In Silico Evaluation of Anticancer Potential of 3,4,5-Trihydroxybenzoic acid Derivatives from *Bougainvillea* Species Using Molecular Docking and ADMET Prediction

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Abstract- This study explores the anticancer potential of phytochemical derivatives derived from Bougainvillea glabra through an in silico molecular docking approach. The plant material was shade-dried, finely powdered, and subjected to maceration for the extraction of bioactive constituents. Following solvent evaporation, standard analytical techniques were employed to identify and characterize the major phytochemicals. Among the identified compounds, 3,4,5-trihydroxybenzoic acid was selected as the lead scaffold and structurally modified using various aromatic aldehydes and aromatic amines to generate a series of derivatives for computational evaluation. Molecular docking studies were performed using Molegro Virtual Docker (version 6.0) against the target protein (PDB ID: 6CUC: represents a protein involved in cancer progression such as a kinase, regulatory enzyme, or signaling protein). Comparative analysis was conducted with the co-crystallized ligand and the standard anticancer drug Adriamycin. The results demonstrated that several synthesized derivatives exhibited improved binding affinity and interaction stability within the active site of the protein. Notably, the aromatic amine derivative coded AA6 showed the highest binding affinity, with a MolDock score of −146.533. This compound established multiple stable hydrogen bond interactions with key amino acid residues, including Glu31, Lys16, Gly15, Thr35, Gly13, Asp33, Val14, Ala18, and Lys17, indicating strong and favorable binding. Furthermore, physicochemical and ADMET properties were evaluated using Molinspiration and PreADMET. The integrative application of phytochemical analysis and computational modeling underscores the efficiency of in silico strategies in accelerating preclinical drug discovery while minimizing cost, time, and reliance on animal experimentation.

Keywords: Docking, ADMET, In Silico, 3,4,5-Trihydroxybenzoic acid, *Bougainvillea Glabra*

I. INTRODUCTION

Lung cancer is a heterogeneous group of malignant epithelial tumors arising from the tracheobronchial tree, characterized by stepwise accumulation of genetic and epigenetic alterations that drive uncontrolled proliferation, invasion, and metastasis. Onthe basis of histological and molecular feature lung cancer is mainly classified as Adenocarcinoma (ADC) and Squamous cell carcinoma (SCC),

In lung cancer as in other malignancies, tumourigenesis relates to activation of growth promoting proteins [e.g., v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS), epidermal growth factor receptor (EGFR), BRAF, MEK-1, HER2, MET, ALK and rearranged during transfection (RET)] as well as inactivation of tumour suppressor genes [e.g., *P53,* phosphatase with tensin homology (*PTEN*), *LKB-1*] (1). Activation of growth promoting oncogenes can occur by gene amplification or other genetic alterations including point mutations and structural rearrangements leading to uncontrolled signalling through oncogenic pathways. “Oncogene addiction” results when cell survival depends on continued activation of the aberrant signalling (2,3) making them ideal candidates for targeted therapies. Oncogenic driver mutations have been identified in over 50% of lung ADC and are almost always exclusive of other driver mutations (4,5)

Tyrosine kinase inhibitors (TKIs) are targeted therapies that treat many kinds of cancer. They block certain substances in cancerous cells that manage how fast the cells grow and divide. Tyrosine kinase inhibitors can't cure cancer, but they can put cancer into long-term remission or help people with certain cancers to live longer.Tyrosine kinase inhibitors disrupt the process that manages how your cells grow and divide. That process involves:

Growth factors: Chemicals that control cell growth.Tyrosine kinases: Enzymes inside your cells that control cell division.Growth factors flip the switch that activates tyrosine kinases. In turn, tyrosine kinases signal cells so they start to divide. The cells continue dividing until tyrosine kinases turn off. Normal tyrosine kinases turn on and off as needed.Treatment for chronic myeloid leukemia (CML) is a good example of how TKIs work. CML is a blood cancer that starts in the blood-forming myeloid cells (stem cells) in your bone marrow. When myeloid cells mutate, they make abnormal tyrosine kinase enzymes that turn on when the growth factor flips the switch. They never turn off.

