ISSN 1068-3674, Russian Agricultural Sciences, 2023, Vol. 49, No. 2, pp. 172–183. © Allerton Press, Inc., 2023.

PLANT GROWING, PLANT PROTECTION AND BIOTECHNOLOGY

# Essential Oil Derived from Underutilized Plants *Cymbopogon khasianus* Poses Diverse Biological Activities against "*Aspergillosis*" and "*Mucormycosis*"

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Received September 10, 2022; revised October 11, 2022; accepted November 22, 2022

**Abstract**—Palmrosa essential oil (PEO) from *Cymbopogon khasianus*, is used as complementary and traditional medicine worldwide. The present study aimed at compositional profiling of PEO and molecular docking of PEO bioactive compound geraniol against fungal enzymes chitin synthase (CS), UDP-glycosyltransferase (UDPG) and glucosamine-6-phosphate synthase (GPS), as apposite sites for drug designing against "Aspergillosis" and "Mucormycosis" and in vitro confirmation. Compositional profile of PEO was completed by GC-FID analysis. For molecular docking, Patch-dock tool was conducted. Ligand-enzyme 3D interactions were also calculated. ADMET properties (absorption, distribution, metabolism, excretion and toxicity) were also calculated. GC-FID discovered the occurrence of geraniol as a major component in PEO, thus nominated for docking analysis. Docking analysis specified active binding of geraniol to GPS, CS and UDPG fungal enzymes. Wet-lab authentication was achieved by three fungal strains *Aspergillus niger*, *A. oryzae* and *Mucor* sp. Docking studies revealed that ligand geraniol exhibited intercations with GPS, CS and UDPG fungal enzymes by H-bond and hydrophobic interactions. Geraniol obeyed LIPINSKY rule, and exhibited adequate bioactivity. Wet lab results indicated that PEO was able to inhibit fungal growth against "Aspergillosis" and "Mucormycosis".

**Keywords:** aspergillosis, COVID-19, mucormycosis, palmrosa oil, Herbal Drug

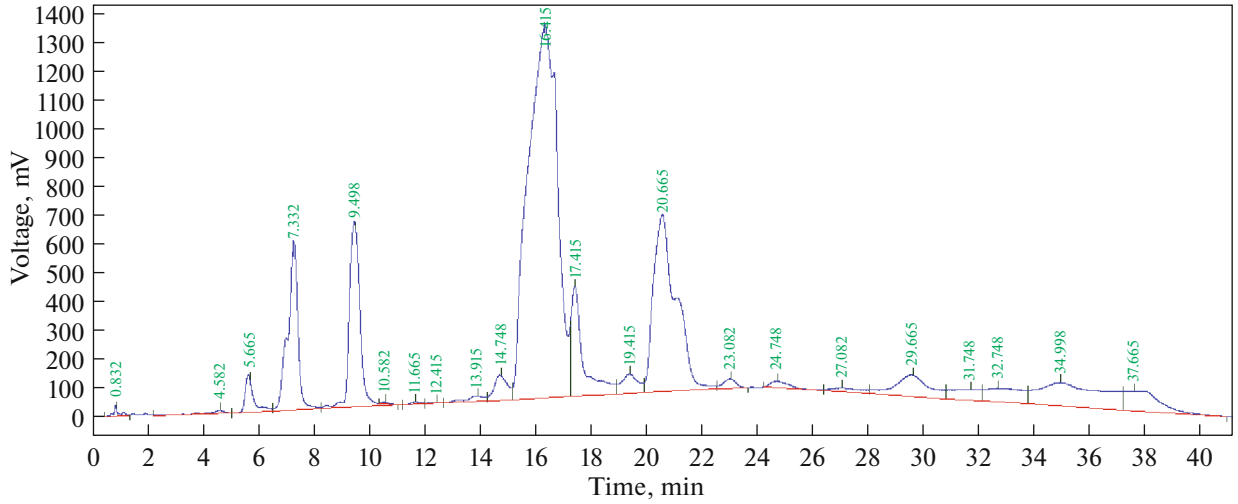
**DOI:** 10.3103/S106836742302012X

## INTRODUCTION

Post COVID-19 period, many co-infections are reported worldwide [1, 2]. Amongst all, oppertuntic fungal infections such as "mucormycosis" and "aspergillosis" are caused by common fungal molds such as *Aspergillus* and *Mucor spp*. backed to a great morbidity and mortality rate of 68% [3, 4] These fungal infections stances a serious health risk for sternly immune-compromised COVID-19 persons cured with uncontrolled use of steroids, hence leading to coined as "COVID-19" associated mucormycosis/aspergillosis (CAM/CAA) [4]. The indications related with aspergillosis comprise: running nose, stiffness, cough with blood, pain, fever, and abridged smelling power [5]. Symptoms associated with mucormycosis include: around the nose blackish discolouration, stuffy and bleeding nose, Black crusts oozing out from nose, teeth and jaw loosening, numbness and one-sided facial pain, swelling of eyes; blurred vision and problems in respiratory symptoms [6].

