International Journal for Multidisciplinary Research (IJFMR)

E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Structure Based Multitargeted Molecular Docking Analysis of Selected Proteins against Breast Cancer

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ABSTRACT

In India, cancer represents the second leading cause of death, claiming roughly 0.3 million lives annually. Among the Indian population, the most frequently diagnosed cancers include those of the breast, colon, lung, liver, rectum, and stomach. Experimentally evaluating the potential of compounds as microtubule inhibitors or protein-targeting anticancer agents is often labor-intensive, costly, and dependent on specialized chemicals, cancer cell lines, and animal models. Consequently, employing in silico approaches prior to experimental validation offers significant advantages by reducing time, cost, and resource consumption. Computational modeling serves as an effective tool for predicting potential drug candidates, assessing their binding affinities to target sites, and estimating their metabolism and possible side effects. Molecular docking was performed to assess the binding interactions and affinities of twenty selected natural and synthetic compounds with the Epidermal Growth Factor Receptor (EGFR) (PDB ID: 4WD5), a critical target implicated in breast cancer progression. Using PyRx software, each ligand was docked into the active site of EGFR to predict its potential inhibitory efficacy. The docking conformations were analyzed based on binding affinity (kcal/mol) and RMSD (root mean square deviation) values, with lower binding energies indicating stronger binding interactions A total of 20 compounds were selected for docking analysis based on their reported or potential anticancer properties, particularly against breast cancer. When figuring out the structure and evaluation of a small-molecule ligand-protein interaction in a complex, molecular docking is an effective technique. It is applied to investigate the behavior of molecules when target proteins bind. Also, it offers a wide set of sample options and is a rapid and easy technique to screen huge collections of ligands and targets. It is a technology that is widely used in the search for new drugs. Future research can focus on lead optimization and pharmacological validation to develop these natural compounds into viable therapeutic agents for breast cancer. The integration of virtual screening helps to reduce time, cost, and the risk of failure in the later phases of drug development.

Keywords: Molecular Docking, Epidermal Growth Factor Receptor, Abemaciclib, Oxypropanoic acid, Pazopanib,

INTRODUCTION

Breast cancer remains one of the most common malignancies among women globally. Despite extensive research, the biomolecular mechanisms underlying breast carcinogenesis are still not fully elucidated due to the complexity of its associated risk factors [1]. In 2022 alone, approximately 2.3 million women were diagnosed with breast cancer, and about 670,000 deaths were recorded worldwide [2]. Cancer originates from abnormal cell division and mutations driven by genetic damage, and breast cancer is specifically classified as a hormone-related malignancy [3]. Understanding the molecular pathways that trigger tumor initiation and promote the transition to cellular migration is therefore essential [4].

Breast tissue is glandular and highly sensitive to fluctuations in systemic hormone levels [5]. In India, cancer represents the second leading cause of death, claiming roughly 0.3 million lives annually. Among the Indian population, the most frequently diagnosed cancers include those of the breast, colon, lung, liver, rectum, and stomach [6]. Various physical and chemical agents—such as hormones, ionizing radiation, ingested asbestos, tobacco smoke, and lifestyle factors—can contribute to carcinogenesis [7]. Alterations in cell-signaling pathways impair the ability of cells to regulate proliferation, ultimately enabling uncontrolled growth [8]. DNA damage or cellular stress can also disrupt apoptotic and cell-cycle regulatory mechanisms, further promoting tumor development [9]. These abnormalities collectively facilitate cancer cell growth, proliferation, and metastasis to distant tissues [10].

Experimentally evaluating the potential of compounds as microtubule inhibitors or protein-targeting anticancer agents is often labor-intensive, costly, and dependent on specialized chemicals, cancer cell lines, and animal models [11]. Consequently, employing in silico approaches prior to experimental validation offers significant advantages by reducing time, cost, and resource consumption [12]. Computational modeling serves as an effective tool for predicting potential drug candidates, assessing their binding affinities to target sites, and estimating their metabolism and possible side effects [13]. Although numerous proteins have been implicated in breast cancer, the present study focuses on RAC1B due to its involvement in multiple cancer types [14]. Furthermore, a recent study published in *Nature* identified Rac1 as a high-priority therapeutic target, supported by compelling evidence of its clinical relevance [15].

Molecular Docking

The structure of the solasodine compound was retrieved from PubChem in SMILES format, and its 3D conformation was generated using an online SMILES translator. The resulting 3D structure was optimized using Discovery Studio. Receptor structures were obtained from the Protein Data Bank (PDB), with breast cancer–associated receptors selected based on their elevated expression levels (Table 1).[16] These structures were prepared by removing water molecules and adding hydrogen atoms in Discovery Studio. Solasodine was then docked against twelve breast cancer-related receptors using AutoDock Vina: estrogen receptors (ER), progesterone receptor (PR), mammalian target of rapamycin (mTOR), epidermal growth factor receptor (EGFR), androgen receptor (AR), mineralocorticoid receptor, retinoid X receptor (RXR)-α, peroxisome proliferator-activated receptor (PPAR), liver X receptor (LXR), vitamin D receptor (VDR), cyclin-dependent kinase 2 (CDK2), and farnesoid X receptor (FXR). Docking outputs were visualized in Discovery Studio, and binding energies along with ligand–receptor interactions were analyzed to identify the most promising receptor for subsequent cytotoxicity assays.