Without an "off" switch, myeloid cells in your bone marrow divide and multiply uncontrollably, making it hard for your bone marrow to make other blood cells and platelets your body needs. Tyrosine kinase inhibitors treat CML by flipping the "on" switch to "off," blocking abnormal enzyme signals that make cancerous cells divide.(6)

Cancers Treated with Tyrosine Kinase Inhibitors

Tyrosine kinase inhibitors treat several kinds of cancer, including:

1. HER2-positive breast cancer.
2. Chronic lymphocytic leukemia.
3. Gastrointestinal stromal tumors.
4. Kidney cancer.
5. Waldenstrommacroglobulinemia.
6. Non-small cell lung cancer.
7. Melanoma.(6)

Recent Advancement in Cancer Therapy

The field of immunotherapy is undergoing rapid advancements, with novel approaches aimed at improving the efficacy and range of treatments available for various cancer types. Prominent strategies include CAR-T cell therapy, immune checkpoint inhibitors (ICIs), tumor-infiltrating lymphocytes (TIL) therapy, and cancer vaccines. These methods mark significant progress in leveraging the immune system to fight cancer more effectively. (7)

Overview of next-generation immunotherapy strategies

Chimeric antigen receptor (CAR) T cell therapy: Patient or donor-derived T cells are engineered to express CARs that recognize tumor antigens, followed by expansion of these modified T cells for re-administration.

Immune checkpoint inhibitors (ICIs): Tumor cells display PD-L1 and CD80 as immune surveillance evasion strategies. They interact with PD-1 and CTLA-4 displayed on T cells which serve as immune checkpoints that inhibit immune responses. ICIs such as anti-CTLA-4 and anti-PD-1/PD-L1 block receptors on T cells, preventing tumor-induced immune suppression and restoring T cell-mediated cytotoxicity.

Cancer vaccines/oncovaccines: Personalized cancer vaccines, derived from tumor cells, are sequenced, and neoantigens are identified to produce synthetic peptides, formulated into personalized vaccines capable of generating an immune response against tumor-specific antigens. Vaccines can be used in conjunction with CAR-T cells or other immunotherapies for enhanced efficacy.(7)

Rational for selection of 6CU6double knot toxin (DkTx): 6CUC represents a protein involved in cancer progression (such as a kinase, regulatory enzyme, or signaling protein), inhibiting its activity can suppress tumor growth, proliferation, or metastasis. Docking studies assess whether designed compounds can effectively bind to and inhibit this protein.

Computational Studies

It is typically the application of computer simulation and other forms of computation from numerical analysis and theoretical computer science to solve problems in various scientific disciplines. The field is

different from theory and laboratory experiments, which are the traditional forms of science and engineering. The scientific computing approach is to gain understanding through the analysis of mathematical models implemented on computers. Scientists and engineers develop computer programs and application software that model systems being studied and run these programs with various sets of input parameters. The essence of computational science is the application of numerical algorithms and computational mathematics. In some cases, these models require massive amounts of calculations (usually floating-point) and are often executed on supercomputers or distributed computing platforms.(8)

Following are the names and descriptive information of computational methods used:

1. Lipinski Rule of Five

Lipinski rule of 5 helps in distinguishing between drug like and non drug like molecules. It predicts high probability of success or failure due to drug likeness for molecules complying with 2 or more of the 5rules.Lipinski's Rule of Five is a guideline in drug discovery to predict if a compound has good oralbioavailability, stating an orally active drug generally has no more than one violation of these criteria (9)

a. Molecular mass less than 500 Dalton
b. High lipophilicity (expressed as LogP less than 5)
c. Less than 5 hydrogen bond donors
d. Less than 10 hydrogen bond acceptors
e. Molar refractivity should be between 40-130

2. ADMET Studies

The PreADMET online web tool was utilized to predict the physicochemical properties, ADME (absorption, distribution, metabolism, and excretion), and toxicity profiles of the desired ligands using the freely accessible web-based program (-https://preadmet.webservice.bmdrc.org/). The chemical structures of the ligands were submitted in SMILES format to evaluate key pharmacokinetic parameters such as human intestinal absorption, Caco-2 cell permeability, blood–brain barrier penetration, plasma protein binding, and cytochrome P450 inhibition potential. In addition, toxicity predictions including Ames mutagenicity, carcinogenicity, and acute toxicity were assessed to estimate the safety profile of the compounds. PreADMET provides a comprehensive in silico platform for early-stage screening of drug-like molecules, helping to identify potential pharmacokinetic and toxicity liabilities and supporting the rational selection and optimization of promising ligands for further experimental studies. (10)