Due to clinical limitations of fungicidal agents, high price, inevitable toxicities, fungal drug resistance, the need of novel antifungal drugs is prerequisite [7]. Previous studies proposed that bioactive molecules that pose cell-wall linked enzymatic antifungal inhibitors can be used as therapeutic drugs to mitigate fungal infections [8]. Cell wall of fungal strains is a tough physical barrier which protects fungal strains against various environmental cues owing to the existence of different cell components such as mannoproteins, glucan, chitin, GPI anchors [9]. These enzymes are more likely to be crucial for fungus viability. Since, no such entity exist in humans, hence these cell wall components may serve as outstanding drug target sites for therapeutic interventions against antifungal drugs. CS, UDPG, GPS are pivotal enzymes convoluted chitin biosynthesis, GPI biosynthesis and *N*-acetyl-glucosamine biosynthesis respectively, by maintaining integrity and building fungal cell wall [9, 10]. This study postulated the view point that bioactive compound geraniol has the impending potential combat fungal infections by targeting CS, GPS and UDPG [11].

*Cymbopogon* genus, commonly known as Palmarosa or rosa grass, are important and valuable essential




| RT (min) | Compound | Concentration |
|---|---|---|
| 5.6 | Terpinolene | 1.2 |
| 7.3 | 6-Methyl hept-5-en-2-one | 7.1 |
| 9.4 | 2-Norbornaneacetic acid | 1.7 |
| 14.7 | Citronellyl acetate | 1.4 |
| 16.4 | Geraniol | 45.8 |
| 17.4 | Borneol | 5.5 |
| 19.4 | Nerol | 1.3 |
| 20.6 | Geranial | 16.9 |
| 29.6 | Elemol | 3.1 |
| 31.7 | Epi-α-acadinol | 1.3 |
| 32.7 | δ-Cadinol | 2.2 |
| 34.9 | Linalool | 6.3 |
| 37.6 | Fenchyl alcohol | 2.9 |

**Fig. 1.** GC-FID analysis of PEO.

oil bearing aromatic crops in the Poaceae family. The palmarosa comprising about 140 species worldwide is a native of most parts of subtropical areas worldwide including: India, UAS, USA, UK, Germany, Spain, Switzerland, Srilanka and Philipines [12]. Several *Cymbopogon* species possessed significant anthelmintic, anti-inflammatory, analgesic, antiageing, pesticidal, antimicrobial, mosquito repellant and larvicidal activities and thus, are used in native medicine for curing a number of diseases [13]. Essential oil is extracted from *Cymbopogon* species by the steam distillation method, and this oil finds extensive application in high grade perfumery, cosmetic, flavouring and aromatherapy industries throughout the world [14,

**Table 1.** Molecular docking of fungal receptors with geraniol

| Fungal Receptor | Dock score | | | | Interacting residues within 4 Å radius | |
|---|---|---|---|---|---|---|
| | Score | Area | ACE | Transformation | Hydrophobic interactions | Hydrogen bonds |
| Chitin synthase (CS) | 3210 | 345.80 | –76.93 | –0.04 0.77 –2.94 –5.19 –29.99 14.59 | TYR25, PRO177 | – |
| UDP-glucosyltransferase (UDPG) | 3410 | 405.80 | –77.29 | 3.13 –0.12 0.57 66.51 76.17 60.31 | PHE40, ALA457 | – |
| Glucosamine-6-phosphate synthase (GPS) | 3733 | 428.90 | –69.28 | 2.08 0.98 –0.27 3.02 26.91 80.05 | LY35, THR37 | SER101, ASN 103 |

