemdock was estimated using:

Energy = vdW + H-bond + Elect…. (1)

whereas the vdW term is van der Waal energy, H-bond term is hydrogen bonding energy, and Elect term is electro statistic energy.

RESULTS AND DISCUSSION

Results

In silico docking is the best method to predict the usefulness of any chemical as a remedy before continuing with any *in vivo* or *in vitro* study to shorten the experiments and ensure cost savings. A literature review was done for the organic compounds, and the chosen compounds were docked later against factor Xa by using iGemdock to evaluate the theoretical effect as a factor Xa inhibitor and conclude its interactive analysis before the compounds are introduced to investigate the *in vitro* anticoagulant activity.

Several studies have emphasized the importance of using Lipinski's rules when developing and researching new drugs. This rule helps to determine if a biologically active chemical is likely to have the chemical and physical properties to be orally bioavailable. Noting that Lipinski's rules allow for one transgression for each molecule[39–41].

Lipinski's Rule

The "Rule of Five" was formulated by Christopher A. Lipinski in 1997, based on the observation that most orally administered drugs are relatively small and moderately lipophilic molecules. The "Rule of Five" describes molecular properties and is used to predict drug pharmacokinetics in the human body, which consists of four important stages that are Absorption, Distribution, Metabolism, and Excretion (ADME). The compounds are more likely to be membrane-permeable and easily absorbed by the body if it matches the following criteria [42]:

1. Molecular weights not more than 500 Da.
2. Calculated octanol-water coefficients (CLogP) not more than 5.
3. Less than 5 hydrogen bond donors
4. Less than 10 hydrogen bond acceptors.

From this point of view, some FDA-proved drugs and organic compounds like those mentioned in **table 1** were selected for docking and were compared to (RIV).

Rivaroxaban which is a proven known factor Xa inhibitor was employed as a positive standard, then the docking investigations were performed using iGemdock v2. 1. The kcal/mol results demonstrated that the best 20 compounds had high binding energy ranging from (–167,702 kcal/ mol) to (-146/,294kcal/mol). This is demonstrated in **Table 2** compared with the standard (–149,661kcal/mol). Therefore, these molecular docking analyses could express the most potent 2w26 inhibitors for the prevention and treatment of thrombosis. **Table 2** summarizes the results of the docking study based on binding energies.

Table 2: The docking binding energy values results using iGEMDOCK.

S. Num.	Common name	IUPAC Name	Total Energy	VDW	HBond	Elec
1	5,3'-dihydroxy-3,7,4'-tribenzoxyflavone	5-hydroxy-2-(3-hydroxy-4-phenylmethoxyphenyl)-3,7-bis(phenylmethoxy)chromen-4-one	-167.702	-152.085	-15.6168	0
2	Otamixaban	methyl (2R,3R)-2-[(3-carbamimidoylphenyl)methyl]-3-[[4-(1-oxidopyridin-1-ium-4-yl)benzoyl]amino]butanoate	-166.342	-126.623	-35.6951	-4.02388
3	Oregonin	(5S)-1,7-bis(3,4-dihydroxyphenyl)-5-[(2S,3R,4S,5R)-3,4,5-trihydroxyoxan-2-yl]oxyheptan-3-one	-166.028	-135.858	-30.17	0

Table 2: Continued.

