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New Metformin Derivatives as Promising Anticancer Agents: A Computational and Experimental Study

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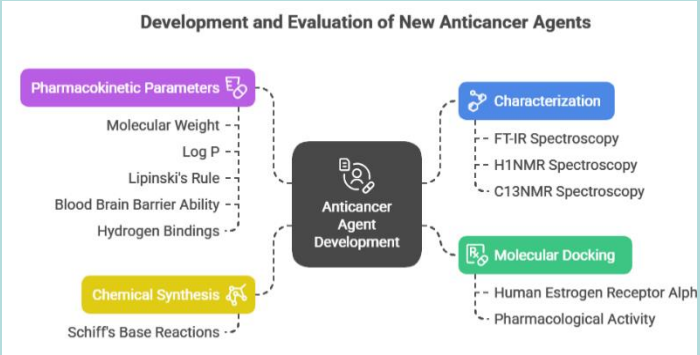
Abstract: Despite significant therapeutic developments, cancer remains a major cause of global mortality, underscoring the urgent need for novel and effective anticancer agents. This study outlines the rational design, in silico evaluation and synthesis of five novel metformin derivatives. Initially, the preliminary activity of these compounds as anticancer agents was assessed through molecular docking using CCDC GOLD suite software (2025) to indicate how the compounds would interact with the human estrogen receptor alpha (ERα, PDB ID: 3ERT), a key therapeutic target. Pharmacokinetic and drug-likeness properties including molecular weight, Log P, Lipinski's Rule of Five, blood-brain barrier permeability, and key hydrogen-bonding interactions with the receptor were subsequently evaluated to confirm their viability as potential drug candidates. All compounds showed favorable binding affinities for the receptor's active site. Notably, compound [1] exhibited a PLP fitness score (62.807) higher than the reference ligand (Methotrexate) which scored 61.76.Following the reliable computational results, all of the designed molecules [C1-C5] were synthesized successfully and characterized by melting point, FT-IR, ^{1}H NMR and ^{13}C NMR spectroscopy. The pharmacokinetic results showed that all the compounds adhered to Lipinski's Rule, expected to be well-absorbed from the gut with high topological polar descriptors. The present research represents a preliminary evaluation of the anticancer activity and requires further investigations by *in vitro* and / or *in vivo* studies.



Keywords: Metformin, Molecular Docking, Estrogen Receptor α, ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy.

Introduction

Metformin is a synthetic chemical compound that includes a guanidine moiety in its structure [1]. Its hydrochloride form is a white crystalline powder that has a hygroscopic property and good solubility in water [2]. Guanidine was first isolated for the first time from *Galega officinalis* as a natural product [3]. Metformin (also known as N, N-dimethyl-biguanide) is a derivative of biguanidine with the chemical formula ($C_4H_{11}N_5$) [4]. Generally, it is available as metformin hydrochloride ($C_4H_{11}N_5$·HCl) because it provides greater stability in its structure. The chemical synthesis of metformin hydrochloride is carried out in a single-step reaction between dimethylamine hydrochloride and 2-cyanoguanidine [5].Historically, metformin hydrochloride has been used to treat Type 2 Diabetes Mellitus (T2DM) due to its ability to reduce intestinal glucose absorption, increase peripheral glucose utilization, decrease fasting plasma insulin levels, and improve insulin sensitivity, thereby helping to maintain blood glucose levels without causing hypoglycemia [6]. Additionally, metformin and its derivatives have shown very potent anticancer activity [7]. Cancer refers to a disease that involves uncontrolled cell division, leading to the formation of a lump called a tumor [8]. Tumor cells can spread from the primary site to other distant organs in the body. Metformin has direct (insulin-independent) and indirect (insulin-dependent) anticancer effect] 9 .[The direct anticancer effect of metformin occurs through the inhibition of Mitochondrial Complex I, resulting in reduced ATP production and activation of adenosine monophosphate-activated protein kinase (AMPK) due to an increased AMP/ATP ratio. AMPK activation subsequently inhibits mTORC1 signaling, which contributes to cell growth and proliferation, ultimately suppressing tumor development [10].