3. Molinspiration

The Molinspiration online web tool was used for the prediction of physicochemical properties of the desired ligands using the online program available at https://www.molinspiration.com/. This tool enables rapid in silico evaluation of key molecular descriptors that are essential for assessing drug-likeness and oral bioavailability. The ligands were uploaded in appropriate structural formats, and parameters such as molecular weight, octanol–water partition coefficient (logP), number of hydrogen bond donors and acceptors, topological polar surface area (TPSA), number of rotatable bonds, and Lipinski's rule of five compliance were calculated. These physicochemical properties provide valuable insights into the absorption, distribution, and permeability characteristics of the compounds. The Molinspiration predictions assisted in the preliminary screening and optimization of ligands by identifying molecules with favorable drug-like characteristics prior to further molecular docking and pharmacokinetic studies.

4. Molecular Docking

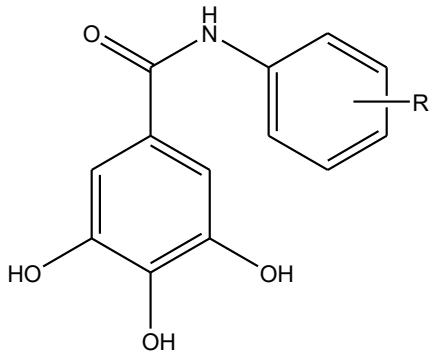
Molecular docking studies were performed using Molegro Virtual Docker (MVD) version6.0 to investigate the binding interactions between the selected ligands and the target protein. The three-dimensional structure of the protein was retrieved from the Protein Data Bank and prepared by removing water molecules, adding hydrogen atoms, and assigning appropriate charges. Ligand structures were energy-minimized before docking. The active site was identified based on the co-crystallized ligand or cavity detection module of MVD. Docking simulations were carried out using the MolDock scoring function with a grid resolution of 0.30 Å, and

multiple poses were generated for each ligand. The best docking conformation was selected based on the lowest MolDock score and favorable interaction energies. Protein–ligand interactions, including hydrogen bonding, hydrophobic interactions, and electrostatic forces, were analyzed to understand the binding affinity and molecular mechanism of action.(12-14)

II. MATERIAL AND METHOD

All computational studies were carried out using a latest-configuration computer system equipped with high-performance processing capabilities to ensure accurate and efficient execution of molecular modeling tasks. Molecular docking and related in silico analyses were performed using Molegro Virtual Docker (MVD) software. The advanced hardware configuration enabled rapid conformational searching, precise scoring, and reliable visualization of protein–ligand interactions. Use of updated computational resources minimized calculation errors and reduced processing time, thereby enhancing the reliability and reproducibility of the docking results. This computational approach provided a robust platform for evaluating binding affinity and interaction patterns of the selected ligands with the target protein at the molecular level.

DATA SET OF COMPOUNDS



Where R= Methyl, Chloro, Bromo, Methoxy, Nitro etc

Methods

computational algorithms that predict ligand binding poses and affinities by exploring conformational space within a protein's binding pocket, categorized mainly by flexibility handling and search/scoring strategies.(15)

1. Methodology of ROF(Rule of Five):

Lipinski's Rule of Five was carried out using the online web program provided by the SCFBio, IIT Delhi drug design server. The chemical structures of the selected ligands were first prepared and converted into SMILES format using standard chemical drawing software. These SMILES strings were then submitted to the Lipinski rule prediction web interface. Upon submission, the server automatically calculated key drug-likeness parameters, including molecular weight, octanol–water partition coefficient (logP), number of hydrogen bond donors, and number of hydrogen bond acceptors. The results were analyzed to determine compliance with Lipinski's Rule of Five, which predicts the oral bioavailability of compounds. This online tool provides a rapid and reliable in silico assessment to screen ligands for drug-like properties prior to further pharmacokinetic and biological evaluation. (16,17)

2. Methodology of Molinspiration

prediction of physicochemical properties was carried out using the Molinspiration online web program. The chemical structures of the selected ligands were initially drawn using standard chemical drawing software and converted into SMILES format. These SMILES strings were then submitted to the Molinspiration property calculation interface. Upon submission, the server automatically calculated important physicochemical parameters such as molecular weight, octanol–water partition coefficient (logP), number of hydrogen bond donors and acceptors, topological polar surface area (TPSA), and number of rotatable bonds. The generated data were used to assess the drug-likeness and oral bioavailability of the ligands in accordance with established medicinal chemistry guidelines.(18-20)

3. Methodology of ADMET

Structure preparation: Draw the chemical structure of the desired ligand using a chemical drawing software (e.g., ChemDraw) and convert it into SMILES format.

