

In-silico analysis of *Tabebuia rosea* phytoconstituents against ovarian cancer targets BRCA 1, BRCA 2 and PALB2

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Abstract

Ovarian cancer, a significant cause of cancer-related mortality globally, often necessitates chemotherapy, which is associated with various adverse effects. Herbal remedies, such as *Tabebuia rosea*, offer potential alternatives due to their affordability and availability. Investigating the pharmacokinetic properties of *Tabebuia rosea* compounds, *in silico* molecular docking studies were conducted to identify potential therapeutic lead molecules. Results indicated that compounds including 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, 7-quinolinol, 2-furan carboxaldehyde, cinnamaldehyde, and Santolina triene effectively inhibit genes associated with ovarian cancer, namely BRCA1, BRCA2, and PALB2. Notably, 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, and 7-quinolinol exhibited the highest binding scores. The novelty lies in the integration of traditional herbal medicine with modern computational techniques to identify potential therapeutic lead molecules. By focusing on inhibiting specific genes implicated in ovarian cancer, the study offers a targeted approach that could potentially mitigate the adverse effects associated with traditional chemotherapy. Experimental validation is essential to confirm the predicted interactions between the identified lead molecules and target genes. While molecular docking provides valuable insights, experimental studies are crucial to verify binding affinities and assess efficacy. Acknowledging the limitations of the *in-silico* approach is necessary for a comprehensive understanding and to guide further research directions. This study aims to assess how well certain compounds from *Tabebuia rosea* can target and inhibit specific genes (BRCA1, BRCA2, and PALB2) associated with ovarian cancer. Experimental validation is imperative to substantiate these attributes and appraise the potential of these compounds as chemotherapy alternatives.

Keywords - *Tabebuia rosea*, BRCA 1, BRCA 2, PALB2 and molecular docking

1. Introduction

The majority of cases of ovarian cancer occur in menopausal-aged women and are complicated diseases with low survival rates. It ranks fifth in terms of cancer-related deaths among women in developed nations and is the sixth most frequent type of cancer overall. Hence, fatalities attributed to ovarian cancer surpass two-thirds of deaths among gynaecologic cancers, despite comprising less than one-third of all gynaecologic cancer cases (Ali *et al.*, 2023).

In the Bignoniaceae family, *Tabebuia* is the largest genus, known for its diverse array of bioactive components present in all parts of the plant. However, the bark is particularly prized for its abundance of active compounds, including quinines, benzoic acid, flavonoids, furanonaphthoquinones, cyclopentenones, naphthoquinones, and dialdehydes. In traditional medicine, *Tabebuia rosea*, commonly known as the "pink trumpet tree," is utilized for its antibiotic, astringent, diuretic, laxative properties, as well as its effectiveness in alleviating symptoms such as fever, discomfort, and inflammation (Nolasco *et al.*, 2023). *Tabebuia* species contain various bioactive phyto compounds familiar for its anti-inflammatory and antioxidant properties, similarly saponins, quinones, tannins, and alkaloids (Castano *et al.*, 2020, Hawary *et al.*, 2021). The primary chemical constituents present in *Tabebuia rosea* leaf extracts include 2-furancarboxaldehyde, Santolina triene, 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, 7-Quinololinol, and Cinnamadehyde (Ramalakshmi and Muthuchelian. 2011).

Identifying potential anticancer candidates can be facilitated by examining natural compounds. Research has revealed that more than 3000 plants possess anticancer properties, and a majority of cancer medications currently in use, accounting for over 60%, have origins in natural sources (Hawary *et al.*, 2021).

Utilizing next-generation sequencing techniques, numerous genes associated with hereditary ovarian cancer have been identified through research endeavors. Approximately 23% of ovarian carcinomas are estimated to possess a genetic predisposition. Predominantly, hereditary cases stem from germline mutations in the BRCA1 or BRCA2 genes, constituting around 20-25% of high-grade serous ovarian cancer instances. Additionally, other hereditary ovarian malignancies, including Lynch syndrome, Peutz-Jeghers syndrome, Li-Fraumeni syndrome, CHEK2, RAD51, BRIP1, and PALB2, are linked to a spectrum of genes pivotal in the DNA damage response mechanism (Pietragalla *et al.*, 2020).

In order for homologous recombination to take place, the DNA repair gene BRCA2 (PALB2) serves as a vital facilitator. PALB2 plays a crucial role in preserving genome integrity by connecting BRCA1 and BRCA2 in the DNA damage response, ensuring recombinational repair and checkpoint functions are maintained (Zhou *et al.*, 2020).

Molecular modeling has emerged as a vital component in biomedical research, aiming to streamline laboratory efforts and pinpoint the most probable molecular targets and signalling pathways. Molecular docking technology has experienced a surge in popularity due to its ability to significantly enhance productivity and decrease research costs. Moreover, in computer-assisted drug design, accurately assessing binding affinity and analysing interaction modes have become indispensable methodologies (Wakil *et al.*, 2023).

The hallmark of safe and effective drugs includes strong potency, affinity, and selectivity towards the molecular target, coupled with meticulously balanced pharmacodynamics (PD) and pharmacokinetics (PK) incorporating appropriate ADMET properties (Ferreira *et al.*, 2019).

The research objectives of this study entail investigating the pharmacokinetic properties of *Tabebuia rosea* compounds, conducting *in silico* molecular docking studies to identify potential therapeutic lead molecules, and assessing the inhibitory effects of these compounds on genes linked with ovarian cancer, namely BRCA1, BRCA2, and PALB2. This investigation integrates traditional herbal medicine with modern computational techniques to identify promising therapeutic leads and offers a targeted approach to mitigate adverse effects associated with traditional chemotherapy.

The novelty of this study lies in its innovative approach, which integrates traditional herbal medicine with modern computational techniques to identify potential therapeutic lead molecules. By leveraging this unique combination, the research offers a targeted strategy focused on inhibiting specific genes associated with ovarian cancer, such as BRCA1, BRCA2, and PALB2. This approach has the potential to mitigate the adverse effects commonly associated with traditional chemotherapy, presenting a promising avenue for improving treatment outcomes. Furthermore, the study underscores the importance of experimental validation to confirm the predicted interactions between the identified lead molecules and target genes, emphasizing the need for comprehensive understanding and guiding future research directions.

Therefore, the focus of the present study is on examining the binding interactions between five bioactive phytochemicals found in *Tabebuia rosea* and the genes BRCA1, BRCA2, and PALB2.