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The indirect effect is mediated by the inhibition of gluconeogenesis, which occurs subsequently after AMPK activation. This leads to lower blood glucose and insulin levels. The decrease in insulin levels reduces signaling through the PI3K pathway, which is involved in tumor growth and proliferation, especially in cancers with high insulin receptor expression (e.g. prostate, breast, and colon) [11]. In an earlier study, diabetic patients who took metformin showed a lower risk of pancreatic cancer [12]. Another study found metformin to be more effective than sulfonylureas in reducing the risk of liver cancer in diabetic patients [13]. In the current study, Estrogen Receptor alpha (ERα) serves as a pivotal therapeutic target in anti-cancer research due to its fundamental function in promoting the growth and proliferation of the predominant subtype of breast cancer. Approximately 70% to 75% of all breast malignancies are designated as ERα-positive (ER+), establishing ERα as a highly validated and clinically significant target for therapeutic intervention [14]. One of the most common derivatives of metformin is Schiff bases, organic compounds characterized by the presence of a carbon-nitrogen double bond. Schiff bases (also known as imines) are formed by the condensation of primary amines with carbonyl compounds [15]. The general formula of Schiff bases is R'-CH=NR, where R' and R can be alkyl, aryl, or hydrogen[16]. The nucleophilic carbon and electrophilic nitrogen of the -C=N- imine bond make Schiff bases capable of binding with both electrophiles and nucleophiles, resulting in active molecules with biological and clinical applications, such as inhibiting diseases and enzymes [17]. Recent studies have indicated the effectiveness of Schiff base compounds against bacteria, fungi, and cancer [18]. Furthermore, Schiff bases derived from salicylaldehydes have been used to regulate plant growth and development [19]. Schiff base derivatives of phenol were synthesized and employed as antibiotics against *Pseudomonas aeruginosa*, *Salmonella typhi*, *Escherichia coli*, and Staphylococcus aureus [20]. Moreover, Schiff bases derived from metformin have exhibited antioxidant and antibacterial properties [21]. Schiff bases have been identified as valuable compounds in medicinal chemistry due to their capacity to add functional groups to their structures [22]. The current study aims to synthesize novel schiff bases derived from metformin and evaluate *in silico* their potential fitting capability as anticancer drugs targeting ERα.

Materials and Methods

The Docking Studies

Molecular docking studies were performed using the CCDC GOLD (Genetic Optimization for Ligand Docking) suite,which is a highly regarded and validated technique in structure-based drug discovery. GOLD is esteemed for its precision in forecasting the binding of tiny, flexible compounds (ligands) to protein binding sites, serving a vital function in lead identification and optimization [23].

Preparation of ligands and target

X-ray diffraction of the human estrogen receptor alpha (PDB code: 3ERT) was downloaded from the Protein Data Bank (PDB). The chemical structures for the designed compounds were generated using ChemOffice software (version 20) and converted into 3D structures using the BIOVIA Discovery studio 2021 client, which is also useful for identifying the important water molecules essential for water-mediated hydrogen bonding with the 3ERT receptor binding site [24].

Molecular docking protocol

The protein identified as human estrogen receptor alpha (PDB code: 3ERT) was downloaded from the Protein Data Bank (PDB) website and prepared using the Hermes program inside the CCDC GOLD suite 2025. The preparation of the protein is multi-step process; The first step is to add all of the hydrogen atoms, which is crucial to correct the tautamerization and ionization state of the amino acids, then the productive water molecules should be extracted, from the Discovery Studio software, water molecules (2, 58, 59) were noticed to be responsible for water-mediated hydrogen bonding between ligands and the protein active site. Thus, these water molecules were extracted and the remaining water molecules were deleted. The third step in protein preparation is to remove any ligand or cofactor co-crystallized with the active core of the protein [25]. The active site prediction was based on the pocket remaining after the extraction of the co-crystal ligand. The protein binding site residues were characterized within a distance of 10 Å (Angstrom) from the co-crystal ligand or the designed compounds for the docking process. Additionally, we used BIOVIA Discovery Studio to visualize the 2D interactions between the co-crystal ligand and the 3ERT target protein, which helped us identify the key amino acid residues in the target's active site. The amino acid residues present at the target active site include: MET421 (2), MET388, ILE424, LEU391, LEU428, ALA350 (2), LEU387, MET343, GLU353, ARG394, TRP383, LEU346. The two-dimensional interactions between the co-crystal ligand and the residues in the 3ERT binding pocket are demonstrated in **Figure 1**. For the other parameters of the docking process, we used the default values. The default setting for the number of produced postures was 10, and the top-ranked solution was left unchanged. In addition, the option to terminate the contract early was disabled. The five designed ligands were added in (.mol2) file format. The ChemScore kinase served as the basis for the setup [26]. Meanwhile the better fitness equals superior binding: GOLD's fitness functions (including PLP, ChemPLP, GoldScore, and ChemScore) are amplifies such that a higher numerical score indicates a more energetically favorable and consequently stronger predicted binding interaction (higher affinity) between the ligand and the protein [27]. In this study, Methotrexate was used a reference ligand compared with our five synthesized compounds as a convenient and efficient anticancer agent.

