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Synthesis, Characterization, *In Silico*, *In Vitro* Antiplatelet Aggregation and Phospholipase A_2 Studies of (*E*)-2(Benzylideneamino)-4-Methylpentanoic Acid, (*E*)-2-((1-Phenyl -ethylidene)Amino)Propanoic Acid and (*E*)-4-Methyl-2-((1-Phenylethylidene)Amino)Pentanoic Acid

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Abstract: *This research investigated the synthesis, characterization, in silico, in vitro antiplatelet aggregation and Phospholipase A_2(PLA_2) activities of Schiff base derivatives (E)-2-(benzylideneamino)-4-methylpentanoic acid, (E)-2-((1-phenylethylidene)amino) propanoic acid and (E)-4-methyl-2-((1-phenylethylidene)amino)pentanoic acid. The Schiff base derivatives were prepared from the condensation reaction between selected amino acids and aromatic aldehydes/ketones under controlled conditions. The FTIR, ^{1}HNMR and HRMS spectra were in agreement with the assigned structures, confirming the formation of imine functional group, which confirmed the successful formation of the target compounds. In silico molecular docking studies were carried out to confirm the binding interactions of the synthesized compounds with COX-2 and PLA_2 enzymes. The results revealed favorable binding affinities, with (E)-2-(benzylideneamino)-4-methylpentanoic acid exhibiting the strongest interaction for in silico antiplatelet study and (E)-2-((1-phenylethylidene)amino)propanoic acid exhibiting the strongest interaction for in silico phospholipase A_2 study. In vitro antiplatelet aggregation assays revealed that (E)-2-(benzylideneamino)-4-methylpentanoic acid showed the highest inhibitory activity achieving 70% inhibition at 8 mg/mL while aspirin achieved 80% inhibition at 8 mg/mL. Furthermore, the PLA_2 inhibitory assay revealed that (E)-2-((1-phenylethylidene)amino)propanoic acid and (E)-4-methyl-2-((1-phenylethylidene)amino) pentanoic acid achieved a complete inhibition at 400 µg/mL, while (E)-2-(benzylidene amino)-4-methylpentanoic acid reached 100% inhibition at 800 µg/mL and this was tested in comparison to Prednisolone which maintained 100% inhibition across all concentrations tested.*

Keywords*: Synthesis, in silico, antiplatelet, Schiff base, phospholipase*

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1.0 Introduction

Cardiovascular diseases, including major cardiovascular events triggered by thrombosis, such as myocardial infarction and ischemic stroke, are the leading causes of morbidity and death worldwide (Stanger *et al*., 2023). A major underlying factor in many cardiovascular events, and subsequent obstruction of blood vessels .Antiplatelet agents reduce the ability of blood to clot or coagulate by reversibly or irreversibly inhibiting platelet activation and aggregation necessary for the initial platelet plug in primary hemostasis (Mohamood *et al*., 2020).The role of antiplatelet drugs is to prevent platelet activation either by inhibiting the platelet activation pathways or by stimulating inhibitory pathways (Zaragozi *et al*., 2022). Platelets play a key role in hemostasis and thrombosis, and targeting the platelet is critical in treating cardiovascular diseases, including acute coronary syndromes, chronic coronary artery disease, and cerebrovascular and peripheral artery disease (Stanger *et al*., 2023).

Phospholipase A_2 (PLA_2) plays a pivotal role in inflammatory and pathological processes thus providing a strong rationale for the development of specific inhibitors. By blocking the activity of this enzyme, it is possible to prevent the production of a cascade of inflammatory mediators, thereby dampening the inflammatory response and mitigating disease symptoms. Existing anti-inflammatory drugs often target downstream enzymes, such as cyclooxygenases (COX-2), but this can lead to side effects. Inhibiting PLA 2 at an earlier stage in the inflammatory pathway offers a strategic advantage (Dennis *et al*., 2011). These enzymes catalyze the hydrolysis of the ester bond at the sn-2 position of phospholipids, releasing fatty acids and lysophospholipids. The fatty acid released is often arachidonic acid, which is a key precursor to a wide range of inflammatory mediators, including prostaglandins, leukotrienes, and thromboxanes (DaSilva *et al*., 2011). Recent studies have highlighted the importance of targeting upstream enzymes such as PLA_2 to achieve broader anti-inflammatory effects compared to conventional therapies.

Beyond inflammation, PLA_2 enzymes are implicated in a variety of other pathological processes. They are found in snake and bee venoms, where their lytic activity is responsible for the destructive effects of the toxins (Lambeau *et al*., 2008).