Access the web tool: Open the PreADMET web server using the official website.

Input of ligand: Paste the SMILES string of the ligand into the input box provided on the PreADMET interface or upload the structure file if the option is available.

Selection of parameters: Choose the required prediction modules, including physicochemical properties, ADME parameters (such as human intestinal absorption, Caco-2 permeability, blood–brain barrier penetration, plasma protein binding, and CYP450 inhibition), and toxicity prediction (Ames test, carcinogenicity, and acute toxicity).

Submission of job: Click on the submit or run option to initiate the prediction process.

Result analysis: After computation, the predicted results are displayed on the screen in tabulated form.

Interpretation: The obtained data are analyzed to assess the drug-likeness, pharmacokinetic behavior, and safety profile of the ligands, aiding in the selection and optimization of promising compounds for further experimental studies. (21,22)

Molecular Docking: The molecular docking procedure was carried out using Molegro Virtual Docker (MVD) for in silico evaluation of ligand–protein interactions. The three-dimensional structure of the target protein was retrieved from the Protein Data Bank and prepared by removing co-crystallized ligands and water molecules, followed by addition of hydrogen atoms and assignment of appropriate charges. Ligand structures were drawn, energy-minimized, and imported into MVD. The active binding site was identified using the cavity detection module of the software. Docking simulations were performed using the MolDock scoring function with default parameters, and multiple binding poses were generated for each ligand. The best docked conformation was selected based on the lowest MolDock score and favorable interaction energy. The protein–ligand interactions, including hydrogen bonds and hydrophobic contacts, were analyzed and visualized to understand the binding mode and affinity of the ligands.(23,24)

III. RESULT AND DISCUSSION

Molinspiration: The physicochemical properties of the fifteen substituted derivatives were evaluated using the Molinspiration online web tool, and the calculated results are presented in Table 1.

Table 1: Drug likeness properties of substituted derivatives

NO.	LOgP	TPSA	natoms	MW	nON	nOHNH	nviolations	Nrotb	Volm
AA1	1.12	102.67	19	260.25	6	4	0	2	223.30
AA2	0.72	102.67	19	260.25	6	4	0	2	223.30
AA3	0.67	102.67	18	246.22	6	4	0	2	206.74
AA4	0.50	102.67	18	246.22	6	4	0	2	206.74
AA5	0.28	102.67	18	246.22	6	4	0	2	206.74
AA6	1.48	147.31	22	305.24	8	6	1	3	245.91
AA7	1.58	99.02	20	275.26	6	4	0	3	236.44
AA8	1.60	99.02	20	275.26	6	4	0	3	236.44
AA9	1.62	99.02	20	275.26	6	4	0	3	236.44
AA10	2.38	89.78	19	324.13	5	4	0	2	228.78
AA11	2.13	135.61	22	324.68	8	4	0	3	247.76
AA12	2.13	135.61	22	324.68	8	4	0	3	247.76
AA13	2.85	89.78	20	314.12	5	4	0	2	237.96
AA14	1.43	89.78	20	273.29	5	4	0	2	244.01
AA15	2.39	89.78	20	273.29	5	4	0	2	244.01

The Molinspiration analysis of the designed 3,4,5-Trihydroxybenzoic acid derivatives indicated that the majority of compounds exhibited acceptable physicochemical properties and complied with standard drug-likeness criteria. Out of the fifteen designed derivatives, only AA6showed violations of

the evaluated parameters, suggesting potential limitations in their oral bioavailability or drug-like behavior. The remaining fourteen derivatives satisfied the required criteria without any violations, indicating favorable physicochemical profiles.

The physicochemical evaluation indicates that most derivatives (AA1–AA15) comply with Lipinski's Rule of Five, as reflected by zero violations in all compounds except AA6, which shows one violation due to its relatively higher TPSA (147.31 Å²) and increased hydrogen bonding capacity (nON = 8, nOHNH = 6). The molecular weight of all compounds remains below 500 Da, and LogP values (0.28–2.85) suggest favorablelipophilicity and potential membrane permeability. Compounds AA7–AA15 demonstrate balanced lipophilicity (LogP ~1.4–2.8) with moderate TPSA values (<140 Å²), indicating good oral bioavailability potential. AA6, although slightly more polar and possessing one rule violation, may exhibit enhanced binding interactions due to its higher hydrogen bonding capacity. Overall, the dataset suggests that the majority of synthesized derivatives possess drug-like properties with acceptable pharmacokinetic profiles, supporting their suitability for further anticancer investigation.

