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In-Silico Analysis of *Agrocybe aegerita* Bioactive Compounds Targeting HER-2 Positive Breast Cancer Protein

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Abstract

This study explores the anti-cancer potential of bioactive compounds derived from *Agrocybe aegerita*, focusing on their interaction with the HER-2 protein, which is commonly overexpressed in aggressive breast cancers. Using in-silico molecular docking techniques via the SwissDock platform and AutoDock Vina algorithm, the binding affinities of three bioactive compounds—ceramide, ganoderic acid, and galectin—were evaluated and compared to standard cancer drugs, including doxorubicin, lapatinib, and pazopanib. The results demonstrated that ganoderic acid exhibited the highest binding affinity to HER-2 (-6.34 to -6.18), comparable to lapatinib and pazopanib, suggesting its strong therapeutic potential. Ceramide and galectin showed moderate affinities, indicating possible roles in complementary or synergistic therapies. The findings suggest that *A. aegerita*, particularly its ganoderic acid compound, holds promise as a natural source for novel anti-cancer agents, potentially offering comparable efficacy to synthetic drugs with fewer side effects. However, the limitations of in-silico studies are acknowledged, and further in vitro and in vivo validation is necessary to confirm these promising results. This research contributes to the growing body of knowledge on natural bioactive compounds, underscoring the potential of mushrooms in cancer therapy and advocating for more extensive studies to harness their medicinal properties.

Keywords: *Agrocybe aegerita*, HER-2, in-silico analysis, molecular docking, ganoderic acid, anti-cancer, breast cancer.

INTRODUCTION

Mushrooms have long fascinated humans, not only for their culinary uses but also for their diverse medicinal properties. These fungi belong to the kingdom Fungi and have been integral to many cultures for millennia, serving as both food and medicine. Their wide variety of species, shapes, and biochemical compositions make mushrooms an exciting subject of study, particularly in the context of human health and agriculture. With over 14,000 known species, mushrooms exhibit an incredible diversity in morphology and habitat, thriving in forests, grasslands, and urban environments. The vast biochemical potential of mushrooms has become a major area of focus in natural product research, where scientists explore their bioactive compounds' medicinal, nutritional, and environmental applications (Abah et al., 2024).

Historically, mushrooms have been used in traditional medicine in many cultures, especially in Asia, where species such as *Ganoderma lucidum* (Reishi) and *Lentinula edodes* (Shiitake) are celebrated for their immune-boosting, anti-inflammatory, and antioxidant properties. In recent years, modern science has begun to uncover the pharmacological potential of mushrooms, revealing them as a rich source of bioactive compounds, including polysaccharides, terpenoids, alkaloids, and phenolic compounds. These compounds have been studied for their roles in combating oxidative stress, inflammation, and microbial infections, among other health benefits (Jantrapanukorn et al., 2018).

Among the many mushrooms under scientific scrutiny, *Agrocybe aegerita*, commonly known as the tea tree mushroom or black poplar mushroom, has gained attention for its unique composition and beneficial bioactive compounds. Native to Europe and Asia, this mushroom grows on decaying wood, especially poplar, oak, and tea trees, from which it derives its common name. Its relatively fast growth, appealing flavour, and adaptability make it a popular choice in both wild foraging and commercial cultivation (Sganzerla et al., 2022).

Beyond its culinary value, *Agrocybe aegerita* is increasingly recognized for its promising bioactive compounds, which exhibit antimicrobial, antioxidant, and anticancer properties.

This mushroom contains various polysaccharides, which are particularly interesting due to their immunomodulatory and anti-tumor activities. Additionally, compounds such as flavonoids and phenolic acids have been identified in *A. aegerita*, contributing to its potential as a natural source of antioxidants, which are crucial in protecting cells from oxidative stress and preventing chronic diseases (Xu et al., 2022).

One of the most significant discoveries in *Agrocybe aegerita* is the presence of compounds with antimicrobial properties. The increasing threat of antibiotic resistance has led researchers to seek alternatives, and mushrooms like *A. aegerita* are proving to be valuable in this regard. Studies have shown that extracts from *A. aegerita* possess potent antibacterial and antifungal activities, making them a promising source for developing new antimicrobial agents. This potential aligns with the broader scientific interest in mushrooms as reservoirs of novel antibiotics, particularly in the fight against multi-drug resistant pathogens (Kumar et al., 2021).