Despite significant advances in pharmacological interventions, the management of chronic inflammatory diseases remains a persistent and complex challenge in global healthcare. While significant pharmacological progress has been made, particularly with the introduction of biologics, the reliance on conventional anti-inflammatory drugs still dominates primary care. These conventional agents, notably Non-Steroidal

Anti-Inflammatory Drugs (NSAIDs) and corticosteroids, often fail to address the root causes of chronic inflammation and are frequently associated with severe, dose-limiting systemic side effects (Ong *et al*., 2007).

Schiff bases and their derivatives have attracted considerable attention due to their wide range of biological activities. Schiff bases are synthesized by the reaction of an aldehyde or ketone with a primary amine in the presence of a dehydrating agent (Chauhan *et al*., 2023). The reaction mechanism involves the formation of an imine intermediate, which is then converted to the final Schiff base product by the elimination of water. The reaction is usually catalyzed by an acid or a base, depending on the nature of the starting materials. Their structural diversity, ease of synthesis, and ability to coordinate with metals have made them important in coordination chemistry and drug design t "Schiff bases are also utilized in cyclization, cycloaddition, and substitution reactions for the synthesis of biologically important compounds in industry and medicine (Thakor *et al*., 2023). However, despite the broad biological activities reported for Schiff base derivatives, there is limited information on the antiplatelet aggregation and phospholipase A_2 inhibitory potentials of amino acid-derived Schiff bases, particularly those incorporating aromatic moieties.

Therefore, this study aims to synthesize, characterize, and evaluate the in silico, in vitro, antiplatelet aggregation, and phospholipase A_2 inhibitory activities of selected Schiff base derivatives derived from amino acids and aromatic aldehydes/ketones.

This study is expected to contribute to the development of novel therapeutic agents with dual antiplatelet and anti-inflammatory properties, potentially offering improved efficacy and reduced side effects compared to existing drugs

2.0 Materials and Method

2.1 *Chemicals and Solvents*

All reagents were of analytical grade and used without further purification unless otherwise stated. Benzaldehyde, Acetophenone, Leucine and Alanine were purchased from Sigma-Aldrich and used without further purification. Infrared (IR) spectra were recorded using KBr discs on an FTIR-8400S Fourier transform infrared spectrophotometer, and absorption bands were reported in wavenumbers (cm^{-1}). The chemical shifts (δ) of ^1H NMR spectra were recorded in ppm using DMSO-d6 as solvent on a Bruker Avance spectrometer (400 MHz). Mass spectrometric analysis was carried out using an Agilent GC–MS system over an appropriate m/z range. The molecular simulations were done using AutoDock vina and PyMOL software.

2.2 Synthesis of Schiff base derivatives (3)

Benzaldehyde **(1)** (1.0612 g, 9.96 mmol) was dissolved with 5ml of ethanol in a beaker and stirred for 10 minutes. Leucine (**2**) (1.312 g, 10.02mmol) was dissolved with 30ml of ethanol in another beaker and stirred for 10 minutes. The two mixtures were transferred into a round bottomed flask and allowed to stir in a magnetic stirrer and refluxed for 2 h. The obtained product was collected by filtration through a funnel and dried at room temperature to give a white crystalline solid.