Pharmacokinetic study

The pharmacokinetic properties, including Absorption, Distribution, Metabolism, and Elimination (ADME) were studied along with other physicochemical properties of the newly synthesized compounds using SwissADME server. This server is an accessible website used to study physicochemical parameters and medicinal chemistry properties. The bioavailability radar is very important for the design and synthesis of new compounds. The newly generated compounds' chemical structures were transformed into SMILE names using chemAxon's Marvin JS [28, 29]. The polarity and lipophilicity of the five compounds along with Methotrexate are shown in the BIOLLED-EGG representation in **Figure 2.**

Chemistry – General

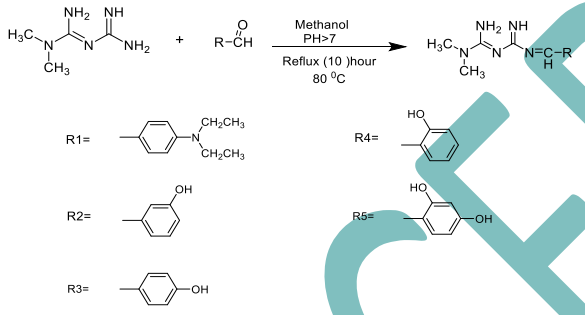
All chemicals and solvents employed in this research were purchased from commercial sources and used precisely as directed. The hydrochloride salt of metformin ($C_4H_{11}N_5$.HCl) was acquired from Samarra, a state-owned pharmaceutical and medical appliance company. The aldehydes: m-hydroxybenzaldehyde, p-hydroxybenzaldehyde, 2,4-dihydroxybenzaldehyde, N,N-diethylaminobenzaldehyde, and salicylaldehyde were all purchased from Sigma-Aldrich (Germany). An electronic device, a CL-726 (India MART Member Since, Noida, India) was used to ascertain the melting points.

The Fourier transform infrared (FT-IR) spectroscopic analysis was done by a Nicolet iS10 spectrophotometer (Thermo Scientific, Waltham, MA, USA). With a spectral resolution of 4 cm^{-1}. The ^{1}H-NMR and ^{13}C-NMR spectroscopic analysis were performed at Al-Basra University, College of Science using a **Bruker** company (Swiss-German origin). **Table1** shows the chemical structures and the IUPAC names of the synthesized compounds.

Chemical Synthesis

Synthesis of Metformin Schiff Bases by Conventional Method

C1–C5 were all produced using Schiff base technique, which included refluxing a mixture of 20 mL of methanolic basic (pH 9–10 using a few drops of 10% w/v sodium hydroxide solution) medium containing equimolar concentrations (10 mmol each) of metformin–HCl and the ortho- or para–substituted benzaldehyde for two to three hours. To keep track of how the reaction was going, Thin-layer chromatography (TLC) was used. The reaction was stopped when a mixture ranging in hue from pale orange to a very vivid orange was produced. After cooling, filtering, drying, and recrystallization with ethanol, the product was packaged [19]. The synthesis of target compounds C1- C5 was accomplished according to the following procedures illustrated in the **scheme 1. Table 2** shows the physical properties of the synthesized compounds.



Scheme (1): Synthesis of Intermediates and Target Compounds.

Results and Discussion

Molecular docking results interpretation

The molecular docking process was done initially in order to identify the possible interactions with the target protein (3ERT) to prove that our synthesized chemicals were interact with the target protein at the same active site. The docking study proved that compound (C1) which showed PLP fitness (62.807) had a high-priority lead candidate with predicted affinity comparable to the reference compound (Methotrexate) which had PLP fitness (61.767) as shown in table 3. A higher score signifies a more favorable interaction between the ligand and the protein, suggesting a more stable and energetically preferred binding pose [23]. **Figure 3** illustrates the 3D pictures of the five synthesized ligands interacted with the target receptor (3ERT) using GOLD suite software as a molecular docking tool along with Methotrexate as a reference ligand.

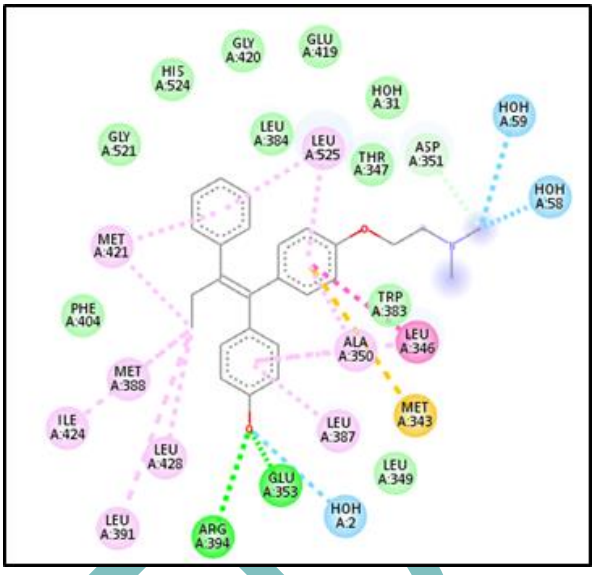


Figure (1): Interactions of the co–crystal ligand with the predicted binding pocket residues of the human estrogen receptor alpha (PDB ID: 3ERT).

