Evaluation of Fungal Activity Through In Silico Analysis of Medicinal Plants Against Exophiala jeanselmei
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ABSTRACT
Phaeohyphomycosis is a fungal infectious disease commonly called as dermal problem which is caused by dematiaceous fungi, Exophiala jeanselmei. Chitin was the main component of fungal cell and no effective inhibitor was identified still in chitin synthase I. The protein chitin synthase I play a major role in drug metabolism as well as signal processing molecule and therefore have been targeted in the present study. The medicinal plants being a solution for several human ailments, also act as a reservoir for secondary metabolites, has taken its credit as a cure from our ancient times. The biological activity of the Myricetin was analysed using the pass online tool. The value of Probability to be active (Pa) = 0.241 Probability to be inactive (Pi) = 0.021. The several compounds retrieved from the plants Acalypha indica, Achyranthus aspera, Brassica niger, Cassia auriculata, Cleome gynandra, Clitoria ternatea, Ipomoea hederacea, Leonc aspera, Mimosa pudica, Phyllanthus niruri, Ocimum basilicum, Ocimum sanctum, Tridax procumbens, Vitex negundo and Waltheria indica were analyzed for its possible significant interaction with the target protein using molecular docking studies. The compound Myricetin had Binding energy of -7.32 Kcal/mol and formed hydrogen bonds with the residue HIS 29 showing the bond length of 1.8 Å and residue THR 3 showing the bond length of 1.9 Å. The future perspective of the study is to determine the stability of the protein-compound interaction through docking studies.

Keywords: Phaeohyphomycosis, Medicinal plants and Molecular docking.

1 Introduction
Bioinformatics is computational biology in terms of molecules and applying informatics techniques from various disciplines to understand and organize the information associated with these molecules, on a large scale [1]. Modern bioinformatics research does not necessarily require more resources than any other field of Computer Science; almost all processes can be efficiently designed and modeled on a personal computer or workstation [2]. For more than a century, vast progress has been made in hereditary qualities and molecular biology. New high-throughput exploratory methods continued to develop rapidly. The mechanization of DNA sequencing set up for the Human Genome Project in 1990 [3], which has prompted genomics and a scope of related disciplines, for example, transcriptomics (the investigation of the total
quality articulation state), proteomics (the investigation of the full arrangement of proteins encoded by a genome), and metabolomics (the investigation of extensive metabolite profiles), here and there every one of these areas are all things considered alluded to as genomics. Numerous institutes use PC bunches to expand handling time, increment information base stockpiling and actualize quicker information putting away and recovering techniques [4]. The significant favorable circumstances of utilizing PC bunches are clear when an association requires enormous scope processing like in bioinformatics educating and research. At the point when utilized along these lines, PC groups offer: Cost productivity: the bunch method is practical for the measure of intensity and preparing speed being delivered. At present, progressed bioinformatics is amassed in a couple of exploration bases and privately owned businesses on the world that have the ability to utilize staff with profoundly particular preparing. Notwithstanding the way that bioinformatics techniques are openly available, there is obviously a hole between the creating and the industrialized world, which must be intentionally limited.

Following the development of the first algorithms in the 1980s, molecular docking became an essential tool in drug discovery [5]. In molecular docking, in light of the protein structures, a great many potential stances of association are attempted and assessed; the posture with the least energy score is anticipated as the "best match", i.e., the coupling mode. Since Kuntz and associates spearheading work [6], critical advancement has been made in mooring exploration to improve the computational speed and precision. Among them, protein-ligand docking is an especially energetic exploration region in view of its significance to structure-based medication design [7] and will be the subject of the current survey [8].

Bioinformatics was characterized as the assortment, order, stockpiling, and investigation of biochemical and biological data utilizing through in silico analysis of molecular genetics and genomics. Phaeohyphomycosis is a rare mycotic infection caused by various heterogeneous groups of black colored fungi (dematiaceous) involving the skin and subcutaneous tissue. Phaeohyphomycosis is due to an irresistible pigment called melanin which is regularly known for dermal issues brought about by dematiaceous growths, Exophiala jeanselmei. It is a crafty microorganism skilled to most regularly display phaeomycotic cyst/subcutaneous phaeohyphomycosis. Chitin a basic segment of parasitic cell divider is one of a kind to contagious realm and interim, no practical inhibitor was so far distinguished for chitin synthesize, however the melanin shade present in the cell mass of Exophiala jeanselmei causes the destructiveness reason for the microorganism. In later phases of this illness goes to the mind and causes the demise [9]. The most widely recognized etiological operators of subcutaneous Phaeohyphomycosis are E. jeanselmei followed by E. dermatitidis [10]. The genus Exophiala is generally right in the earth and may cause contaminations in both immune compromised and once in a while, in immunocompetent people. E. jeanselmei ordinarily causes gentle cutaneous and subcutaneous diseases which are often limited and singular (phaeohypomycotic blister) [11]. Indeed, even in seriously immune suppressed patients Exophiala contamination regularly will in general remain restricted [12]. Ajello recorded 71 types of dematiaceous organisms from 39 genera which have been found to cause phaeohyphomycosis in people and in lower creatures [13]. There have been two distributed reports of Phaeohyphomycosis brought about by Exophiala jeanselmei in a household feline [14] and in Australia Phaeohyphomycosis brought about by Exophiala spinifera in two felines [15]. There are various cases in the writing in which the analysis was founded exclusively on histopathology, which, albeit trademark, gives in sign with regards to the character of the organism included [16]. Phaeohyphomycosis is a less frequent, progressively disfiguring and sometimes fatal infection. Although the diseases will be quite opposite, their drug therapy has become a common feature for both infections [17]. Exophiala jeanselmei is clinically deflected as an uncommon operator of subcutaneous. Our results will be discussed about its extraordinary clinical introduction and etiological operator, Exophiala jeanselmei. The patient recouped totally after treatment with Ketoconazole [18].