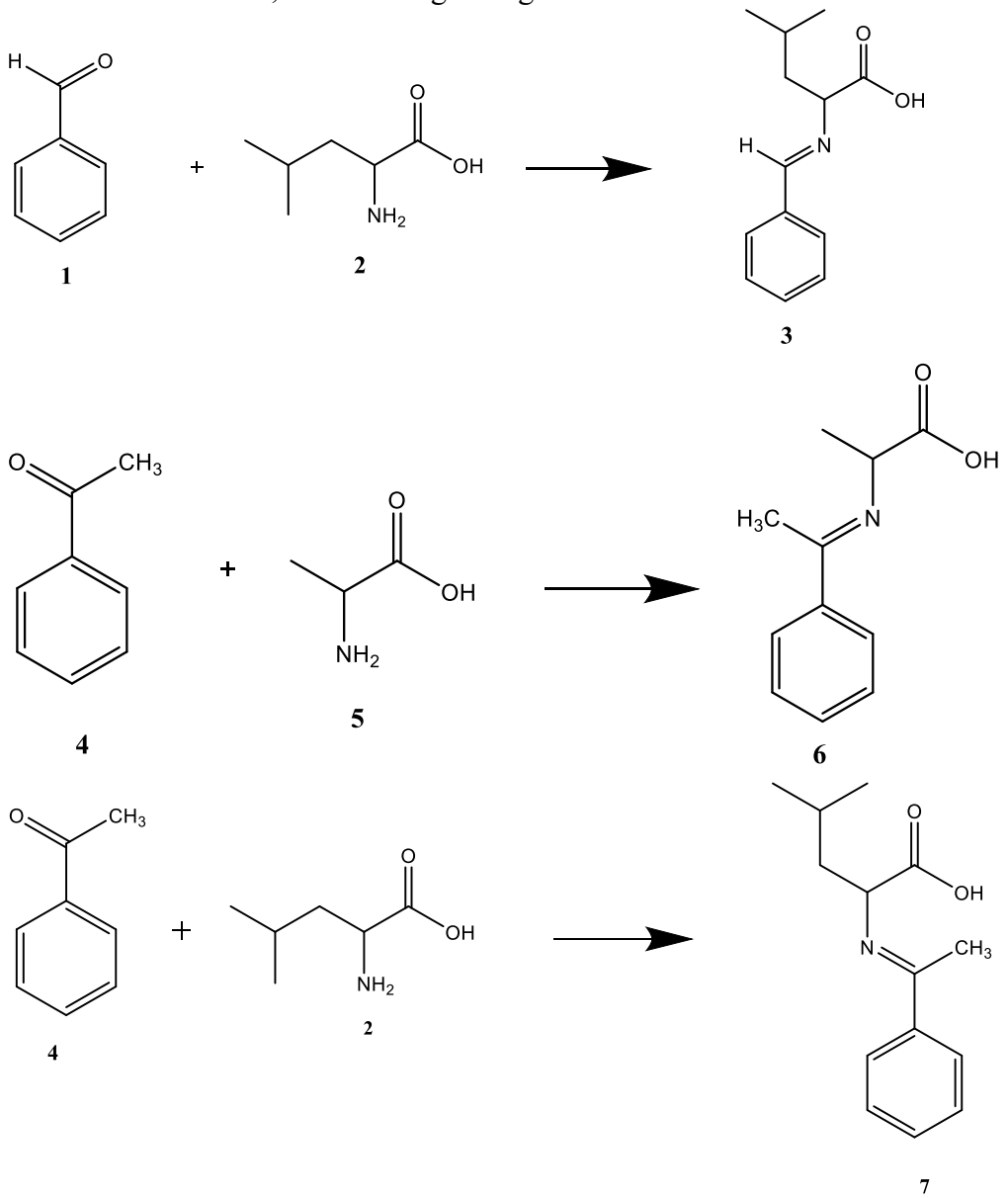
2.3 Synthesis of Schiff base derivatives (6)

Acetophenone (**4**) (1.205 g, 10 mmol) was dissolved with 5 ml of ethanol in a beaker and stirred for 10 minutes. Alanine (**5**) (0.891g, 10.01mmol) was dissolved with 30ml of ethanol in another beaker and stirred for 10 minutes. The two mixtures were transferred into a round bottomed flask and allowed to stir in a magnetic stirrer and refluxed for 2 h. The obtained product was collected by filtration through a funnel and dried at room temperature to give a white crystalline solid.

2.4 Synthesis of Schiff base derivatives (7)

Acetophenone (**4**) (1.205 g, 10 mmol) was dissolved with 5ml of ethanol in a beaker and stirred for 10 minutes. Leucine (**2**) (1.312g,

10.02mmol) was dissolved with 30ml of ethanol in another beaker and stirred for 10 minutes. The two mixtures were transferred into a round bottomed flask and transferred into a round-bottom flask, stirred using a magnetic stirrer, and refluxed for 2 h The obtained product was collected by filtration and dried at room temperature to ontain a white crystalline solid.



Scheme 1: Synthesis of Schiff base derivatives (3, 6, and 7)

2.5 Molecular Docking

2.5.1 Protein Retrieval

The crystal structures of the target proteins for antiplatelet study (PDB ID: 5F19, aspirin-acetylated human cyclooxygenase-2) and phospholipase A_2 study (PDB ID: 1KQU, human phospholipase A_2) were retrieved from the Protein Data Bank (PDB) in 3D format.

2.5.Ligand Preparation (Synthesized Compounds and Standard Drugs)

The 2D structures of the synthesized compounds and standard drugs were drawn using ChemDraw Professional (2021). These structures were converted to 3D using Chem3D and saved in PDB format for docking studies.

2.5.3Protein and Ligand Preparation

The target proteins and ligands were prepared prior to molecular docking using AutoDock Tools (MGL). Preparation steps included the addition of Gasteiger charges, energy minimization, addition of polar hydrogens, and grid box generation.

For COX-2 (PDB ID: 5F19), the grid box center coordinates were set at X = 20.904, Y = 37.495, Z = 59.306, with 40 grid points in each dimension and a spacing of 0.375 Å.

