VOLUME 8 ISSUE 1 2022

ISSN 2454-3055

INTERNATIONAL JOURNAL OF ZOOLOGICAL INVESTIGATIONS

Forum for Biological and Environmental Sciences

Published by Saran Publications, India

International Journal of Zoological Investigations Vol. 8, No. 1, 320-337 (2022)

International Journal of Zoological Investigations
Contents available at Journals Home Page: www.ijzi.net
Editor-in-Chief: Prof. Ajai Kumar Srivastav
Published by: Saran Publications, Gorakhpur, India

ISSN: 2454-3055

In-Silico Research to Screen Various Phytochemicals as Potential Therapeutics Against Beta Glucan Synthase Enzyme from Black Fungus Endangering Covid Patients in India

Sarkar Diptendu

Department of Microbiology, Ramakrishna Mission Vidyamandira, Belur Marh, Howrah 711202, West Bengal, India

Received: 29th January, 2022; **Accepted:** 11th March, 2022; **Published online:** 15th March, 2022

https://doi.org/10.33745/ijzi.2022.v08i01.035

Abstract: Mucormycosis, has reportedly decimated numerous Indian states. This malady has already been deemed a catastrophe in several Indian states. Black fungus appears to have been a deadly, existence situation that needs medical assistance. Mucormycosis has indeed been medicated using antagonists of glucan biosynthesis processes, however, the discovery is now in its beginning stages. Because of its main functions in glucan biosynthesis, beta-glucan synthase was picked as nothing more than a great option for therapeutic development in this investigation. The objectives of this research were about to conduct in-silico assessment plus molecular docking analysis on a number of phytocompounds (a total of 32 phytochemicals) in regard towards 1,3-beta-glucan synthase protein (4M80). There have been very few studies done on *in-silico* investigation by using beta-glucan synthase as target protein for various phytochemicals to date. The strongest interacting phytomolecule was found to be rhamnazin 3-rutinoside, with the largest negative correlating -10.54 Kcal/mol. The interacting energy of hesperidin, the second-best interacting chemical, would have to be -10.47 Kcal/mol, whereas pectolinarin, the third-best dealing compound, had been -10.38 Kcal/mol. This study, which aimed to predict the repressive exercises of plant-derived materials that specifically target 4M80 proteins, found a number of interesting findings, including how the pharmaceutical had a vastly greater posture as well as complexation than hydroxychloroquine and the antibiotic fluconazole. Furthermore, ADME was also carried out with all the selected compounds. More studies in animal and clinical prototype may lay the groundwork for some of these compounds to be utilised in drug research.

Keywords: Mucormycosis, Black fungus, Glucan biosynthesis, Molecular docking, Pharmaceutical, Phytochemical

Citation: Sarkar Diptendu: *In-silico* research to screen various phytochemicals as potential therapeutics against beta glucan synthase enzyme from black fungus endangering COVID patients in India. Intern. J. Zool. Invest. 8(1): 320-337, 2022.
https://doi.org/10.33745/ijzi.2022.v08i01.035

Introduction

Mucormycosis, popularly known as "black fungus," is indeed a rare but deadly disease spread by mostly mucormycetes, a fungus family. Due to their tendency for invading blood vessels, they trigger terrible tissue hemorrhage, strokes, with apoptosis, ending in complications and death (Garg *et al.*, 2021). Black fungus seems to be a dangerous, life-threatening ailment that needs to be medicated as soon as possible (Garg *et al.*, 2021). Antifungal medicines as well as surgical intervention have been typically used to treat fungal infections (Sharma *et al.*, 2021). Mucormycosis instances have recently increased in India. This ailment has been labeled pandemic

