RESEARCH ARTICLE

Arun Dev Sharma
Inderjeet Kaur
Amrita Chauhan

Unveiling anti-aspergillosis and anti-mucormycosis potential of fruit extracts from naturally growing *Chamaedorea seifrizii:* Chemical profiling, *in silico* studies, pharmacokinetics and wet lab validation

Authors' address:
Post Graduate Department of Biotechnology,
Lyallpur Khalsa College,
Jalandhar, 144001, Punjab,
India.

Correspondence:
Arun Dev Sharma
Post Graduate Department of Biotechnology, Lyallpur Khalsa College, Jalandhar, 144001, Punjab, India.
Tel.: 91-181-2241466
Fax: 91-181-2241465
e-mail: arundevsharma47@gmail.com

Article info:
Received: 17 August 2025
Accepted: 31 March 2026

ABSTRACT

Chamaedorea seifrizii is a bamboo plant that is mainly used for its air-purifying properties and ornamental value. Due to the absence of reports on its phytochemical constitutes, this study was aimed at chemical profiling, and evaluation of its *in vitro* anti-aspergillosis and anti-mucormycosis potential of acetone extracts of fruits of *Chamaedorea seifrizii* accompanied by *in silico* analysis. In this study, the chemical profile of *Chamaedorea seifrizii* fruit acetone extract (CFE) was determined, and major component hinokione was molecularly docked against fungal enzymes involved in the cell wall synthesis, specifically lanosterol 14α-demethylase (LD), chitin synthase (CS) and 1,3-beta-glucan synthase (GS), followed by with *in vitro* validation. Bioactive compounds in fruit extracts were studied using a gas chromatography-flame ionization detector (GC-FID). The CB-dock 2 tool was used for molecular docking. Using the poisoned food approach, antifungal activity was assessed against three test pathogens. Since hinokione was found to be a significant component of CFE by GC-FID, it was utilized for docking analysis. According to docking study, hinokione binds actively to the fungal enzymes LD, CS and GS. According to docking experiments, ligand hinokione interacted via H-bonds with the fungal enzymes 3 with vina score ranged from -9.0 to -10.6 kcal/mol. Hinokione complied with the LIPINSKY criteria. According to wet lab studies, CFE mitigated the growth of test pathogens. *Chamaedorea seifrizii* may be used in this study to produce new herbal remedies to cure for a range of illnesses including aspergillosis and mucormycosis. However, it needs further validation by *in vivo* and clinical studies.

Key words: aspergillosis, COVID-19, mucormycosis, *Chamaedorea seifrizii*, herbal drug

Introduction

The prevalence of invasive fungal diseases (IFD) is rising due to the aging of the population, the rise in diabetes mellitus (DM) and malignant tumors, and the widespread use of immunosuppressants during the coronavirus disease 2019 (COVID-19) pandemic (Ling et al., 2024). Numerous co-infections were documented globally during the COVID-19 pandemic (Alanio et al., 2020). Fungi such as *Aspergillus* and *Mucor* species are opportunistic infections that are responsible for fungal diseases, including mucormycosis and aspergillosis, that can infiltrate the lungs and bronchus of individuals with significantly compromised immune systems, causing acute inflammation of the lungs. Due to their high invasiveness, these pathogens can enter the bloodstream through the pulmonary blood vessels, causing necrotic inflammation, lung tissue ischemia, and blood vessel embolization. The mortality rate from invasive pulmonary aspergillosis (IPA) ranges from 35 to 80%, while invasive pulmonary mucormycosis (IPM) ranges from 76 – 87% (Hoenig et al, 2022; Ling et al., 2024). These fungal infections are known as "COVID-19 associated mucormycosis/aspergillosis (CAM/CAA)" because they pose a major health concern to those with impaired immune systems and can be treated with excessive steroid usage (John et al., 2021).

The need to find new antifungal medications is necessary because of the therapeutic limits of fungicidal medicines, such as their high cost, unavoidable toxicities, and fungal

http://www.jbb.uni-plovdiv.bg DOI: 10.69085/jbb20261009

drug resistance (Chen et al., 2025). According to earlier research, bioactive compounds that function as anti-fungal compounds may be employed as medicinal medications to lessen fungal growth (Chen et al., 2025). The intricate architecture of fungal cell walls, which is mostly made of chitin, glucans, and other polymers, are dynamically remodeled and degraded by enzymes such as lanosterol 14α-demethylase (LD), chitin synthase (CS), and 1,3-beta-glucan synthase (GS) (Ene et al., 2015; Gow et al., 2017; Chen et al., 2025). Numerous functions, including cell development, division, morphogenesis, and interactions with the environment, depend on these enzymes. The creation and degradation of fungal cell walls depend heavily on these enzymes, which are dynamic structures. Since the fungal cell wall is necessary for fungal life and absent from human cells, fungal enzymes can serve as useful targets for the development of novel antifungal medications since they are necessary for fungus but not for humans (Madhavan et al., 2022). The development of antifungal agents primarily targets enzymes involved in cell wall production and remodeling. New antifungal tactics that target the enzymes in fungal cell walls are still being investigated. Cell damage and death can result from defects in the integrity of the cell wall, which is frequently brought on by abnormalities in enzyme activity. Fungal cell wall enzymes are a focus for research and possible antifungal treatments since they are crucial to fungal physiology and interactions with the environment.

Chamaedorea seifrizii belongs to the Arecaceae family and is often referred to as bamboo palm, parlor palm, or reed palm. It is one of the members of the palm family (Agostini-Costa, 2018). There are several accounts of these ethnomedical applications for palm family members. *Chamaedorea seifrizii* is classified as a plant that has traditional and complementary medicine values to cure Goiter, bronchial asthma, and vaginal disorders (Bernal et al., 2010). This plant is considered as ornamental and generally used as an indoor air toxins and chemical vapor/pollutant remover. Nowadays, a lot of people grow *C. seifrizii* both indoors and outdoors. Earlier research pointed out that because this plant can absorb toluene, it can be used to treat neurological, ocular, and eye, nose, and throat irritations as well as unsteadiness (Inbathamizh et al., 2020). Lack of proper medicinal reports on this plant prompted us to do further studies for its possible therapeutic uses. Extracts from *C. sefrizii* reported in cancer chemoprevention via NQO1 enzyme induction in the Hepa-1c1c7 murine hepatoma cell line (Farag et al, 2019). By virtue of having bioactive compounds, *Chamaedorea seifrizii*, extracts from this plant should have antioxidant properties and anti-inflammatory potential as well. However, there are few specific studies on the bioactive compounds found in this plant; more research is required to fully identify the exact composition of its extracts. Even though this plant belongs to a well-known family of medicinal herbs, there haven't been many reports on it, which have led to more research. Although it is known that *Chamaedorea seifrizii* may contain beneficial biochemicals, there aren't many thorough investigations of its particular phytochemical profile. To completely comprehend the unique bioactive substances found in *Chamaedorea seifrizii* and their possible medical uses, more investigation is required. To the best of our knowledge, there are not many reports that describe the existence and assessment of distinct bioactive chemicals in *Chamaedorea seifrizii*. We hypothesized that due to the abundance of bioactive compounds, CFE has therapeutic potential to mitigate fungi like *Aspergillus* spp. and *Mucor* spp. Therefore, the current study concentrated on identifying bioactive compounds from the acetone extract of *Chamaedorea seifrizii* fruits, followed by docking and molecular simulation of bioactive component hinokione against LD, CS, and GS, and wet-lab validation. Its ability to prevent mucormycosis and aspergillosis is yet unclear, though. It would also provide fresh perspectives on the possible predictions in order to identify the most important antifungal medications. The structures and formulas of the bioactive chemicals found in *Chamaedorea seifrizii* will be predicted with the help of this study, which might be crucial for the development of novel therapeutic formulations. This is the first comprehensive report on the phytochemical and antifungal potential of *Chamaedorea seifrizii*, distinguishing it from general studies on the Arecaceae family.