Method and Materials

Retrieval of Target Protein Structure

The three-dimensional structure of the target protein, Epidermal Growth Factor Receptor (EGFR), was retrieved from the Protein Data Bank (PDB) under the accession ID 4WD5 in .pdb format. EGFR was selected due to its well-established involvement in breast cancer initiation and progression through dysregulated signaling and abnormal cell proliferation. Prior to docking, the protein structure was prepared using Discovery Studio Visualizer 2020 by removing non-essential components—including crystallographic water molecules, heteroatoms, and co-crystallized ligands. Polar hydrogen atoms and Kollman charges were subsequently added to enhance structural accuracy and facilitate reliable ligand–receptor interactions during docking [17].

Selection and Preparation of Ligand

A total of 20 natural and synthetic compounds previously reported to possess anticancer activity or suspected to exhibit such effects were selected for molecular docking. These included phytochemicals such as Curcumin, Genistein, Epigallocatechin Gallate, and Biochanin A, along with clinically approved anticancer agents including Abemaciclib, Afatinib, and Pazopanib. Chemical structures of all ligands were retrieved from the PubChem database in SDF format, and their corresponding PubChem IDs were recorded for documentation. Selection of Compounds. A total of 20 compounds were selected for docking analysis based on their reported or potential anticancer properties, particularly against breast cancer. These included natural phytochemicals such as *Curcumin, Genistein, Epigallocatechin gallate,* and *Biochanin A*, along with clinically approved anticancer drugs such as *Abemaciclib, Afatinib,* and *Pazopanib*. Each compound was retrieved from the PubChem database, with corresponding PubChem IDs and literature references listed in Table 1. The combination of both natural and synthetic molecules provided a diverse structural basis for evaluating EGFR inhibitory potential. Energy minimization of each ligand was performed using Open Babel, integrated within PyRx 0.8, employing the Universal Force Field (UFF) and the conjugate gradient optimization algorithm. This process ensured that each ligand adopted a low-energy conformation suitable for accurate docking. The minimized ligand structures were then converted into PDBQT format, the required input format for AutoDock Vina.

Preparation of Protein for Docking

The EGFR structure (PDB ID: 4WD5) was imported into PyRx for docking analysis. Active site residues were identified using published literature, CASTp 3.0 server predictions, and structural evaluation in Discovery Studio. A grid box was then defined to fully envelop the catalytic binding pocket, ensuring coverage of all potential ligand-binding regions.

Protein preparation involved the following steps:

- Removal of crystallographic water molecules
- Addition of polar hydrogen atoms
- Assignment of Gasteiger charges
- Conversion of the optimized structure into PDBQT format for compatibility with Auto Dock Vina

This preparation protocol ensured accurate ligand–receptor recognition and preserved the geometry and integrity of the EGFR active site.

Molecular Docking Using PyRx

Molecular docking was conducted using AutoDock Vina integrated into PyRx 0.8. Each ligand was individually docked into the predicted active binding region of EGFR. The docking parameters were configured to generate multiple binding poses, from which the pose exhibiting the lowest binding energy (kcal/mol) was selected as the most favorable conformation.
Docking scores were used to estimate binding affinity, while RMSD values were assessed to determine the consistency of generated conformations. Ligands demonstrating more negative binding energies were considered to exhibit stronger interactions with EGFR, indicating higher inhibitory potential.

Visualization and Interaction Analysis
Docking results were analyzed using Discovery Studio Visualizer (BIOVIA, 2020). The ligand–protein complexes were examined to identify key amino acid residues and the specific types of non-covalent interactions involved. These interactions included:

- Conventional hydrogen bonds
- π–π stacking and π–sigma interactions
- Alkyl and π–alkyl hydrophobic contacts
- Halogen bonds
- van der Waals interactions

Three-dimensional interaction diagrams were generated to illustrate ligand orientation within the EGFR binding pocket, while 2D interaction maps were constructed to highlight the nature and strength of individual interactions. This combined visualization approach provided detailed insight into the binding mechanism and potential inhibitory effect of each compound.

Validation of Docking Protocol
To ensure reliability and reproducibility, the clinically approved EGFR inhibitor **Abemaciclib** was employed as a reference standard. Its binding energy and interaction profile served as a benchmark against which all other test ligands were evaluated. Concordance between key amino acid interactions of Abemaciclib and those of top-performing ligands confirmed the robustness and validity of the docking protocol.

Comparative and Statistical Evaluation
Docking scores for all 20 ligands were compiled and compared to identify the compounds with the most favorable binding affinities. Structure–activity relationship (SAR) trends were examined to determine functional groups associated with enhanced binding. Ligands exhibiting binding energies equal to or better than the reference compound were shortlisted as promising EGFR inhibitors meriting further experimental investigation.

RESULT
When figuring out the structure and evaluation of a small-molecule ligand-protein interaction in a complex, molecular docking is an effective technique [18]. It is applied to investigate the behavior of molecules when target proteins bind. Also, it offers a wide set of sample options and is a rapid and easy technique to screen huge collections of ligands and targets [19]. It is a technology that is widely used in the search for new drugs. Top docking software includes AutoDock, Vina, PyRx MOE-Dock, FLexX, and

GOLD [20]. In this study, AutoDock Vina has been used to perform molecular docking. Using AutoDock Vina (https://vina.scripps.edu/), molecular docking has been carried out in this work wherein the ligands were docked to the protein active sites to assess the selected compounds' affinity for atomic binding [21]. The initial grid parameters were as follows: Size Z = 20, Size X = -2.444440, Center Z = 35.521089, Center Y = 69.964664. The active site-specific docking is aided by these parameters. The docking simulations employed an exhaustiveness parameter of 8, an energy range, and a random seed. The docked complexes were loaded into BIOVIA Discovery Studio Visualizer for further analysis and display of the active amino acid residues and 2D-3D interaction diagram.