2. Materials and Methods

2.1. Prediction of drug likeness properties

The Quikprop v.11.8 module within Schrödinger offers a convenient and efficient tool for predicting ADME properties of organic molecules. ADMETox (Adsorption, Distribution, Metabolism, Excretion, and Toxicity) enables the physical structure prediction and relevant pharmaceutical property estimation of these molecules. ADMETox is utilized to assess drug-like properties, being adherence to Lipinski's Rule of Five and human oral absorption. Specifically, parameters including molecular weight, hydrogen bond donors, hydrogen bond acceptors, and log P are evaluated in conformance with Lipinski's rule. Following this, the most promising compounds are subjected to filtration steps based on Lipinski's rule to evaluate their pharmacokinetic properties.

2.2. Retrieval of 3D structures from database

The chosen three-dimensional configuration of compounds was annexed from the PubChem database (<https://pubchem.ncbi.nlm.nih.gov/>), while the targets associated with ovarian cancer were sourced from the Protein Data Bank database (<https://www.rcsb.org/>).

2.3. Docking protocol

Using the Schrodinger software (Maestro 11.5), molecular docking of the five proposed compounds was carried out to choose ligands that exhibit favorable interactions with target proteins. The processes listed in Figure-1 are taken into account when conducting a molecular docking study.

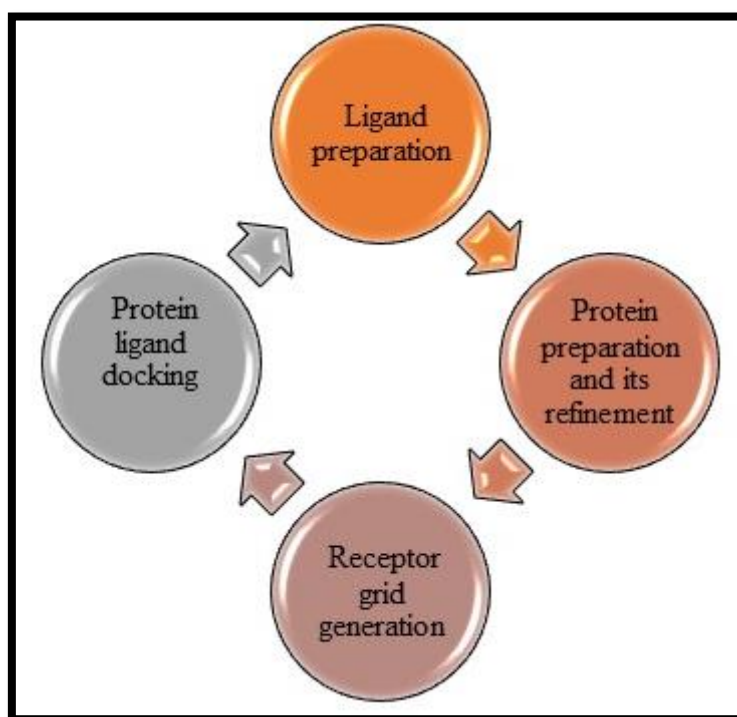


Figure 1: Molecular docking steps - The important stages in the molecular docking process include ligand and protein preparation, encompassing refinement, as well as receptor grid generation, followed by the actual docking of the protein and ligand.

2.4. Preparation of the ligand

The LigPrep module within the Maestro 11.8 interface of Schrödinger 2018 was employed to prepare the ligands. LigPrep generates multiple structures for each ligand input, considering different ionization states, tautomers, stereochemistries, and ring conformations. Subsequently, molecules are filtered based on criteria such as molecular weight and types of functional groups. Additionally, LigPrep facilitates tasks such as adding hydrogen atoms, eliminating undesired molecules, and neutralizing charged groups. The chosen ligands' tautomers were produced and optimized, with partial atomic charges computed utilizing the default energy parameters of the OPLS3e force field. Each conformer underwent energy minimization, employing a consistent window of 10 kcal/mol and a minimum atomic deviation of 1.00 Å. Subsequently, redundant structures were eliminated from the results file, and the resulting ligand structures were saved in Maestro format as a.maegz file for subsequent docking protocols.

2.5. Preparation of the protein

Before engaging in ligand docking, it's essential to minimize the energy of the protein molecule, a vital aspect in molecular docking investigations. The Maestro, serving as the Graphical User Interface (GUI) for the Schrödinger suite, provides the protein preparation wizard, facilitating the importation of proteins from the Protein Data Bank (PDB) and their subsequent preparation for ligand docking studies. This wizard accepts proteins in their raw form, including hydrogen bonds.

The three-dimensional structures of the ovarian cancer target proteins BRCA1, BRCA2, and PALB2 were obtained and underwent protein preparation using the protein preparation wizard. Subsequently, the prepared protein structures were saved individually for each protein.

Proteins that are sourced from the PDB, vendors, and other sources often have entire loop regions, side chains, incomplete charges, and missing hydrogen. Therefore, to get past all of these obstacles in the docking study, the proteins had to undergo pre-processing, which was accomplished by choosing the parameters shown in Figure 2.

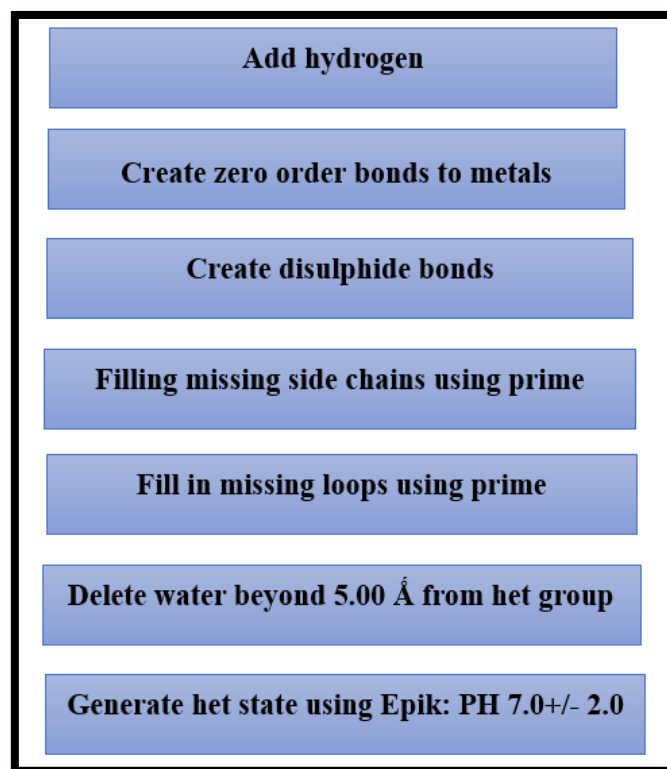


Figure 2: Pre-processing parameters – the pre-processing parameters was accomplished by choosing the parameters stated in the figure.