For PLA_2 (PDB ID: 1KQU), the grid box center coordinates were X = 56.624, Y = 34.044, Z = 42.741, with the same grid parameter

2.6 Biological Studies.

In vitro platelet aggregation assay. The platelet aggregation rates were determined following the Born's turbidimetric method on an LG-PABER-I platelet aggregator (Beijing Steellex Tech Instru Co., Ltd. China). The percent change in light transmission was recorded to indicate the aggregation rate: PRP and PPP were used to set the the baseline and maximal transmission, respectively. The platelet number was determined by an automatic counter (6.7×10^8 cell/mL) and PRP was adjusted to 3 $\times10^8$/mL with PPP. PRP samples (200 µL) with samples A-C at a concentration of 0.15 mg/ml (5µL) were added into the microbasin. PRP samples were pre-incubated at 37°C for 2 min in the aggregometer, and then 20 µL of ADP (AA, COLL) was added to the PRP samples to induce acute thrombosis. In blank and positive control experiments, DMSO (5µL) and aspirin (5µL) were added instead of the test samples, respectively. Tests were performed within 3 h to avoid platelet inactivation. The percent inhibition was used to evaluate the effects of samples A-C and aspirin compared with blank control samples. Maximum aggregation was recorded for the blank control (CA) and the different tests (TA). The inhibition rate (IA) was calculated as:

$$\text{IA}(\%) = \frac{(CA-TA)}{CA} X\ 100\% \qquad (1)$$

In vitro A_2 phospholipase A_2 activity. A volume (5ml) of blood sample was used to obtain red blood cells which was used as PLA_2solution while cultured asparagillusnijer was prepared as source of enzyme. A volume (1ml) of phosphate buffer saline, red blood cells which was suspension (0.2ml) and $CaCl_2$ (0.2ml) were added into each set of test tubes labeled blank and test before the addition of 1ml of boiled and free enzyme to the blank and rest tube, respectively. Then, 1ml of reneging concentration of each fraction (100-800ug/ml) and (200-400ug/ml) of indomethacin and phosphate buffer saline were dispersed into the respective test tube. The control test tube to RBC suspension, free enzyme and $CaCl_2$. All the test tubes were incubated at room temperature for 1 hour before centrifugation was done at 3000 rpm for 10 minutes. Absorbable was measured at a wavelength of 418nm.

% inhibition of enzyme activity = Ab(c) -Ab(t)/ Ab(c) (2)

All experimental procedures involving blood samples were conducted in accordance with institutional ethical guidelines

3.0 Results and Discussion

(E)-2-(benzylideneamino)-4-methylpentanoic acid(**3**). yield 0.40g(18.24%). FT-IR (KBr, cm^{-1}) 3673.44, 3646.22, (O-H) 3565.17(N-H), 1506(C=C), 847.51, 621.87(C-H). ^{1}HNMR ($DMSOd_6$, 400MHz)δ: 8.02-7.98 (m, 2H, ArH), 7.89-7.88(d, J= 4.0Hz, 2H, ArH), 7.51-7.48(t, J=6.0Hz, 4H, ArH), 7.39-7.36(t, J6.0Hz, 1H, ArH), 4.18(s, 4H, OCH_3), 3.45-3.41(m, 1H, O=C-H), 1.04-1.01(m, 3H, CH_3). HRMS(m/z) for $C_{13}H_{17}NO_2$: calculated 219.1255, a peak was observed at 201.0439.

(E)-2-((1-phenylethylidene)amino)propanoic acid(**6**). yield 0.33g(17.3%). FT-IR (KBr, cm^{-1}) 3851.90, 3799.54, 3710.02, 3674.23(OH),

1683.31, 1540.01(C=O), 678.40, 594.25, 484.25, 437.72, 427.58(C-H). ^{1}HNMR (DMSOd_6, 400MHz)δ: 8.00-7.97(m, 5H, ArH), 1.37-1.35(m, 2H, CH_2), 1.16(s, 3H, CH_3), 0.80-0.79(m, 3H, CH_3). HRMS(m/z) for $C_{11}H_{13}NO_2$: calculated 191.0971, a peak was observed at 168.0692.

(E)-4-methyl-2-((1-phenylethylidene)amino)pentanoic acid(**7**). Yield 0.52(22%). FT-IR (KBr, cm^{-1}) 3851.89, 3837.34, 3800.06, 3709.82, 3647.50(OH), 1771.64, 1716.34,1558.20, 1506.75(C=O), 529.39, 508.16, 462.45(C-H).^{1}HNMR (DMSOd_6, 400MHz)δ: 7.96-7.94(m, 7H, ArH), 1.16(s, 6H, CH_3), 0.87-0.84(t, J=6.0Hz, 4H, CH_2), 0.78-0.77(m, 2H, CH_2).HRMS(m/z) for $C_{14}H_{19}NO_2$ calculated: 233.1451, base peak was observed at 234.0249.The FT-IR spectra confirmed the formation of the imine (C=N) functional group, a characteristic feature of Schiff bases. The ^{1}H NMR spectra further supported the proposed structures through the presence of aromatic proton signals and characteristic imine proton signals. The HRMS data were consistent with the expected molecular weights, confirming the successful synthesis of the target compounds.