Therapeutic plants were made use of customary medication rehearses since ancient occasions. Plants incorporate many compounds for size comprises guard against parasites, infections, and herbivorous warm-blooded creatures. Various photochemical with potential or set up organic action had been recognized.
Restorative plants are the "spine" of customary medicine, which implies more than 3.3 billion people in the less evolved nations use therapeutic plants all the time [19]. There are about 2000 ethnic gatherings on the planet, and pretty much every gathering have their own conventional clinical information and encounters [20]. Recent screenings of most of the medicinal plant extracts with antibacterial, antifungal and antidermatophytic efficacy shown better because of those active compounds which could be isolated and has been able to identify promising compounds that might represent future solutions in critical areas of human health [21, 22]. Therapeutic plant compounds have just been utilized to effectively treat various viral illnesses. Thus, we screened a therapeutic plant information base containing 32,297 potential enemies of viral phytochemicals and chosen the main nine hits that may repress SARS-CoV-2 3CLpro action also, thus infection replication [23].

As indicated by WHO, the vast majority of the developing and developed nations accept on home grown items for its therapeutic accessibility, in light of this philosophy the accompanying medicinal plants are utilized for the treatment of Phaeohyphomycosis. The aim of this study is to cure this dermal disease by knockout the Melanin pigment which is the main virulent factor by Molecular docking studies (Acalypha indica, Achyranthus aspera, Brassica niger, Cassia auriculata, Cleome gynandra, Clitoria ternatea, Ipomoea hederaceae, Leucas aspera, Mimosa pudica, Phyllanthus niruri, Ocimum basilicum, Ocimum sanctum, Tridax procumbens, Vitex negundo and Waltheria indica)

2 Materials and Methods

2.1 Pdb, Pubchem & Pass Online

The 3D protein structure for Chitin synthases (Chs) of Exophiala jeanselmei is recovered from the Protein Data Bank database (PDB ID: 2MPK). Dynamic web page region was anticipated utilizing LigSite online apparatus. The concoction mixes from the referenced plants are recovered from the PubChem database. The PASS ONLINE predicts 4130 types of biological activities, for which the difference between probabilities will be active (Pa) and probabilities will be inactive (Pi) was calculated. The Pa-Pi values for activities randomly selected from the total list of predicted biological activities will be used as independent regression variables are perused.

2.2 Drugability

Lipinski rule of 5 helps in distinguishing between drug like and non-drug like molecules. It predicts high probability of success or failure due to drug likeness for molecules complying with 2 or more of the following rules [22 & 24]. Molecular mass less than 500 Dalton

- High lipophilicity (expressed as LogP less than 5)
- Less than 5 hydrogen bond donors
- Less than 10 hydrogen bond acceptors
- Molar refractivity must be between 40-130

2.3 Molecular Docking Study

MGL tools with AutoGrid 4 and AutoDock 4 [25] will be used to set up and to perform blind docking calculations between the Ligands and Protein. Crystallized 3-dimensional structure was obtained from the Protein Data Bank (PDB). Receptor (protein) and ligand (complex) files were prepared using Auto Dock Tools. The protein was enclosed in a box with grid points in x, y and z directions and a grid spacing of 0.375 Å. The center of the grid set to -6.516, 30.278 and -1.951 Å. Lamarckian genetic algorithms, as implemented in Auto Dock, were employed to perform docking calculations. All other guidelines are default settings. For every individual the docking cases, the lowest energy docked conformation, according to the Auto Dock scoring function and number hydrogen bonds was selected as the binding mode. The output from Auto Dock was rendered with PyMol [26].
2.4 PyMOL

PyMOL is one of a few open source visualization tools which are used in a structural biology. A part of the software’s name refers to the fact that it extends, and is extensible by the python programming language. All the bindings are visualized by using the Structure Visualizing tool Pymol viewer, the interaction between the chemical compounds and target protein.