Materials and Methods

Collection of samples

Auxiliary fruit samples from wild-growing *Chamaedorea seifrizii* (Figure 1) plants were gathered from a garden in the research region (31.30 latitudes North and 75.60 longitudes East). The botany department confirmed the plant, and BT106 was entered on the voucher. The climate of this city is humid subtropical, with long, hot summers and cold winters. The experiment was conducted in January – April 2025. After being cut into smaller pieces using a knife, the plant material (fruits) was taken to the study area, where it was left to shade dry at room temperature in the dark. A mortar and pestle were used to further decrease the size in powder form. After that, it was sieved, processed using an electrical grinder, and kept at 4°C for further examination.

http://www.jbb.uni-plovdiv.bg DOI: 10.69085/jbb20261009

Preparation of extracts

The powdered *Chamaedorea seifrizii* fruits (3g) were extracted in acetone/water (8:2 v/v). Before being spun down for fifteen minutes at 10,000 rpm and 4°C, the mixtures were manually mixed by agitating, vortexed, and incubated at room temperature for the whole night in an orbital shaker. Whatman filter paper 1 was used to filter the resulting supernatant, designated as *Chamaedorea seifrizii* auxiliary fruit methanol extract (CFME). The filtrate was then evaporated at 40°C using a rotary evaporator (BUCHI Rotavapor R¬200), and the concentrated extract (0.3 g, yield: 10%) was finally stored at -20°C until it could be further examined.

GC-FID analysis of extracts

The study of biologically active compounds in the fruits of *Chamaedorea seifrizii* acetone fruit extract was conducted using a gas chromatography flame ionization detector (GC-FID) apparatus (Chemtron Pvt ltd., 2045), according to Amrita et al. (2023). The extract was subjected to GC-FID analysis in order to determine and quantify the bioactive compounds. A 2-meter stainless steel column that was a component of the GC apparatus was filled with a sample volume of 10 µl at a volume of 10% OV-17. The sample was deposited onto 80 – 100% mesh Chromosorb W (HP). The nitrogen gas utilized for the mobile phase was 30 milliliters per minute. The injector and detector were kept at 200°C and 250°C, respectively. The oven was ramped up from 64°C to 200°C at an inflation rate of 3°C per minute. Bioactive compounds were identified through matching the relative duration time frame with published data or standards (Adams, 2012).

Computational studies

Preparation of ligands

On the basis of GC-FID, the main bioactive substance hinokione was chosen as ligand for docking studies following Amrita et al. (2023). Ketoconazole was used as a standard antifungal inhibitor. SMILES from the NCBI-PubChem (https://pubchem.ncbi.nlm.nih.gov/) database were used to prepare the ligands, and UCSF-chimera was used to create 3-D structures using build structure option.

Target protein preparation

The crystal structures of three structurally related members of fungal cell wall enzymes lanosterol 14α-demethylase (LD), chitin synthase (CS) and 1,3-beta-glucan synthase (GS) were employed as target enzymes in this study. The target receptors pdb ID's were: lanosterol 14α-demethylase: 4uym, 1,3-beta-glucan synthase: 8jzn, Chitin synthease: 8k52. The RCSB-PDB database (https://www.rcsb.org/) provided their structures. The dock prep setup in the Chimera program was used to prepare target enzyme receptors for docking research. Dock prep is an algorithm optimization step that fixes atomic bond length, charge anomalies, and structure.

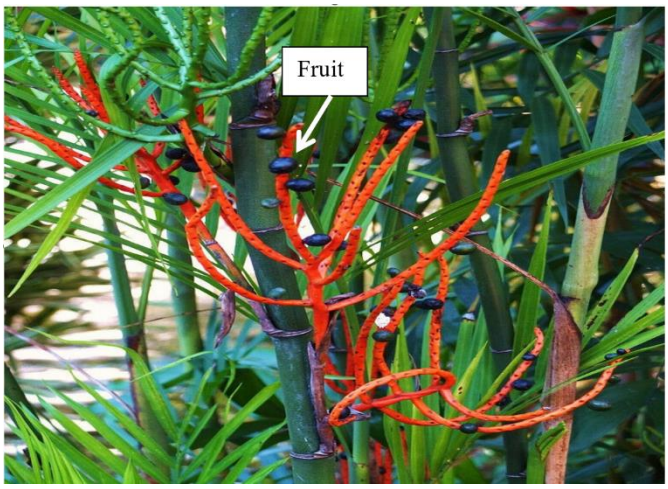


Figure 1. *Representative image fruit of Chamaedorea seifrizii. Photograph by AD Sharma.*

Molecular Docking

Bioactive chemicals chosen as ligands were subjected to molecular docking using Cb-dock2 (https://cadd.labshare.cn/cb-dock2/php/index.php) to examine the binding mechanism with members of the fungal cell wall family. The ligand and target enzyme molecules were uploaded to the cb-dock2 program in a.pdb file to initiate the docking process. The best-generated model is downloaded and stored in the.pdb file. The Biovia 2020 and UCSF Chimera tools were used to estimate the 2-D interactions between the enzyme and the ligand.

Molecular dynamic simulation (MDS)

The molecular dynamic simulation was evaluated in accordance with Chauhan & Sharma (2025) in order to determine the binding stability, orientation, and interaction styles between the selected best docked bioactive chemical (hinokione) and receptor (Lanosterol 14α-demethylase: 4uym). The selected complex file was subjected to molecular dynamics studies using GROMACS 2019.2 software. As functions of structural stability, the outcomes of the post-MD simulation studies were shown as RMSD.

Drug-likeness and ADMET

Using SWISSADME (http://www.swissadme.ch/http://lmmd.ecust.edu.cn/ admetsar/predict/), pharmacokinetics studies, drug-likeness, and ADMET (Absorption, Metabolism, Toxicity, and Excretion) of ligand (Hinokione) were carried out. Toxicity profile of ligands was studied using ProTox tool using SMILES of ligands (https://tox.charite.de/protox3/).

In vitro antifungal activity of CFE

The poison food method outlined by Gakuubi et al. (2017) was used to assess the antifungal activity of CFE. Using the food poisoning technique, the anti-aspergillosis and anti-mucormucosis capability of CFE was investigated on the fungal strains *A. niger* (MTCC 277), *A. oryzae* (MTCC 343), and *M. indicus* (MTCC 3473). Every microbe was purchased from the Institute of Microbial Technology in Chandigarh, India, or IMTECH. To PDA medium (HiMedia), 50 µl of CFE was added. The mixture was then divided across sterile Petri plates (9 cm in diameter) and left to harden for three hours at about 37°C. Using a sterile cork borer, mycelial fungal discs (8 mm) were extracted from fungal plates, aseptically transferred to Petri plates, and cultured for 15 days at 29°C. Ketoconazole (25 mg) of (Leford Pvt Ltd, India) was employed as a positive control. The following formula was used to measure MGI (mycelia growth inhibition): (MGI %) = DC-DT/DC × 100, where DC and DT are the control and test colony diameters. Experiments on antifungal activity were carried out three times.

Results and Discussion

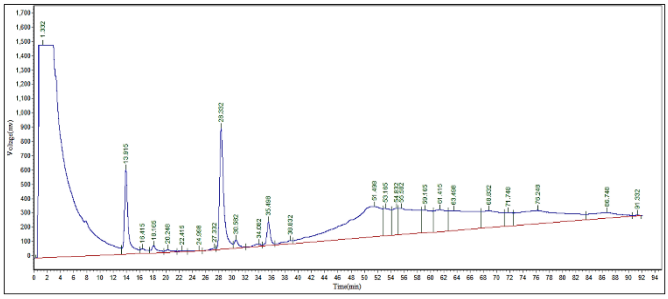
GC-FID identification and quantification of bioactive compounds present in Chamaedorea seifrizii fruit acetone extracts

Using color developments and/or precipitate, phytochemical fingerprinting is a qualitative test (Bouzidi et al., 2023). One of the modern techniques for locating and separating phytoconstituents is GC-FID phytochemical analysis. Plant phytoconstituents may be identified and isolated using GC-FID, a contemporary method (Bouzidi et al., 2023; Nkwocha et al., 2023).