In addition to its antimicrobial properties, *Agrocybe aegerita* has demonstrated significant antioxidant activity, largely attributed to its phenolic and flavonoid content. These compounds are known for neutralising free radicals, thereby reducing oxidative stress and preventing cellular damage. Oxidative stress is a key factor in the development of numerous chronic conditions, including cardiovascular diseases, neurodegenerative disorders, and cancers. The antioxidant capacity of *A. aegerita* thus makes it a promising candidate for use in nutraceuticals and functional foods aimed at promoting health and longevity (Abdelshafy et al., 2022; Hamza et al., 2024).

Moreover, preliminary studies have suggested that *Agrocybe aegerita* might possess anticancer properties. Polysaccharides extracted from the mushroom have shown potential in inhibiting the growth of cancer cells in vitro, suggesting that *A. aegerita* could play a role in developing novel cancer therapies. This aligns with findings from other mushroom species, such as *Trametes versicolor* and *Cordyceps sinensis*, which have long been studied for their anti-tumor effects (Yang et al., 2018).

As scientific interest in natural products grows, mushrooms like *Agrocybe aegerita* are becoming increasingly important in the search for bioactive compounds with health-promoting properties. The study of these compounds enhances our understanding of mushroom biology and contributes to the development of novel therapies for a wide range of diseases (Diyabalanage et al., 2008).

Mushrooms are far more than just a food source; they are a rich reservoir of bioactive compounds with tremendous potential for improving human health. *Agrocybe aegerita*, with its unique composition and array of beneficial compounds, stands out as a mushroom of great interest. Its antimicrobial, antioxidant, and potential anticancer properties make it a valuable subject of research, with the promise of contributing to the development of natural products that can address some of the most pressing health challenges of our time (Bains et al., 2021).

Molecular docking is a widely used computational technique in drug discovery that predicts the preferred orientation of a ligand (bioactive compound) when bound to a protein receptor. This approach allows researchers to estimate the binding affinity of bioactive compounds, providing valuable insights into their potential therapeutic efficacy (Meza Menchaca et al., 2020).

This research has as its primary objectives

1. Investigation of the potential anti-cancer potential of already discovered bioactive compounds present in *Agrocybe aegerita* against HER-2 breast cancer protein using Swiss Dock (AutoDock Vina algorithm).
2. Comparison against standard drugs to determine if they possess higher anti-cancer potential.

METHODS

Software and Tools

Swissdock platform was used to conduct the docking utilizing the autodock vina algorithm embedded to predict the binding modes and affinities of ligands to a receptor.

Target Selection

HER-2 breast cancer protein will be utilized for this study. The 3d structure of the protein was downloaded from the public database Protein Data Bank (PDB). The protein structure was cleaned using UCSF Chimera to remove water molecules, ions and heteroatoms that could interfere.

Ligand Preparation

1. Bioactive compound selection

TABLE 1: Bioactive compounds in *Agrocybe aegerita*

S/N	BIOACTIVE COMPOUNDS	REFERENCES
1	Ceramide	(Diyabalanage et al., 2008)
2	Ganoderic acid	(Yuan et al., 2022)
3	Galectin	(Yang et al., 2018)

2. Ligand structure retrieval

   The 3D structure of the compounds was obtained from Pubchem in .sdf format.

3. Energy minimization

   The energy of the ligands was minimized to ensure optimal conformation for docking. This was done using Chimera.

Docking procedure

The prepared receptor and ligands were imported into the Swissdock server. Blind docking explored all potential binding sites on the receptor surface.