3 Results and discussion

3.1 PDB, PUBCHEM & Pass Online

In a progression of novel InhA inhibitors was recognized through a virtual screening technique. The creators utilized a multistage approach, incorporating pharmacophore demonstrating and atomic docking [27]. Most of the plants tried are a significant wellspring of hostile to parasitic aggravates that may give sustainable wellsprings of helpful antifungal medications against dermatophytic diseases in people [28]. Plants produce a combination of restorative portions as helper metabolites, for instance, phenolic blends, principal oils, tannins, terpenes, etc that can stifle microorganism advancement and are for the most part surveyed for its sensibility and reasonableness [29] various components add to anti-toxin opposition remembering abuse and abuse of anti-microbials for people, creatures and horticulture; patient's interest for and receipt of anti-infection agents when they needn't bother with them; and inability to complete an anti-microbial solution. Accordingly, the utilization of Ayurveda drugs has expanded now days [30]. The aeronautical pieces of C. auriculata L. shows higher antibacterial and antifungal action against bacterial and contagious microbes, for example, Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Candida albicans and Aspergillus niger [31].

| ORGANISM NAME         | PROTEIN NAME & ID   | STRUCTURE | RESIDUES COUNT |
|-----------------------|---------------------|-----------|----------------|
| Exophiala jeanselmei  | Chitin Synthase I & 2MPK | ![Diagram](image) | 74             |

The 3D structure of a protein (Chitin synthase I) was recovered from the Protein Data Bank (PDB) and the information was mentioned (Table 1). It was visualized by utilizing the visualizing tool pymol. The three dimensional structure of the protein was distinguished utilizing Lãgsite online device. The 3D structures of the phytochemical compounds of the plants chosen in the current investigation were retrieved from Pubchem Chemical database. The compounds which are segregated and revealed from earlier mentioned restorative plants were organized (Table 2) along with their molecular weight, molecular formula and pubchem ID, where pubchem is the database for getting small molecules. The biological activity of the Myricetin was broke down utilizing the pass online device which predicts the pharmacological and biochemical properties. The estimation of Probability to be dynamic (Pa) = 0.241 Probability to be idle (Pi) = 0.021. The properties anticipated for each plant compounds were recorded (Table 3).
**Table 2: List of compounds isolated from medicinal plants**