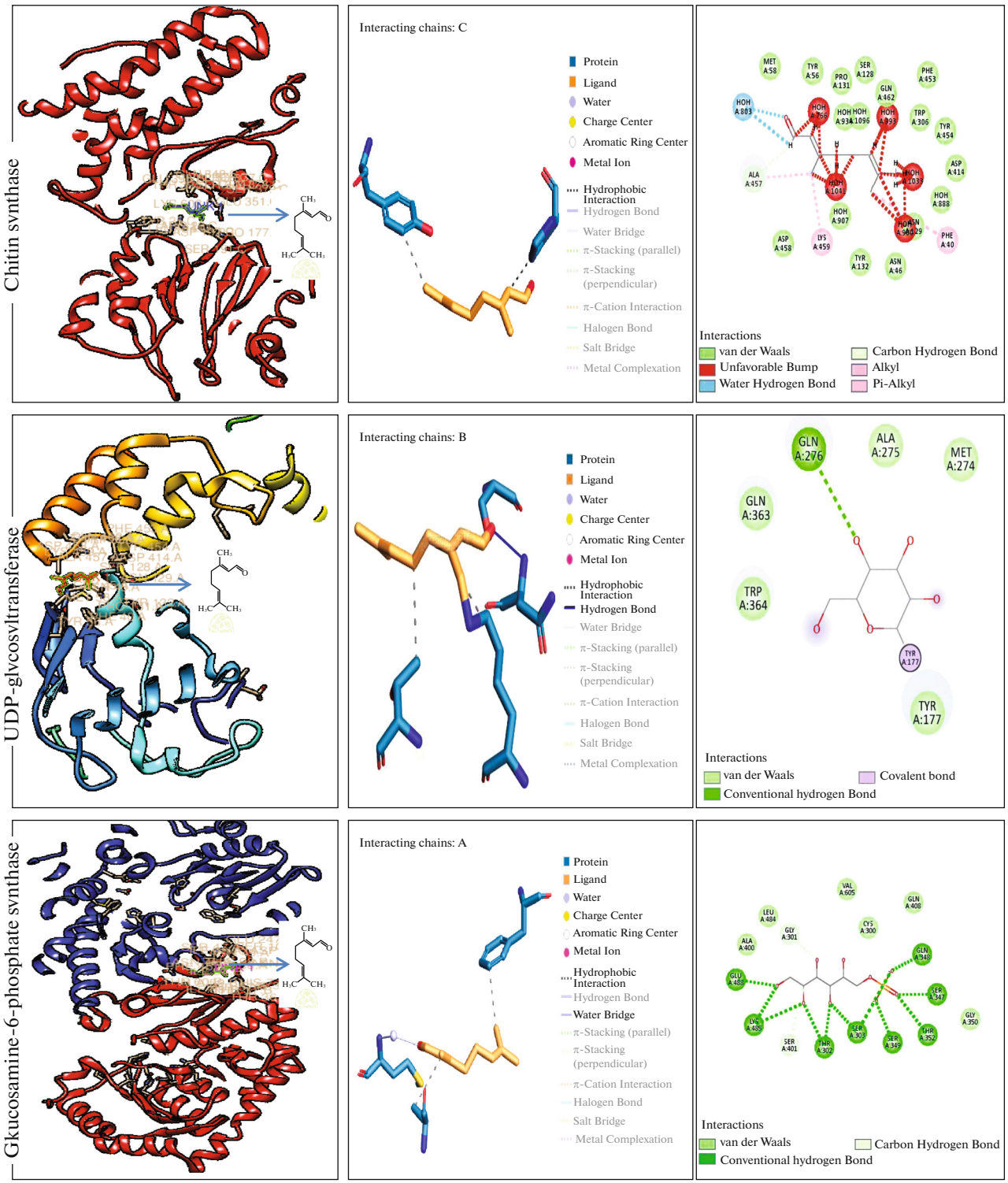
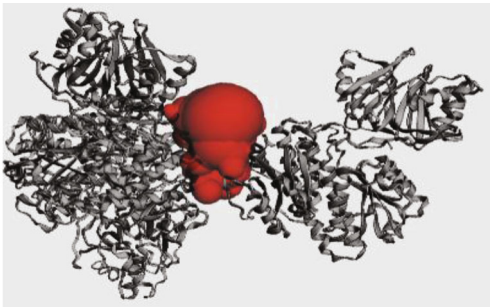
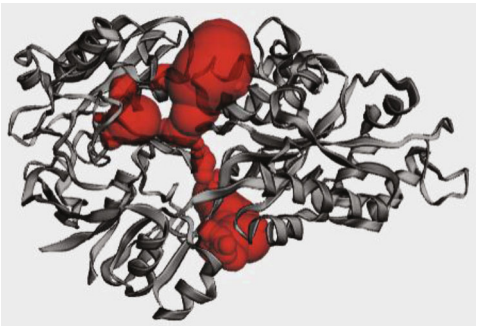
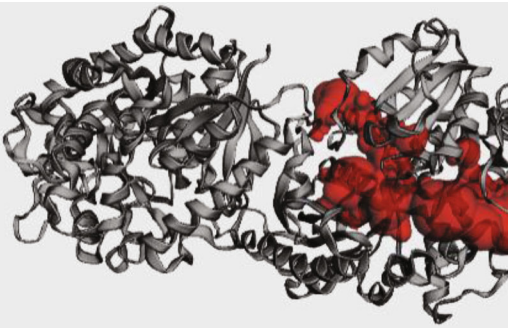



**Fig. 2.** 3D ligand-receptor model and molecular interactions of geraniol with fungal receptors.

15]. Palmrosa grass essential oil (PEO) from *Cymbopogon* genus, encompasses a number of bioactives with abundant pharmacological and aroma properties. The characteristic odour of Palmarosa oil is due to its high content of total alcohol, mainly geraniol (also known as Genanial, Lemonal, trans-3,7-Dimethyl-2,6-octadienal) and small but varying amount of esters associated with geraniol. We presented our viewpoint that due to the abundance of geraniol, PEO from *Cymbopogon khasianus* have potential to mitigate

**Table 2.** Protein target structure, native ligand and active site amino acids

| Fungal receptor | 3D model | Interacting active site residues | Cavity | |
|---|---|---|---|---|
| | | | area | volume |
| CS |  | TYR 454, ASP458, THR456,457, PRO48, 131, LYS459, ASN129, PHE40, SER128, TYR 132,454, TRP306, ALA457, GLN412, TYR25, PRO177 | 949.053 | 3379.091 |
| UDPG |  | ASN333, 332, LEU 331, PHE354, LYS415, 419, 334, ARG422, SER332, ALA335, VAL 356 , PHE40, ALA457 | 1097.766 | 1086.959 |
| GPS |  | ALA400, VAL399, GLY 505, HIS 504, TYR 304, GLN348, SER 303, LEU 346, LYS 603, GLU 396, GLN 348, CYS300, THR352, 302, GLU 396, LY35, THR37 | 1688.961 | 1193.342 |

"Aspergillosis" and "Mucormycosis". Therefore, the aim of present study was intended to study 3D docking of geraniol against CS, UDPG and GPS and wet-lab authentication. PEO contains bioactive molecules, phyto-compounds, endowed with pharmacological activities like: antifungal and mosquito repellent activity, antimicrobial properties, used in Ayurvedic traditional and complementary medicine to treat skin problems and relieve nerve pain, and Immunomodulatory action [16], therefore poses a key role as therapeutics in the scientific community. Nevertheless, its potential against "Aspergillosis" and "Mucormycosis" is still a matter of conjuncture. It would additional add new visions into the potential forecasts to ascertain the key anti-fungal drugs during COVID-19 medications.