RESULT OF ADME: The ADMET properties of the fifteen substituted derivatives were evaluated using the PreADMET online web tool, and the calculated results are presented in Table 2and 3

Table 2: ADME properties of designed derivatives

COMP	BBB	CaCO2	CYP2D6	HIA	MDCK	PGP	PPB	SKIN P.
AA1	0.166	16.00	Non	75.62	33.23	Non	74.74	-4.44
AA2	0.119	14.91	Non	75.62	26.19	Non	67.81	-4.43
AA3	0.265	10.06	Non	74.04	15.69	Non	67.40	-4.49
AA4	0.095	13.42	Non	74.55	4.529	Non	67.92	-4.63
AA5	0.077	0.490	Non	74.56	3.909	Non	69.70	-4.64
AA6	0.056	14.52	Non	39.78	16.68	Non	83.69	-4.44
AA7	0.159	18.80	Non	78.49	67.91	Non	81.02	-4.25
AA8	0.167	4.307	Non	78.49	34.01	Non	82.98	-4.28
AA9	0.282	1.827	Non	78.49	10.06	Non	82.60	-4.28
AA10	0.704	19.46	Non	86.66	0.40	Non	100.0	-4.09
AA11	0.044	17.96	Non	70.25	0.833	inhibitor	97.39	-4.20
AA12	0.232	8.751	Non	70.25	12.73	inhibitor	97.23	-4.20
AA13	1.160	17.98	Non	87.57	32.83	Non	95.53	-4.13
AA14	1.423	5.506	Non	81.17	187.1	Non	86.26	-3.98
AA15	0.577	10.71	Non	81.17	108.5	Non	88.06	-4.01

The ADMET prediction results indicate that most compounds exhibit moderate to low blood–brain barrier (BBB) penetration, with values generally below 1.0, suggesting limited central nervous system exposure. Compounds AA13 and AA14 show relatively higher BBB values, whereas AA6 demonstrates minimal BBB permeability (0.056), which may reduce the risk of CNS-related side effects for an anticancer candidate. Caco-2 and MDCK permeability values suggest variable intestinal absorption and membrane transport characteristics. Compounds AA7, AA14, and AA15 display comparatively higher MDCK permeability, indicating better passive diffusion potential. Human intestinal absorption (HIA) is generally favorable (>70%) for most derivatives, except AA6 (39.78%), suggesting comparatively lower oral absorption for this compound. Importantly, all compounds are predicted as non-inhibitors of CYP2D6, indicating a low probability of metabolic drug–drug interactions. Only AA11 and AA12 show P-glycoprotein (PGP) inhibitory potential, which may influence drug efflux and bioavailability. Plasma protein binding (PPB) values are high for several compounds (AA10–AA15), indicating strong protein binding that may prolong systemic circulation but reduce free drug concentration. Skin permeability values (log Kp ≈ −4.0 to −4.6) indicate low transdermal permeability.

Overall, the ADMET profile suggests that most derivatives possess acceptable pharmacokinetic characteristics, with AA7, AA14, and AA15 showing comparatively balanced absorption and permeability properties, while AA6 demonstrates stronger polarity with limited absorption despite favorable docking performance.

Table 3: Result of Toxicity study of designed derivatives

COMP	AMES TEST	CARCINO MO	CARCINO RAT	HERG
AA1	mutagen	negative	positive	medium
AA2	mutagen	negative	positive	medium
AA3	mutagen	negative	positive	Medium
AA4	mutagen	negative	positive	medium
AA5	mutagen	negative	positive	medium
AA6	mutagen	negative	positive	medium
GA7	mutagen	negative	positive	Medium
AA8	mutagen	negative	Positive	medium
AA9	mutagen	negative	positive	medium
AA10	mutagen	negative	positive	medium
AA11	mutagen	negative	positive	medium
AA12	mutagen	negative	positive	medium
AA13	Non mutagen	negative	positive	medium
AA14	mutagen	negative	positive	medium
AA15	mutagen	negative	positive	medium