Figure 2 shows the typical GC-FID chromatogram, which depicts the peaks that correspond to several bioactive compounds found in the extracts of *Chamaedorea seifrizii* acetone fruit extracts (CFE). It lists the compounds present in the CFE of *Chamaedorea seifrizii*, together with their percentage (%) compositions and retention time (RT). The GC–FID analysis of CFE led to the identification of 22 components. The major compound identified was hinokione (10.68%). These findings are similar to those of Duru (2020), who used gas chromatography and a flame ionization detector to measure the phytochemical content in solvents and observed the maximum amount in an ethanolic extract of *Zea mays* husk. Additionally, there have been reports of some of these components' biological activity. According to El Hachlafi et al. (2021), hinokione, a naturally occurring substance, may be found in the wood of several trees, particularly those in the Cupressaceae family. It is a form of thujaplicin and a derivative of tropolone. Hinokione has antibacterial, anti-inflammatory, and anticancer qualities and is utilized in a variety of goods, including cosmetics, dental care products, and even food additives in Japan. Based on this data, it was concluded that *Chamaedorea seifrizii* is rich in phytochemical constituents with key biological activities, such as antioxidant activity, according to the reviewed literature. Consequently, the diverse range of physiological potentials and biological activities exhibited by *Chamaedorea seifrizii* may be attributed to the existence of these bioactive chemicals.

In silico docking

In order to validate anti-aspergillosis and anti-mucormycosis potential of CFE, major bioactive phytocomponent hinokione was molecularly docked against fungal enzymes involved in the cell wall synthesis, specifically lanosterol 14α-demethylase (LD), chitin synthase (CS) and 1,3-beta-glucan synthase (GS). *In silico* docking is a technique for structure-based drug design used to find new ligands for protein structures. Molecular docking is a productive and economical



Ser. №	Ret. Time	Bioactive compound	Concentration (%)
1	1.332	-	51.4174
2	13.915	*Pentyl cyc1ohcxa-I.3-diene*	2.8765
3	16.415	*Linalool formate*	0.2753
4	18.165	*Linalool acetate*	0.3653
5	20.248	*Terpinyl acetate <Irans-dihydro-α->*	0.1529
6	22.415	*Citronellyl acetate*	0.0434
7	24.998	*Isocyclogeraniol*	0.0283
8	27.332	*Caryophyllene <9-epi(E)->*	0.0620
9	28.332	*Pinocampheol*	4.5506
10	30.582	*Isoamyl nonanoate*	0.3154
11	34.082	*Eudesmol <γ->*	0.1433
12	35.498	*Dodecanoic acid*	0.7490
13	38.832	*Ambroxide*	0.2751
14	51.498	*Hinokione*	10.6801
15	53.165	*Incensole acetate*	1.7397
16	54.832	*γ-Sitosterol*	1.3654
17	55.582	*Sandaracopimarinol*	4.4496
18	59.165	*Labd-7.13-dien-15-ol. acetate*	2.1026
19	61.415	*Abietol <neo->*	2.4677
20	63.498	*Hentriacontane*	4.7799
21	68.832	-	2.8643
22	71.748	*Nonacosane*	0.9219
23	76.248	*Nezukol*	5.8320
24	86.748	-	1.5115
25	91.332	-	0.0310

Figure 2. *Identification of chemical constituents by GC-FID from fruit-based acetone extracts from naturally growing Chamaedorea seifrizii.*

http://www.jbb.uni-plovdiv.bg DOI: 10.69085/jbb20261009

method of developing and testing medications (Kabir & Muth, 2022). This method provides information on the interactions between drugs and receptors, which may be utilized to predict how the drug model will bind to target proteins and achieve dependable binding at ligand binding sites. The interaction between the chemicals and the receptor is crucial when formulating medications. While *Chamaedorea* has been used traditionally to treat illnesses, we looked at the binding ability of bioactive major chemical from *Chamaedorea seifrizii* extracts with important anti-fungal targets in this work.

Table 1 lists compounds' docking scores with all receptors (vina score: binding energy) and other crucial information against the fungal cell wall family. The higher negative docking score demonstrated strong binding affinity between the ligand and receptor molecules by indicating the lowest binding free energy and vice versa. The binding energy of hinokione phytochemical as a ligand with receptors was between −9.6 kcal/mol and −10.6 kcal/mol. Docking analysis revealed that hinokione docked efficiently with all fungal cell wall enzymes. However, among all receptors, lanosterol 14α-demethylase (4uym) exhibited more affinity towards hinokione as evidenced by its binding energy value of −10.6 kcal/mol. Notably, when compared with the synthetic drug ketokinazole, docking of hinokione was apparently higher towards lanosterol 14α-demethylase as evidenced from its binding energy values (−10.3 kcal/mol vs −10.6 kcal/mol). 3D images exhibiting best docked structures are shown in Figure 3. In-depth analysis revealed that, like synthetic drug ketokinazole, the bioactive compound hinokione showed strong affinity towards lanosterol 14α-demethylase by targeting the C-terminal domain via conserved residues involving “A chain”. The activity of lanosterol 14α-demethylase is linked to its C-terminal domain, which also interacts with medications such as ketoconazole (Chen et al., 2025). This domain is crucial for the catalytic activity of the enzyme and the contact with the substrate. It has structural components that aid in binding to substrates and inhibitors like azoles. The C-terminal domain of lanosterol 14α-demethylase is thought to be a possible target for drug development because of its function in substrate and inhibitor binding, especially for medications intended to treat disorders linked to fungi. Lanosterol 14α-demethylase is a crucial enzyme involved in ergosterol synthesis that is a key component of the fungal cell wall. It controls membrane permeability and offers structural stability. Based on this investigation, it was hypothesized that the bioactive chemical hinokione functions similarly to the synthetic medicine ketoconazole by blocking the enzyme lanosterol 14α-demethylase, which is necessary for the formation of ergosterol in fungi (Cupp-Vickery et al., 2001). The fungal cell membrane becomes leaky and loses its structural integrity due to hinokione's interference with ergosterol production. Fungal cell death results from hinokione's disruption of the structure and function of the fungal cell membrane by preventing its production. Insufficient ergosterol causes the fungal cell membrane to become unstable and leaky, which hinders its capacity to control the flow of chemicals into and out of the cell.

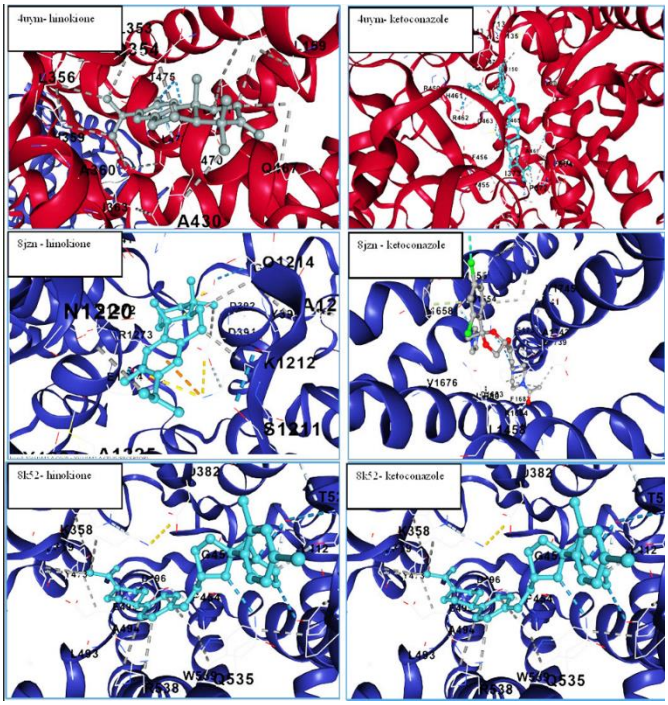


Figure 3. *3D-images showing molecular docking conformation of hinokione in the active sites of receptors.*