## MATERIALS AND METHODS

### *GC-FID Analysis*

PEO was extracted from fresh green leaves of plants growing in CSIR AROMA nursery in campus by hydrodistillation method. Formal identification of the plant material used in your study was done by Dr Inderjeet Kaur and voucher specimen bearing number BT 103 was deposited to dept. Oil was stored in dark colored vials at 4°C till further analysis. To identify bioactive compounds in PEO, GC-FID study was carried out (GC-FID, Chemtron 2045). The specifications of column was: 2 m long, stainless steel having 10% OV-17 on 80–100% mesh Chromosorb W (HP). Nitrogen was used as carrier gas at flow rate of 35 mL/min. 0.2 μL PEO sample was used. The temperatures for detector and injector were: 220 and 270°C. Oven ramping conditions were: 100°C (firstly

**Table 3.** ADME properties of geraniol

| Physicochemical Properties | |
|---|---|
| Formula | $C_{10}H_{18}O$ |
| Molecular weight | 154.25 g/mol |
| Num. heavy atoms | 11 |
| Num. arom. heavy atoms | 0 |
| Fraction Csp3 | 0.60 |
| Num. rotatable bonds | 4 |
| Num. H-bond acceptors | 1 |
| Num. H-bond donors | 1 |
| Molar Refractivity | 50.40 |
| TPSA | 20.23 Å$^2$ |
| Lipophilicity | |
| Log $P_{o/w}$ (iLOGP) | 2.75 |
| Log $P_{o/w}$ (XLOGP3) | 3.56 |
| Log $P_{o/w}$ (WLOGP) | 2.67 |
| Log $P_{o/w}$ (MLOGP) | 2.59 |
| Log $P_{o/w}$ (SILICOS-IT) | 2.35 |
| Consensus Log $P_{o/w}$ | 2.78 |
| Water Solubility | |
| Log $S$ (ESOL) | –2.78 |
| Solubility | 2.59e-01 mg/mL; 1.68e-03 mol/L |
| Class | Soluble |
| Log $S$ (Ali) | –3.67 |
| Solubility | 3.30e-02 mg/mL; 2.14e-04 mol/L |
| Class | Soluble |
| Log $S$ (SILICOS-IT) | –1.84 |
| Solubility | 2.20e+00 mg/mL; 1.43e-02 mol/L |
| Class | Soluble |
| Pharmacokinetics | |
| GI absorption | High |
| BBB permeant | Yes |
| P-gp substrate | No |
| CYP1A2 inhibitor | No |
| CYP2C19 inhibitor | No |
| CYP2C9 inhibitor | No |
| CYP2D6 inhibitor | No |
| CYP3A4 inhibitor | No |
| Log $K_p$ (skin permeation) | –4.71 cm/s |
| Druglikeness | |
| Lipinski | Yes; 0 violation |

**Table 3.** (Contd.)

| Physicochemical Properties | |
|---|---|
| Formula | $C_{10}H_{18}O$ |
| Ghose | No; 1 violation: MW<160 |
| Veber | Yes |
| Egan | Yes |
| Muegge | No; 2 violations: MW < 200, Heteroatoms <2 |
| Bioavailability Score | 0.55 |
| Medicinal Chemistry | |
| PAINS | 0 alert |
| Brenk | 1 alert: isolated_alkene |
| Leadlikeness | No; 2 violations: MW < 250, XLOGP3 > 3.5 |
| Synthetic accessibility | 2.58 |

maintained) ramped to 2100°C at 3°C/min. Bioactive constituents in PEO were identified by comparing relative retention times (RT) of GC-FID spectra of PEO with authentic standards and literature data [16, 17].

### *Ligand Preparation*

For fungal receptors (CS, UDPG and GPS), geraniol was used as ligand for structures. To build 3D structure of ligand, SMILES (CC(=CCCC(=CC=O)C)C) of geraniol was recovered from NCBI-Pubchem database. The structure was built by using UCSF-chimera.

### *Molecular Docking*

Crystal structures of CS, UDPG and GPS fungal enzymes were recovered from PDB (https://www.rcsb.org/). Before docking analysis, all target enzymes were cleaned from selected $H_2O$ molecules, cofactors, co-crystallized ligand, and energy minimized. Then all protein target structures were prepared by means of the dock prep set up in UCSF-chimera. It is the process under optimization that bond length, charges anomalies and corrects atomic structure. For docking, PatchDock tool was used for docking of ligand geraniol over CS, UDPG, GSP (https://bioinfo3d.cs.tau.ac.il/PatchDock/). To execute docking, both receptors and ligand molecules as "pdb files" were uploaded to the PatchDock and docking was performed. For 2D and 3D interactions in docked complexes, Biovia 2020, UCSF Chimera and Plip tools were used.

### *Drug-Likeness and Toxicity*

ADMET (Absorption, Metabolism, Toxicity and Excretion), drug likeness, physiochemical properties and pharmacokinetics were studied using SWISSADME tool (http://www.swissadme.ch/). ProTox-II was used for toxicity profile, oral toxicity, hepatotoxicity, immunotoxicity, mutagenicity, carcinotoxicity, cytotoxicity, and analysis (http://tox.charite.de/protox_II). Bioactivity potential of geraniol was studied by using web based molinspiration tool (https://www.molinspiration.com/cgi-bin/properties).