RESULTS

TABLE 2: *Agrocybe aegerita* bioactive compounds

S/N	COMPOUND	BINDING AFFINITY (kcal/mol)
1	CERAMIDE	-3.91 -3.18 -3.07
2	Ganoderic acid	-6.34 -6.27 -6.18
3	Galectin	-4.97 -4.82 -4.61

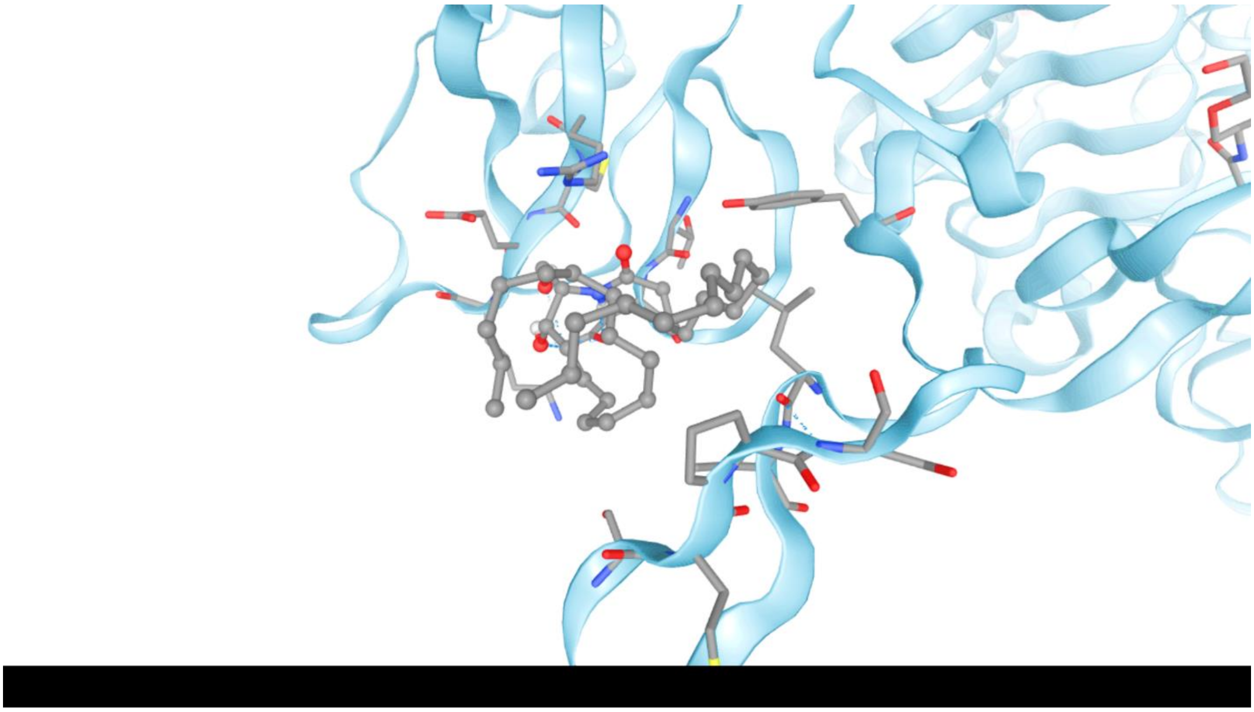

FIGURE 1: CERAMIDE AND HER 2 DOCKING PROCESS

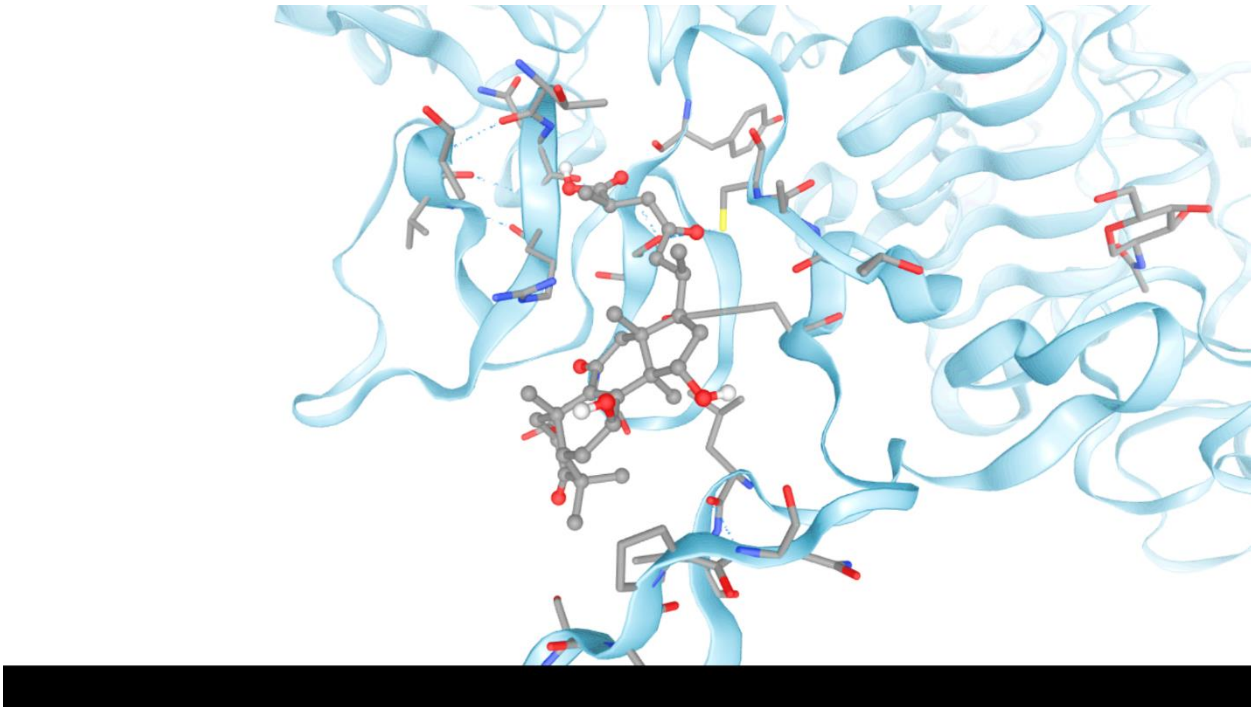