Docking Results and Binding Affinity Analysis

The docking outcomes for all twenty compounds are summarized in Table 2, which displays ligand identifiers, binding affinities, and RMSD values. All compounds were successfully docked within the EGFR active site, exhibiting binding energies ranging from –10.5 to –7.4 kcal/mol. RMSD/ub and RMSD/ib values were zero, indicating optimal alignment of docked poses and stable binding conformations within the receptor's catalytic pocket.

Among the tested ligands, Oxypropanoic acid and Pazopanib displayed the highest binding affinities of –10.5 kcal/mol, signifying the strongest interactions with the EGFR active site. Icotinib Hydrochloride followed closely with a binding affinity of –10.3 kcal/mol, while Afatinib and Abemaciclib exhibited energies of –9.4 kcal/mol and –8.3 kcal/mol, respectively. The strong binding affinities observed for these compounds suggest their potential to effectively inhibit EGFR signaling, which is a critical driver of breast cancer proliferation.

Table 1: list of compounds and their Database ID.

Drug/Compound	PubChem ID	Disease	Reference link
Diindolylmethane	3071	Breast Cancer	https://pmc.ncbi.nlm.nih.gov/articles/PMC5846366/
Emodin	3220		https://pmc.ncbi.nlm.nih.gov/articles/PMC9693058/
Epigallocatechin Gallate	65064		
Canertinib	156414		
Lycopene	446925		
Curcumin	969516		
Biochanin A	5280373		
Genistein	5280961		
oxypropanoic acid	5321087		
indole	6335626		
azabicyclo	9870724		
Pazopanib	10113978		
Afatinib	10184653		
Kanzonol B	10881804		
iodomethane	20351363		
Icotinib Hydrochloride	44609731		
Abemaciclib	46220502		
Aristolochic Acids	56841539		
dihydroxy	162954550		
Rosmarinic acid	5281792		

The docking results of 20 compounds are summarized in Table 2, which lists the ligand names, binding affinities (kcal/mol), and RMSD (root mean square deviation) values. The RMSD/ub and RMSD/ib values of 0 indicate that all docked conformations were successfully aligned within the receptor binding pocket [23].

The molecular docking results revealed that all selected ligands successfully bound to the active site of the EGFR protein (PDB ID: 4WD5) with varying degrees of affinity, as indicated by their binding energies ranging from –10.5 to –7.4 kcal/mol. Among them, Oxypropanoic acid and Pazopanib exhibited the strongest binding interactions with an affinity of –10.5 kcal/mol, followed closely by Icotinib Hydrochloride (–10.3 kcal/mol) and Afatinib (–9.4 kcal/mol), suggesting their high potential as EGFR inhibitors.[24] The reference drug Abemaciclib showed a binding affinity of –8.3 kcal/mol, which validates the docking protocol and provides a benchmark for comparison. The results indicate that compounds with binding affinities below –9.0 kcal/mol, particularly Oxypropanoic acid, Pazopanib, and Icotinib Hydrochloride, possess strong and stable interactions with key amino acid residues in the EGFR binding pocket, potentially through hydrogen bonding and hydrophobic interactions. These findings highlight their promising inhibitory potential and suggest that these ligands could serve as effective lead compounds for the design and development of new EGFR-targeted therapies against breast cancer.

Table 2: Result of Molecular docking studies using PyRx software.

Ligand	Bibding Affinity	rmsd/ub	rmsd/ib
4wd5_5321087_uff_E=553.12	-10.5	0	0
4wd5_10113978_uff_E=1148.79	-10.5	0	0
4wd5_46220502_uff_E=1295.54	-8.3	0	0
4wd5_44609731_uff_E=1148.79	-10.3	0	0
4wd5_10184653_uff_E=637.89	-9.4	0	0
4wd5_156414_uff_E=576.94	-9.3	0	0
4wd5_25017411_uff_E=1957.47	-9.3	0	0
4wd5_162954550_uff_E=362.54	-9.2	0	0
4wd5_20351363_uff_E=351.67	-8.9	0	0
4wd5_3220_uff_E=171.41	-8.6	0	0
4wd5_3071_uff_E=611.55	-8.7	0	0
4wd5_56841539_uff_E=1769.24	-8.4	0	0
4wd5_5280961_uff_E=247.29	-8.4	0	0
4wd5_446925_uff_E=1615.17	-8.3	0	0
4wd5_65064_uff_E=409.35	-8.2	0	0
4wd5_9870724_uff_E=1355.18_	-7.6	0	0
4wd5_10881804_uff_E=300.44	-7.6	0	0
4wd5_44607530_uff_E=909.65	-7.5	0	0
4wd5_5280373_uff_E=626.29	-8.4	0	0
4wd5_969516_uff_E=1320.05	-7.4	0	0