### *Active Sites Prediction*

In fungal receptors, identification and dimension of cavities on 3D active sites were computed by using CASTp web tool. For this all structures in "pdb" format were uploaded to server and prediction was executed with probe radius value of 1.4 Å.

### *In vitro Antifungal Activity of Palmrosa Oil*

Anti-aspergillosis and anti-mucormucosis potential of PEO was studied on using fungus strains *Aspergillus niger* (MTCC 277) and *A. oryzae* (MTCC 343), and *Mucor* sp. (MTCC 3473). A 10–15 µl/ml of palmrosa oil was added with liquid autoclaved PDA medium. 25 ml of PEO mixed PDA was distributed into disinfected petri-plates (8 cm in diameter) and allowed to solidify at ~37°C for 3 h, Mycelial fungal discs (8 mm) were taken from fungal plates with the help of sterile cork borer and aseptically placed in petri plates and incubated for 15 days at 29°C. As positive control, antibiotic discs of 15 µg fluconazole was used. MGI (Mycelial growth inhibition) was premeditated by following equation: (MGI%) = DC – DT/DC × 100, DC and DT: diameter of control and test colony.

## RESULTS AND DISCUSSION

### *GC-FID Profiling*

Aroma profile and bioactives identified by GC-FID is displayed in Fig. 1. GC-FID analysis of PEO displayed the incidence of 22 peaks including major and minor peaks. The major bioactive components were Geraniol (45%), Geranial (16%), 6-Methyl hept-5-en-2-one (7.4%), Linalool (6%) and Borneol (5%), Elemol (3%) and Fenchyl alcohol (2%). The small peaks may be attributed to the crumbled major bioactive components or existent in minor amounts. As described in literature, PEO was rich in Geraniol [16, 17]. Due to these bioactives molecules, PEO has rose-like aroma and has immense applications in high grade perfumery, cosmetic, flavouring and aromatherapy, fragrances, soaps, detergents, toiletry, tobacco products and pharmaceutical industries [16, 17]. Therefore, geraniol was selected as a ligand for docking studies against fungus cell wall receptors.

### *Molecular Docking*

3D docking results illustrated that fungal enzyme GPS depicted strong binding with ligand geraniol (Table 1), as apparent from its docking score of 3733. Docking score for CS and UDPG was 3210 and 3410, respectively. 3D model displaying docking pose and 2D/3D interactions of geraniol with CS, UDPG and GPS fungal enzymes are displayed in Fig. 2. From docking analysis it was apparent that ligand geraniol efficiently docked with CS, UDPG and GPS fungal enzymes. With CS, ligand geraniol docked with catalytic domain between C- (trans-membrane) and N- (a catalytic) domains [18]. With GPS, geraniol docked with domains involved in sugar-phosphate isomerization and glutamine hydrolysis [19]. With UDPG, ligand geraniol showed interaction with UDP-glucose binding domain at C terminal which is likely site of UDP-glucose binding [20]. These results were in agreement with earlier studies reporting docking interactions of essential oil based bioactives from plants *Trachyaspermum ammi*, *Thymus vulgaris*, and *Boswellia carteri* with fungal enzyme [21]. Based on analysis, it was highlighted that PEO can be used as effective source of anti-fungicidal compounds.

**Table 4.** Bioactivity score of geraniol

| Bioactivity | Score |
|---|---|
| GPCR ligand | −0.60 |
| Ion channel modulator | −0.07 |
| Kinase inhibitor | −1.32 |
| Nuclear receptor ligand | −0.20 |
| Protease inhibitor | −1.03 |
| Enzyme inhibitor | 0.28 |

Through 3D docking, with site residues of receptors, ligand could form H-bonds or hydrophobic bonds which designate affinity of ligand with receptor [22]. Hence, docking interactions of geraniol with CS, UDPG and GPS were further evaluated. It was observed that ligand geraniol forms both H-bond and hydrophobic interactions with CS, UDPG and GPS. With GPS hydrophobic interactions were detected via LYS 35 and THR 37 (Fig. 2). Number of H-bonds among ligand and receptor describe the power of binding [23]. It was noted that geraniol exhibited H-bond with GPS by SER 101 and ASN 103 residues. Due to this geraniol exhibited tight binding with GPS as compared to other fungal receptors that was also apparent from its docking score. Hydrophobic interactions with CS, were mediated via TYR25, and PRO177. With UDPG, Hydrophobic interactions, were detected via PHE40 and ALA457. No H-bond interactions were observed with CS and UDPG receptors. CASTp active sites prediction quantified interacting residues in the active site cavities of CS, UDPG and GPS receptors (Table 2). In CS enzymes, a main pocket was documented with Volume (SA) of 3379 and Area (SA) of 949. For UDPG Volume (SA) of 1086 and Area (SA) of 1097, for GPS Volume (SA) of 1688 and area (SA) 1193 were noticed. Meanwhile geraniol shown good affinity to all fungal enzymes so it was conjectured that upon binding with ligand CS, UDPG and GPS becomes closed thus in-turn persuades change in conformation of fungal enzymes. All these events halts fungal cell wall synthesis thus mitigate infectivity of fungus into the host cell. Similar in silico results citing antifungal potential of polypharmacological agents to control growth of Aspergillosis among COVID-19 patients have been stated [23, 24].