The in vitro antiplatelet aggregation results (Table 1) revealed that all synthesized compounds exhibited inhibitory activity in a concentration-dependent manner. As the concentration increased from 1 to 8 mg/mL, the percentage inhibition of platelet aggregation also increased.

Compound 3 showed the highest inhibitory activity (70%) at 8 mg/mL, closely followed by compound 6 (69%), while compound 7 exhibited comparatively lower activity (59%). The standard drug aspirin showed the highest inhibition (80%), indicating superior efficacy.

The observed activity of the synthesized compounds suggests their potential as antiplatelet agents, although they are less potent than aspirin

Table 1: *In vitro* platelet aggregation activity of synthesized compounds

Compound	Concentration(μg/mL)			
	%inh of 1 mg/mL	%inh of 2 mg/mL	%inh of 4 mg/mL	%inh of 8 mg/mL
3	41	46	49	70
6	38	41	52	69
7	35	38	46	59
Aspirin	46	52	59	80

The in vitro phospholipase A_2 (PLA_2) inhibitory activity (Table 2) demonstrated that all synthesized compounds exhibited significant enzyme inhibition compared to the standard drug prednisolone.

Compound 3 showed moderate activity at lower concentrations, with 76% inhibition at 50 μg/mL, increasing to complete inhibition (100%) at 800 μg/mL. Compound 6 exhibited higher potency, achieving 80–81% inhibition at 50 μg/mL and complete inhibition at 400 μg/mL. Similarly,

Compound 7 showed strong inhibitory activity, with 82–83% inhibition at 50 μg/mL and complete inhibition at 400 μg/mL.

Prednisolone maintained 100% inhibition across all concentrations, confirming its high potency and validating the assay.

These results suggest that compounds 6 and 7 possess stronger PLA_2 inhibitory activity at lower concentrations, indicating better anti-inflammatory potential compared to compound 3

Table 2: Phospholipase A2 Biological Activities

Compound	% Inhibition	50 (µg/mL)	100 (µg/mL)	200 (µg/mL)	400 (µg/mL)	800 (µg/mL)
Compound 3	1	76	79	89	96	100
	2	76	80	89	95	100
	3	76	79	87	96	100
Compound 6	1	80	88	90	100	100
	2	81	89	90	100	100
	3	81	88	90	100	100
Compound 7	1	82	87	93	100	100
	2	81	86	93	100	100
	3	83	86	94	100	100
Prednisolone	1	100	100	100	100	100
	2	100	100	100	100	100
	3	100	100	100	100	100

The molecular docking results were further analyzed using both 2D interaction diagrams and 3D binding conformations to understand the binding modes of the synthesized Schiff base derivatives within the active sites of COX-2 and phospholipase A_2 (PLA_2).

Docking with COX-2 (Antiplatelet Target)

The 3D docking structures show that all synthesized compounds were well accommodated within the active site cavity of COX-2, similar to the reference drug aspirin. The binding poses indicate that the compounds interact with key amino acid residues through a combination of hydrogen bonding, hydrophobic interactions, and π–π stacking.

Compound 3 exhibited the most favorable binding orientation among the synthesized compounds, which correlates with its highest binding affinity (−7.3 kcal/mol). The 2D interaction analysis revealed that this compound forms multiple stabilizing interactions, including hydrogen bonds and hydrophobic contacts with residues lining the COX-2 active site. The presence of the aromatic benzylidene moiety likely enhances π–π interactions with aromatic residues, contributing to stronger binding.

Compounds 6 and 7 also demonstrated stable binding within the COX-2 pocket but with slightly lower binding affinities. Their interactions were predominantly hydrophobic, with fewer hydrogen bond interactions compared to compound 3, which may explain their relatively lower antiplatelet activity observed experimentally.

Aspirin, used as the reference drug, showed strong and well-defined interactions within the COX-2 active site, validating the docking protocol. The similarity in binding orientation between aspirin and compound 3 suggests that the synthesized compounds may exert their antiplatelet effects through a similar inhibitory mechanism.

The docking results with PLA_2 revealed that all compounds effectively bind within the enzyme's active site, forming stable ligand–protein complexes. The 3D surface representations show deep penetration of the ligands into the hydrophobic binding pocket, indicating strong enzyme affinity.

Compound 6 exhibited the best binding affinity (−6.9 kcal/mol) among the synthesized compounds, which aligns with its superior in vitro PLA_2 inhibitory activity. The 2D interaction diagrams indicate that compound 6

forms key hydrogen bonds and hydrophobic interactions with catalytic and neighboring residues, enhancing binding stability.

Compound 7 also showed strong binding interactions with PLA_2, forming multiple hydrophobic contacts and moderate hydrogen bonding. This supports its high inhibitory activity observed experimentally, particularly at lower concentrations.