2.6. Grid generation

The prepped protein is brought into the Maestro interface, where the active site is delineated utilizing Glide version 11.8. The centre of the grid is determined for the active site, and dimensions for the boxes are defined. Afterwards, a cubic grid box is created and enlarged to a measurement of 20 Å. The next step involves

generating the Glide grid. After the grids are effectively created, the prepped ligands are imported into Maestro. Ligands are kept flexible while the protein remains fixed, and the docking process begins utilizing both standard and extra precision modes (SP and XP modes). The docking calculation generates multiple positions for each ligand. The choice of the best position relies on the interaction energy between the ligand and the protein, along with the ligand's interactions with experimentally confirmed essential residues. Typically, a lower interaction energy yields a superior pose for the ligands.

2.7. Protein ligand docking simulation

Glide 11.8 utilizes a structured cascade of filters to investigate potential binding sites within the active region of the receptor. The receptor grid is created at the receptor location, either when it's bound by a ligand or by specifically choosing the active site residue of the protein. Following that, the prepped ligands undergo docking with the target proteins using Glide 11.8 within the Schrödinger software suite. The handling of conformational flexibility in Glide 11.8 entails a thorough exploration of different conformations, supported by a heuristic screening process that efficiently eliminates inappropriate ones.

Standard Precision (SP) was employed for flexible docking, while Extra Precision (XP) mode was utilized for enhanced refinement. The ligand docking methodology facilitates the prediction of ligand conformation and orientation within a specific binding site, aiding in the interpretation of ligand-protein interactions and determination of binding affinity. The procedures outlined in Figure 3 were followed to conduct the ligand docking. The docked protein-ligand complexes were visualized using the Glide Pose Viewer. The optimal docked structure was selected based on parameters such as the Docking score function and Glide energy, and the compound was identified accordingly. Images illustrating the optimal docking positions of both the ligand and protein were stored in "jpg" format.

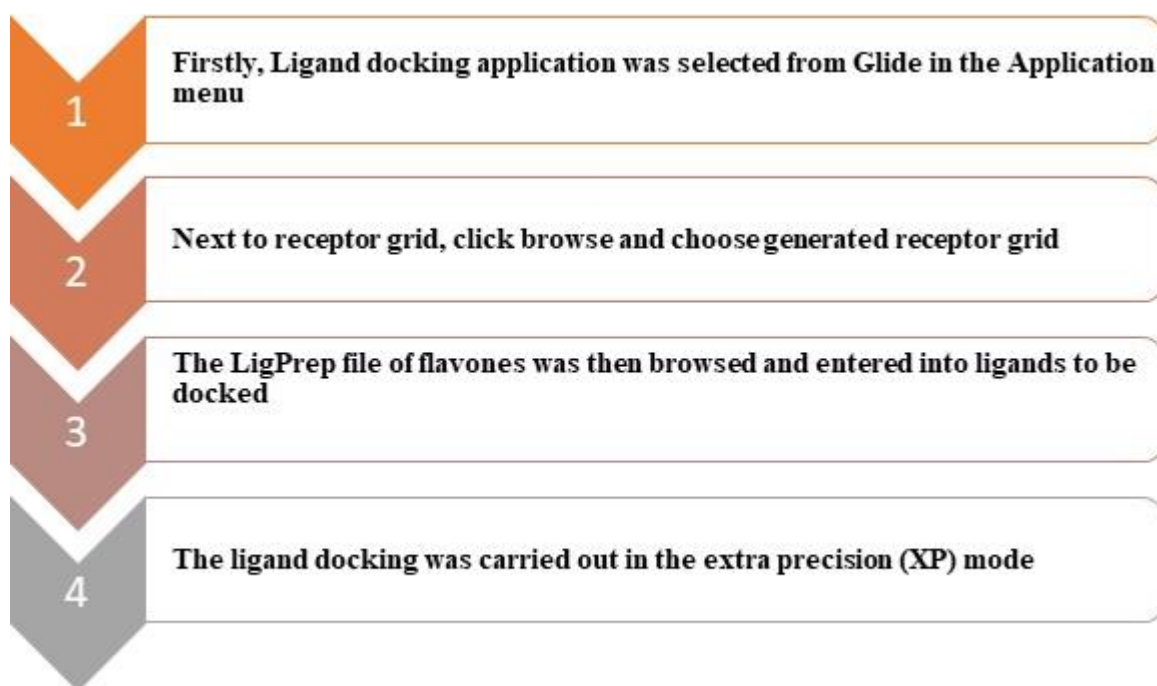


Figure 3: Ligand docking steps – The steps outlined in Figure 3 were employed to execute the ligand docking procedure. This involved a series of systematic steps designed to accurately position the ligand molecule within the binding site of the target protein.

2.8. Ligands (Compounds) and target proteins

The compounds Santolina triene, 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, Cinnamaldehyde, 7-quinolinol, and 2-furan carboxaldehyde were selected for molecular docking analysis against BRCA1, BRCA2, and PALB2 based on their potential bioactivity against cancer targets, structural similarity to known inhibitors, availability, diverse chemical structures for comprehensive exploration, and recognition of their anticancer potential from literature. These compounds represent promising candidates for investigating their therapeutic efficacy against ovarian cancer-associated genes. By strategically combining *Tabebuia rosea* bioactive compounds with precise targeting of ovarian cancer-related proteins, this approach aims to develop targeted therapies, leveraging the plant's natural anti-cancer potential.

2.8.1. List of the Ligands

-  Santolina triene
-  4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl
-  Cinnamaldehyde
-  7-quinolinol
-  2-furan carboxaldehyde

2.8.2. List of the Target Proteins

-  BRCA 1 (8GRQ)
-  BRCA 2 (7BDX)
-  PALB2 (3EU7)

Results

3.1 Prediction of ADME properties of the compounds using the QikProp module of Schrodinger

For a prospective drug candidate to be a successful therapeutic agent for oral delivery, it must possess a few favorable pharmacokinetic features. Early on in the drug development process, the analysis of *in silico* ADMET (absorption, distribution, metabolism, excretion, and transport) features helps to minimize drug toxicity failures (Shanmugam *et al.*, 2024).