4	Dabigatran	3-[[2-[(4-carbamimidoylanilino)methyl]-1-methylbenzimidazole-5-carbonyl]-pyridin-2-ylamino]propanoic acid	-160.084	-125.897	-30.4908	-3.69672
5	Apixaban	1-(4-methoxyphenyl)-7-oxo-6-[4-(2-oxopiperidin-1-yl)phenyl]-4,5-dihydropyrazolo[3,4-c]pyridine-3-carboxamide	-159.772	-144.192	-15.5794	0
6	Quercetin Pentaallyl Ether	2-[3,4-bis(prop-2-enoxy)phenyl]-5-hydroxy-3,7-bis(prop-2-enoxy)-2,3-dihydrochromen-4-one	-159.467	-137.807	-21.66	0
7	4-benzylidene curcumin	(1E,6E)-4-benzylidene-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione	-155.201	-132.163	-23.0375	0
8	2-{[4,5-Bis(Nitrooxy)Pentanoyl]Oxy}Benzoic Acid	2-(4,5-dinitrooxypentanoyloxy)benzoic acid	-153.588	-105.261	-48.7256	0.398419
9	Curculigoside A	[5-hydroxy-2-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]methyl 2,6-dimethoxybenzoate	-152.852	-121.316	-31.5365	0
10	Genistein 4'-Rhamnoside	5,7-dihydroxy-3-[4-(3,4,5-trihydroxy-6-methyloxan-2-yl)oxyphenyl]chromen-4-one	-152.844	-136.155	-16.6892	0
11	Betrixaban	N-(5-chloropyridin-2-yl)-2-[[4-(N,N-dimethylcarbamimidoyl)benzoyl]amino]-5-methoxybenzamide	-149.967	-129.353	-20.6141	0
12	Quercetin 7-Xyloside	2-(3,4-dihydroxyphenyl)-3,5-dihydroxy-7-[(2S,4S,5R)-3,4,5-trihydroxyoxan-2-yl]oxychromen-4-one	-149.873	-111.563	-38.3104	0
13	Rivaroxaban	5-chloro-N-[[(5S)-2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]-1,3-oxazolidin-5-yl]methyl]thiophene-2-carboxamide	-149.661	-135.591	-14.0703	0
14	4,4'-Methylenebis(3-acetoxy-2-naphthoic acid)	3-acetyloxy-4-[(2-acetyloxy-3-carboxynaphthalen-1-yl)methyl]naphthalene-2-carboxylic acid	-148.409	-125.63	-21.6073	-1.17161
15	Tioclomarol	3-[3-(4-chlorophenyl)-1-(5-chlorothiophen-2-yl)-3-hydroxypropyl]-4-hydroxychromen-2-one	-148.066	-130.376	-17.6898	0
16	Kaempferol Tetraacetate	[4-(3,5,7-triacetyloxy-4-oxochromen-2-yl)phenyl] acetate	-147.846	-129.15	-18.6958	0
17	Daidzin	3-(4-hydroxyphenyl)-7-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxychromen-4-one	-147.178	-134.08	-13.0978	0

Table 2: Continued.

18	2-{[6,7-Bis(Nitrooxy)Heptanoyl]Oxy}Benzoic Acid	2-(6,7-dinitrooxyheptanoyloxy)benzoic acid	-146.932	-102.624	-46.6379	2.32975
19	Curcumin	(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione	-146.585	-135.735	-10.8502	0
20	Letaxaban	1-[1-[(2S)-3-(6-chloronaphthalen-2-yl)sulfonyl-2-hydroxypropanoyl]piperidin-4-yl]-1,3-diazinan-2-one	-146.294	-137.082	-9.21217	0

Post Screening Analysis

Most of the investigated compounds in the post-screening analysis with PDB ID: 2w26, compared to the reference (RIV), were potential anticoagulant drugs that had good docking energy with the target protein. The compound (1) [5-hydroxy-2-(3-hydroxy-4-phenylmethoxyphenyl)-3,7-bis (phenylmethoxy) chromen-4-one] showed the highest binding intensity (–167,702 kcal/ mol) and **figure 3** shows the predicted docking pose while **figure 4** illustrates the predicted interaction of compound (1) with amino acid residues. It was synthesized as a derivative of quercetin, and then its antibacterial and antioxidant effects were measured. However, the results showed that this derivative is less effective than Quercetin as an antibacterial and antioxidant[43], however, the anti-coagulant effect hasn't been investigated yet. Whereas, quercetin has many biological effects as a powerful antioxidant, antibacterial, anti-inflammatory, and anticoagulant, especially as an inhibitor of activated factor X[44–47].

Table 3: Shows pharmacological interactions and residues of the amino acids involved in the binding site for compound (1) compared with the loaded ligand RIV. the previous pharmacological interactions help understand the ligand-binding mechanisms of a therapeutic target.