| S.No | Compound Name         | Pubchem ID | Molecular formula | Molecular Weight     |
|------|-----------------------|------------|-------------------|----------------------|
| 1.   | Myricetin             | 5281672    | C_{15}H_{10}O_{8} | 318.237 g/mol        |
| 2.   | Quercetin             | 5280343    | C_{15}H_{10}O_{7} | 302.238 g/mol        |
| 3.   | Dauosterol            | 5742590    | C_{35}H_{60}O_{6} | 576.859 g/mol        |
| 4.   | Baicalein             | 5281605    | C_{15}H_{10}O_{5} | 270.24 g/mol         |
| 5.   | Cosmosin              | 5280704    | C_{21}H_{20}O_{10}| 432.381 g/mol        |
| 6.   | Kaempferol            | 5280863    | C_{15}H_{10}O_{6} | 286.239 g/mol        |
| 7.   | Robinetin             | 5281692    | C_{15}H_{10}O_{7} | 302.238 g/mol        |
| 8.   | Luteolin              | 5280445    | C_{15}H_{10}O_{6} | 286.239 g/mol        |
| 9.   | Acacetin              | 5280442    | C_{16}H_{12}O_{5} | 284.267 g/mol        |
| 10.  | Catechin              | 9064       | C_{15}H_{14}O_{6} | 290.271 g/mol        |
| 11.  | Epicatechin           | 72276      | C_{15}H_{10}O_{6} | 290.271 g/mol        |
| 12.  | Isovitexin            | 162350     | C_{21}H_{20}O_{10}| 432.381 g/mol        |
| 13.  | (+)-Gallacatechin     | 65084      | C_{15}H_{12}O_{7} | 306.27 g/mol         |
| 14.  | 3-O-Methyl-D-Glucose  | 8973       | C_{7}H_{14}O_{6}  | 194.183 g/mol        |
| 15.  | Chanoclavine          | 5281381    | C_{15}H_{20}N_{2}O| 256.349 g/mol        |
| 16.  | Adenosine             | 60961      | C_{10}H_{13}N_{3}O_{4} | 267.245 g/mol     |
| 17.  | Naringenin            | 932        | C_{15}H_{12}O_{2} | 272.256 g/mol        |
| 18.  | Daidzein              | 5281708    | C_{15}H_{16}O_{4} | 254.241 g/mol        |
| 19.  | Penninclavine         | 115247     | C_{16}H_{18}N_{2}O_{2} | 270.332 g/mol   |
| 20.  | Isopenniclavine       | 12311156   | C_{16}H_{18}N_{2}O_{2} | 270.332 g/mol   |
| 21.  | Esculetin             | 5281416    | C_{6}H_{6}O_{4}   | 178.143 g/mol        |
| 22.  | Ciprofloxacin         | 2764       | C_{17}H_{16}N_{3}O_{3} | 331.347 g/mol     |
| 23.  | Lyserol               | 14987      | C_{16}H_{18}N_{2}O | 254.333 g/mol        |
| 24.  | Pueranin              | 5281807    | C_{21}H_{20}O_{9} | 416.382 g/mol        |
| 25.  | 6-Hydroxy lavone      | 72279      | C_{15}H_{10}O_{3} | 238.242 g/mol        |
| 26.  | Teucladiol            | 1604618    | C_{15}H_{26}O_{2} | 238.371 g/mol        |
| 27.  | Ethyl caffetate       | 5317238    | C_{11}H_{12}O_{6} | 208.213 g/mol        |
| 28.  | Buetin                | 5281222    | C_{15}H_{12}O_{5} | 272.256 g/mol        |
| 29.  | 20-hydroxyecdysone    | 5459840    | C_{22}H_{24}O_{7} | 480.642 g/mol        |
| 30.  | Rubiadin              | 5124062    | C_{15}H_{10}O_{6} | 473.943 g/mol        |
|   | Compound             | Molecular Weight | Molecular Formula | Molecular Mass (g/mol) |
|---|----------------------|------------------|-------------------|-----------------------|
| 31. | Mimosic acid         | 190359           | C_{7}H_{2}NO_{4}   | 169.136               |
| 32. | Octadecatrienoic acid | 5739740         | C_{28}H_{34}O_{4}  | 434.576               |
| 33. | Tetracaine           | 5411             | C_{15}H_{24}N_{2}O_{2} | 264.369           |
| 34. | Chicanine            | 5336043          | C_{20}H_{20}O_{3}  | 342.391               |
| 35. | Saupirin             | 181128           | C_{19}H_{22}O_{6}  | 346.379               |
| 36. | Elymocline           | 440904           | C_{16}H_{18}N_{2}O | 254.333               |
| 37. | Tyrosine             | 6057             | C_{9}H_{11}NO_{3}  | 181.191               |
| 38. | p-coumaric acid      | 637542           | C_{9}H_{8}O_{3}    | 164.16                |
| 39. | Nectandrin-b         | 156517           | C_{20}H_{20}O_{5}  | 344.407               |
| 40. | Caffeic acid         | 689043           | C_{9}H_{8}O_{4}    | 180.159               |
| 41. | Linoleic acid        | 5280450          | C_{18}H_{32}O_{2}  | 280.452               |
| 42. | Negundin A           | 10043572         | C_{20}H_{16}O_{6}  | 352.342               |
| 43. | Buchariol            | 101009028        | C_{13}H_{26}O_{2}  | 238.371               |
| 44. | Phyllmirurin         | 179963           | C_{20}H_{20}O_{3}  | 342.391               |
| 45. | Waltherine A         | 100978900        | C_{31}H_{42}N_{4}O_{4} | 534.701           |
| 46. | Steroid O sulfate    | 439761           | C_{18}H_{24}O_{4}S | 336.446               |
| 47. | 9,12-octadecadiynoic acid | 1931   | C_{18}H_{26}O_{2}  | 276.42                |
| 48. | Silymarin            | 5213             | C_{25}H_{20}O_{10} | 482.441               |
| 49. | Oleic acid           | 445639           | C_{18}H_{34}O_{2}  | 282.468               |
| 50. | Waltherine C         | 100994181        | C_{30}H_{37}N_{4}O_{4} | 531.657           |
| 51. | Phyllanthin          | 358901           | C_{24}H_{34}O_{8}  | 418.53                |
| 52. | 9-Octadecenoic acid  | 965              | C_{18}H_{34}O_{2}  | 282.468               |
| 53. | Viteagnuside A       | 38362716         | C_{26}H_{42}O_{9}  | 498.613               |
| 54. | Niranethin           | 13989915         | C_{24}H_{32}O_{7}  | 432.513               |
| 55. | Bufadienolide        | 46173848         | C_{24}H_{34}O_{2}  | 354.534               |
| 56. | Palmitic acid        | 985              | C_{16}H_{32}O_{2}  | 256.43                |
| 57. | Adouetine X          | 5281577          | C_{28}H_{42}N_{2}O_{4} | 500.684           |
| 58. | Lignans              | 443013           | C_{22}H_{34}O_{8}  | 414.41                |
| 59. | Oleanolic acid       | 10494            | C_{30}H_{48}O_{3}  | 456.711               |
| 60. | Gledigenin 1         | 45483610         | C_{10}H_{30}O_{3}  | 456.711g/mol           |
Table 3: Prediction of pharmacological activity for plant compounds

| Compound Name & Id | Compound structure | Compound Activity |
|--------------------|--------------------|-------------------|
| Myricetin 5281672  | ![Compound Structure](image) | 0.269 0.042 Chemopreventive |
|                    |                    | 0.242 0.018 Protein kinase stimulant |
|                    |                    | 0.282 0.059 CYP2E1 substrate |
|                    |                    | 0.280 0.060 CYP2E substrate |
|                    |                    | 0.241 0.021 Melanin inhibitor |
|                    |                    | 0.311 0.097 CYP3A4 inhibitor |
|                    |                    | 0.244 0.032 UGT1A4 substrate |

★ The Symbol indicates the main activity of the compound for the disease.