Compound 3, although active, displayed comparatively weaker interactions, with fewer stabilizing contacts within the PLA_2 active site. This is consistent with its lower inhibitory potency relative to compounds 6 and 7.

Prednisolone, the standard drug, demonstrated the strongest binding affinity and extensive interaction network within the PLA_2 active site, confirming its high potency and serving as a benchmark for comparison.

The docking results suggest that structural features such as:

(i) Aromatic rings (enhancing π–π interactions)
(ii) Imine (C=N) functional group (facilitating hydrogen bonding)
(iii) Alkyl substituents (improving hydrophobic interactions)

play crucial roles in stabilizing ligand–protein interactions.

Compounds 6 and 7, which contain phenylethylidene moieties, appear to have enhanced hydrophobic interactions within the PLA_2 binding pocket, contributing to their superior anti-inflammatory activity. In contrast, compound 3 shows better interaction with COX-2, likely due to its structural compatibility with the enzyme's active site.

A good correlation was observed between the docking results and the in vitro biological assays:

(i) Compound 3 showed the best COX-2 binding and the highest antiplatelet activity
(ii) Compounds 6 and 7 showed better PLA_2 binding and higher anti-inflammatory activity

This agreement validates the docking study and suggests that the computational approach is reliable in predicting biological activity.

Overall, the docking analysis demonstrates that the synthesized Schiff base derivatives possess favorable binding interactions with both COX-2 and PLA_2 enzymes. While their activity is lower than that of standard drugs, their moderate-to-strong binding affinities indicate that they could serve as promising lead compounds for further structural optimization.

Table 3: Molecular Docking Results of Synthesized Compounds Against COX-2 and PLA_2

Compound	COX-2 (kcal/mol)	PLA_2 (PDB ID: 1KQU) (kcal/mol)
Compound 3	-7.3	-6.3
Compound 6	-6.8	-6.9
Compound 7	-6.5	-6.6
Aspirin	-7.0	—
Prednisolone	—	-8.2

Table 3 is the result of the *in silico* studies using COX-2 and 1KQU as a target. The results showed that all compounds have good binding affinity against the target protein. When compared with the reference Aspirin and Prednisolone, the reported compounds showed good binding affinity, ranging from -6.3 to -7.3 kcal/mol compared to the reference drugs .The most active for antiplatelet being compound **3** with binding affinity -7.3 could serve as a substitute for Aspirin if developed further while the most active for

phospholipase A2 being compound **6** with binding affinity of -6.9 could serve as a substitute for Prednisolone if developed further. Overall, the experimental and computational results are in agreement, as compounds with higher docking scores also exhibited better biological activity. This correlation supports the reliability of the molecular docking approach in predicting the biological potential of the synthesized compounds.

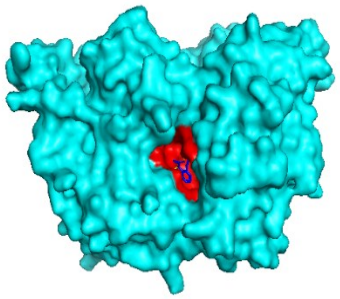


Fig 1: structure of Aspirin docking with COX-2

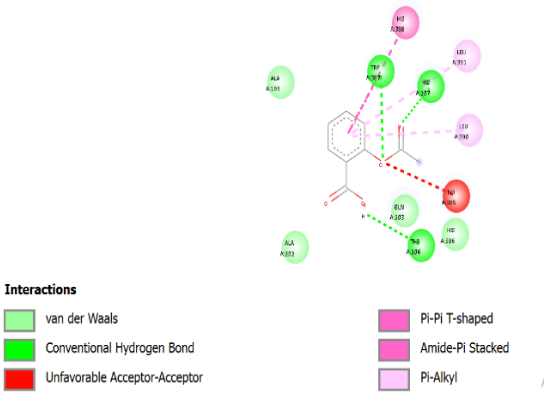


Fig 2: 2Dstructure of Aspirin docking with COX-2

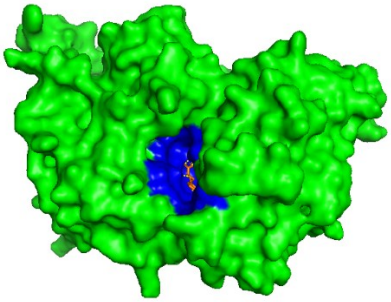


Fig 3: 3D structure of (E)-2-(benzylideneamino)-4-methylpentanoic acid docking with COX-2