Lipinski developed the "Rule of 5" (Ro5) qualities along with a chemical explanation of the substances. The rule is useful while creating new drugs. To find compounds with the best chance of being developed into possible drugs, Ro5 is a useful tool. It is intended that drugs be readily absorbed, broken down, and removed from the bloodstream without having any harmful side effects. To engage with receptor molecules, these medications are delivered to the body's intended location of action (Saravanan *et al.*, 2022).

The ability of a chemical agent to function as a drug is assessed by the ADME property. Table 1 displays the pharmacokinetic profile of the chosen drugs and shows that none of the criteria for the Lipinski rule have been broken. The QikProp software module was utilized to examine the ADME parameters of the chosen ligands. Each of the compounds displayed characteristics consistent with drug-like behavior, evidenced by a molecular mass below 500 Da, fewer than 5 hydrogen bond donors, fewer than 10 hydrogen bond acceptors, and an octanol-water partition coefficient ($\log P_{o/w}$) below 5. These properties were assessed using Lipinski's rule of five. These chemicals show promise as therapeutic alternatives for the treatment of ovarian cancer, as the pharmacokinetic parameters analysed fell well within the permissible range for human use.

Table 1: ADME Properties

S.No.	Compounds	Compound CID	$\log P_{o/w}$	Molecular weight	Hydrogen Bond Donor	Hydrogen Bond Acceptor	Rule of Five	Human oral absorption
1.	Santolina triene	519872	4.342	136.236	0	0	0	High
2.	4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	119838	-0.619	144.127	2	5.2	0	High
3.	Cinnamaldehyde	637511	1.879	132.162	0	2	0	High
4.	7-quinolinol	135426866	2.090	145.160	1	1.750	0	High
5.	2-furan carboxaldehyde	237332	0.037	96.085	0	2.5	0	High

The table 1 presents ADME properties of selected ligands and the results revealed that Santolina triene (CID: 519872) exhibits a $\log P_{o/w}$ value of 4.342 and a molecular weight of 136.236. It lacks both hydrogen bond donors and acceptors and meets the Rule of Five criteria, indicating high human oral absorption. Following this, 4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl (CID: 119838) displays a $\log P_{o/w}$ of -0.619 and a molecular weight of 144.127. With two hydrogen bond donors and 5.2 acceptors, it also meets the Rule of Five, resulting in high oral absorption. Cinnamaldehyde (CID: 637511) boasts a $\log P_{o/w}$ of 1.879 and a molecular weight of 132.162. Similar to Santolina triene, it lacks hydrogen bond donors but possesses two acceptors, aligning with high human oral absorption. Meanwhile, 7-quinolinol (CID: 135426866) registers a $\log P_{o/w}$ of 2.090 and a molecular weight of 145.160. It contains one hydrogen bond donor and 1.750 acceptors, adhering to the Rule of Five for high oral absorption. Lastly, 2-furan carboxaldehyde (CID: 237332) presents a $\log P_{o/w}$ of 0.037 and a molecular weight of 96.085. Without any hydrogen bond donors but with 2.5 acceptors, it also meets the Rule of Five for high oral absorption.

Following the ADME analysis, the compounds demonstrating favorable properties were selected for further investigation through molecular docking analysis against the target genes BRCA1, BRCA2, and PALB2 associated with ovarian cancer. The rationale behind the selection of these compounds was primarily driven by their potential anticancer effects and their suitability for interaction with the target genes of interest. This approach ensured that the compounds chosen for molecular docking analysis possessed both favorable pharmacokinetic properties and the potential to inhibit the target genes implicated in ovarian cancer.

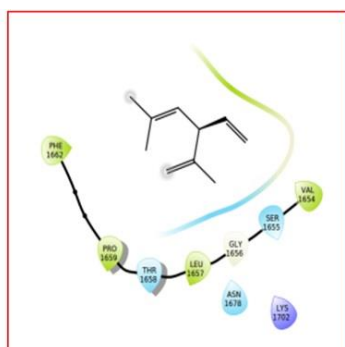
3.2 Molecular docking of *Tabebuia rosea* phytoconstituents with BRCA 1, BRCA 2 and PALB2

After the docking phase, the ligands were ranked by their binding affinities. Analysis of the results involved examining the interactions between specific proteins and the chemicals, along with the interaction energies.

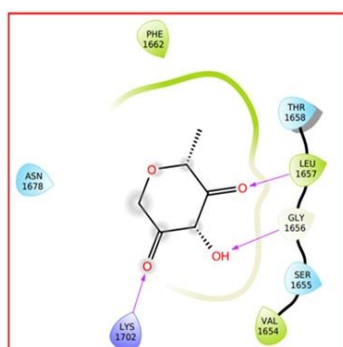
Molecular docking analysis of *Tabebuia rosea* phytoconstituents with BRCA 1 results revealed that 7-quinolinol exhibited the best glide score of -5.422 followed by 4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl, 2-furan carboxaldehyde, Cinnamaldehyde, and Santolina triene. The findings are showcased in Table 2 and Figure 4 and 5.

Table 2: Glide SP docking of the compounds with BRCA 1

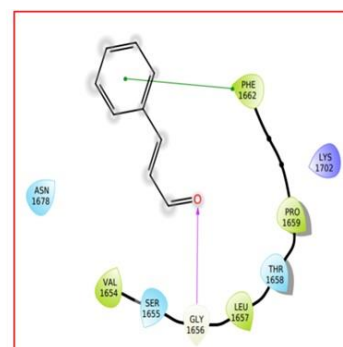
S.No.	Ligand	Compound CID	Glide Score (kcal/mol)	Glide Energy (kcal/mol)	H Bond
1.	Santolina triene	519872	-1.658	-14.756	0
2.	4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	119838	-4.916	-28.209	3
3.	Cinnamaldehyde	637511	-2.917	-18.889	1
4.	7-quinolinol	135426866	-5.422	-27.096	1
5.	2-furan carboxaldehyde	237332	-3.836	-18.326	1



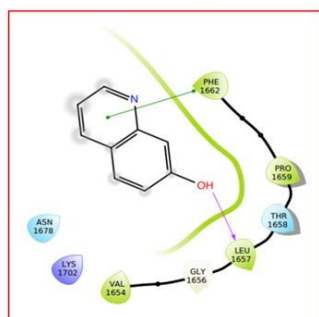
Santolina triene



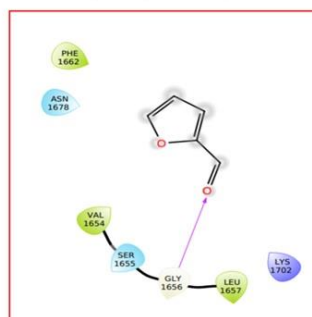
4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl



Cinnamaldehyde



7-quinolinol



2-furan carboxaldehyde

Figure 4: 2D docking interactions of *Tabebuia rosea* phytoconstituents with BRCA 1- Illustration of the docking interactions between *Tabebuia rosea* phytoconstituents and the BRCA1 protein, depicted in 2D formats.