Table 1. *Molecular docking of bioactive compound hinokione and synthetic drug ketoconazole with fungal cell wall enzymes.*

Receptors	Ligand name	Binding energy kcal/mol (Vina score)	Cavity volume (Å^3)	Center (x, y, z)	Docking size (x, y, z)
Lanosterol 14α-demethylase: 4uym		-10.6	2737	123, 195, -10	20, 30, 26
1,3-beta-glucan synthase: 8jzn	hinokione	-10.2	2664	143, 158, 141	27, 20, 20
Chitin synthease: 8k52		-9.6	3570	140, 171, 164	27, 35, 27
Lanosterol 14α-demethylase: 4uym		-10.3	6068	137, 199, 2	34, 27, 27
1,3-beta-glucan synthase: 8jzn	ketoconazole	-10.1	2285	152, 169, 182	27, 27, 27
Chitin synthease: 8k52		-9.0	2495	136, 168, 147	20, 20, 20

http://www.jbb.uni-plovdiv.bg DOI: 10.69085/jbb20261009

During docking, the ligand's affinity for the receptor is based on polar and non-polar interactions with active site residues of the receptor. As a result, as indicated in Figure 4, the molecular interactions between bioactive substances and target receptor proteins were further examined. Figure 3 shows the ligand-target interactions of the bioactive compound hinokione with fungal cell wall enzymes and proteins. The in-depth analyses demonstrated that the docked ligand leveraged a strong network of polar interactions with several residues aligning the binding cavity of the receptors. Such interactions included H-bond, alkyl, Pi-alkyl, and Pi-anion interactions. The details of polar interactions for each candidate molecule in terms of the ligand's atom, amino acid, and bond length are also shown in Figure 2. Further, It was observed that the most stable complex lanosterol 14α-demethylase- hinokione was also stabilized by alkyl, pi-alkyl, and two conventional H-bond interactions. Additionally, our investigation confirmed that tested bioactive candidate hinokione like synthetic drug ketokinazole were able to orient themselves in the same binding pose and demonstrated a tendency to target conserved residues LEU125 THR126 PHE130 VAL134 VAL135 TYR136 LEU143 GLN146 LYS147 VAL150 MET300 ALA303 LEU304 ALA307 ILE373 SER375 ILE376 ILE377 ARG378 PHE504 in the binding site of the lanosterol 14α-demethylase enzyme. These observations suggested a common mechanism pathway evolved by the synthetic drug ketokinazole and the bioactive compound hinokione to mitigate fungal growth. These results were in consonance with earlier studies reporting docking interactions of ursolic acid and noscapine bioactive compounds from *Syzygium aromaticum* and *Inula racemosa* with a binding energy value of − 8.7 kcal/mol for *Bipolaris oryzae* BMK-1 enzyme (Bhat et al., 2024). Singh et al (2022) reported molecular docking studies of stigmasterol and γ-sitosterol from fruit extracts of *Cyamopsis tetragonoloba* against the fungal target protein, i.e., lanosterol 14α-demethylase and observed potential binding mode and binding affinity. There have been reports of carvacrol, α-thujene, and thymol bioactives based on essential oils from the plants *Boswellia carteri*, *Thymus vulgaris*, and *Trachyspermum ammi* that include fungal enzymes with binding affinity ranging from -4.1 to -6.9 kcal/mol for the active regions of pathogen proteins (Biswal et al., 2019; Omar et al., 2021). Antifungal biochemical urosolic acid derived from leaf extracts from *Breonadia salicina* was found to be effective in mitigating fungal diseases derived from *Penicillium* spp. (Mahlo & Eloff, 2014). In order to ascertain the binding mechanism and affinity of various phytochemical substances for lanosterol 14α-demethylase, Singh et al. (2022) also used an *in silico* docking technique. Taken together, this study cited that extracts made from *Chamaedorea seifrizii* may be considered the most important source of anti-fungal compounds. Based on analysis, it was highlighted that CFE can be used as an effective source of anti-fungicidal compounds. Therefore, following more research, the recently discovered chemical may be used as a possible next-generation plant-based medication to treat mucormycosis and aspergillosis. Nevertheless, a more thorough examination of each compound's unique activity and method of action as potent inhibitors is required. This study will assist in predicting the structures and formulas of bioactive chemicals contained in *Chamaedorea seifrizii* extracts that might be vital for novel medicine formulations.

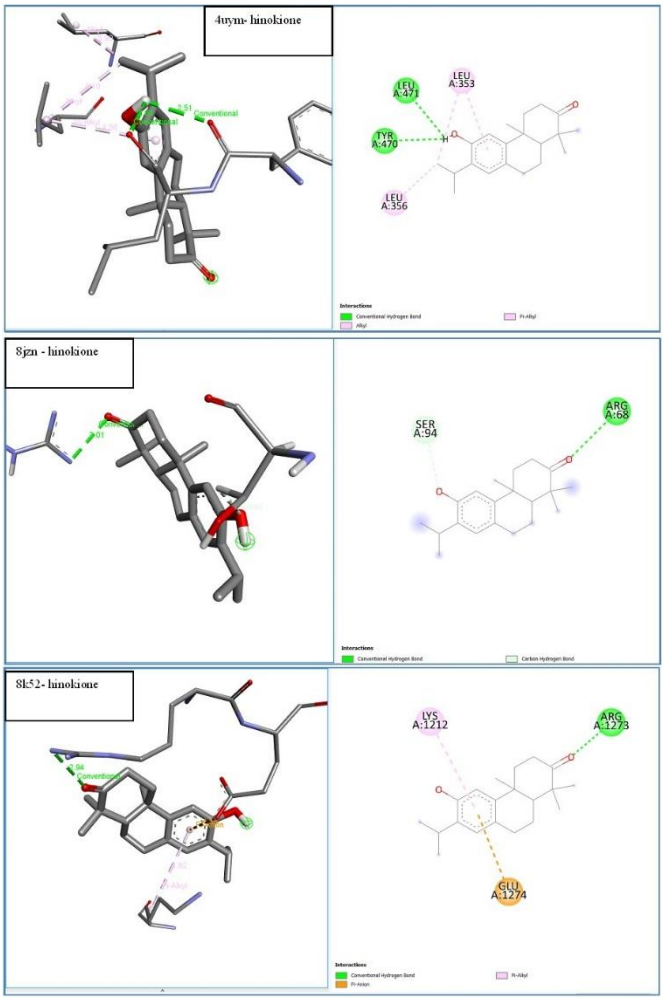


Figure 4. *2D images showing ligand hinokione interactions with receptor.*

Molecular dynamics studies

Molecular dynamics (MDS) simulation was used to verify docking results. In a regulated physiological environment, MDS facilitates precise analysis of biological macromolecule dynamics. MDS, a computer technique for examining a biophysical system's physical interactions, the flexibility and structural alterations of docked complexes may be seen over the simulation time. According to Liu et al. (2017), such an investigation would also evaluate the ligand's crucial binding interactions with important catalytic site residues and provide

valuable insights into the dynamic behavior of the ligand and protein. The best-docking scored models of the most promising lead, Hinokione -Lanosterol 14α-demethylase: 4uym complex, was chosen for a 50 ns all-atom MDS (Figure 5). Crucial structural metric RMSD was utilized to describe the MDS of biomolecular systems (Ishak et al., 2017). The results of the post-MD simulation investigations are shown in Figure 5, where the RMSD of the resulting complexes as a function of structural stability following ligand attachment to the appropriate proteins is represented. RMSD determines the average distance among atoms in a model at a specific moment in the simulation compared to the reference starting structure. Thus, we analyze the overall time-dependent structural deviation or similarity among the structures recorded in the trajectory. Examining how RMSD values vary over time or under various circumstances might help one understand the complex's dynamics and stability (Ishak et al., 2017). This graph displays the degree of ligand-protein binding site compatibility during the simulation. A falling pattern might indicate that the ligand is adopting a more advantageous binding position, whereas a rising pattern would indicate that it is exploring other orientations. A stable fit means that the ligand's binding form remains constant. Important information on the orientation and structure of the simulated ligands in relation to their binding pocket might be obtained by tracking RMSD trajectories. After a few nanoseconds, the target achieved stable confirmation, as the plot of the Hinokione -Lanosterol 14α-demethylase: 4uym complex demonstrates. The first binding to the substrate causes massive fluctuations between 0.1 nm and 0.8 nm in the RMSD trajectory upon ligand binding till 30 ns, followed by the equilibrium state at 0.6 nm during simulation time. The ligand-protein's RMSD trajectory suggests that it could be trying to find a better binding posture during the simulation, based on the initial binding position. The trajectory seems to have established a more suitable binding position toward the conclusion of the experiment, stabilizing