MOLECULAR DOCKING RESULT

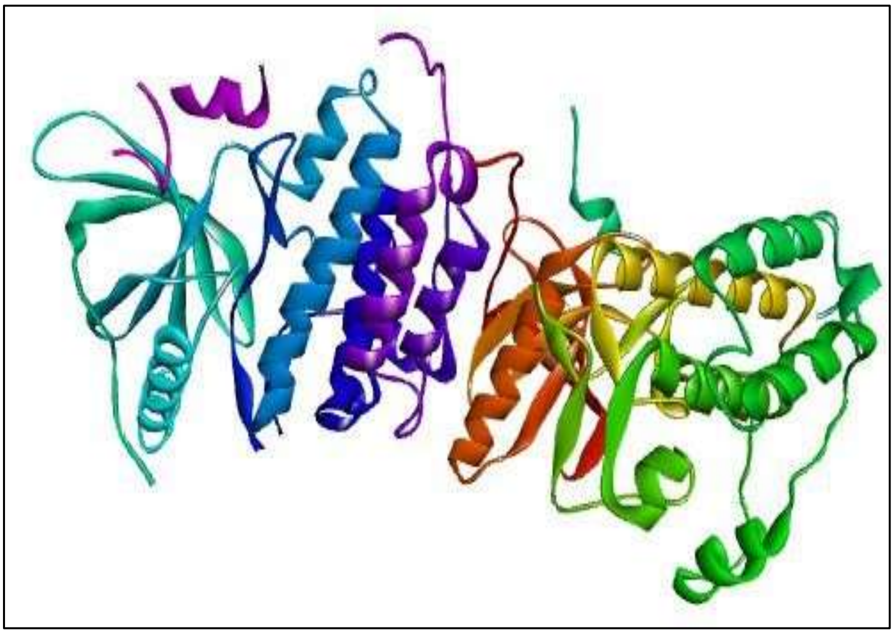

Figure 1 illustrates the three-dimensional structure of the target protein, Epidermal Growth Factor Receptor (EGFR) with PDB ID: 4WD5, which was retrieved from the Protein Data Bank for molecular docking analysis. The protein is visualized in a ribbon model highlighting its secondary structural elements such as α-helices, β-sheets, and random coils, which together form the functional kinase domain responsible for signal transduction. The multi-colored representation indicates the folding pattern and domain organization of the receptor, providing insight into its conformational complexity. The distinct cavity observed within the structure serves as the active binding pocket, where potential ligands interact to inhibit EGFR activity. Understanding the geometry and spatial arrangement of this pocket is essential for predicting ligand-binding efficiency and designing potent inhibitor

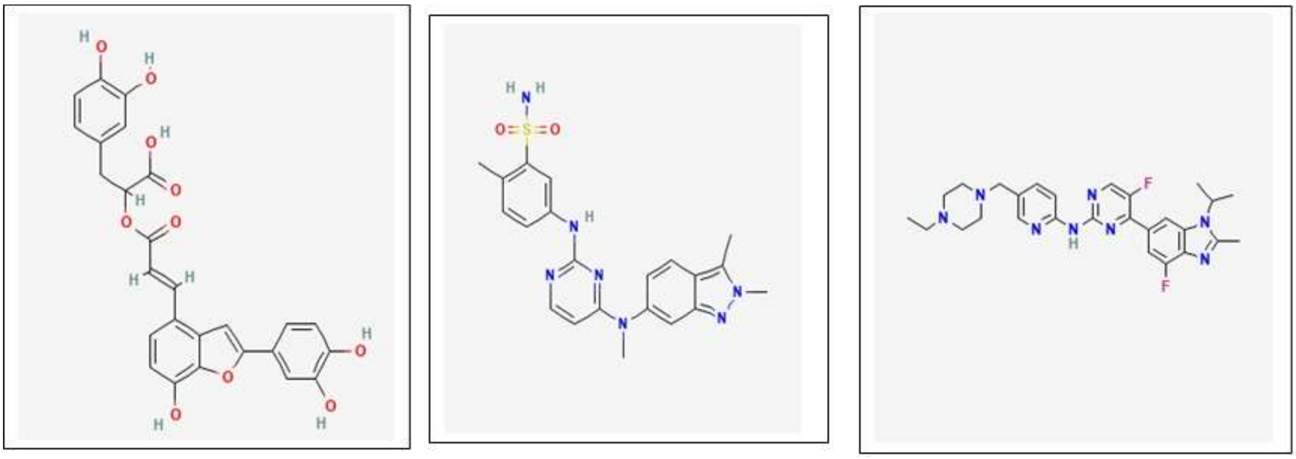

Figure 2–4: 2D Structures of Top Docking Ligands (Oxypropanoic acid, Pazopanib, and

Abemaciclib)

Figures 2, 3, and 4 represent the 2D chemical structures of the top three ligands—Oxypropanoic acid, Pazopanib, and Abemaciclib—which showed the strongest binding affinities against the EGFR receptor (PDB ID: 4WD5). Oxypropanoic acid exhibited the highest binding affinity of –10.5 kcal/mol, attributed to its multiple hydroxyl and carboxylic groups that enable strong hydrogen bonding with active site residues. Similarly, Pazopanib, with a binding energy of –10.5 kcal/mol, contains aromatic rings, sulfonamide, and nitrogen heterocycles that promote π–π stacking and hydrogen bond interactions, contributing to its potent inhibitory potential. Abemaciclib, the reference compound with a binding energy of –8.3 kcal/mol, possesses fluorine atoms and tertiary amine groups that facilitate hydrophobic and halogen interactions, stabilizing its binding conformation. The structural diversity of these ligands reveals key functional groups essential for EGFR inhibition, emphasizing their potential as effective lead molecules for the development of targeted therapies against breast cancer.