Molecular docking Validation

Ligand re-docking is the primary and essential method for validating a docking protocol. The protocol begins with the selection of a co-crystal structure: we initiated the validation with the X-ray crystallographic structure of the target protein complexed with a known ligand (PDB ID: 3ERT). The co-crystallized ligand functions as the reference structure. Subsequently, the co-crystallized ligand was removed from the protein. Both the protein and ligand were prepared by including hydrogens, assigning charges, and implementing other requisite alterations, employing the same criteria specified for docking your distinct molecules. Re-docking: the reference ligand was then reinstated into the active site of the generated protein as shown in **Figure 4**. This re-docking resulted in a PLP fitness (97.91) with RMSD = 1.161 A°. Since this value is less than the accepted threshold of 2.0 Å, the docking protocol is validated and reliable [30].

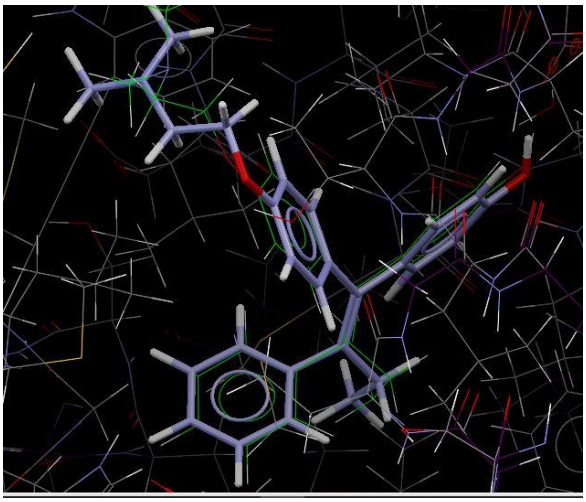


Figure (4): The docking pose of the co-crystal ligand with 3ERT.

Table (1): The chemical structure of the synthesized derivatives with their IUPAC names.

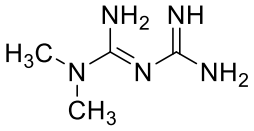
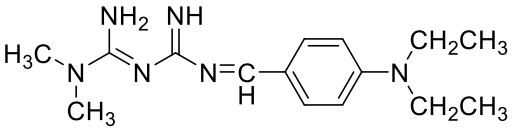
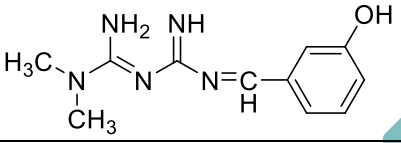
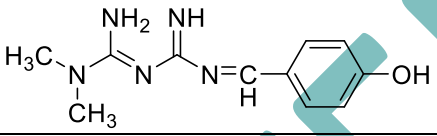
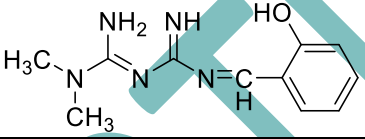
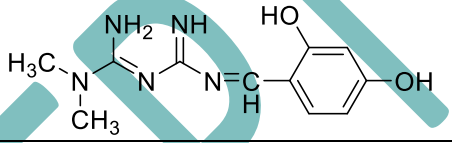
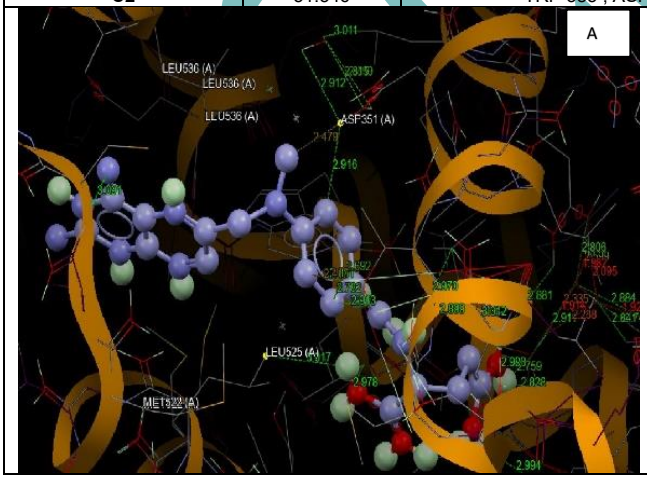
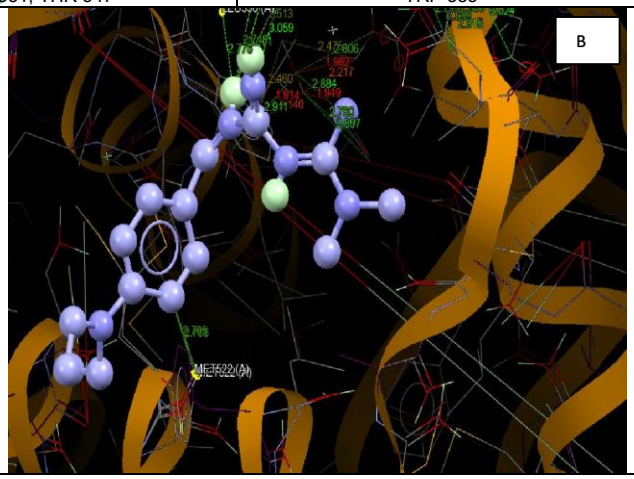
Compound	Chemical formula	Structure	Name of the compounds
Standard	$C_4H_{11}N_5$		**Metformin**
C1	$C_{15}H_{24}N_6$		**(E)-2-(N-(4-(diethylamino)benzylidene)carbamimidoyl)-1,1-dimethylguanidine**
C2	$C_{11}H_{15}N_5O$		**(E)-2-(N-(3-hydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine**
C3	$C_{11}H_{15}N_5O$		**(E)-2-(N-(4-hydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine**
C4	$C_{11}H_{15}N_5O$		**(E)-2-(N-(2-hydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine**
C5	$C_{11}H_{15}N_5O_2$		**(E)-2-(N-(2,4-dihydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine**