### *PASS Analysis*

PASS analysis and ADMET properties of bioactive geraniol were calculated. It was cited that these properties are pivotal for any therapeutic drug to be used in living organisms [25]. Drug-likeness was calculated by following Lipinski rule of five (RO5). It was observed that geraniol obeyed RO5. For this rule drug must have log $P \leq 5$, H-bond acceptors ≤10, and H-bond donors ≤5 and violation no more than 1 (Table 3). PASS analysis advocated that geraniol was low molecular weight ligand (LMW). It was reported that drugs ligands having less LMW poses high propensity to transportation across the cellular membranes and diffuse effortlessly than high MW compounds [26]. The Log $P_{o/w}$ value (v) was also in acceptable range. In pharmaco-analysis, Log $P_{o/w}$ is a potential factor to measure lipophilicity of any drug and its movement in body after absorption (Abraham, 2003). TPSA (topological polar surface area) value was 9.23 Å squared, indicating geraniol possess nice oral bioavailability [21]. Wu et al. [25] cited that TPSA is a key factor of drug transport properties like efficient permeability

**Table 5.** Toxicity profile of geraniol

| Classification | Target | Prediction |
|---|---|---|
| Toxicity end points | Carcinogenicity | Inactive |
| Toxicity end points | Mutagenicity | Inactive |
| Toxicity end points | Cytotoxicity | Inactive |
| Tox21-Nuclear receptor signalling pathways | Aryl hydrocarbon Receptor (AhR) | Inactive |
| Tox21-Nuclear receptor signalling pathways | Androgen Receptor (AR) | Inactive |
| Tox21-Nuclear receptor signalling pathways | Androgen Receptor Ligand Binding Domain (AR-LBD) | Inactive |
| Tox21-Nuclear receptor signalling pathways | Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma) | Inactive |
| Tox21-Stress response pathways | Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE) | Inactive |
| Tox21-Stress response pathways | Heat shock factor response element (HSE) | Inactive |
| Tox21-Stress response pathways | Mitochondrial Membrane Potential (MMP) | Inactive |
| Tox21-Stress response pathways | Phosphoprotein (Tumor Supressor) p53 | Inactive |
| Tox21-Stress response pathways | ATPase family AAA domain-containing protein 5 (ATAD5) | Inactive |
| $LD_{50}$ | – | 2100 |
| $-\log_{10}(LD_{50})$ | Poison scale [0–13] | 3.3 |
| Predicted toxicity class | 1 2 3 4 5 6 | 5 |

and absorption. To exert toxic affect, drug has to be absorbed thoroughly in human body. GI (Gastrointestinal tract absorption) of geraniol was high (Table 3). Against P-glycoprotein (P-gp) efflux transporters, geraniol was non-substrate. In human body P-gp pumps drugs back into the lumen, lessening their absorption [27]. Further, geraniol was non-substrate to CYP450 series of enzyme. In human body, CYP450 are series of enzymes intricated in liver detoxification [26]. These results indicated that geraniol can effectively target receptors thus can be further evaluated for biological activity score.

Biological activity (BA) is a key factor that defines the capability of any drug binding to respective drug or biological targets (Khan et al., 2017). In living systems, biological targets usually are: ion channels or biological receptors. BA score of geraniol was computed as shown in Table 4. BA rule states that if BA score is more than 0, drug is active, if less than –5.0, drug is silent and if between –5.0 to 0, drug is sufficient active. BA score for geraniol was from –5.0 and 0, displayed to be act a likely drug. Khan et al., [28] reported these types of observations on drug formulations. These kinds of annotations have been described by researchers working on different drug formulations. Toxicity profile of geraniol was calculated by ProTox tool. To be used as an effective therapeutic drug in pharmaceutical companies, in-silico toxicity analysis is prerequisite [11]. Raies et al., [29] aptly pointed that toxicity must be analyzed for drugs that could be damaging to humans, environment or animals. Prediction results reveled that geraniol was mostly non-toxic, non-mutagenic and non-carcinogenic (Table 5). For instance: negative hepatotoxicity was observed for geraniol. Liver hepatotoxicity is most common cause of failure of any therapeutic in drug market [30]. It was reported that mutagenicity nature of any drug is dangerous to living cells and main cause of diseases like cancer [31]. Nevertheless, geraniol displayed passiveness to target based biological pathways like: stress response or nuclear receptor signaling pathways. As listed in Table 5, it was cited that in human body these are valuable biological targets [31]. Further, prediction results revealed that geraniol belong to toxicity class 5, indicating safe nature of bioactive compound. Predicted $LD_{50}$ value was 2100 mg/kg. $LD_{50}$ is the toxic unit that measures lethal toxicity dose of drug. On toxic scale, $-\log_{10}(LD_{50})$ value of geraniol was 3.3, indicating non-toxic nature of bioactive compound. On poison scale, $-\log_{10}(LD_{50})$ on a linearized toxicity

**Table 6.** Mycelial growth inhibition rate (%) of Palmrosa essential oil (PEO), TI: total inhibition (SD ± $n$ = 3)

| PEO, µL/mL) | Growth inhibition, % | | |
|---|---|---|---|
| | MTCC 277 | MTCC 343 | MTCC 3473 |
| 10 | 20[a] | TI | 15[a] |
| 15 | 45[b] | TI | TI |
| +control | 10 | 48 | 41 |

Different letters with in column indicates significant difference at $P \leq 0.05$ vs. control with in column.