The ADME and toxicity profiles of the designed 3,4,5-Trihydroxybenzoic acid derivatives were evaluated using the PreADMET online web tool to assess their pharmacokinetic behavior and safety. The in silico analysis revealed that most of the derivatives exhibited favorable human intestinal absorption and acceptable Caco-2 cell permeability, indicating good potential for oral bioavailability. The predicted blood–brain barrier penetration values suggested that the compounds were unlikely to cause undesirable central nervous system effects. Plasma protein binding predictions showed moderate binding affinity, which is desirable for maintaining sufficient free drug concentration in systemic circulation. Furthermore, the majority of the derivatives demonstrated low risk of cytochrome P450 inhibition, suggesting a reduced likelihood of metabolic drug–drug interactions. Toxicity predictions, including Ames mutagenicity and carcinogenicity assessments, indicated that most compounds were non-mutagenic and non-carcinogenic. Overall, the PreADMET results support the favorable ADME characteristics and acceptable safety profiles of the designed 3,4,5-Trihydroxybenzoic acid derivatives, highlighting their potential as promising candidates for further experimental and biological investigations.

Molecular docking: Molecular docking studies were carried out using Molegro Virtual Docker (MVD) version 6.0 to assess the binding affinity and interaction patterns of the designed compounds with the target protein. The docking results are summarized in Table 4, while the detailed protein–ligand interactions are illustrated in Figure 1.

Table 4: Mol dock score, Hydrogen bond and Steric Interaction of Designed 3,4,5-Trihydroxybenzoic acid derivatives

COMP.	DOCKING SCORE	HYDROGEN BOND INTERACTON	STERICINTERACTION
AA-1	-125.175	Ala18, Lys16, Gly15, Gly13, Tyr32, Arg12	Ala18, Gly15, Ser17, Asp33, Arg12, Tyr32

AA-2	-130.696	Lys16, Gly15, Val14, Thr35, Tyr32, Arg12, Ser17, Gly13	Gly15, Asp33, Ser17, Tyr32, Arg12
AA-3	-123.376	Lys16, Gly15, Val14, Tyr32, Thr35, Arg12, Ser17, Gly13	Lys16, Arg12, Tyr32, Ser17, Asp33, Gly15
AA-4	-122.907	Lys16, Gly15, Tyr32, Arg12, Thr35	Tyr32, Ser17, Asp33
AA-5	-123.849	Lys16, Gly15, Tyr32, Thr35, Arg12, Ser17, Lys17	Gly13, Ser17, Tyr32
AA-6	-146.533	Gly13, Tyr32, Lys16, Gly60, Gly15, Val14	Arg12, Tyr32, Asp33, Ser17, Lys117, Gly15, Val29, Lys16.
AA-7	-123.956	Thr35, Lys16, Gly15, Val14, Ala18	Pro34, Ser17
AA-8	-134.267	Arg12, Tyr32, Thr35, Lys16, Gly15, Gly13	Gly15, Tyr32, Asp33, Ser17
AA-9	-128.835	Lys16, Gly15, Gly13, Arg12, Tyr32, Thr35, Lys117	Gly15, Asp33, Ala18, Ser17, Arg12, Tyr32
AA-10	-129.116	Thr35, Lys16, Gly15, Ala18	Pro34
AA-11	-130.948	Asp33, Thr35, Lys16, Gly15, Gly17, Glu31,val14,ala18	Tyr32, Pro34
AA-12	-132.806	Thr35, Lys16, Gly15, Val14, Ala18, Asp33	Tyr32, Pro34
AA-13	-124.588	Tyr32, Arg12, Thr58, Gly60, Asp57, Ser17, Thr35, Gly15	Tyr32, Thr35, Ser17, Gly13, Asp33
AA-14	-108.64	Gly31, Asp33, Ser17, Thr35, Gly15	Tyr32, Asp33, Gly13, Gly15, Ala18
AA-15	-125.175	Asp33, Thr35, Lys16, Gly15, Gly31, Ala18, Val14	Pro34
Std drug	-112.967	Tyr32,Ala18,Asp33 Ala146,Asn116	Glu31.Asp33,Gly15 Tyr32,Phe28,Ala18 Ala146,Asn116,Asp30