Table (2): The Binding Energies (PLP fitness) for the synthesized derivatives and Methotrexate Docked With 3ERT protein.

Compound	PLP fitness	H-bond acceptor	Short contact
Methotrexate	61.767	ARG394, CYS530	ARG394,CYS530
C1	62.807	LEU 536	THR347 , ASP 351
C4	53.437	TRP 383	TRP 383, M3T 522
C3	53.253	LEU 354 through water bridge (HOH AM3), ASP 351, THR 347 (2), MET 343 , MET 528 (2).	THR 347 (2) , ASP 351
C5	52.600	ASP 351 , TRP 383, THR 347 , LEU 525 (2)	TRP 383 , MET 522
C2	51.346	TRP 383 , ASP 351, THR 347	TRP 383





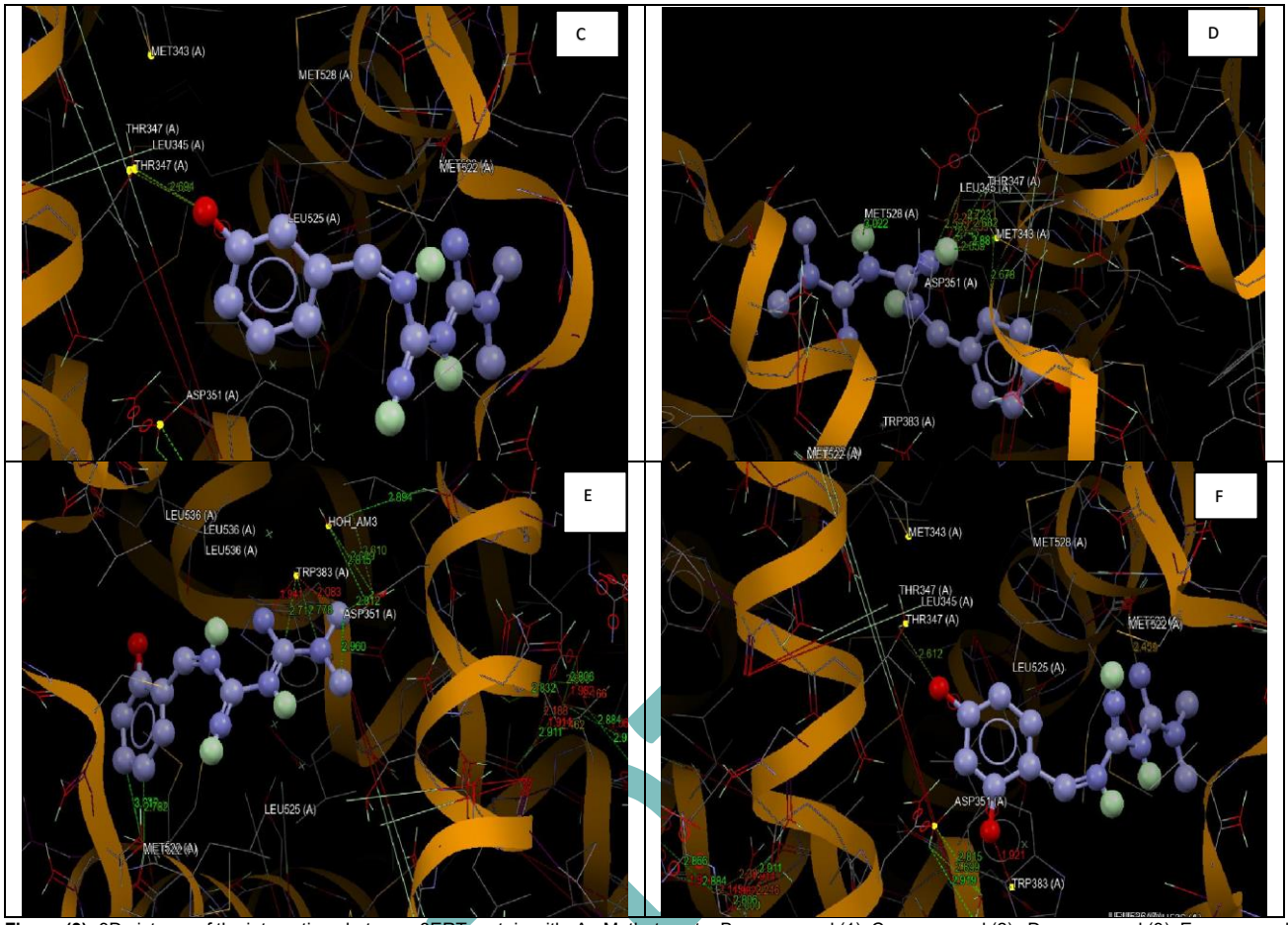


Figure (3): 3D pictures of the interactions between 3ERT protein with: A= Methotrexate, B= compound (1), C= compound (2) , D= compound (3), E=compound (4), F= compound (5).

Pharmacokinetic results interpretation

The Swiss ADME server used to evaluate the physicochemical parameters of the synthesized compounds [31]. The ADME features may be detected before synthesis and biological testing using this affordable and helpful technology. This helps to exclude ligands that are insufficient or have an unsatisfactory pharmacokinetic profile [32]. Among these factors is the Topological Polar Surface area (TPSA), which used to describe the ability of drugs to permeate cells, Compounds with TPSA<140Å^2 have high cellular permeability and bioavailability; the low value of TPSA <140 Å^2 is a good indicator of good human oral bioavailability. Low TPSA values indicate a lower molecular polarity which assists in permeating the lipid membrane of intestinal cells