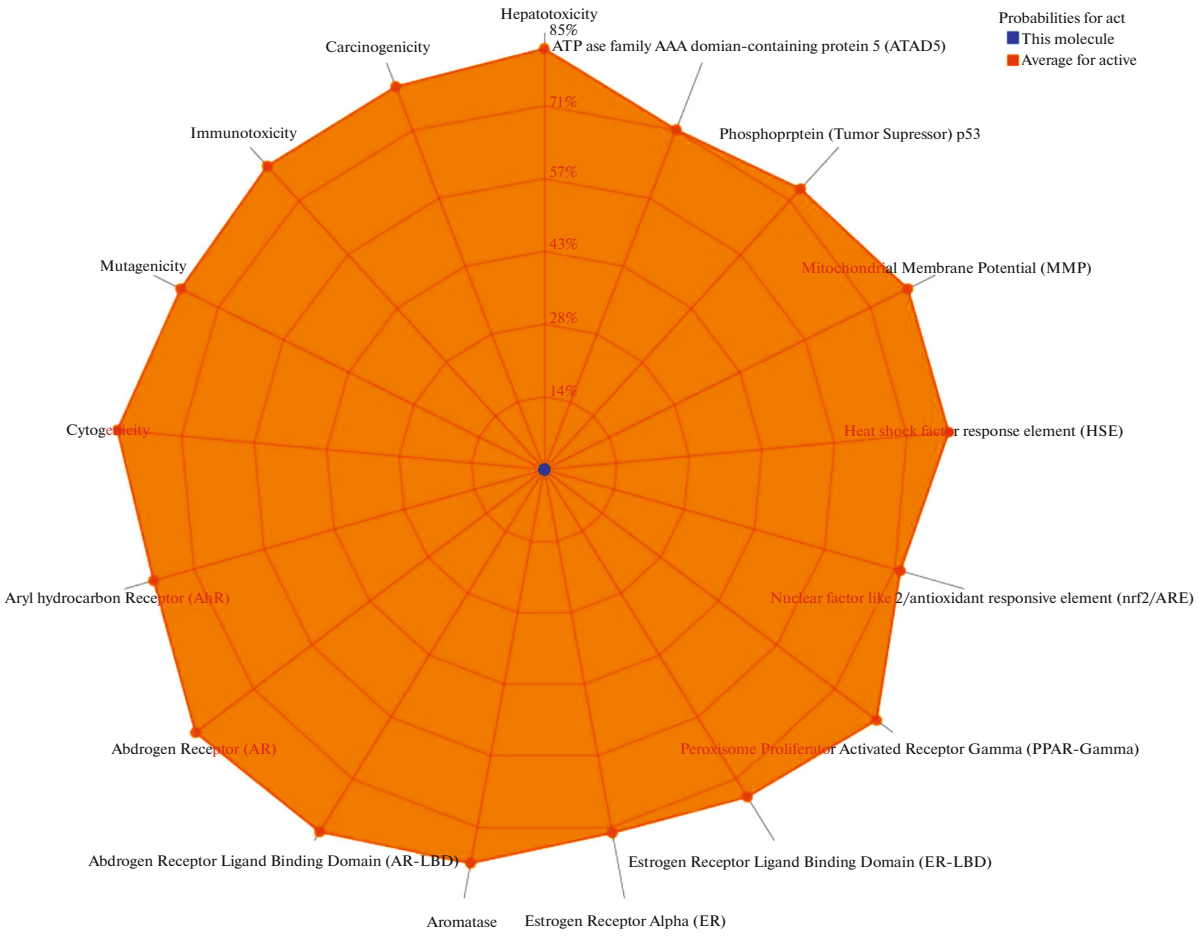



**Fig. 3.** Toxicity radar chart of geraniol, toxicity profile of the input compound is shown using orange dots/lines which represents the predicted probabilities of the input compound for respective ProTox-II models.

scale covering 13 orders of magnitude with less values indicates non-toxic nature of drugs [32]. Toxicity radar chart is likewise displayed in Fig. 3, that rapidly typifies the reassurance of affirmative poisonousness consequences compared to the average of its class.

### *In vitro Antifungal Activity of PEO*

Wet lab authentication was further corroborated with the in silico findings by using three fungal strains viz: *A. niger* (MTCC 277), *A. oryzae* (MTCC 343), *Mucor* sp. (MTCC 3473). At 15 µL/mL, ample mycelial growth inhibition was detected in MTCC 343 and MTCC 3473 fungal strains, whereas 45% mycelial growth inhibition was observed with MTCC 277 (Fig. 4, Table 6). At concentration of 10 µl/ml, PEO displayed total growth inhibition against *A. oryzae* than *A. niger* anti-fungal potential of PEO may be due to presence of major component geraniol or minor components in toto. It is possible that PEO easily enters fungal cell wall thus cause membrane leakage of electrolytes or lipid peroxidation of membrane which eventually hindered fungal hyphal-growth and germination of conidia of fungal strains. These finding were in consonance with earlier studies demonstrating anti-fungal activity of PEO against *Fusarium graminearum*, causing leaf spot infection in plants [33]. Fungicidal effect of PEO has also been pronounced for other pathogenic fungus like: *Saccharomyces cerevisiae*, *Botrytis cinerea*, *Penicillium digitatum* and *P. italicum* [34–37].