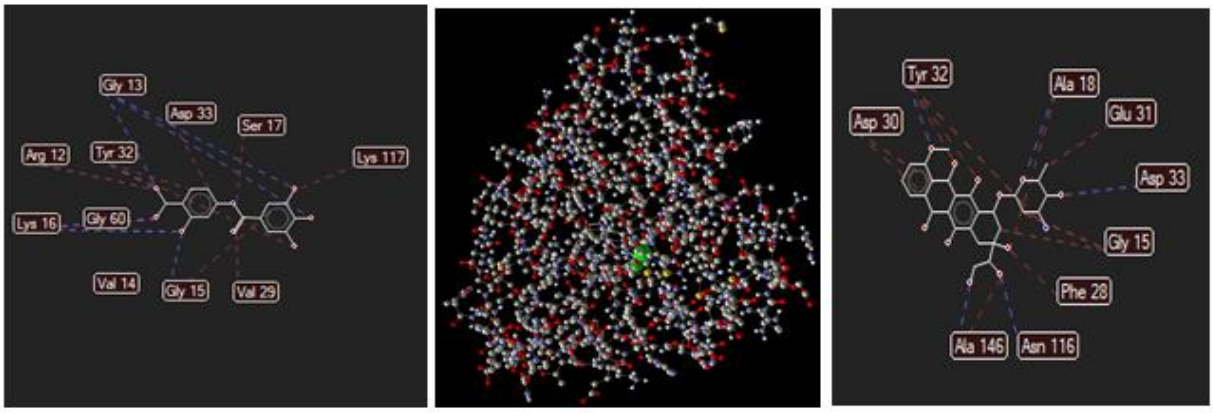


Fig 1.Representation of most active compound AA6 (having most H-bond interaction and having highest dock score) and Adriamycin for (PDB: 6CU6). Hydrogen bond Interactions are represented as dotted lines

Molecular docking analysis was performed using Molegro Virtual Docker (version 6.0) to evaluate the binding affinity and interaction profile of the synthesized derivatives within the active site of the selected target protein. The docking results demonstrated that compound AA-6 exhibited a markedly superior binding affinity compared with the reference drug Adriamycin. Compound AA-6 showed a MolDock score of −146.533, indicating a strong and energetically favorable interaction with the target protein. Detailed interaction analysis revealed that AA-6 formed multiple stabilizing hydrogen bonds with key amino acid residues, including Gly13, Tyr32, Lys16, Gly60, Gly15, and Val14. In contrast, the standard anticancer drug Adriamycin exhibited a comparatively lower MolDock score of −112.967, reflecting reduced binding affinity under identical docking conditions. Adriamycin formed hydrogen bond interactions with Tyr32, Ala18, Asp33, Ala146, and Asn116, indicating reasonable but less extensive

stabilization within the binding cavity. The substantial difference in docking scores (approximately 33.5 units) suggests that AA-6 possesses a stronger predicted binding potential than the standard drug. Overall, the docking findings indicate that AA-6 may serve as a promising lead candidate, warranting further validation through molecular dynamics simulations and experimental in vitro anticancer assays.

IV. CONCLUSION:

The present study demonstrates the significant anticancer potential of phytochemical derivatives derived from *Bougainvillea glabra*, particularly 3,4,5-Trihydroxybenzoic acid and 4-hydroxy-3-methoxycinnamic acid, through an integrated phytochemical extraction and in silico molecular docking approach. The designed aromatic aldehyde and aromatic amine derivatives exhibited enhanced binding affinities toward the target protein PDB ID: 6CUC when compared with the co-crystallized ligand and the standard anticancer drug Adriamycin. Among all evaluated compounds, the aromatic amine derivative of 3,4,5-Trihydroxybenzoic acid (AA6) showed the highest binding affinity with a MolDock score of −146.533 and formed multiple stable hydrogen bond interactions with key active-site residues, indicating strong binding stability and specificity. In silico ADMET and physicochemical property analysis using Molinspiration and PreADMET further supported the drug-likeness and favorable pharmacokinetic profiles of the selected derivatives. Overall, this study highlights the effectiveness of combining phytochemical investigation with advanced computational tools to identify promising plant-based anticancer candidates, thereby providing a strong foundation for further in vitro and in vivo validation and future anticancer drug development.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

AUTHORS' CONTRIBUTIONS

All authors contributed collaboratively to this research work. The study conception and design, literature review, data compilation, and manuscript preparation were carried out jointly. All authors were involved in drafting and critically revising the manuscript and have approved the final version for publication.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding this study.

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