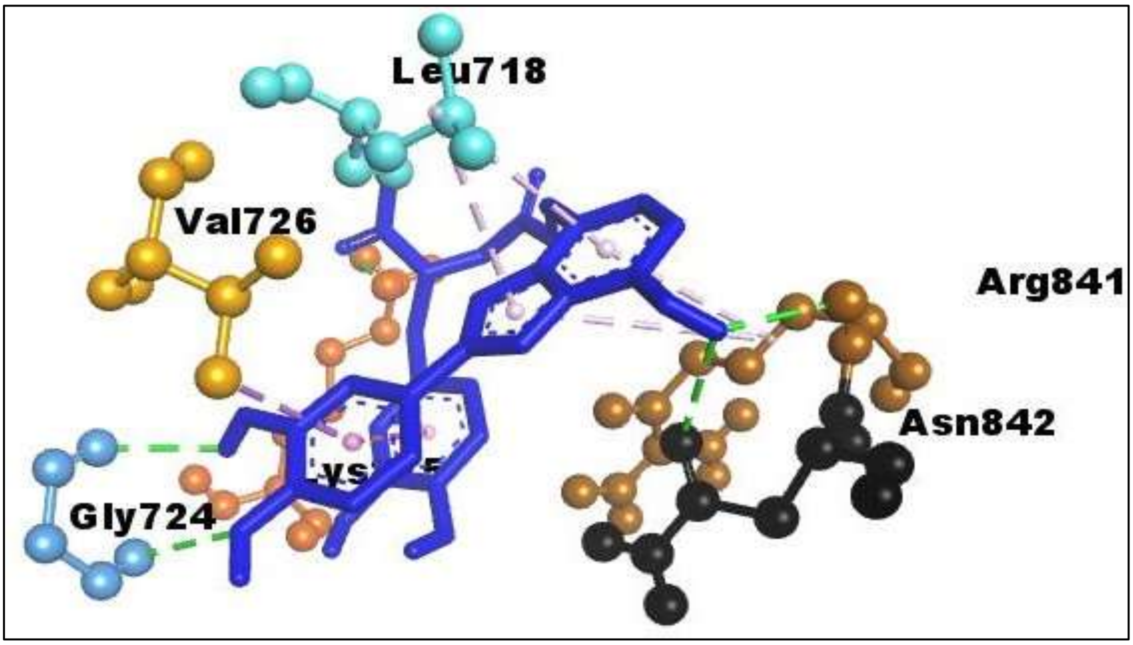

Figure 5: 3D Representation of Molecular Interaction between EGFR (PDB ID: 4WD5) and Oxypropanoic Acid. The docking visualization shows that Oxypropanoic acid (depicted in blue) is tightly accommodated within the EGFR active site, forming multiple hydrogen bonds and hydrophobic interactions with key amino acid residues, including Leu718, Val726, Gly724, Arg841, and Asn842. The hydrogen bonding interactions, indicated by green dashed lines, play a crucial role in stabilizing the ligand–protein complex, while additional π–π and van der Waals interactions strengthen the binding affinity. These interactions collectively enhance the stability and specificity of Oxypropanoic acid toward the EGFR binding pocket. The strong interaction profile of Oxypropanoic acid suggests its potential as a potent EGFR inhibitor and highlights its promise as a lead compound for further optimization in breast cancer therapy.