3.2 Drugability

The compounds were first oppressed for dissecting Absorption, Distribution, Metabolism and Excretion properties. Earlier ADME profiling of little atoms are noteworthy committed to the field of medication revelation by having sway on cost, work request and length [32]. Computational estimation of the docked phytochemical's medication likeliness was found based on limits set by "Lipinski's Rule of Five" through Drug examine apparatus at Molinspiration server. The subjective appraisals of ingestion, statement, digestion, discharge and poisonousness profile of these hits were anticipated basically by utilizing ADMET sar worker [33].

In the current investigation, Lipinski's standard of five in any case called Pfizer's standard of five or general guideline to assess tranquilize similarity shows the accompanying properties like atomic weight, octanol/water parcel coefficient, hydrogen bond giver and acceptor. After the filtration involving through Lipinski rule totally 39 out of 60 bioactive compounds from medicinal plants. Since the standard has a cutoff point in products of five, the name has been given as rule of five. Aside from the above properties, extra boundaries, such as, surface territory in square Armstrong (polar surface region, PSA); cerebrum/blood hindrance and level of human oral assimilation were additionally anticipated (Table 4).

Table 4: ADME toxicity for plant molecules

| Molecular ID | Molecular weight | Donor Hydrogen Bonds | Acceptor Hydrogen Bonds | High lipophilicity (Log P) | Molar refractivity |
|--------------|------------------|----------------------|-------------------------|---------------------------|-------------------|
| Normal range | 500              | 5                    | 10                      | <5                        | 40-130            |
| 8973         | 194              | 4                    | 6                       | -2.72                     | 41.96             |
| 5411         | 264              | 1                    | 2                       | 2.89                      | 80.43             |
| 5280704      | 432              | 5                    | 10                      | -0.10                     | 103.54            |
| 5280863      | 286              | 4                    | 6                       | 0.64                      | 62.82             |
| 5281672      | 318              | 5                    | 8                       | 1.71                      | 75.715            |
| 5280343      | 302              | 5                    | 7                       | 0.52                      | 64.36             |
| 637542       | 164              | 2                    | 3                       | 0.15                      | 40.19             |
| 124062       | 254              | 2                    | 4                       | 1.66                      | 61.13             |
| 181128       | 346              | 2                    | 6                       | 2.65                      | 87.76             |
|     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|
| 6057| 181 | 3   | 3   | 0.56| 44.23|
| 932 | 272 | 3   | 5   | 1.17| 64.16|
| 2764| 331 | 2   | 3   | 1.49| 81.89|
| 9064| 290 | 5   | 6   | 1.09| 68.13|
| 14987|254  | 2   | 1   | 2.35| 74.53|
| 60961|267  | 5   | 5   | -2.45|55.22|
| 65084|306  | 6   | 7   | 0.79| 69.01|
| 72276|290  | 5   | 6   | 1.09| 68.34|
| 72279|238  | 1   | 3   | 1.8 | 58.81|
| 94477|154  | 3   | 2   | 0.55| 40.135|
| 115247|270  | 3   | 2   | 2.06| 75.35|
| 190359|169  | 2   | 4   | -0.9|44.862|
| 440904|254  | 2   | 1   | 2.35| 74.53|
| 162350|432  | 6   | 10  | 1.63| 97.03|
| 5280442|284  | 2   | 5   | 1.65| 67.17|
| 5280445|286  | 4   | 6   | 0.83| 63.34|
| 5281222|272  | 4   | 5   | 1.19| 64.86|
| 5281381|256  | 3   | 1   | 2.67| 76.63|
| 5281416|178  | 2   | 4   | 0.45| 46.6 |
| 5281605|270  | 3   | 5   | 1.42| 61.24|
| 5281692|302  | 5   | 7   | 0.52| 64.36|
| 5281708|254  | 2   | 4   | 1.24| 61.06|
| 5281807|416  | 6   | 9   | 1.74| 96.34|
| 5317238|208  | 2   | 4   | 1.31| 51.03|
| 5459840|480  | 4   | 7   | 5.6 | 141.7|
| 5742590|312  | 5   | 6   | -0.05|77.62|
| 57397401|434  | 0   | 4   | 5.77| 130.09|
| 16046185|238  | 1   | 2   | 3.778|78.84|
| 12311156|270  | 3   | 2   | 2.06| 75.6 |
| 53360432|342  | 1   | 5   | 3.468|91.73|
3.3 Molecular Docking Study