## CONCLUSIONS

Aroma profile of PEO displayed geraniol as major component along with some other minor ones. Molecular docking study revealed that geraniol from PEO was an effective ligand which docked with fungal cell wall enzymes like CS, UDPG and GPS. It was further authenticated by wet-lab results which displayed total inhibition of fungal strains causing "aspergilosis" and "mucormycosis" diseases mutilating COVID-19 persons. Thus, results stemmed from in silico and wet-lab established that, Palmrosa essential oil plant might be promising antifungal therapeutic drug against Aspergillosis and Mucormycosis.

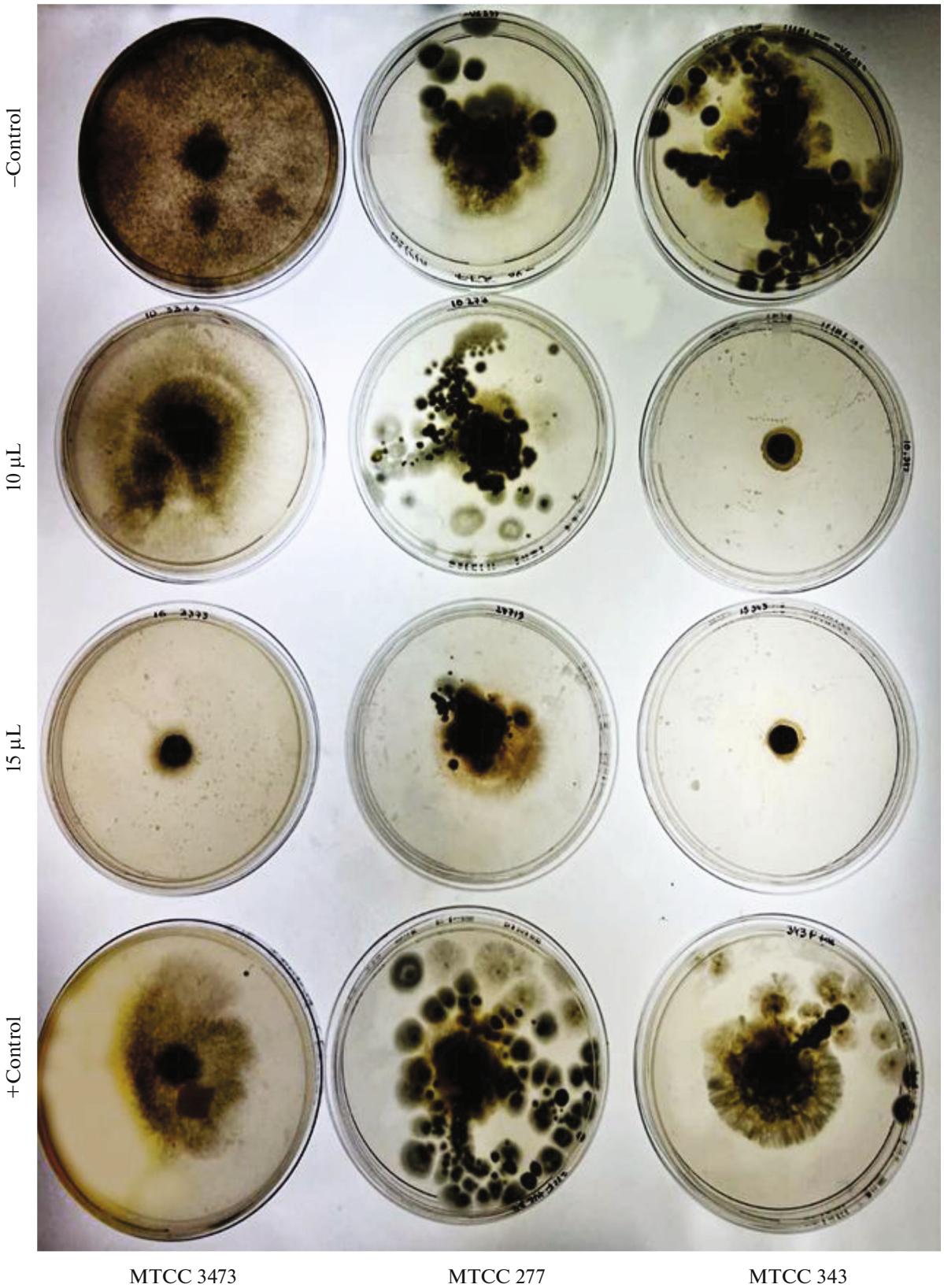



**Fig. 4.** Anti-fungal potential of PEO against Aspergillosis (MTCC 277, 343) and Mucormycosis (MTCC 3473) causing fungal strains.

ACKNOWLEDGMENTS

DST, Government of India.

STATEMENTS

Ethics approval and Consent to participate (include appropriate approvals or waivers): Not applicable.

Consent for publication (include appropriate statements): Yes.

Availability of data and materials (data transparency): Not applicable.

Competing interests (include appropriate disclosures): Nil.

Funding (information that explains whether and by whom the research was supported): DST.

SEED

Authors' contributions: ADS: Designed the study, IJK: Manuscript preparation.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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