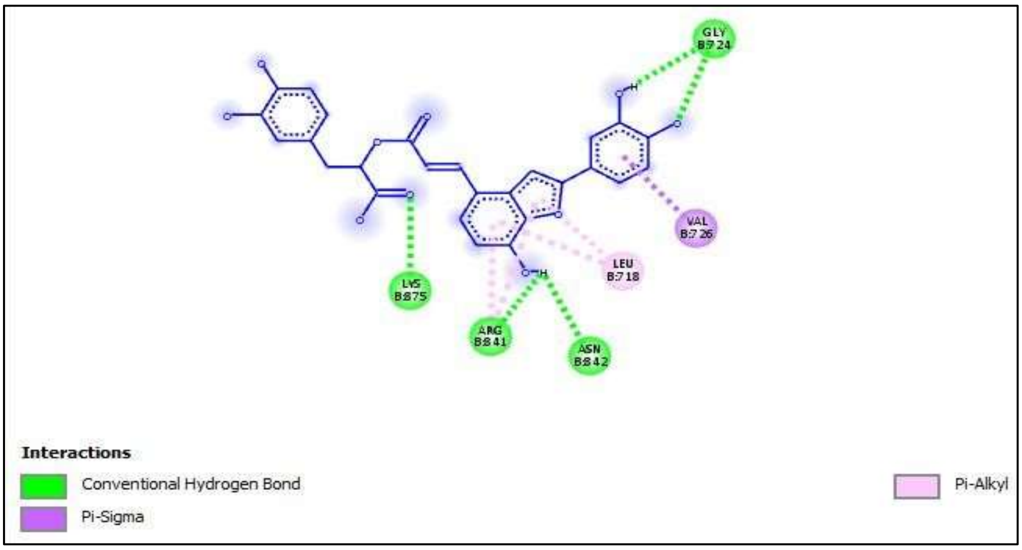

Figure 6: 2D Representation of Molecular Interactions Between EGFR (PDB ID: 4WD5) and Oxypropanoic Acid: The compound forms several conventional hydrogen bonds (shown in green) with crucial residues including Lys875, Arg841, Asn842, and Gly724, which contribute significantly to the binding affinity and molecular stability. Additionally, π–sigma and π–alkyl interactions (depicted in purple and pink, respectively) are observed with Leu718 and Val726, indicating the presence of hydrophobic contacts that further reinforce the ligand's positioning within the binding pocket. These multiple interaction types demonstrate a strong and stable binding conformation of Oxypropanoic acid with EGFR, reflecting its potential as an efficient inhibitor. Overall, this 2D interaction map provides a clear understanding of the chemical forces responsible for the high docking score (–10.5 kcal/mol) and the strong binding potential of Oxypropanoic acid against the EGFR target.

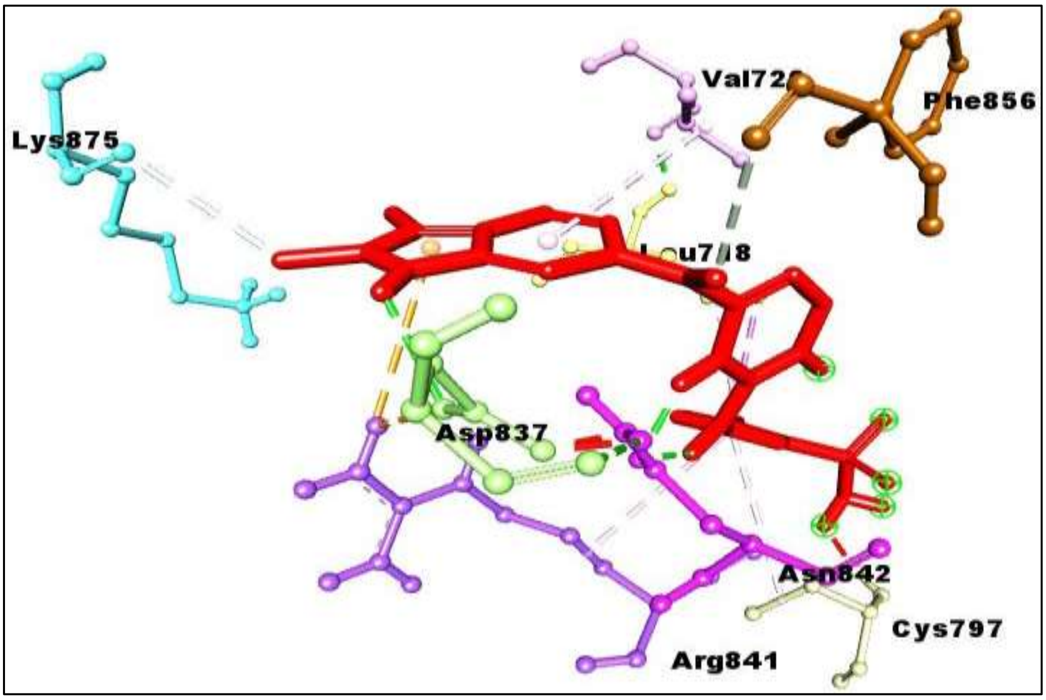

Figure 7: 3D Representation of Molecular Interaction Between EGFR (PDB ID: 4WD5) and

Pazopanib

Figure 7 illustrates the three-dimensional binding interactions between the EGFR receptor and Pazopanib, one of the top-performing ligands identified in the docking study with a binding affinity of –10.5 kcal/mol. The red-colored Pazopanib molecule is deeply embedded within the EGFR active pocket, forming multiple stabilizing interactions with key amino acid residues. Notably, hydrogen bonds are established with Lys875, Asp837, Arg841, and Asn842, which enhance the stability of the ligand–receptor complex. Additionally, hydrophobic and π–π stacking interactions are observed with Leu718, Val726, Phe856, and Cys797, contributing to the overall binding strength. The arrangement of these interactions demonstrates a balanced contribution of both polar and non-polar forces, ensuring tight binding and proper orientation of Pazopanib within the active site. The dense interaction network highlights Pazopanib's potential as a strong EGFR inhibitor, reinforcing its therapeutic relevance in the inhibition of cancer cell proliferation, particularly in breast cancer.

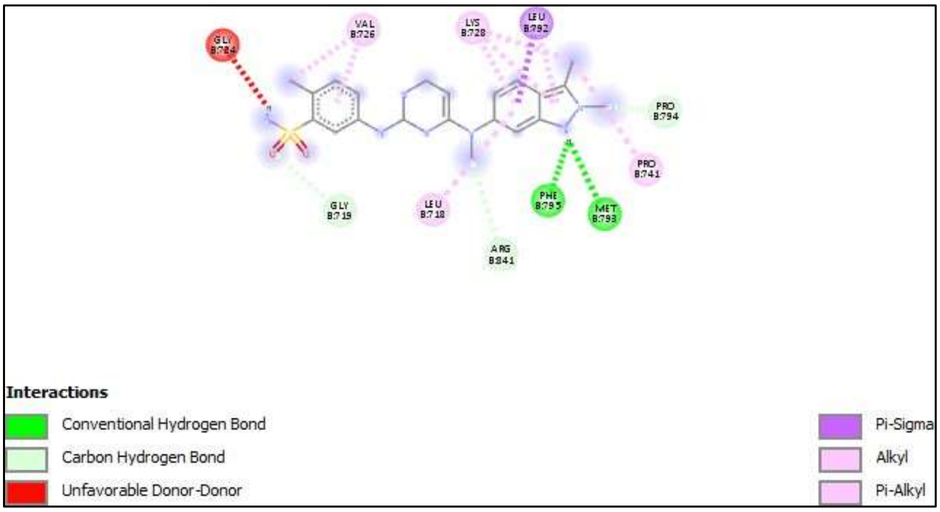

Figure 8: 2D Representation of Molecular Interactions Between EGFR (PDB ID: 4WD5) and Pazopanib