Molecular docking and pharmacology studies are beneficially involved to screen the anti-inflammatory constituents of *Cinnamomum cassia* twigs, with a total of 69 bioactive compounds found to have potential drug-like properties. These findings will facilitate the development of bioactive compounds from *C. cassia* twigs for the treatment of inflammatory disorders [34]. *Senna alata* leaves are generally antifungal specialists they were exposed to *in silio* Molecular docking studies to locate their antifungal activities. As per Glide docking score selective compounds were exposed for drug-likeliness (ADME/T) investigation to foresee their conceivable potential to be used as a normally determined antifungal agent. As finalizing the results, the anthraquinones are promising applicants as an antifungal agent [35]. The results of docking studies 29 compounds were recorded (Table 5). The compound Myricetin had Binding energy of -7.32 Kcal/mol and formed hydrogen bonds with the residue HIS 29 showing the bond length of 1.8 Å and residue THR 3 showing the bond length of 1.9 Å. The compound Quercetin had Binding energy of -6.82 Kcal/mol and formed hydrogen bonds with the residue ALA 26 (H-O), ASP 6 (H-O), HIS 29 (O-H) showing the bond length of 2.2, 1.7, 1.8 Å. The compound Daucosterol had Binding energy of -6.64 Kcal/mol and formed hydrogen bonds with the residue HIS-66 showing the bond length of 1.6 Å. The compound Baicalein had Binding energy of -6.62 Kcal/mol and formed hydrogen bonds with the residue HIS 29 and THR 3 showing the bond length of 2.2 and 2.5 Å. The compound Cosmosin with binding energy of -6.58 Kcal/mol and formed hydrogen bonds with the residue ASP 32 and ASP 6 showing the bond length of 1.9 and 1.7Å. Further, the interactions of plant compounds with the target would compare to the presently available drug molecule, to study its potency. As well as the simulation studies would provide an insight about the stability of protein-compound complex. The plant compounds indicating collaboration with the protein are arranged with the Binding energy. The plant compounds and the information of their hydrogen bond, collaborating deposits and individual bond lengths were organized independently (Table 6). Utilizing Pymol tool, the cooperation between the synthetic mixes and target protein are visualized and the communication of the Compound Myricetin was appeared in the figure 1.

**Table 5: Docking result for plant molecules**

| S.No | Plant name       | Compounds                                      | Binding energy |
|------|------------------|------------------------------------------------|----------------|
| 1.   | *Achyranthus aspera* | 20-hydroxyecdysone (5459840)                   | -4.74          |
| 2.   | *Brassica niger*  | Tetracaine (5411)                              | -4.25          |
| 3.   | *Cassia auriculata* | Myricetin (5281672)                            | -7.32          |
|      |                   | Naringenin (932)                               | -5.17          |
|      |                   | Quercetin (5280343)                            | -6.82          |
|      |                   | Rubiadin (124062)                              | -4.67          |
| 4.   | *Cleome gynandra* | Daucosterol(5742590)                           | -6.64          |
|      |                   | Teucladiol(16046185)                           | -4.81          |
| 5.   | *Clitoria ternatea* | Adenosine (60961)                             | -5.53          |
|      |                   | p-coumaric acid (637542)                       | -4.13          |
| 6.   | *Ipomoea hederacea* | Chanoclavine (5281381)                        | -5.65          |
|      |                   | Penniclavine (115247)                          | -4.93          |
|      |                   | Isopen niclavine (12311156)                    | -4.93          |
|      |                   | Lysergol (14987)                               | -4.87          |
|      |                   | Ethyl Caffeate (5317238)                       | -4.78          |
|      |                   | Elymoclavine (440904)                          | -4.18          |
| 7.   | *Leucas aspera*    | Catechin (9064)                                | -5.76          |
|      |                   | Acacetin (5280442)                             | -5.91          |
|      |                   | Chicanine (53360432)                           | -4.22          |
| 8.   | *Mimosa pudica*    | 6-hydroxy flavones (72279)                     | -4.86          |
### Evaluation of Fungal Activity Through In Silico Analysis of Medicinal Plants Against Exophiala Jeanselmei