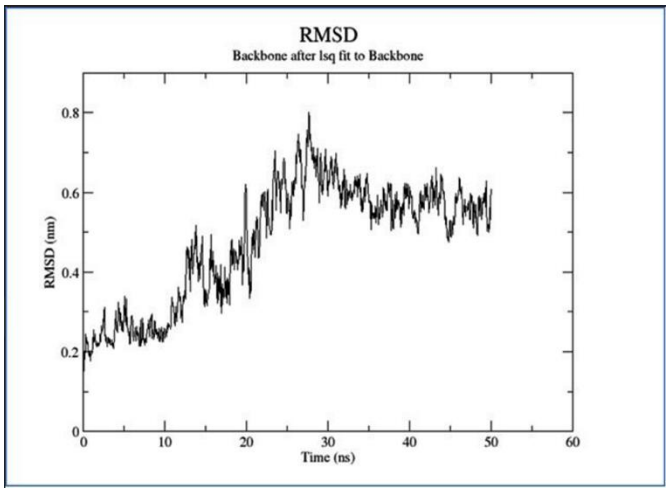


Figure 5. *Molecular dynamics (MD) analysis of Lanosterol 14α-demethylase: 4uym-hinokione complex.*

at around 0.6 nm until 20 ns. Similar RMSD variations within an acceptable limit of 10 Å (1 nm) have been documented using simulation-based analysis and molecular docking based on drug development (Muralidharan et al., 2020). This finding proved that ligand binding stabilizes the protein structure. From the aforementioned, it can be inferred that the ligands' binding does not jeopardize the structural integrity of the Lanosterol 14α-demethylase enzyme and that they may act as enzyme inhibitors. These results also validated docking studies, indicating the impactful role of *Chamaedorea seifrizii* as an anti-fungal agent having therapeutic applications.

In vitro antifungal activity of CFE

The *in silico* results were further supported by wet lab authentication using three fungus strains. Using CFE (50 µl), 75% mycelial growth inhibition (MGI) was detected in the MTCC 277 pathogen, whereas 67% MGI was observed with MTCC 343 and MTCC 3373 after 6 days of incubation (Table 2 and supplementary Figures 1-3). Changes in mycelia

Table 2. *Mycelia growth inhibition (MGI) by CFE against various fungal strains.*

Fungal culture	**Sample/ Control name**	**MGI (%) Days**			
		3	6	10	15
MTCC277	NC	CI	NI	NI	NI
MTCC277	PC	CI	80	70	50
MTCC277	CFE	CI	75	70	50
MTCC343	NC	CI	NI	NI	NI
MTCC343	PC	CI	40	NI	NI
MTCC343	CFE	CI	67	28	28
MTCC3373	NC	CI	NI	NI	NI
MTCC3373	PC	CI	80	60	50
MTCC3373	CFE	CI	67	30	30

Legend: CI - complete inhibition, NI - nil inhibition, PC - positive control (synthetic drug), CFE - *Chamaedorea seifrizii* fruit extract.

DOI: 10.69085/jbb20261009

growth diameter at different days is also shown in Figure 6.

Surprisingly, CFE was able to inhibit growth of MTCC 277 pathogen even after 15 days of growth, whereas with MTCC 343 and MTCC 3373 MGI was 28% and 30% respectively. Notably, when compared with the synthetic drug ketoconazole, with the MTCC 273 pathogen, the drug was able to show only 40% MGI as compared to 67% with CFE after 6 days of growth. After 15 days of growth, the synthetic drug ketoconazole was unable to inhibit the growth of pathogen MTCC 273, whereas CFE showed 28% MGI. With MTCC 277 after 15 days of growth, MGI of CFE was equivalent (50%) to that of the synthetic drug. Hinokione, a main component of CFE, or other minor components, may be responsible for its antifungal properties. Additionally, it was mentioned that many antifungal drugs prevent fungi by prohibiting ergosterol synthesis, which is the key component of fungal cell walls. This disrupts fungal growth and proliferation, osmosis, and the integrity and function of membrane-bound proteins (Bendaha et al., 2011). This observation was in agreement with the report of Abirami et al.'s (2021), citing the anti-fungal potential of medicinal plant extracts such as *Allium sativum*, *Lawsonia inermis* against fungal pathogens like *Curvularia* spp. and *Trichophyton* spp. Similar findings were reported by Hua et al. (2014), who examined the essential oils of eucalyptus, camphor, peppermint, litsea, and anise and reported antifungal effectiveness against *Aspergillus ochraceus*, with growth rate inhibition ranged from 50 – 70% decreased by 250 – 500 µL of oils. *Aspergillus nigri* growth was suppressed by Boldo essential oil, according to Passone et al. (2012).

ADMET analysis

The ligand Hinokione has been evaluated for drug-likeness using the Lipinski rule of five (RO5). The data for all parameters was estimated using the SwissADME web server. These ideas could be a good indicator of medication safety (Lipinski et al., 1997; Veber et al., 2002). This proved that all molecules possessed properties similar to those of drugs. Other chemical properties like the partition coefficient and polar surface area can be used to predict each ligand molecule's oral action. Both ligands have modest molecular weights, per PASS and ADMET tests. Srimai et al. (2013) found that ligands with smaller molecular weights had a higher probability of diffusing rapidly and overcoming biological membranes. Hinokione had log Po/w ratios of 4.37 (Table 3). Based on our research, the ligand is highly bioavailable orally. Wu et al. (2020) claim that TPSA is a

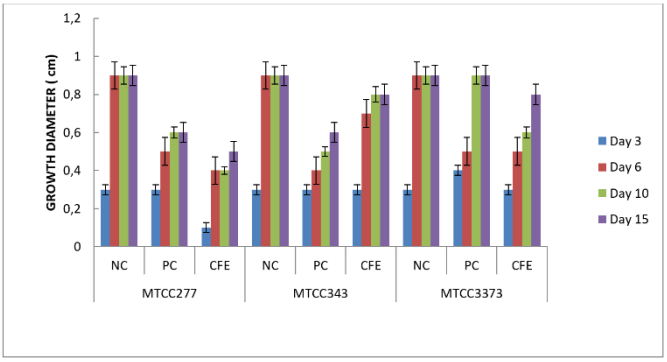


Figure 6. *Fungal mycelia growth under CFE against various fungal strains, NC: negative control, PC: positive control, CFE: Chamaedorea seifrizii extract.*