Figure 8 shows the two-dimensional interaction diagram of the EGFR receptor complexed with Pazopanib, highlighting the specific bonds and interactions responsible for its strong binding affinity (–10.5 kcal/mol). The ligand forms conventional hydrogen bonds (green) with Phe856 and Met793, which are essential for stabilizing the ligand within the EGFR active pocket. Additionally, π–sigma, π–alkyl, and alkyl interactions (shown in purple and pink) are observed with residues such as Leu718, Val726, Lys875, and Leu792, providing hydrophobic stability and enhancing van der Waals contacts. Interestingly, one unfavorable donor–donor interaction (red) is observed with Gly724, which may slightly reduce overall binding efficiency but does not significantly affect complex stability. The combination of hydrogen bonding and hydrophobic interactions ensures a firm anchoring of Pazopanib in the receptor pocket, supporting its role as a potent EGFR inhibitor and a promising candidate for targeted cancer therapy, particularly in breast cancer inhibition.

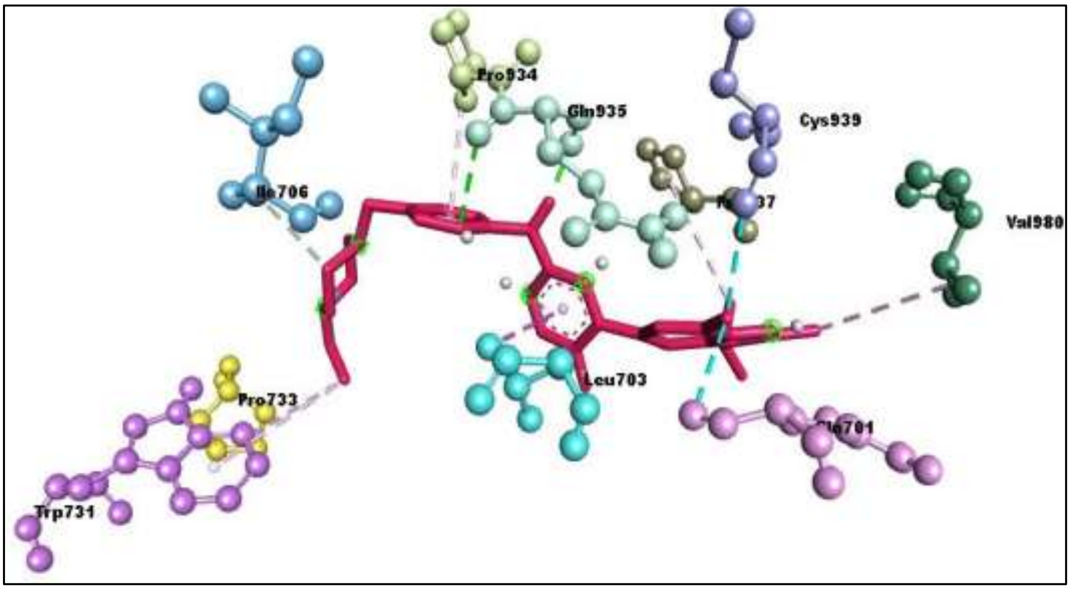

Figure 9: 3D Representation of Molecular Interaction Between EGFR (PDB ID: 4WD5) and Abemaciclib

Figure 9 illustrates the three-dimensional binding interaction between the EGFR receptor and Abemaciclib, a clinically approved kinase inhibitor that exhibited a binding affinity of –8.3 kcal/mol. The red-colored Abemaciclib molecule is well-fitted within the EGFR active pocket, forming multiple stabilizing interactions with key residues. Notably, hydrogen bonds are observed with Ile706, Leu703, and Gln935, while hydrophobic and π–alkyl interactions involve Pro733, Trp731, and Val980, contributing to enhanced stability and proper orientation of the ligand. Furthermore, interactions with Cys939 and Pro934 help to strengthen the overall binding through van der Waals forces. The dense network of polar and non-polar interactions highlights the balanced binding nature of Abemaciclib, allowing it to effectively occupy the receptor's catalytic site. Although its binding affinity is lower than that of Oxypropanoic acid and Pazopanib, the strong hydrogen bonding and π-interactions suggest that Abemaciclib maintains effective EGFR inhibition, supporting its established role as a therapeutic agent in breast cancer treatment