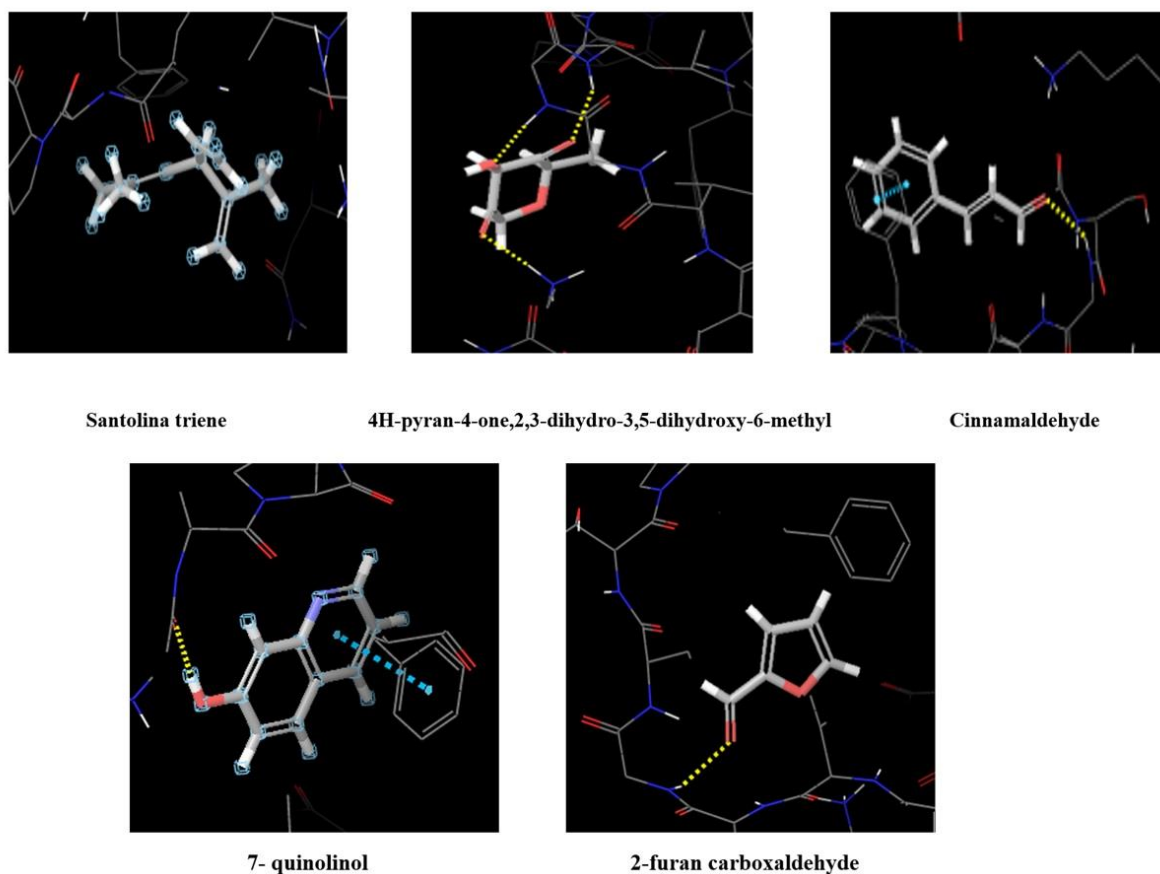
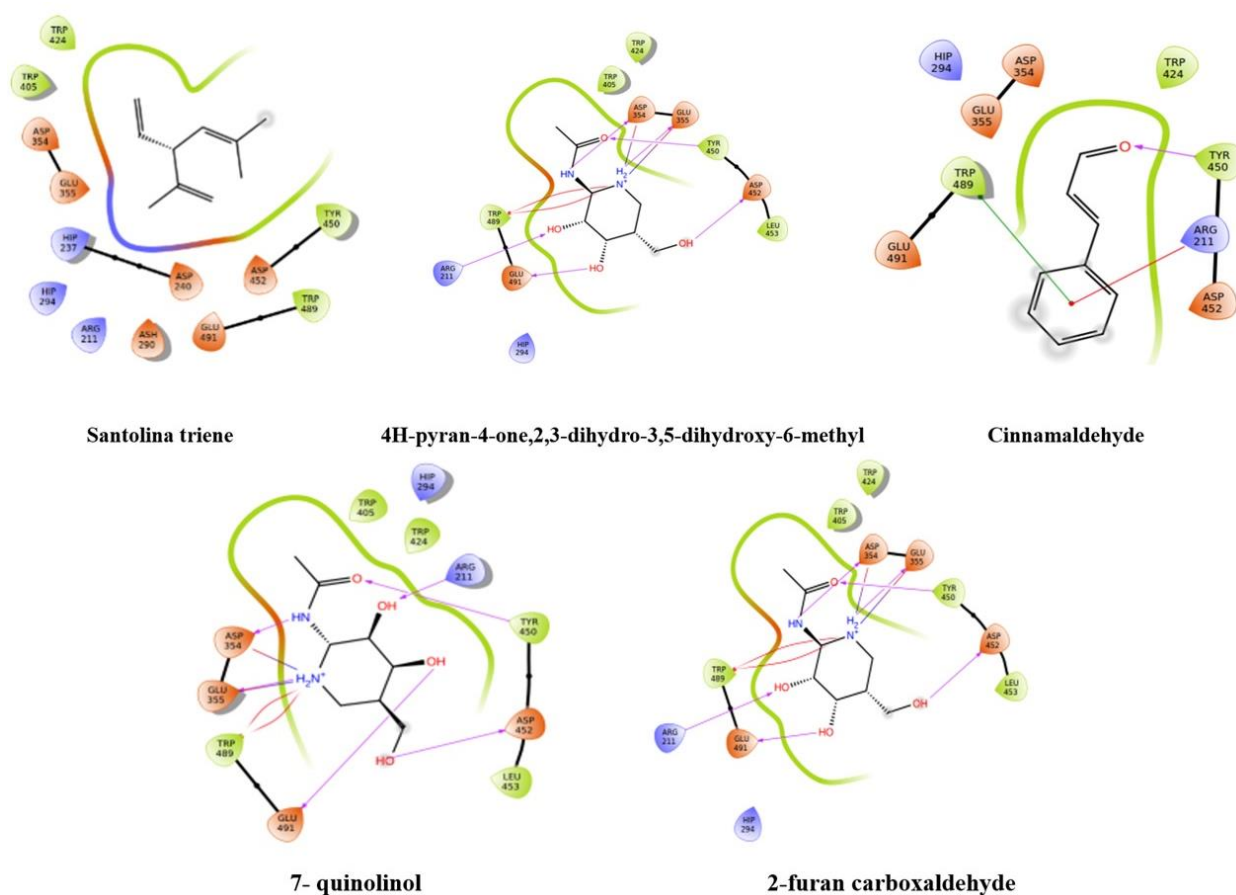