before entering into the bloodstream when orally administered. On the other hand, higher TPSA values are associated with higher molecular polarity which could lead to poor permeability and hence poor oral bioavailability [33, 34]. From the SwissADME results it was found that all of the synthesized compounds have TPSA <140 Å^2 the TPSA values ranged from (81.07-118.29) which means the five compounds expected to be absorbed passively and thoroughly from the GIT and do not pass through the blood brain barrier (BBB). The Lipinski's "rule of five" (Ro5) is a common guideline for predicting if a compound can be orally absorbed. It requires a molecular mass of under 500 Daltons, no more than 5 hydrogen bond donors, and no more than 10 hydrogen bond acceptors, along with a log P value below 5. In our study, all compounds satisfied the RO5 criteria. [35] The boiled egg plot (**Figure .3)** is a graphical representation used to easily assess the pharmacokinetic parameters. The white area represents molecules that are passively absorbed through the GIT, while the yolk area of the egg represents molecules pass the blood brain barrier (BBB). If the molecules appeared outside the boiled egg, that means the molecules have low GI passive absorption and low BBB penetration. The red dots indicates that the molecules are not effluxed by p-glycoprotien [36]. The results showed all of the compounds appeared as red dots, but only Compounds C1–C5 appeared in the yolk region of the plot, indicating predicted BBB penetration.