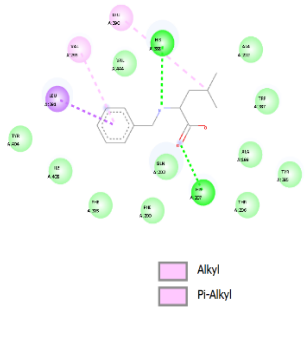


Fig 4: 2D structure of (E)-2-(benzylideneamino)-4-methylpentanoic acid docking with COX-2

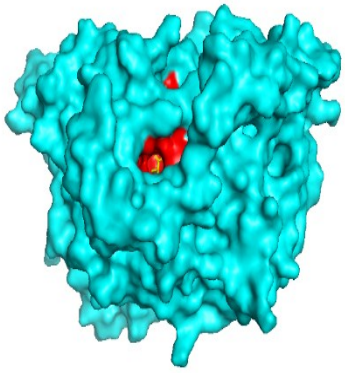


Fig 5:3D structure of (E)-2-((1-phenylethylidene)amino)propanoic acid docking with C0X-2

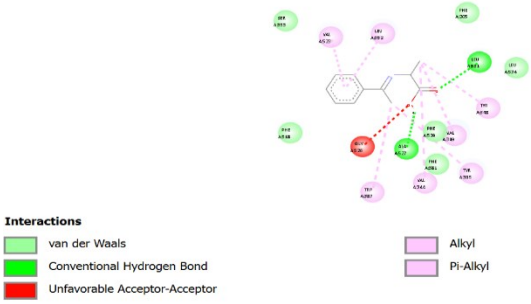


Fig 6: 2D structure of (E)-2-((1-phenylethylidene)amino)propanoic acid docking with C0X-2

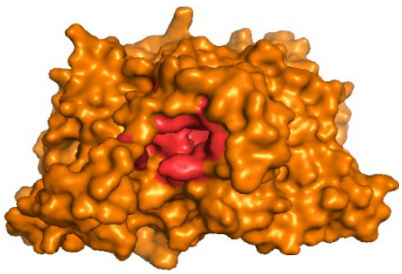


Fig 7:3D structure of (E)-4-methyl-2-((1-phenylethylidene)amino)pentanoic acid docking with COX-2

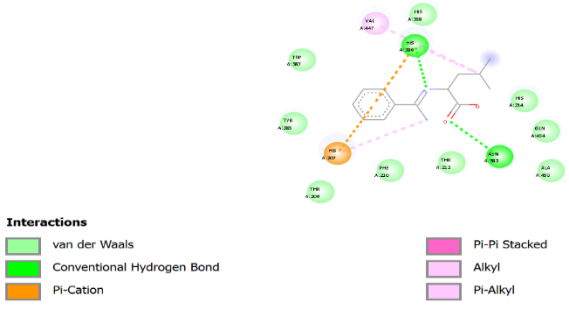


Fig 8: 2D structure of (E)-4-methyl-2-((1-phenylethylidene)amino)pentanoic acid docking with COX-2

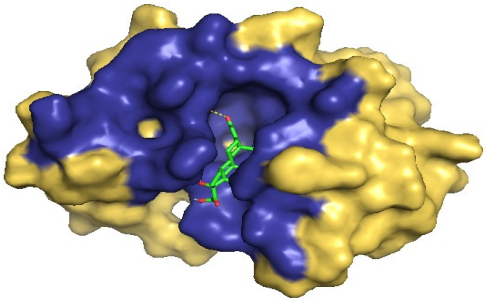


Fig 9: 3D structure of prednisolone docking with 1KQU

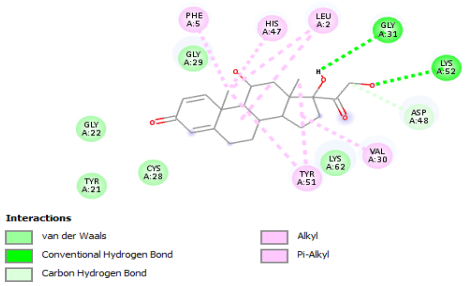


Fig 10: 2D structure of prednisolone docking with 1KQU

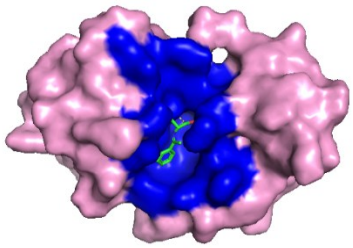


Fig 11: 3D structure of (E)-2-(benzylideneamino)-4-methylpentanoic acid docking with 1KQU

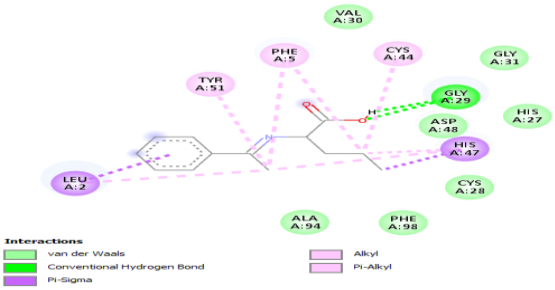


Fig 12: 2D structure of (E)-2-(benzylideneamino)-4-methylpentanoic acid docking with 1KQU