Figure 5: 3D docking interactions of *Tabebuia rosea* phytoconstituents with BRCA 1- Illustration of the docking interactions between *Tabebuia rosea* phytoconstituents and the BRCA1 protein, depicted in 3D formats.

Molecular docking analysis of *Tabebuia rosea* phytoconstituents with BRCA 2 results revealed that 4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl exhibited the best glide score of -5.737 followed by 7-quinolinol, 2-furan carboxaldehyde, Cinnamaldehyde, and Santolina triene. The findings are showcased in Table 3 and Figure 6 and 7.

Table 3: Glide SP docking of the *Tabebuia rosea* phytoconstituents with BRCA 2

S.No.	Ligand	Compound CID	Glide Score (kcal/mol)	Glide Energy (kcal/mol)	H Bond
1.	Santolina triene	519872	-1.829	-20.818	0
2.	4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	119838	-5.737	-37.575	6
3.	Cinnamaldehyde	637511	-3.052	-24.878	1
4.	7- quinolinol	135426866	-5.373	-34.659	6
5.	2-furan carboxaldehyde	237332	-4.296	-26.299	6

**Figure 6: 2D docking interactions of *Tabebuia rosea* phytoconstituents with BRCA 2-** Illustration of the docking interactions between *Tabebuia rosea* phytoconstituents and the BRCA2 protein, depicted 2D formats.

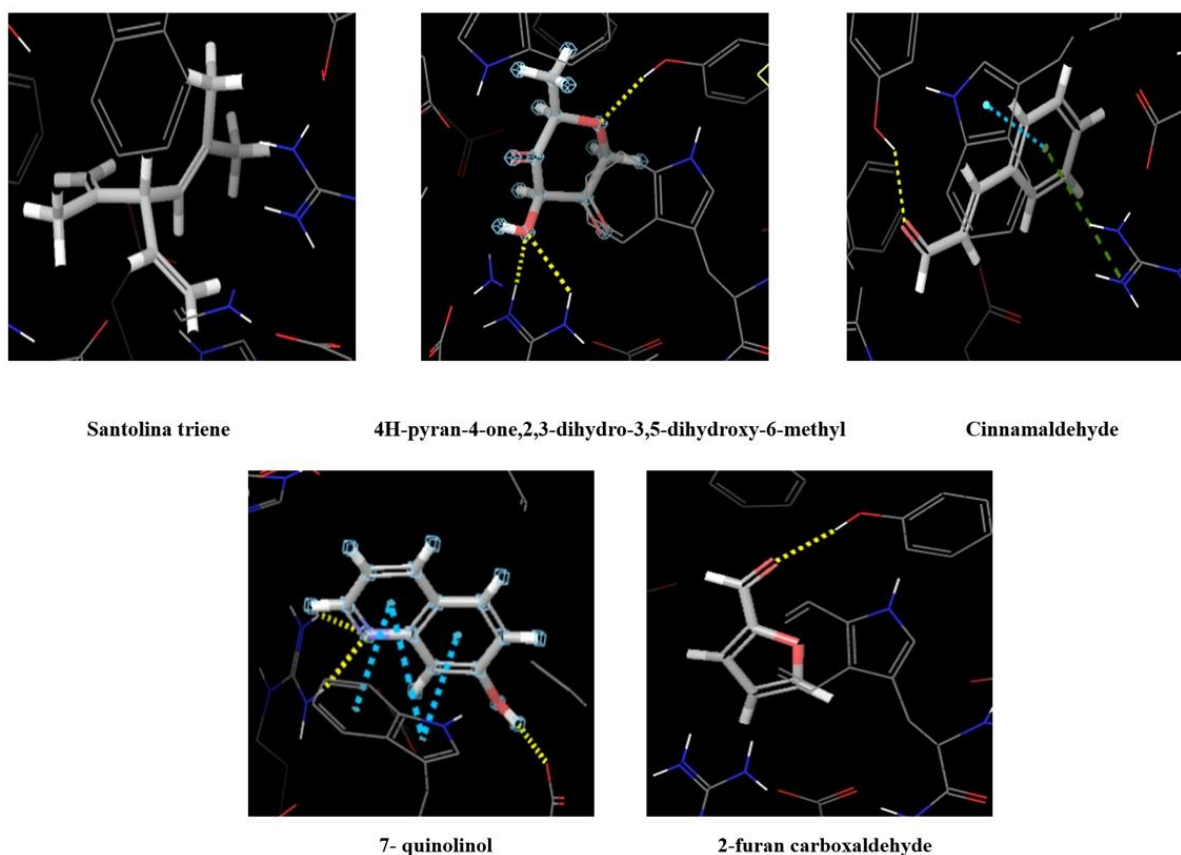


Figure 7: 2D docking interactions of *Tabebuia rosea* phytoconstituents with BRCA 2- Illustration of the docking interactions between *Tabebuia rosea* phytoconstituents and the BRCA2 protein, depicted 3D formats.

Molecular docking analysis of *Tabebuia rosea* phytoconstituents with PALB2 target results revealed that 4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl displayed best glide score of -5.120 followed by 7-quinolinol, 2-furan carboxaldehyde, Cinnamaldehyde, and Santolina triene. The findings are showcased in Table 4 and Figure 8 and 9.