Table 3. *ADMET properties of bioactive compounds hinokione used as ligand.*

Physicochemical properties	
Formula	C20H28O2
Molecular weight	300.44 g/mo
Num. heavy atoms	22
Num. arom. heavy atoms	6
Fraction Csp3	0.65
Num. rotatable bonds	1
Num. H-bond acceptors	2
Num. H-bond donors	1
Molar Refractivity	91.84
TPSA	37.30 Å²
Lipophilicity	
Log Po/w (iLOGP)	3.18
Log Po/w (XLOGP3)	4.87
Log Po/w (WLOGP)	4.72
Log Po/w (MLOGP)	3.90
Log Po/w (SILICOS-IT)	5.19
Consensus Log Po/w	4.37
Water solubility	
Log *S* (ESOL)	-4.91
Solubility	3.73e-03 mg/ml; 1.24e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.39
Solubility	1.23e-03 mg/ml; 4.09e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-5.65
Solubility	6.74e-04 mg/ml; 2.24e-06 mol/l
Class	Moderately soluble
GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	No
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-4.67 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	yes
Bioavailability Score	0.55
PAINS	0 alert
Brenk	0 alert
Leadlikeness	No; 1 violation: XLOGP3>3.5
Synthetic accessibility	3.29

very accurate measure of drug absorption. Ligand showed enormous GI (gastrointestinal tract) absorption, as Table 3 demonstrates. Ligand also exhibited good oral bioavailability as evidenced from bioavailability score of 0.55. A score of 0.55 or above is frequently regarded as ideal, indicating that a significant amount of the medication will be absorbed and reach the bloodstream, which is the crucial factor in drug design. These results validate the compounds' excellent drug-likeness and absorption capacity. A crucial pharmacokinetic characteristic for drug development is lipophilicity, which is represented by consensus Log Po/w, which indicates how well a substance may pass through cell membranes. It was observed that the Log Po/w value was 4.37, indicating the lipophilic nature of all compounds. A chemical is more lipophilic (fat-soluble) if its Log Po/w value is higher, and more hydrophilic (water-soluble) if it is lower. For predicting drug absorption, distribution, metabolism, and excretion (ADME) characteristics and evaluating drug-likeness, this consensus value offers a more accurate approximation of lipophilicity. With a LogKp value score of compounds were in the range of -4.67 cm/s. Greater skin permeability is indicated by a larger LogKp value (e.g., a LogKp > -2.5 is considered high permeability), whereas a lower or negative value denotes a low rate of absorption. This number is usually associated with the molecular size and lipophilicity (fat solubility, commonly expressed as log P) of the molecule. Moreover, the ligand that was assessed was P-glycoprotein (P-gp) efflux exporter substrates. By pumping drugs back into the lumen, P-gp decreases the absorption of drugs in the stomach, according to Konig & Muller (2013). According to Srimai et al. (2013), the liver is home to the CYP450 class of enzymes that aid in the organism's detoxification process. Hinokione had an inhibitory effect on the CYP2D6, CYP2C19 enzymes and non-inhibitory capabilities for other enzymes. Thus, the findings are preliminary and need *in vivo* validation before therapeutic relevance can be claimed.

PASS prediction

Further evaluation of the discovered compounds' biological activity analysis was conducted using the structure-based PASS Online biological activity prediction program (Adnan et al., 2020). A new phytochemical may be indicated by pharmacological activity (Khurana et al., 2011). If a chemical's probable activity (Pa) value is greater than its likely inactivity (Pi), it is said to have pharmacological potential. According to the likely Pa values in this case, the bioactive chemicals found have a variety of biological and pharmacological activities in addition to potential targets against certain receptors, indicating that they may be innovative therapeutic essential components. As seen in Table 4, the ligand has been predicted to possess significant anti-neoplastic and anti-inflammatory characteristics. The strong biological activity of the isolated compound, including its ROS-scavenging capabilities, is demonstrated by its Pa value. In their study of the antioxidant and anti-proliferative qualities of the bioactive edible vegetable fraction of *Achyranthes ferruginea* Roxb, Reza et al. (2021) also observed similar results.

Toxicity profile of ligands

Both ligands' toxicity profiles were ascertained using the ProTox tool. Predication was based on different level of toxicity such as organ toxicity (neurotoxicity, cardiotoxicity, hepatotoxicity, respiratory toxicity, and nephrotoxicity), toxicological endpoints (like cytotoxicity, immunotoxicity, mutagenicity, carcinogenicity, BBB-permeability, clinical toxicity, ecotoxicity, and nutritional toxicity), toxicological pathways (AOPs), toxicity targets, targets for molecular initiating events (MIEs), and six molecular targets for metabolism are among the diverse levels of toxicity that the prediction scheme is divided into, thereby providing insights into the possible molecular mechanism behind such toxic response. According to the toxicity profiles, which include hepatotoxicity, neurotoxicity, cardiotoxicity, immunotoxicity, and cytotoxicity, the ligand was not harmful to any organs (Table 5). Furthermore, bioactive compound used as ligands was not mutagenic or carcinogenic by nature. A thorough toxicological analysis showed that the bioactive material utilized as a ligand was insensitive to target-dependent

Table 4. *Bioactivity score of the ligand.*

Ligand name	Activity	Pa	Pi
Hinokione	Nitric oxide antagonist	0.919	0.002
	CYP2J substrate	0.713	0.014
	Ecdysone 20-monooxygenase inhibitor	0.695	0.003
	Transcription factor NF kappa B stimulant	0.882	0.002
	Transcription factor stimulant	0.682	0.003
	Antineoplastic	0.671	0.014
	Apoptosis agonist	0.762	0.010
	Gluconate 2-dehydrogenase (acceptor) inhibitor	0.656	0.031
	Mucomembranous protector	0.852	0.033
	Testosterone 17beta-dehydrogenase (NADP+) inhibitor	0.753	0.034
	Antiinflammatory	0.722	0.012

biological processes, such as the nuclear receptor signaling pathways or the stress response. Furthermore, the projections indicated that phenethyl cinnamonate and hinokione are safe bioactive components since they fall within toxicity class 5. A radar chart showing the toxicity profile is displayed in Figure 7. The lethal toxicity dosage of a medicine is determined by the hazardous unit called LD_{50}. Hinokione's expected lethal dose (LD_{50}) was 5000 mg/kg. The log10 (LD_{50}) values of 3.5 for hinokione on the hazardous scale demonstrated the bioactive chemical's non-toxic nature. On the dangerous scale, ligands' −log10 (LD_{50}) values range from 2.8 to 3.7, meaning that the bioactive substance is not toxic. According to Raies et al. (2016), a toxicity study is required for drugs that might endanger humans, animals, or the environment. Liver hepatotoxicity is the most common cause of therapeutic pharmacological failures on the market, according to Tiwari et al. (2025). Furthermore, none of the bioactive compounds used as ligands had the ability to induce mutations or malignancy. Tiwari et al. (2025) state that if all medications are mutagenic, meaning they damage live cells

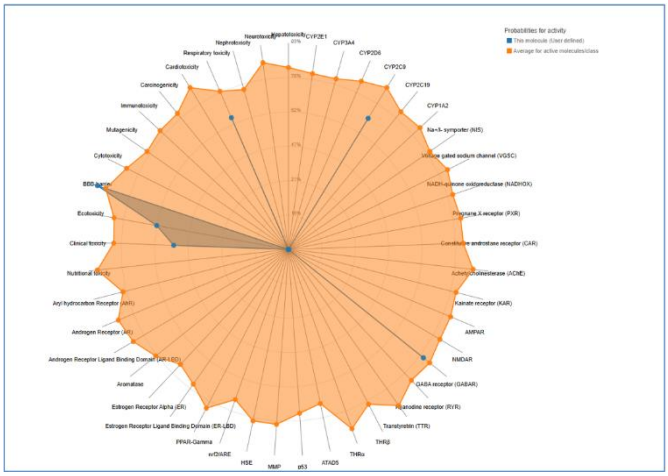


Figure 7. *The toxicity radar chart is intended to quickly illustrate the confidence of positive toxicity results compared.*