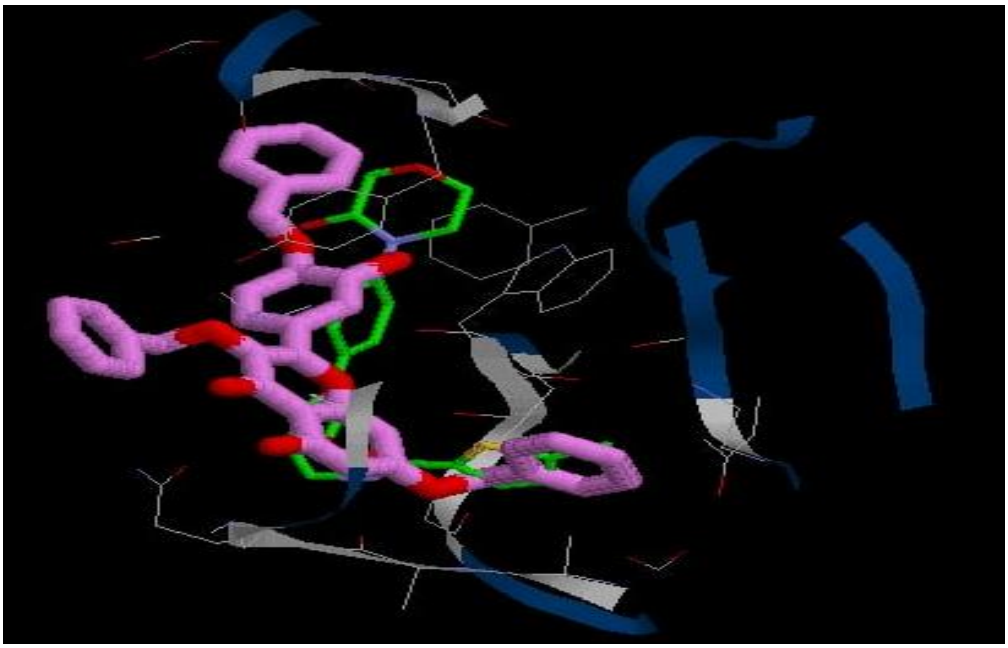


Fig. 3: Shows the predicted docking pose of compound (1) in comparison with the ligand RIV. The pink color represents compound (1) and the green color represents the corresponding reference ligand that was loaded on the enzyme.

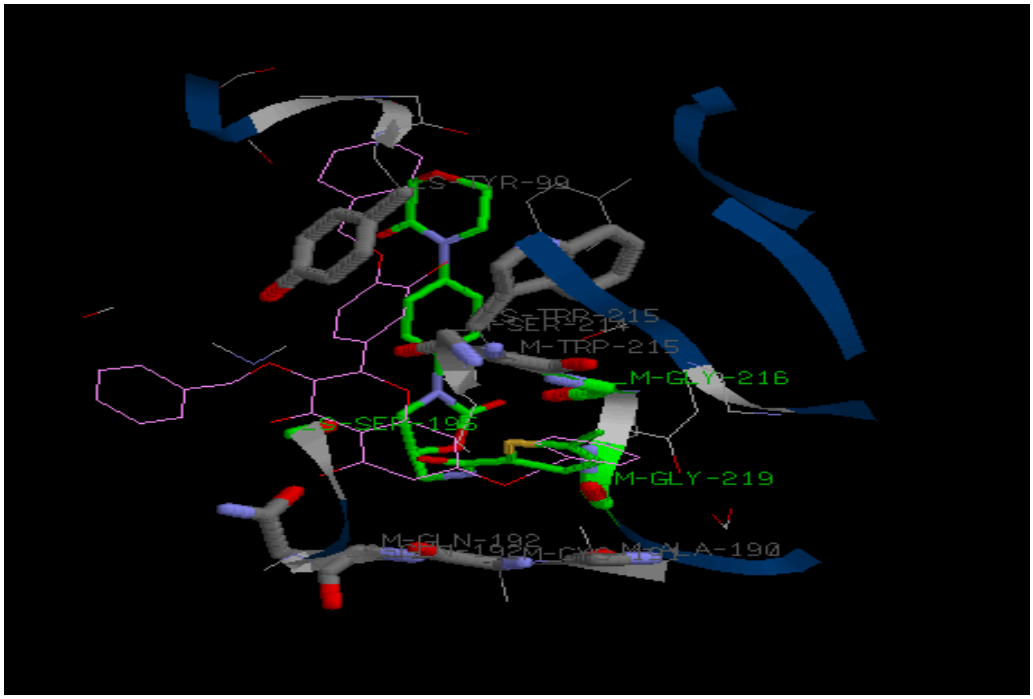


Fig. 4: The Predicted interaction of compound (1) with amino acid residues in the active pocket of (PDB ID:2w26) using iGEMDOCK. The pink color represents the corresponding ligand molecule and the green color represents the corresponding reference. The Green and grey color represent the amino acids involved in hydrogen bonding and van der Waals interactions respectively.