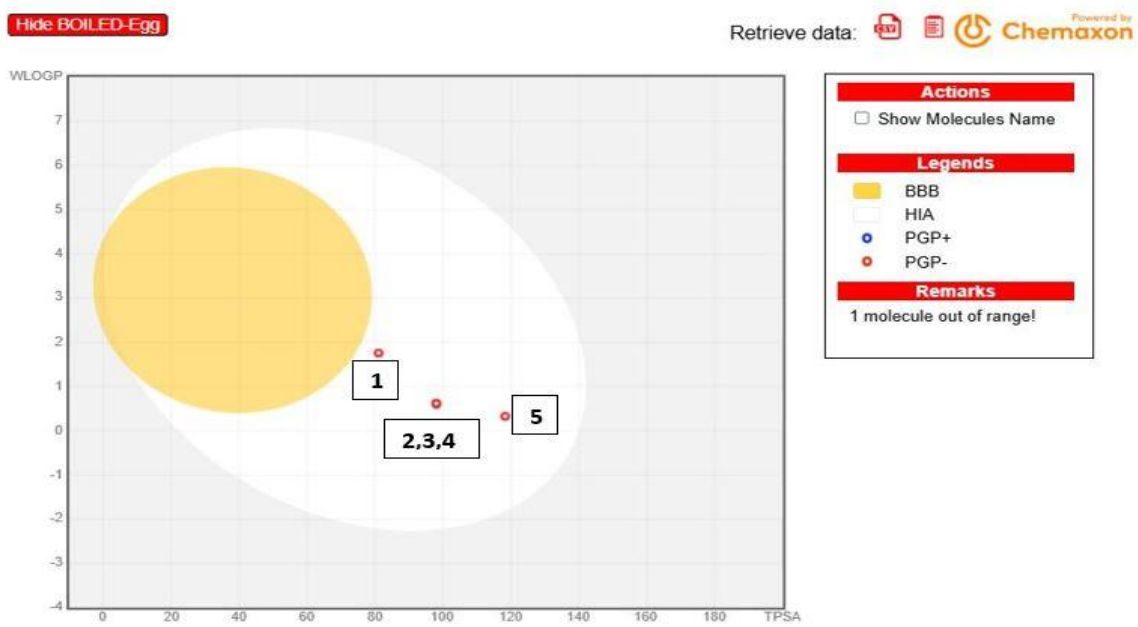


Figure (2): The BOILED-Egg analysis for compounds [1-5].

Table (3): ADME results of synthesized compounds.

Compound	H-donor	H-acceptor	MR	TPSA (Å^2)	GI-absorb.	BBB permeability	Bioavailability	Lipinski's violation
Metformin	3	2	36.93	91.49	high	No	0.55	0
Methotrexate	5	9	118.40	210.54	low	No	0.11	1
C1	2	3	91.02	81.07	high	No	0.55	0
C2	3	3	69.87	85.70	high	No	0.55	0
C3	3	4	69.22	98.06	high	No	0.55	0
C4	3	4	69.22	98.05	high	No	0.55	0
C5	4	5	71.25	118.29	high	No	0.55	0

Structure and Spectral Analysis

The structure of the five synthesized compounds were confirmed by FTIR, ^{1}H NMR and ^{13}C NMR.

E)-2-(N-(diethylamino)benzylidene)carbamimidoyl)-1,1-dimethylguanidine [C1]

Yield 70%, Yellowish-orange powder, Melting point (266-267), Molecular Weight(288.4 g/mol) **The FTIR spectrum showed** broad band at 3161-3371 (cm^{-1}) for v(N–H), 1627–1568 (cm^{-1}) for v(C=N) (imine) group and 1568-1583 (cm^{-1}) for v(C=C) aromatic group. **The ^{1}H NMR spectrum showed that** the aromatic groups are observed at 6.713-7.312ppm, while the proton corresponding to amine appears at 3.406 ppm. The characteristic bands of the aromatic protons (N-CH_2) are seen in the range of 3.026–3.043 ppm. The -N(CH_3)$_2$ band observed at 2.749-2.927 ppm and the CH=N Imine band observed at 8.8 ppm. **The ^{13}C NMR spectrum showed** bands at 159.63–151.17 ppm for C=N / Aromatic C–N, 128.30–111.53 ppm band for Aromatic CH, 62.30 ppm band for N-CH_2 , 34.33–39.95 ppm bands for Additional ethyl/methylene carbons.

(E)-2-(N-(3-hydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine [C2]

Yield 72%, Pale brown powder, Melting point (231-233), Molecular Weight (233.28 g/mol) **The FTIR spectrum showed** broad band at 3319-3371 (cm^{-1}) for v(O–H) phenolic group, 3174-3294 (cm^{-1}) for v(N–H), 1581-1670 (cm^{-1}) for v(C=N) (imine) and band at 1581(cm^{-1}) for v(C=C) aromatic double bonds. **The ^{1}H NMR spectrum showed** that the aromatic groups are observed at 6.782–7.592 ppm, while the proton corresponding to amine appears at 5.283 ppm. The phenolic hydroxide proton observed at 10.123 ppm. The characteristic bands of the aromatic protons (N-CH_2) are seen in the range of 3.026–3.043 ppm. The N(CH_3)$_2$ band observed at 3.035–2.754 ppm and the CH=N Imine band observed at 9.906 ppm. **the ^{13}C NMR spectrum showed** bands at 191.34–191.79 ppm C=N (Imine), 155.24-161.42 ppm bands for C–OH, C=NH, 115.72-145.76 ppm bands for Aromatic Carbons , 58.21-69.37 ppm bands for C–N(CH3)2 and 22.10-40.56 ppm bands for CH_3 groups.