- Isovitexin (162350)
- Mimosamine (94477)
- Mimosinic acid (190359)
- Tyrosine (6057)
- 5.73
- 5.00
- 4.66
- 4.18

| S.No | Name of the ligand / PubChem ID | Residues Interaction | Bond length | No of Bonds | Binding energy |
|------|---------------------------------|----------------------|-------------|-------------|---------------|
| 1.   | Myricetin/5281672               | HIS - 29 (H-O)       | 1.7         | 2           | -7.32         |
|      |                                 | THR - 3 (H-O)        | 2.1         |             |               |
| 2.   | Quercetin/5280343               | ALA - 26 (H-O)       | 2.2         | 3           | -6.82         |
|      |                                 | HIS - 29 (O-H)       | 1.8         |             |               |
|      |                                 | ASP - 6 (H-O)        | 1.7         |             |               |
| 3.   | Daucosterol/5742590             | HIS - 66 (H-O)       | 1.6         | 1           | -6.64         |
| 4.   | Baicalein/5281605               | THR - 3 (O-H)        | 2.5         | 2           | -6.62         |
|      |                                 | HIS - 29 (O-H)       | 2.2         |             |               |
| 5.   | Cosmosin/5280704                | ASP - 32 (H-O)       | 1.9         | 2           | -6.58         |
|      |                                 | ASP - 6 (H-O)        | 1.7         |             |               |
| 6.   | Kaempferol/5280863              | HIS - 29 (O-H)       | 1.8         | 3           | -6.43         |
|      |                                 | ALA - 26 (H-O)       | 2.1         |             |               |
|      |                                 | ASP - 6 (H-O)        | 1.7         |             |               |
| 7.   | Robinetin/5281692               | HIS - 29 (H-O)       | 1.7         | 3           | -6.4          |
|      |                                 | HIS - 29 (O-H)       | 2.6         |             |               |
|      |                                 | ASP - 6 (O-H)        | 2.1         |             |               |
| 8.   | Luteolin/5280445                | HIS - 29 (H-O)       | 2.2         | 3           | -6.29         |

Table 6: Interaction of plant compounds with 2MPK
| No. | Compound | Nucleus 1 | Nucleus 2 | Nucleus 3 | Nucleus 4 | Nucleus 5 | Nucleus 6 | Nucleus 7 | Nucleus 8 | Nucleus 9 | Nucleus 10 | Nucleus 11 | Nucleus 12 | Nucleus 13 | Nucleus 14 | Nucleus 15 | Nucleus 16 | Nucleus 17 | Nucleus 18 | Nucleus 19 | Nucleus 20 | Nucleus 21 | Nucleus 22 | Nucleus 23 | Nucleus 24 |
|-----|----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 9.  | Acacetin/5280442 | ALA - 26 (H-O) | 1.9 | THR - 3 (O-H) | 2.4 | | | | | | | | | | | | | | | 2 | 5.91 | | | | | | |
| 10. | Catechin/9064 | HIS – 29 (O-H) | 2.2 | GLY - 2 (O-H) | 2.6 | | | | | | | | | | | | | | | | | | | | | | |
| 11. | Epicatechin/72276 | ASP - 6 (H-O) | 1.7 | THR - 3 (H-O) | 1.8 | | | | | | | | | | | | | | | | | | | | | | |
| 12. | Isovitexin/162350 | ASP - 6 (H-O) | 2.1 | ASP - 6 (H-O) | 2.3 | ASP - 6 (H-O) | 1.6 | MET - 1 (O-H) | 2.2 | | | | | | | | | | | | | | | | |
| 13. | (+)- Gallatechin/65084 | ASP - 6 (H-O) | 2.1 | THR - 3 (H-O) | 1.9 | | | | | | | | | | | | | | | | | | | | | | |
| 14. | 3-o-Methyl-D-glucose/8973 | ALA - 7 (H-O) | 2.0 | ALA - 26 (H-O) | 1.8 | | | | | | | | | | | | | | | | | | | | | | |
| 15. | Chanoclavine/5281381 | ASP - 6 (H-O) | 1.7 | ASP - 6 (H-O) | 1.3 | | | | | | | | | | | | | | | | | | | | | | |
| 16. | Adenosine/60961 | THR - 3 (H-O) | 2.0 | ASP - 6 (H-O) | 1.7 | ASP - 6 (H-O) | 2.1 | | | | | | | | | | | | | | | | | | | | | | |
| 17. | Naringenin/932 | HIS - 29 (O-H) | 2.3 | | | | | | | | | | | | | | | | | | | | | | |
| 18. | Daidzein/5281708 | HIS - 29 (O-H) | 2.0 | | | | | | | | | | | | | | | | | | | | | | |
| 19. | Penninclavine/115247 | ASP - 6 (H-O) | 1.6 | HIS - 29 (H-N) | 1.9 | | | | | | | | | | | | | | | | | | | | | | |
| 20. | Isopenniclavine/12311156 | ASP - 6 (H-O) | 1.6 | HIS – 29 (H-N) | 1.9 | | | | | | | | | | | | | | | | | | | | | | |
| 21. | Esculetin/5281416 | HIS - 29 (O-H) | 2.2 | | | | | | | | | | | | | | | | | | | | | | |
| 22. | Ciprofloxacin/2764 | GLU - 59 (H-O) | 1.9 | | | | | | | | | | | | | | | | | | | | | | |
| 23. | Lysergol/14987 | ASP - 6 (H-O) | 1.7 | THR - 3 (H-O) | 1.9 | | | | | | | | | | | | | | | | | | | | | | |
| 24. | Puerarin/5281807 | ASP - 6 (H-O) | 2.3 | ASP - 6 (H-O) | 1.8 | | | | | | | | | | | | | | | | | | | | | | |
| No. | Plant Name                  | Coordinates | Activity | IC50 (μM) |
|-----|----------------------------|-------------|----------|-----------|
| 25  | 6-Hydroxy flavone/72279    | HIS - 29(O-H) | 2.1      | -4.81     |
|     |                            | THR - 3 (O-H) | 2.5      |           |
| 26  | Teucladiol/16046185        | ALA - 26 (H-O) | 2.0      | -4.8      |
| 27  | Ethyl caffeate/5317238     | HIS - 29 (O-H) | 2.4      | -4.78     |
|     |                            | ASP - 6 (H-O) | 1.8      |           |
| 28  | Buetin/5281222             | ASP - 5 (H-O) | 2.0      | -4.74     |
|     |                            | ASP - 5 (H-O) | 1.9      |           |
|     |                            | ARG - 9 (O-H) | 2.1      |           |
| 29  | 20-hydroxyecdysone/5459840 | PHE - 8 (H-O) | 2.0      | -4.74     |
|     |                            | THR - 3 (O-H) | 2.5      |           |
| 30  | Rubiadin/5124062           | ASP - 6 (H-O) | 1.8      | -4.67     |
| 31  | Mimosic acid/190359        | THR - 3 (H-O) | 1.9      |           |
|     |                            | THR - 3 (O-H) | 1.6      | -4.66     |
|     |                            | GLY - 2 (O-H) | 2.3      |           |
| 32  | Octadecatrienoic acid/57397401 | LYS - 56 (O-H) | 2.4      | -4.46     |
| 33  | Tetracaine/5411            | ALA - 26 (H-O) | 2.0      | -4.25     |
| 34  | Chicanine/53360432         | ARG - 9 (O-H) | 2.1      | -4.22     |
|     |                            | ASP - 5 (O-H) | 1.8      |           |
| 35  | Saupirin/181128            | ASP - 6 (H-O) | 1.7      | -4.21     |
|     |                            | ALA - 26 (H-O) | 1.8      |           |
| 36  | Elymoclavine/440904        | ASP - 6 (H-O) | 1.6      | -4.18     |
| 37  | Tyrosine/6057              | THR - 3 (O-H) | 2.3      | -4.18     |
|     |                            | ASP - 6 (H-O) | 1.8      |           |
|     |                            | ALA - 26 (H-O) | 1.9      |           |
| 38  | p-coumaric acid/637542     | ALA - 26 (H-O) | 2.1      | -4.13     |
|     |                            | THR - 3 (O-H) | 2.2      |           |
|     |                            | GLY - 2 (O-H) | 2.3      |           |
The ligand was exposed in TV orange color and interacting residues in yellow color. The dotted lines indicating the hydrogen bond formation. The compound Myricetin had Binding energy of -7.32 Kcal/mol and formed hydrogen bonds with the residue HIS 29 showing the bond length of 1.9 Å.