FIGURE 2: Ganoderic acid AND HER 2 DOCKING PROCESS

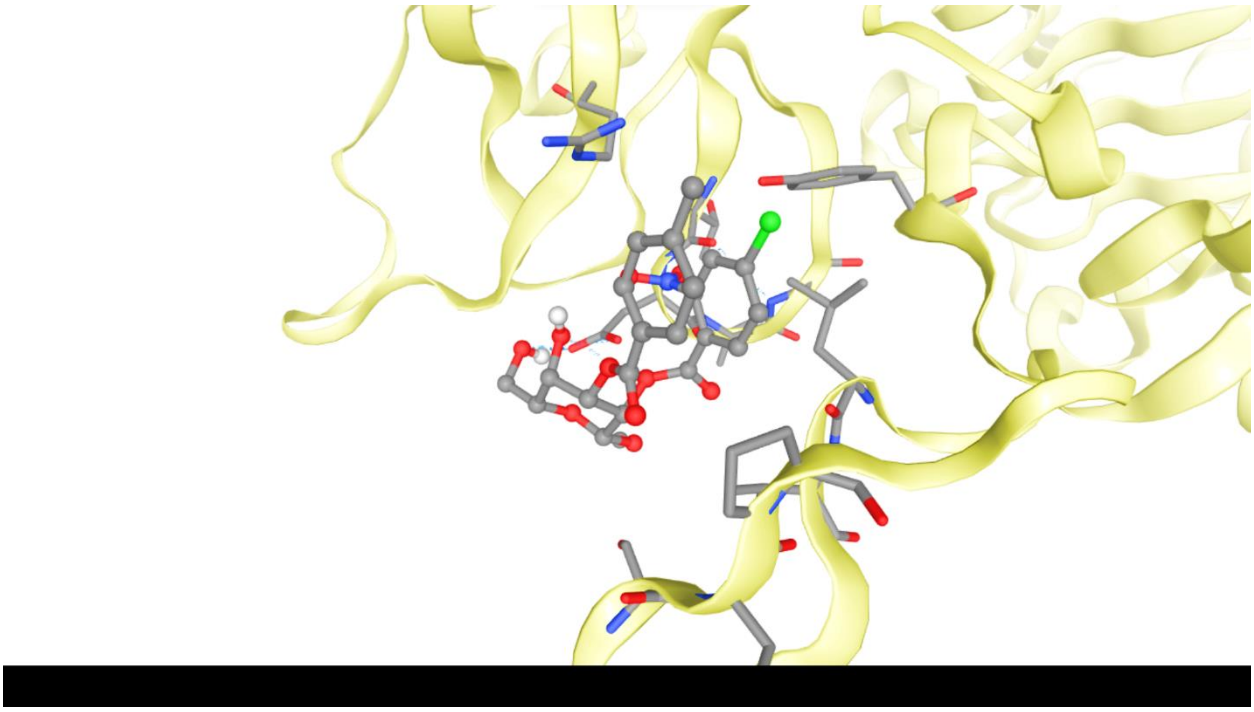

FIGURE 3: Galectin AND HER 2 DOCKING PROCESS

TABLE 3: STANDARD DRUGS

S/N	MOLECULE	BINDING AFFINITY (kcal/mol)
1.	DOXORUBICIN	-5.43 -5.43 -5.42
2.	LAPATINIB	-6.16 -5.86 -5.63
3.	PAZOPANIB	-6.20 -6.14 -6.05