Table 3: Pharmacological interactions and residues involved in the binding site.

PDB ID	Compound	Ligand (RIV)	compound (1)
2w26	Energy	-149.7	-167.7
	H-S-HIS-57	0	-3.40286
	H-M-GLN-192	-3.5	-0.0423223
	H-S-GLN-192	0	-2.65669
	H-M-GLY-193	0	-3.36205
	H-S-SER-195	0	-4.29202
	H-M-GLY-219	-9.44214	0
	V-S-HIS-57	0	-12.84
	V-M-GLU-97	-2.58794	-4.73172
	V-S-GLU-97	0	-4.24404
	V-S-TYR-99	-15.0936	-20.4176
	V-S-PHE-174	-13.8583	-5.40014
	V-M-ALA-190	-6.24742	-8.04601
	V-M-CYS-191	-6.86731	-4.08871

Table 3: Continued.

PDB ID	Compound	Ligand (RIV)	compound (1)
	V-S-GLN-192	-4.26744	-11.849
	V-M-SER-214	-2.314	-6.6039
	V-M-TRP-215	-9.16184	-13.1932
	V-S-TRP-215	-15.1944	-8.90527
	V-M-GLY-216	-9.63745	-10.1749
	V-M-GLU-217	-5.51945	-0.376411
	V-M-GLY-219	-9.21602	-2.54287
	V-M-ILE-227	-2.71267	-4.18128
	V-S-TYR-228	-2.76803	-5.17575

The results also showed the superiority of the synthetic drug [methyl (2R,3R)-2-[(3-carbamimidoylphenyl)methyl]-3-[[4-(1-oxidopyridin-1-ium-4-yl) benzoyl] amino] butanoate], which is known as Otamixaban as a drug approved by FDA over the original ligand loaded on the target protein (ID: 2w26), which is RIV, where the values of the binding energies were (– 166.342 kcal/mol) (-149.661 kcal/mol) respectively.

Conclusions

The current research has provided an insight into the search for new phenolic compounds or phenolic acids compounds as a suggested Factor Xa inhibitor. Various *in silico* tools like Lipinski's rule. Molecular docking has been applied to select the best compounds as anticoagulant inhibitors whereas the derivative [5-hydroxy-2-(3-hydroxy-4-phenylmethoxyphenyl) -3, 7- bis (phenylmethoxy) chromen-4-one] showed great anticoagulant activity theoretically. Later, further *in vitro* investigations should be applied to determine the biological effect. Therefore, the *in-silico* investigation has been essential in predicting molecules enabling the minimization of time spent searching for compounds, and can be recognized as an appropriate technique for screening novel compounds to target other enzymes.

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دراسة في السيليكو لبعض المركبات الطبيعية والاصطناعية كمثبطات محتملة للعامل العاشر

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أظهرت الأبحاث الحديثة أهمية العامل العاشر FXa ومثبطاته كنهج علاجي مُحتمل. وحيث أنَّ الأدوية المُعتمدة حاليًا لها مجموعة متنوعة من الآثار الجانبية، كان من الواجب تطوير مضادات تخثر جديدة. لذلك كان الهدف من هذه الدراسة الحاسوبية إيجاد الجزيئات التي قد تعمل كمثبطات للعامل العاشر .

تم الحصول على بنية العامل العاشر (2w26) من موقع ارشيف بنك بيانات البروتين، بينما تم الحصول على هياكل المركبات العضوية من موقع بيانات ZINC أو عبر وسائل أخرى. وللتحقق من تأثير المركبات الكيميائية المثبط للعامل العاشر، تم استخدام برنامج iGemDock لإجراء الارساء الجزيئي .

أظهر المركب (١) [٥-هيدروكسي-٢- (٣-هيدروكسي-٤-فينيل ميثوكسيفينيل) -٣،٧- ثنائي (فينيل ميثوكسي) كرومون -٤-واحد] أفضل قيمة وكانت طاقة الربط (-١٦٧.٧٠٢ kcal / mol)، بينما كانت طاقة ربط المرجع الريفاروكسابان (-١٤٩.٦٦١ kcal / mol). هذه النتائج أدّت إلى تحديد مركبات عضوية جديدة كمثبطات للعامل العاشر وهناك حاجة إلى مزيد من الدراسات في المختبر لتأكيدها.