(E)-2-(N-(4-hydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine [C3]

Yield 88%, Gray powder, Melting point (235-236), Molecular Weight (233.28 g/mol) **The FTIR spectrum showed** broad bands for O-H phenolic group at 3371 (cm^{-1}), band at 1643, 1600 (cm^{-1}) for v(C=N) (imine), band at 1512-1575 (cm^{-1}) for v(C=C) aromatic double bonds and band at 1286–1215 (cm^{-1}) for v(C–O) phenolic group**. The ^{1}H NMR spectrum showed** that the aromatic groups are observed at 7.75–6.78 ppm, while the proton corresponding to amine appears at 5.7 ppm. The phenolic hydroxide proton observed at 10.36 ppm.The characteristic bands of the CH=N and C=NH (Imine and Amidine protons) are seen in the range of 9.99–8.86 ppm. The N(CH_3)$_2$ band observed at 3.92–2.50 ppm , **the ^{13}C NMR spectrum showed** bands at 191.42 ppm bands for Imine carbon atom, 164.16 ppm bands for C=N & C=NH carbons. 132.52–115.76 ppm band for Aromatic carbons. 156.25-159.65 ppm bands for Phenolic carbon atoms, 40.54–34.44 ppm band for Dimethylamine carbons and 62.34 ppm band for Alkyl-N carbon atoms.

(E)-2-(N-(2-hydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine [C4]

Yield 85%, Dark brown powder, Melting point (228-230), Molecular Weight (233.28 g/mol) **The FTIR spectrum showed** broad band at 3327-3371(cm^{-1}) for v(O–H) phenolic group, 3174-3294 (cm^{-1}) for v(N–H) group, 1627 (cm^{-1}) band for imine

functional group , 1577 (cm^{-1}) band for aromatic v(C=C) group and a band appeared at 1168-1269 (cm^{-1}) for v(C–O) phenolic group. **the ^{1}H NMR spectrum showed** the phenolic hydroxide group observed at 10.28 ppm, 8.71 ppm for C=NH , and 8.51 ppm for CH=N imine**. The ^{13}C NMR spectrum showed** bands at 191–161 ppm bands for C=N, C=NH, guanidine carbons, 158–120 ppm bands for Phenyl ring, phenolic C–OH, for Aliphatic carbon atoms ; bands appeared at 60–40 ppm and bands at 30–20 ppm region observed possibly for methyl groups or solvent residuals

(E)-2-(N-(2,4-dihydroxybenzylidene)carbamimidoyl)-1,1-dimethylguanidine [C5]

Yield 91%, Reddish-Orange, Melting point (248-249), Molecular Weight (249.27 g/mol) **The FTIR spectrum showed** a broad band at 3371 (cm^{-1}) for v(O–H, phenolic) group , a band at 3174-3294 (cm^{-1}) for v(N–H) group, a band at 1627(cm^{-1}) for v(C=N) of imine, a band at 1575(cm^{-1}) for aromatic C=C double bond and 1064-1068 (cm^{-1}) for v(C–O) phenolic group**. the ^{1}H NMR spectrum showed** bands at 2.94-3.07 ppm for -N(CH_3)$_2$) , 4.39 ppm band for amine protons, 8.14 ppm for CH=N , OH (Phenolic) and 6.32–7.17 ppm for aromatic protons**. The ^{13}C NMR spectrum showed** bands at 160-167 ppm probably for C=N (Imine), 151-157 ppm for C–OH, C=NH, 115-122 ppm for aromatic carbons and bands at 35-39 ppm for CH_3 groups.

Conclusion

The five compounds (C1–C5) were designed and studied for their hypothetical pharmacological activity using fully licensed CCDC GOLD suite 2025 software rather than other freely available docking programs to produce precise *in silico* binding predictions. The docking results showed that Compound C1 was a high-priority lead candidate with predicted affinity comparable to the reference compound (Methotrexate) at the active site of the target protein (**ERα**, 3ERT). The compounds then synthesized successfully starting from Metformin as Schiff bases, the molecules characterized using melting point, FT-IR, ^{1}H-NMR and ^{13}C-NMR spectroscopic analysis. It is important to mention that the pharmacological activity remains hypothetical and requires further confirmation by *in vitro* and / or *in vivo* evaluation.

Disclosure Statements

- **Ethics Approval:** None to declare
- **Conflict of Interest:** The authors declare no conflict of interest.
- **Author Contribution:** All Authors contributed equally to this work
- **Funding Source:** None
- **Limitations of the Study:** This study's molecular design technique possesses numerous drawbacks. Our methodology was solely based on molecular docking with the human estrogen receptor-α. This constrained our capacity to thoroughly investigate essential elements like as conformational flexibility and solvation, which could influence the precision of our predictions. The docking parameters and scoring systems employed may not have accurately reflected the actual binding free energies, thereby affecting the reliability of the projected binding modes. Moreover, docking is incapable of forecasting dynamic protein alterations or allosteric effects that transpire inside a biological system. Consequently, further researched are planned to evaluate the activity of the synthesized compounds in vitro and in vivo to confirm their hypothetical effectiveness.
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