Table 4: Glide SP docking of the *Tabebuia rosea* phytoconstituents with PALB2

S.No.	Ligand	Compound CID	Glide Score (kcal/mol)	Glide Energy (kcal/mol)	H Bond
1.	Santolina triene	519872	-1.965	-17.148	0
2.	4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	119838	-5.120	-27.336	2
3.	Cinnamaldehyde	637511	-3.138	-19.101	0
4.	7-quinolinol	135426866	-4.410	-23.468	0
5.	2-furan carboxaldehyde	237332	-4.154	-20.367	0

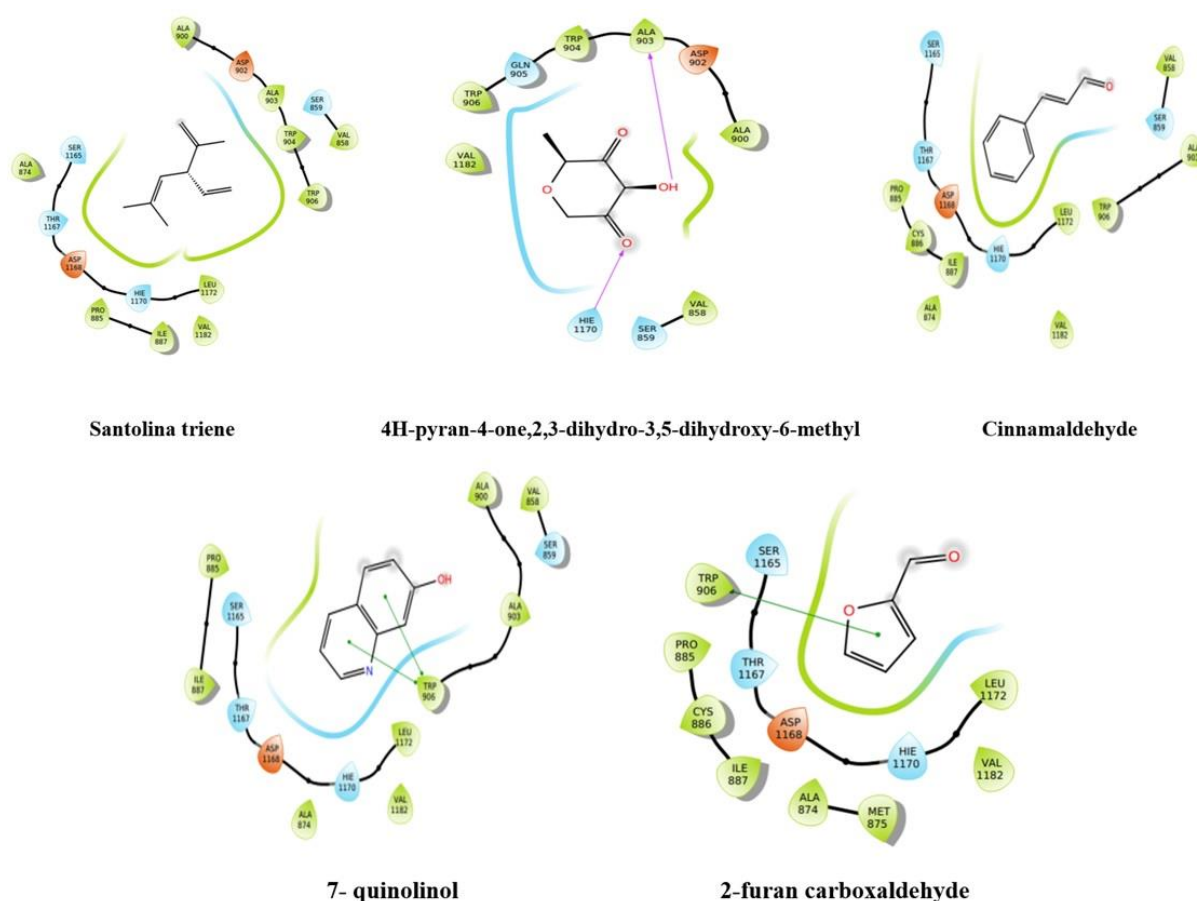


Figure 8: 2D docking interactions of *Tabebuia rosea* phytoconstituents with PALB2- Illustration of the docking interactions between *Tabebuia rosea* phytoconstituents and the PALB2 protein, depicted in 2D formats.