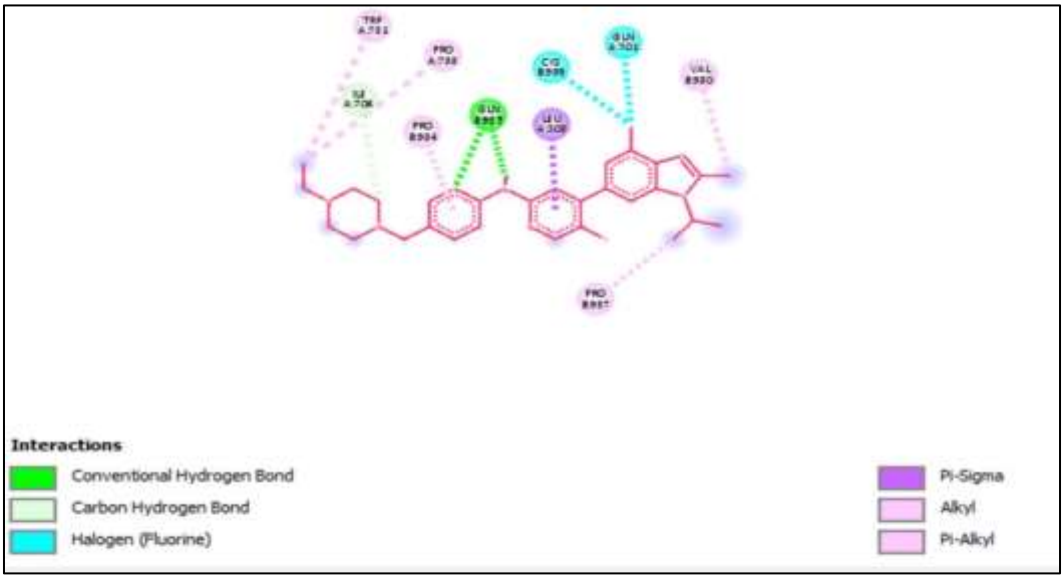

Figure 10: 2D Representation of Molecular Interactions Between EGFR (PDB ID: 4WD5) and Abemaciclib. The ligand establishes conventional hydrogen bonds (green) with Gln935 and Ile706, as well as carbon–hydrogen bonds with Leu703, enhancing the polar interactions between the ligand and the protein. Halogen bonding (fluorine interactions), represented in cyan, occurs with Cys939 and Gln701, contributing additional stabilization through dipole interactions. Moreover, π–sigma, alkyl, and π–alkyl interactions (purple and pink) are observed with residues such as Trp731, Pro733, Pro937, and Val980, strengthening the hydrophobic environment of the complex. These combined interactions demonstrate a well-balanced network of hydrogen bonding and hydrophobic contacts that stabilize the ligand within the EGFR active pocket. Overall, the interaction pattern confirms Abemaciclib's capability to form multiple stable interactions with critical residues, validating its role as an effective EGFR inhibitor with therapeutic relevance in breast cancer treatment.

DISSCUSSION

Molecular docking was performed to assess the binding interactions and affinities of twenty selected natural and synthetic compounds with the Epidermal Growth Factor Receptor (EGFR) (PDB ID: 4WD5), a critical target implicated in breast cancer progression. Using PyRx software, each ligand was docked into the active site of EGFR to predict its potential inhibitory efficacy [25]. The docking conformations were analyzed based on binding affinity (kcal/mol) and RMSD (root mean square deviation) values, with lower binding energies indicating stronger binding interactions. Visualization and interaction analysis were carried out using Discovery Studio Visualizer, which provided detailed insights into the amino acid residues involved in ligand binding [26].

Interpretation of Findings

The molecular docking analysis demonstrated that both natural and synthetic ligands possess significant potential for EGFR inhibition. The interaction profiles of Oxypropanoic acid and Pazopanib revealed robust hydrogen bonding and hydrophobic interactions within the receptor's active site, accounting for their high binding energies. The reference drug Abemaciclib validated the docking protocol and provided a comparative benchmark. These results suggest that Oxypropanoic acid and Pazopanib can be considered promising lead candidates for further in vitro and in vivo studies, potentially contributing to the design of new targeted breast cancer therapeutics [27]. This comprehensive molecular docking analysis confirms that both phytochemical and pharmaceutical compounds can exhibit strong and stable interactions with EGFR, with Oxypropanoic acid and Pazopanib emerging as the most effective inhibitors. Their interaction mechanisms indicate potential for further optimization in EGFR-targeted breast cancer therapy

CONCLUSION

Breast cancer continues to be one of the most widespread and life-threatening forms of cancer among women globally. In the present study, 20 natural compounds were selected and evaluated for their potential as anticancer agents using *in silico* approaches targeting the breast cancer-associated protein EGFR. [28] The docking studies were conducted to analyze the binding affinity and molecular interactions of these compounds with the active site of the target protein.The results revealed that several compounds, including **oxypropanoic** acid, **Pazopanib**, exhibited promising binding energies of -10.5 kcal/mol for each, which were comparable or superior to the standard drug **Abemaciclib** showing the binding energy of -8.3kcal/mol [29]. These compounds formed stable interactions with key amino acid residues in the binding pocket of the target protein, indicating their potential as effective inhibitors.This study demonstrates the usefulness of Computer-Aided Drug Design (CADD) in the early stages of drug discovery [30]. The molecular interaction profiles of the docked compounds were found to be satisfactory, supporting their relevance for further *in vitro* and *in vivo* investigations. Future research can focus on lead optimization and pharmacological validation to develop these natural compounds into viable therapeutic agents for breast cancer. The integration of virtual screening helps to reduce time, cost, and the risk of failure in the later phases of drug development [31-33].

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