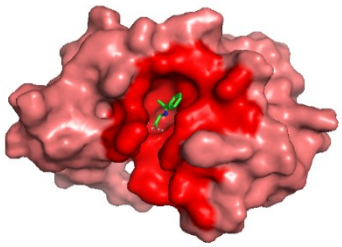


Fig 13 : 3D structure of (E)-2-((1-phenylethylidene)amino)propanoic acid docking with 1KQU

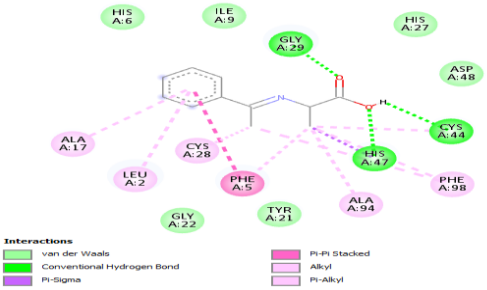


Fig 14: 2D structure of (E)-2-((1-phenylethylidene)amino)propanoic acid docking with 1KQU

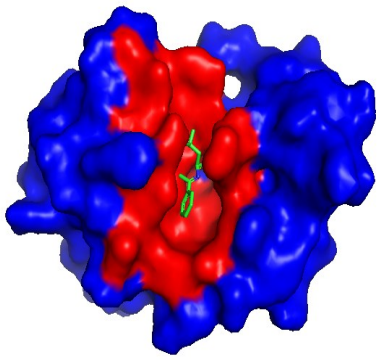


Fig 15: 3D structure of (E)-4-methyl-2-((1-phenylethylidene)amino)pentanoic acid docking with 1KQU

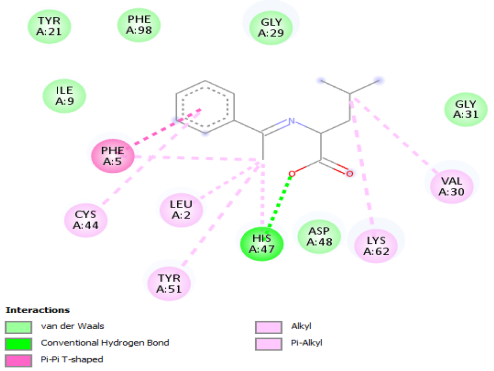


Fig 16: 2D structure of (E)-4-methyl-2-((1-phenylethylidene)amino)pentanoic acid docking with 1KQU

4.0 Conclusion

This research has been geared towards the synthesis, characterization, *in silico, in vitro,* antiplatelet aggregation and phospholipase A_2 studies of Schiff base derivatives, (E)-2-(benzylideneamino)-4-methylpentanoic acid, (E)-2-((1-phenylethylidene)amino)propanoic acid and (E)-4-methyl-2-((1-phenyl ethylidene)amino)pentanoic acid. The synthesized compounds were characterized using various spectroscopic techniques to confirm their structures. *In silico* molecular docking studies revealed significant binding interactions between the synthesized ligands and proteins. The synthesized compounds are novel antiplatelet recommendations for the treatment of these diseases: Cardiovascular diseases and ischemic diseases, based on their activity when compared to Aspirin. Phospholipase A2 (PLA2) was used as the biological target for *insilico* molecular docking because of its significance in inflammatory activity. With the active site residues of PLA2, all three Schiff bases showed significant binding affinities and favorable interaction profiles, with binding energies that were on par with or superior to those of standard molecules that are frequently tested against this target. These findings suggest that the synthesized compounds are potential agents for enzymes modulation or inflammation reduction. The results of this study demonstrate that Schiff bases derived from amino acids are computationally active, structurally stable substances with significant biological potential. Although the results are encouraging, they also imply that before the molecules can be moved closer to potential drug development, they might need more optimization and thorough biological testing. However, this work offers a solid basis for further research into the therapeutic value of Schiff bases and their derivatives.

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Ethics consideration

Not applicable

Data Availability.

All data generated or analysed during this study are included in this published article[and its supplementary information files]

Author Contributions

The first author (Florence Uchenna Eze) carried out investigation, data curation, supervision and manuscript review; the second and third authors (Chisom Praise Obiakalusi and Mmesoma Maryrose Obianika) carried out synthesis, writing of draft and methodology; the fourth, fifth and sixth authors (Chinwendu Faustina Achilionu, Vivian Ifeoma Okonkwo and Joshua Toochukwu Okoro) did data curation and methodology while the seventh author (David Izuchukwu Ugwu) did conceptualization, supervision and manuscript review.