4 Conclusions

The development of computational methods for protein flexibility is still in its infancy and thereby remains one of the major future directions in protein ligand docking. Rising new contagious species and the occurrence of raised medication obstruction for fungal infections keeps on rising and the height of contagious contaminations is disturbing. Medicinal plants are an important part of our natural health. They serve as important therapeutic agents as well as valuable raw materials for manufacturing numerous traditional and modern medicines. Cassia auriculata leaves have been traditionally used worldwide for its versatile therapeutic properties. A study of molecular docking stimulation undertaken to identify and accesses the binding capacity of ligands. The chemical compounds are used to cure disease and those compounds are found in aerial parts of the plant. The purpose of this study is to analyze the inhibitory potential Chitin synthase I through in silico molecular docking studies on active compounds of plant extract. The protein and ligand docking studies are done by using 3D structure of protein. Most of the molecular docking studies successfully predict the binding modes of small-molecule ligands within receptor binding sites. The phytochemical compounds of Myricetin were isolated from C. auriculata exhibit a good binding efficiency with the target showing high binding energy of -7.32 Kcal/mol is used to cure the Phaeohyphomycosis. The biological activity of plant compounds is predicted using pass prediction and the results are proved the chemical compounds have a dermatological property. This indicates that the Myricetin compound has the highest Melanin (main virulent factor) inhibiting activity and also other plant compounds. Those bioactive compounds should be explored more in order to identify an efficient and
potential drug molecule. As shown in the highlighted case studies, molecular docking has been able to identify promising compounds that might represent future solutions in critical areas of human health.

5 Declarations

5.1 Acknowledgements

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5.2 Competing Interests

The authors declared that they do not have any conflict of interest.

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