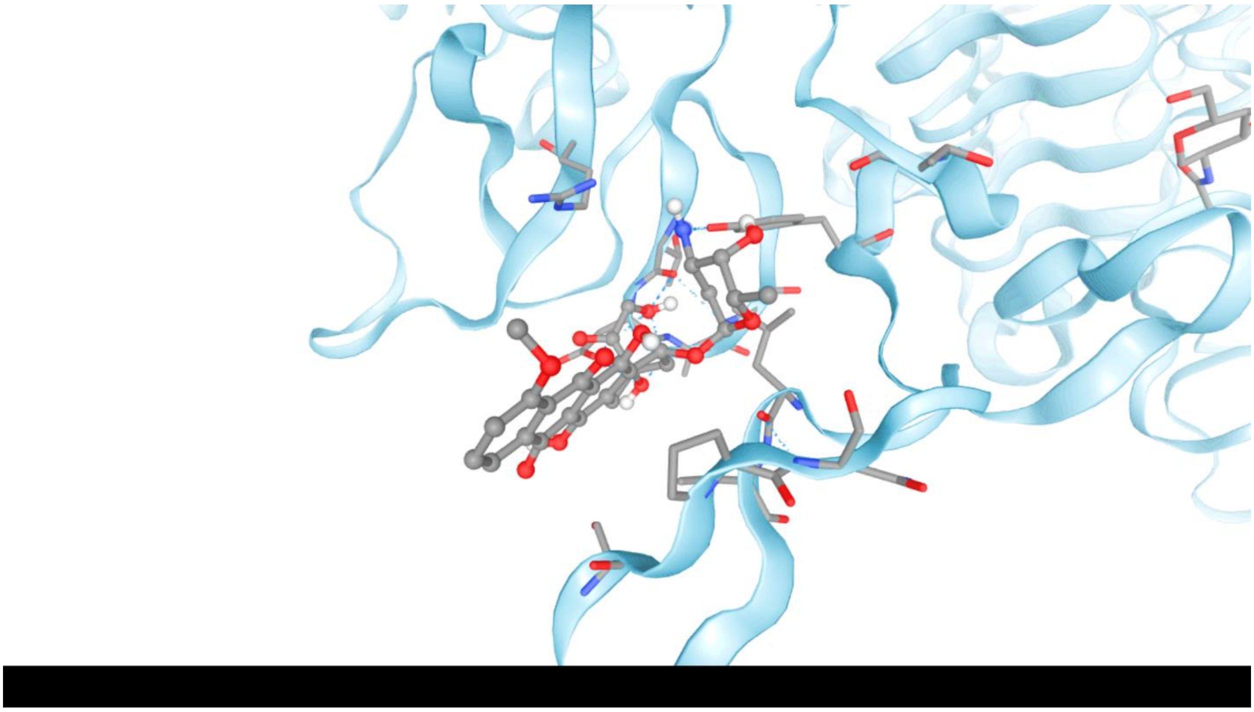

FIGURE 4: DOXORUBICIN AND HER 2 DOCKING PROCESS

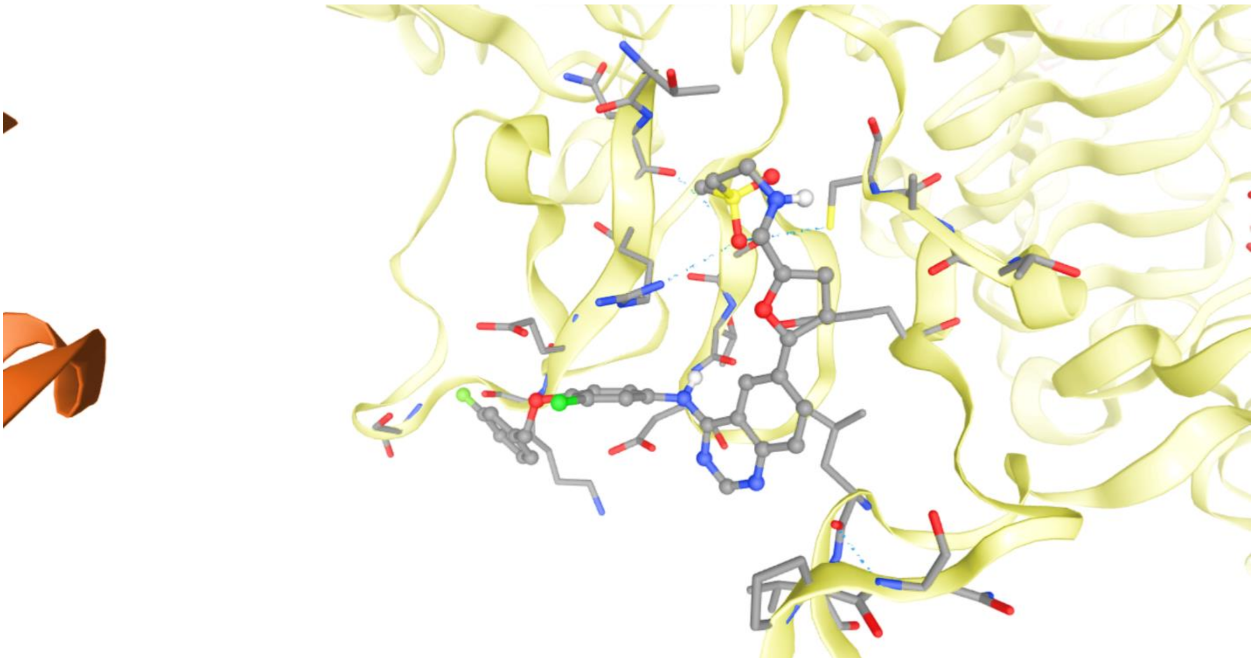

FIGURE 5: LAPATINIB AND HER 2 DOCKING PROCESS

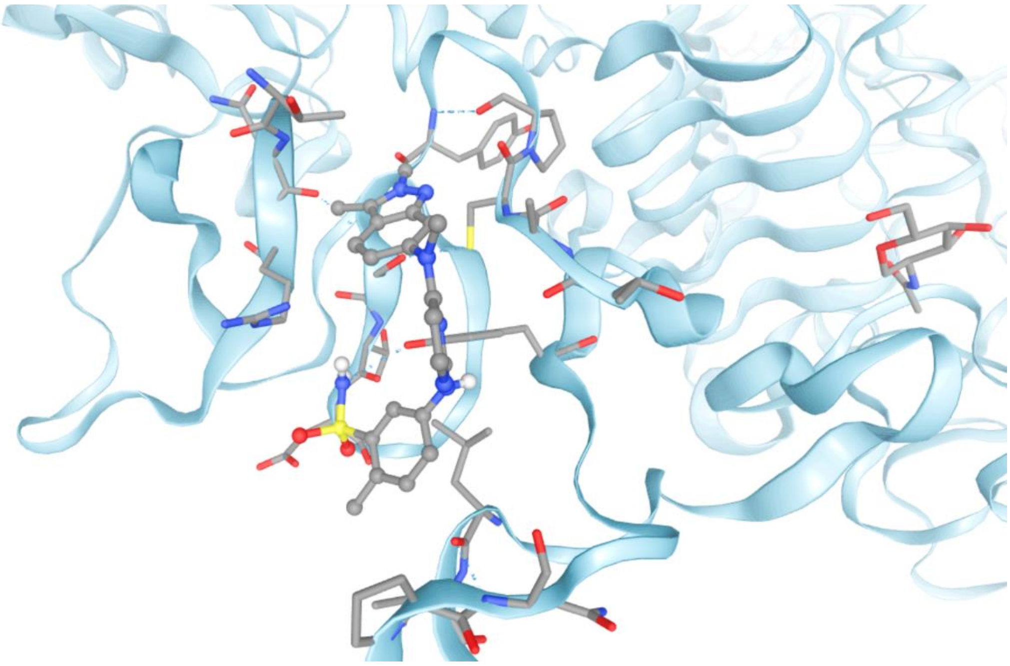

FIGURE 6: PAZOPANIB AND HER 2 DOCKING PROCESS

DISCUSSION

This study delves into the anti-cancer potential of bioactive compounds found in *Agrocybe aegerita*, using in-silico docking to explore their interactions with HER-2, a protein commonly overexpressed in certain aggressive breast cancers. The computational docking results provide important insights, revealing that among the bioactive compounds tested, ganoderic acid stands out with the highest binding affinity to HER-2, showing values in the range of -6.34 to -6.18. This high affinity indicates that ganoderic acid could effectively bind to and inhibit the HER-2 protein, suggesting its potential as a promising therapeutic agent in treating HER-2-positive breast cancer. When compared with standard cancer drugs, such as lapatinib (-6.16 to -5.63) and pazopanib (-6.20 to -6.05), ganoderic acid's similar or even superior binding affinities demonstrate its potential to serve as a viable natural alternative or complement to these well-established treatments (Yuan et al., 2022).