Table 5. *Toxicity profile of Hinokione.*

Classification	Target	Prediction	Probability
Organ toxicity	Hepatotoxicity	Inactive	0.74
Organ toxicity	Neurotoxicity	Inactive	0.53
Organ toxicity	Nephrotoxicity	Inactive	0.90
Organ toxicity	Cardiotoxicity	Inactive	0.81
Toxicity end points	Carcinogenicity	Inactive	0.73
Toxicity end points	Immunotoxicity	Inactive	0.91
Toxicity end points	Mutagenicity	Inactive	0.85
Toxicity end points	Cytotoxicity	Inactive	0.82
Toxicity end points	Nutritional toxicity	Inactive	0.55
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	Inactive	0.93
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	Inactive	0.85
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	Inactive	0.93
Tox21-Nuclear receptor signalling pathways	Aromatase	Inactive	0.91
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	Inactive	0.72
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	Inactive	0.79
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	Inactive	1.0
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	Inactive	0.70
Tox21-Stress response pathways	Heat shock factor response element (HSE)	Inactive	0.70
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	Inactive	0.72
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	Inactive	0.98
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	Inactive	0.95
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	Inactive	0.82
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	Inactive	0.93
Molecular Initiating Events	Transtyretrin (TTR)	Inactive	0.73
Molecular Initiating Events	Ryanodine receptor (RYR)	Inactive	0.86
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	Inactive	0.88
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	Inactive	1.0
Molecular Initiating Events	Kainate receptor (KAR)	Inactive	1.0
Molecular Initiating Events	Achetylcholinesterase (AChE)	Inactive	0.85
Molecular Initiating Events	Constitutive androstane receptor (CAR)	Inactive	0.96
Molecular Initiating Events	Pregnane X receptor (PXR)	Inactive	0.66
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	Inactive	0.78
Molecular Initiating Events	Voltage gated sodium channel (VGSC)	Inactive	0.95
Molecular Initiating Events	Na+/I- symporter (NIS)	Inactive	0.94
Metabolism	Cytochrome CYP1A2	Inactive	0.90
Metabolism	Cytochrome CYP2C19	Inactive	0.62
Metabolism	Cytochrome CYP2D6	Inactive	0.90
Metabolism	Cytochrome CYP3A4	Inactive	0.85
Metabolism	Cytochrome CYP2E1	Inactive	0.99

and are the main cause of diseases like cancer. Over all, it was observed that the compound was inactive for the majority of pathways, thus exerting non-toxic effects.

Conclusion

The present study concludes by highlighting the strong anti-fungal properties of fruit acetone extract of native plants like *Chamaedorea seifrizii*. In addition, *in silico* analysis coupled with MDS also validated the strong therapeutic significance as an anti-fungal agent of bioactive compound hinokione from fruit acetone extracts of *Chamaedorea seifrizii*. Experimental validation indicated that CFE was capable of mitigating fungus growth causing aspergillosis and mucormycosis, and validated the *in silico* findings. This suggests that *Chamaedorea seifrizii* is an excellent source of physiologically active chemicals that may be exploited to the creation of pharmacological products. Our study was limited to *in vitro* tests. However, further studies based on clinical trials are required. The clinical transferability of these results might be improved by examining the bioactive components of these plant extracts. More broadly, our research adds to the expanding corpus of knowledge focused on utilizing nature's arsenal to create plant-based medicines that lessen anti-inflammatory diseases.

Acknowledgement

This research was carried out with the support of the Dept. of Science and Technology, Govt. of India, DST/SEED/SCSP/STI/2019/253.

References

Abirami S, Edwin Raj B, Soundarya T, Kannan M, Sugapriya D, Al-Dayan N, Ahmed Mohammed A. 2021. Exploring antifungal activities of acetone extract of selected Indian medicinal plants against human dermal fungal pathogens. Saudi J. Biol. Sci., 28(4): 2180-2187.

Adams RP. 2012. Identification of essential oils components by gas chromatography/mass spectroscopy, 4th edn. Carol Stream, IL: Allured Business Media.

Adnan M, Chy MNU, Kamal ATMM, Chowdhury KAA, Rahman MA, Reza ASMA, Moniruzzaman M, Rony SR, Nasrin MS, Azad MOK, Park CH, Lim YS, Cho DH. 2020. Intervention in neuropsychiatric disorders by suppressing inflammatory and oxidative stress signal and exploration of *in silico* studies for potential lead compounds from *Holigarna caustica* (Dennst.) Oken leaves. Biomolecules, 10(4): 561.

Agostini-Costa TDS. 2018. Bioactive compounds and health benefits of some palm species traditionally used in Africa and the Americas - A review. J. Ethnopharmacol., 224: 202-229.

Alanio A, Dellière S, Fodil S, Bretagne S, Mégarbane B. 2020. Prevalence of putative invasive pulmonary aspergillosis in critically ill patients with COVID-19. Lancet Respir. Med., 8(6): 48-49.

Amrita Kaur I, Sharma AD. 2023. Underutilized plant *Cymbopogan martinii* derived essential oil is excellent source of bioactives with diverse biological activities. Russ. Agric. Sci., 49(1): 100-117.

Bakkali F, Averbeck S, Averbeck D, Idaomar M. 2008. Biological effects of essential oils – a review. Food Chem. Toxicol., 46(2): 446-475.

Bendaha H, Yu L, Touzani R, Souane R, Giaever G, Nislow C, Boone C, El Kadiri S, Brown GW, Bellaoui M. 2011. New azole antifungal agents with novel modes of action: synthesis and biological studies of new tridentate ligands based on pyrazole and triazole. Eur. J. Med. Chem., 46(9): 4117-24.

Bernal R, Galeano G, García N, Olivares IL, Cocomá C. 2010. Uses and commercial prospects for the wine palm, *Attalea butyracea*, in Colombia. Ethnobot. Res. Appl**.,** 5(8): 255-268.

Bhat S, Rather M, Gani S, Nabi A, Ganai SA, Shah MD, Sofi P, Jeelani F, Hussain A, Ashraf S, Anwar A, Iqbal I, Nisa TU, Summuna B, Banday S. 2024. Identification of plant based potential antifungal compounds against BMK-1 protein of *Bipolaris oryzae* using molecular docking approach. Sci. Rep., 14(1): 15665.

Biswal A, Venkataraghavan R, Pazhamalai V. 2019. Molecular docking of various bioactive compounds from essential oil of *Trachyaspermum ammi* against the fungal enzyme Candidapepsin-1. J. Appl. Pharm. Sci., 9(5): 021-032.

Bouzidi A, Azizi A, Messaoudi O, Abderrezzak K, Vidari G, Hellal AN, Patel CN. 2023. Phytochemical analysis, biological activities of methanolic extracts and an isolated flavonoid from Tunisian *Limoniastrum monopetalum* (L.) Boiss: an *in vitro* and *in silico* investigations. Sci. Rep., 13(1): 19144.

Chauhan A, Sharma AD. 2025. Unlocking the therapeutic potential of phytocompounds from essential oils of *Melaleuca alternifolia* and *Rosmarinus officinalis* targeting bacterial penicillin-binding proteins by computational and experimental validation. Discov. Chem., 2(1): 28.

Chen F, Liang R, Zhang J, Kang R, Tang D, Liu J. 2025. CYP51A1 in health and disease: from sterol metabolism to regulated cell death. Cell Death Discov., 11(1): 322.

Cupp-Vickery JR, Garcia C, Hofacre A, McGee-Estrada K. 2001. Ketoconazole-induced conformational changes in the active site of cytochrome P450eryF. J. Mol. Biol., 311(1): 101-110.

Duru CE. 2020. Mineral and phytochemical evaluation of *Zea mays* husk. Sci. Afr., 7: e00224.

Ene IV, Walker LA, Schiavone M, Lee KK, Martin-Yken H, Dague E, Gow NA, Munro CA, Brown AJ. 2015. Cell wall remodeling enzymes modulate fungal cell wall elasticity and osmotic stress resistance. mBio., 6(4): e00986.