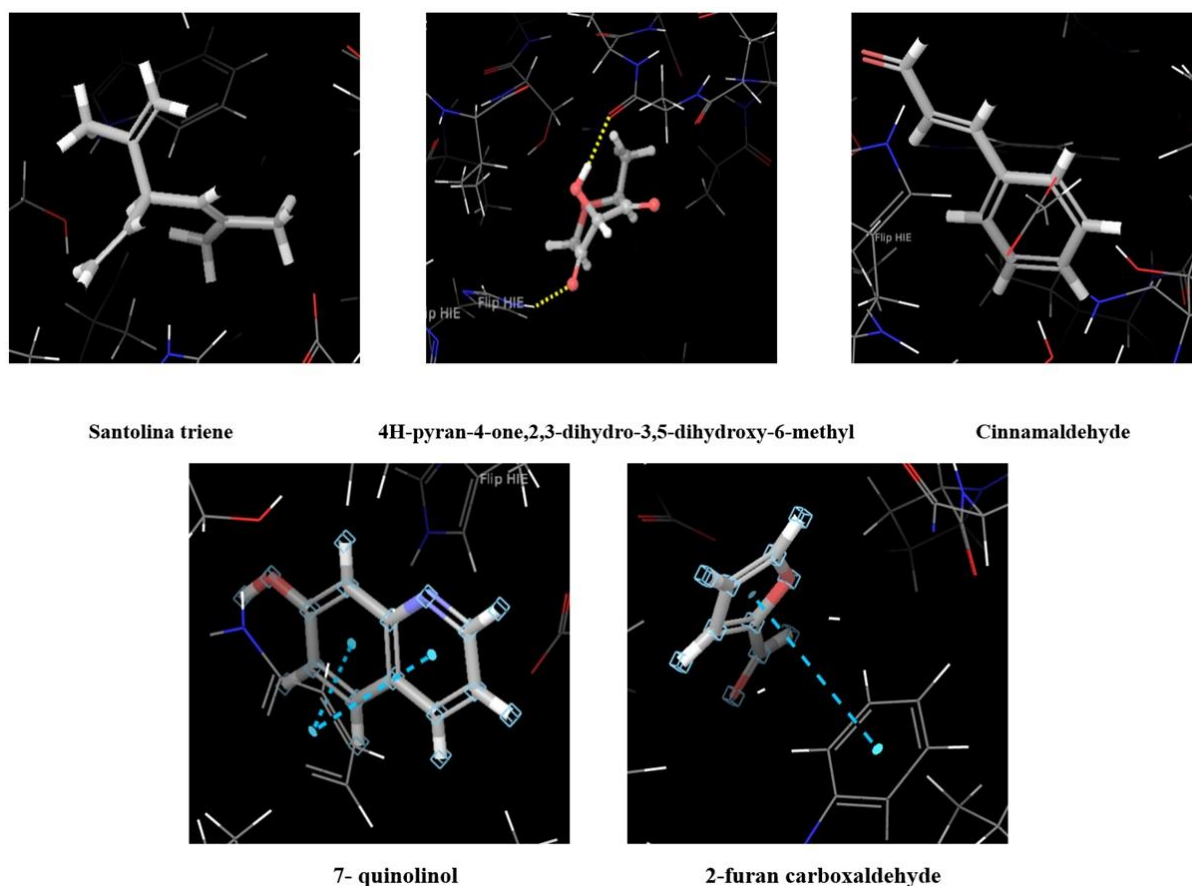


Figure 9: 3D docking interactions of *Tabebuia rosea* phytoconstituents with PALB2- Illustration of the docking interactions between *Tabebuia rosea* phytoconstituents and the PALB2 protein, depicted in 3D formats.

4. Discussion

In a virtual way, computational drug discovery techniques offer important insights into the comprehension of protein–ligand interaction systems. One crucial tool for *in silico* drug discovery is molecular docking (Singh *et al.*, 2023).

Ovarian cancer, a leading cause of cancer-related deaths worldwide, often requires chemotherapy, which can entail various adverse effects. Herbal remedies, such as *Tabebuia rosea*, present promising alternatives due to their affordability and accessibility. Investigating the pharmacokinetic properties of *Tabebuia rosea* compounds, *in silico* molecular docking studies were conducted to pinpoint potential therapeutic lead molecules (Muruganandham *et al.*, 2023).

Compared to mucinous or borderline tumours, serous adenocarcinomas have been found to be more common in women with hereditary BRCA1 or BRCA2 pathogenic mutations (Petrucelli *et al.*, 2022). The BRCA gene is crucial in the homology-directed repair pathway, used for double-strand break repair, and it significantly influences the development of epithelial ovarian cancer in many individuals (Lorenzo *et al.*, 2022).

When PALB2 was first discovered, it was shown to occur frequently in ovarian cancer. In comparison to population incidence particular to each nation, the largest research of patients with PALB2 mutations to date, involving over 500 families, found a relative risk of 2.91 (95% CI 1.40-6.04) for ovarian cancer. After RRBSO, a patient with a PALB2 mutation has also been documented to have primary peritoneal cancer (Samuel *et al.*, 2022).

The mechanism by which BRCA1, BRCA2, and PALB2 mutations trigger ovarian cancer involves disruption of the DNA damage response system. These mutations typically lead to functional impairment of the proteins encoded by these genes. For instance, mutations may result in misfolding of the protein, reducing its stability and half-life. Additionally, mutations can interfere with the protein's ability to bind to its targets or interact with other essential proteins involved in DNA repair processes. Such disruptions compromise the cell's ability to repair double-stranded DNA breaks effectively, leading to genomic instability and an increased predisposition to ovarian cancer (Page *et al.*, 2021 and Guo *et al.*, 2021).

Molecular docking interactions between the 5IAE receptor protein of HeLa cells and the Uox enzyme receptor, utilizing various *Tabebuia rosea* phyto compounds revealed that Pelargonidin-3-O-glucoside exhibited top ranked docking affinity against Uox and HeLa cell 5IAE receptor protein. These results suggest that Pelargonidin-3-O-glucoside forms robust and favorable associations with the respective receptors (Alam *et al.*, 2021).

The current state of research in this field suggests that there is still much to be explored and understood. Despite the efforts made thus far, the existing body of literature is relatively limited, underscoring the need for further investigation and exploration. Many important aspects of this topic have not yet been adequately studied or fully understood. This gap in knowledge presents a significant opportunity for future research to delve deeper into various facets of the subject matter. By expanding our studies and addressing these gaps, researchers can uncover new insights, refine existing theories, and ultimately enhance our understanding of the topic. This ongoing exploration holds promise for advancing scientific knowledge and potentially leading to novel discoveries that could have significant implications for clinical practice, public policy, and further research directions.

Findings revealed that compounds like 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, 7-quinolinol, 2-furan carboxaldehyde, cinnamaldehyde, and Santolina triene effectively target genes associated with ovarian cancer, including BRCA1, BRCA2, and PALB2. Notably, 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, and 7-quinolinol displayed the highest binding scores. The study's novelty lies in integrating traditional herbal medicine with modern computational techniques to identify potential therapeutic leads. By focusing on inhibiting specific ovarian cancer-associated genes, this research offers a targeted approach that could mitigate the adverse effects linked to conventional chemotherapy.

While the study integrates traditional herbal medicine with modern computational techniques to identify potential therapeutic lead molecules for ovarian cancer treatment, several limitations should be acknowledged. Molecular docking studies, while informative, may not fully represent the complexities of protein-ligand interactions in real biological systems, introducing uncertainties. Cancer is multifaceted, and targeting individual genes like BRCA1, BRCA2, and PALB2 might overlook the broader molecular landscape and mechanisms of resistance. Experimental validation, crucial for confirming predicted interactions, is resource-intensive and time-consuming. Moreover, understanding the pharmacokinetics, specificity, and safety

of *Tabebuia rosea* compounds *in vivo* remains a challenge. Clinical translation requires rigorous trials, facing obstacles like patient recruitment and funding. Ethnopharmacological variability and long-term safety effects further complicate the potential use of these compounds. Addressing these limitations is essential for advancing *Tabebuia rosea*'s potential as a cancer therapeutic and guiding future research and clinical endeavors.

5. Conclusion

The study on *Tabebuia rosea* compounds offers promising implications for ovarian cancer treatment and drug development. These compounds present alternative therapies to traditional chemotherapy, particularly beneficial where conventional treatments are limited. They effectively target genes like BRCA1, BRCA2, and PALB2, crucial in ovarian cancer progression, fueling the development of targeted therapies for more effective and less toxic treatments. Understanding their pharmacokinetic properties is vital for personalized medicine approaches, while combining them with existing therapies could address drug resistance. Experimental validation of findings is crucial for clinical translation, highlighting the potential of integrating herbal medicine with modern techniques for innovative cancer treatments. Yet, further research and validation are needed to ensure efficacy and safety in clinical settings, ultimately improving patient outcomes.

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