While not as remarkable as ganoderic acid, the results regarding ceramide and galectin still provide valuable insights into their potential applications. With binding affinities ranging from -3.91 to -3.07, Ceramide exhibited relatively lower interaction strength with HER-2. However, this should not discount ceramide's known biological role in inducing apoptosis in cancer cells. It may be that ceramide's therapeutic value lies not in its direct inhibition of

HER-2 but through complementary pathways that could act synergistically with other treatments. Similarly, galectin showed moderate binding affinity (-4.97 to -4.61), and while its docking scores are not as high as ganoderic acid, galectin is recognized for its involvement in tumor progression and metastasis, opening avenues for further investigation into its anti-cancer properties in combination therapies.

When considering the standard drugs, both lapatinib and pazopanib exhibited strong binding affinities, validating their efficacy in treating HER-2-positive cancers. However, doxorubicin, a commonly used chemotherapy drug, showed comparatively lower binding affinity (-5.43). This discrepancy highlights a key insight from the study: natural bioactive compounds like ganoderic acid could potentially offer comparable, if not improved, therapeutic benefits, particularly with fewer side effects than synthetic chemotherapy drugs, which are often associated with significant toxicity.

CONCLUSION

The in-silico analysis conducted in this study sheds light on the anti-cancer potential of *Agrocybe aegerita* bioactive compounds, particularly against HER-2 breast cancer protein. Among the compounds tested, ganoderic acid emerged as a standout, exhibiting binding affinities comparable to or better than some standard cancer drugs like lapatinib and pazopanib. This suggests that ganoderic acid holds promise as a natural anti-cancer agent with the potential to be developed into a therapeutic drug for HER-2-positive breast cancer. Ceramide and galectin, while showing lower binding affinities, should not be discounted, as they may offer therapeutic value in complementary pathways or combination with other treatments.

This research underscores the importance of exploring natural bioactive compounds in the fight against cancer. While standard chemotherapy drugs are effective, they often come with severe side effects. Natural compounds like ganoderic acid could offer a less toxic alternative, providing similar therapeutic benefits with potentially fewer adverse effects.

DECLARATION

The author declares that there is no conflict of interest.

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