Gakuubi MM, Maina AW, Wagacha JM. 2017. Antifungal Activity of Essential Oil of *Eucalyptus camaldulensis* Dehnh. against Selected *Fusarium* spp. Int. J. Microbiol., 2017: 8761610.

Gow NAR, Latge JP, Munro CA. 2017. The fungal cell wall: structure, biosynthesis, and function. Microbiol. Spectr., 5(3): 10.1128.

Hoenigl M, Seidel D, Sprute R, Cunha C, Oliverio M, Goldman GH, Ibrahim AS, Carvalho A. 2022. COVID-19-associated fungal infections. Nat. Microbiol., 7(8): 1127-1140.

Hua H, Xing F, Selvaraj JN, Wang Y, Zhao Y, Zhou L, Liu X, Liu Y. 2014. Inhibitory effect of essential oils on *Aspergillus ochraceus* growth and ochratoxin A production. PLoS One., 9(9): e108285.

Inbathamizh L. 2020. Indoor medicinal plants: Beneficial biocatalysts for air filtration and bioremediation – A review**.** Int. J. Green Pharm**.,** 14(02).

Ishak SNH, Aris SNAM, Halim KBA, Ali MSM, Leow TC, Kamarudin NHA, Masomian M, Rahman RNZRA. 2017. Molecular dynamic simulation of space and earth-grown crystal structures of thermostable T1 lipase *Geobacillus zalihae* revealed a better structure. Molecules, 22(10): 1574.

John TM, Jacob CN, Kontoyiannis DP. 2021. When uncontrolled diabetes mellitus and severe COVID-19 converge: The perfect storm for Mucormycosis. J. Fungi, 7(4): 298

Kabir A, Muth A. 2022. Polypharmacology: The science of multi-targeting molecules. Pharmacol. Res., 176: 106055.

Kalagatur NK, Nirmal Ghosh OS, Sundararaj N, Mudili V. 2018. Antifungal activity of chitosan nanoparticles encapsulated with *Cymbopogon martinii* essential oil on plant pathogenic fungi *Fusarium graminearum*. Front. Pharmacol., 9: 610.

Khurana N, Ishar MP, Gajbhiye A, Goel RK. 2011. PASS assisted prediction and pharmacological evaluation of novel nicotinic analogs for nootropic activity in mice. Eur. J. Pharmacol., 662(1-3): 22-30.

König J, Müller F, Fromm MF. 2013. Transporters and drug-drug interactions: important determinants of drug disposition and effects. Pharmacol. Rev., 65(3): 944-66.

Ling FX, Qu DM, Lu YQ, Li R, Zhao L. 2024. Successful treatment of mixed pulmonary *Aspergillus* and *Mucor* infection using intrabronchial amphotericin B infusion: a case report and literature review. BMC Pulm. Med., 24(1): 436.

Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. 2001. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug Deliv. Rev., 46(1-3): 3-26.

Liu K, Watanabe E, Kokubo H. 2017. Exploring the stability of ligand binding modes to proteins by molecular dynamics simulations. J. Comput. Aided. Mol. Des., 31(2): 201-211.

Madhavan Y, Sai KV, Shanmugam DK, Manimaran A, Guruviah K, Mohanta YK, Venugopal DC, Mohanta TK, Sharma N, Muthupandian S. 2022. Current treatment options for COVID-19 associated mucormycosis: present status and future perspectives. J. Clin. Med., 11(13): 3620.

Mahlo SM, Eloff JN. 2014. Acetone leaf extracts of *Breonadia salicina* (Rubiaceae) and ursolic acid protect oranges against infection by *Penicillium species*. S. Afr. J. Bot., (93): 48-53.

Farag MA. 2019. Chemopreventive activity of *Chamaedorea sefrizii* and *Attalea butyracea* leaf extracts in relation to its metabolite fingerprints analysed via UPLC-qtof-MS and chemometrics. Biosci. Res., 16(4): 3330.

Muralidharan N, Sakthivel R, Velmurugan D, Gromiha MM. 2021. Computational studies of drug repurposing and synergism of lopinavir, oseltamivir and ritonavir binding with SARS-CoV-2 protease against COVID-19. J. Biomol. Struct. Dyn., 39(7): 2673-2678.

Nkwocha CC, Felix JO, Michael LO, Ale BA. 2024. Phytochemical screening and GC-FID identification of bioactive compounds in n-hexane, ethylacetate and methanol fractions of methanolic leaves extract of *Azanza garckeana*. Food Chem. Adv., 4: 100712.

Omar HS, Abd El-Rahman SN, AlGhannam SM, Reyad NHA, Sedeek MS. 2021. Antifungal evaluation and molecular docking studies of *Olea europaea* leaf extract, *Thymus vulgaris* and *Boswellia carteri* essential oil as prospective fungal inhibitor candidates. Molecules, 26(20): 6118.

Passone MA, Girardi NS, Etcheverry M. 2012. Evaluation of the control ability of five essential oils against *Aspergillus* section Nigri growth and ochratoxin A accumulation in peanut meal extract agar conditioned at different water activities levels. Int. J. Food Microbiol., 159(3): 198-206.

Raies AB, Bajic VB. 2016. *In silico* toxicology: computational methods for the prediction of chemical toxicity. Wiley Interdiscip. Rev. Comput. Mol. Sci., 6(2): 147-172.

Reza ASMA, Haque MA, Sarker J, Nasrin MS, Rahman MM, Tareq AM, Khan Z, Rashid M, Sadik MG, Tsukahara T, Alam AK. 2021. Antiproliferative and antioxidant potentials of bioactive edible vegetable fraction of *Achyranthes ferruginea* Roxb. in cancer cell line. Food Sci. Nutr., 9(7): 3777-3805.

Rincón-Cervera MÁ, Lahlou A, Chileh-Chelh T, Lyashenko S, López-Ruiz R, Guil-Guerrero JL. 2023. Arecaceae seeds constitute a healthy source of fatty acids and phenolic compounds. Plants (Basel)., 12(2): 226.

Shirley M. 2021. Correction to: Ketoconazole in Cushing's syndrome: a profile of its use. Drugs Ther. Perspect., 37(3): 14.

Singh S, Kaushal S, Hunjan MS, Sharma P. 2022. Chemical composition and molecular docking studies of *Cyamopsis tetragonoloba* (L.) Taub. leaves and fruits extracts as antifungal agents against rice phytopathogenic fungi. Arch. Phytopathol. Plant Prot., 55(10): 1179-1200.

Srimai V, Ramesh M, Satya Parameshwar K, Parthasarathy T. 2013. Computer-aided design of selective Cytochrome P450 inhibitors and docking studies of alkyl resorcinol derivatives. Med. Chem. Res., 22(11): 5314-5323.

Tiwari V, Shandily S, Albert J, Mishra V, Dikkatwar M, Singh R, Sah SK, Chand S. 2025. Insights into medication-induced liver injury: Understanding and management strategies. Toxicol Rep., 14: 101976.

Van Tyle JH. 1984. Ketoconazole. Mechanism of action, spectrum of activity, pharmacokinetics, drug interactions, adverse reactions and therapeutic use. Pharmacotherapy, 4(6): 343-373.

Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. 2002. Molecular properties that influence the oral bioavailability of drug candidates. J. Med. Chem., 45(12): 2615-2623.

Ventoulis I, Sarmourli T, Amoiridou P, Mantzana P, Exindari M, Gioula G, Vyzantiadis TA. 2020. Bloodstream infection by *Saccharomyces cerevisiae* in two COVID-19 patients after receiving supplementation of *Saccharomyces* in the ICU. J. Fungi (Basel)., 6(3): 98.

Wu C, Liu Y, Yang Y, Zhang P, Zhong W, Wang Y, Wang Q, Xu Y, Li M, Li X, Zheng M, Chen L, Li H. 2020. Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. Acta Pharm. Sin. B., 10(5): 766-788.