in various states in India, including Maharashtra and Gujarat, as well as Rajasthan (Garg *et al.*, 2021). The goal towards preventing COVID-19-correlated mucormycosis should have been to improve glucose tolerance in COVID-19 sufferers and thus to supervise use of immunosuppressive drugs in the management of severe illnesses (Mondal *et al.*, 2021). Black fungus resurgence has been anticipated to rise to 140 cases per million individuals in India, about 80 times higher than with the global average (Garg *et al.*, 2021). According to latest projections, someone with pre-existing hyperglycemia, those who are on immunosuppressants, especially individuals having COVID-19, including those rehabilitating again from condition, are more likely to have an increase (Amani *et al.*, 2021). Mucormycosis diagnosed based on how the fungus has been developing in the organism. A respiratory contamination (sinusitis) seems to be the most prevalent symptom, which seems preceded with rhinitis, runny nose, with sinus headaches. A temperature and even a migraine are other possible side effects (Zhang *et al.*, 2020).

Due to the general practical drawbacks of fungicidal drugs, such as their heavy price, unpredictable complications, and the growth of chemoresistance, the design of secure and reliable fungicidal therapeutics depending on novel antifungal target has been sorely needed (Padmini *et al.*, 2020). Since no structure exists in people, a previous study reported that 1,3-beta-glucan synthase could be a potential candidate for antifungal medication development (Mondal *et al.*, 2020). The major pharmacological compounds like amphotericin that block beta-1,3-glucan production was suggested as possible treatment medicines against illnesses (Garg *et al.*, 2021). In fungi, 1,3-beta-glucan synthase appears to be a glucosyl-transferase that generates beta-glucan, which would be an important part of cell walls (Amani *et al.*, 2021). The possible use of 32 different phytochemical compounds as a therapy strategy for black fungus through addressing the fungal enzyme 1,3-beta-glucan synthase is presented herein.

Conventional healthcare has been utilized by people all over the globe as an alternative to replace for a variety of ailments (Ricciutelli *et al.*, 2021). A herb is a horticultural or vegetal portion that is used for its odor, fragrance, or therapeutic potential. Medicinal herbs are one component of food supplementation. There have been pills, pellets, smoothies, teas, infusions, along with fresh or dried plants, currently offered. Humans adopt herbal medicine for protection/even lengthen their livelihoods (Mirzavandi *et al.*, 2021). Herbal medicines seem to be popular as they have a diverse variety of therapeutic compounds containing minimal hazardous chemicals, low-cost preparations, less complications, and therefore easily accessible (Padmini *et al.*, 2020). Some of the phenolic compounds present in herbal medicines and recovered from them are phenolic acids, flavonoids, tannins, as well as coumarins. Polyphenols' antimicrobial property was already widely researched, primarily towards microorganisms (Moosavian *et al.*, 2020). Naturally phenolic compounds have been among the most antifungal efficient active ingredients in essential oils, with minimal mammalian toxicity (Sangouni *et al.*, 2020).

Molecular docking would be an important approach in structural molecular biology including machine drug creation (Chen *et al.*, 2020). The purpose of ligand-protein coupling should be to anticipate a ligand's most common binding type(s) with something like a protein with a specified three-dimensional geometry. Molecular docking has been used to assist rationalize ligand interaction towards a target molecule and thus to execute structure-based high - throughput efforts (Sharma *et al.*, 2021). We believe that the abundance of bioactive ingredients in diverse medicinal herbs makes them capable of preventing black fungus attack. *In-silico* analysis and molecular docking investigations of several chosen compounds (total 32 phytochemicals) in relation to 1,3-beta-glucan synthase were thus the objectives of this study.

Materials and Methods

The *in-silico* study was carried out by using PyRx virtual screening tool (Shereen *et al.*, 2021). Protein preparation was carried out by AutoDock Tools (Amani *et al.*, 2021). Ligand preparation and grid generation were carried out by AutoDock Vina. Receptor-ligand docking were carried out by PyRx. The Swiss ADME server was used for drug likeness prediction of all compounds selected for study (Padmini *et al.*, 2020; Ricciutelli *et al.*, 2020).

Selection of target protein and Preparation of Protein Target Structure:

At 1.85A^0 resolution, the architecture of Candida albicans' E292S glycosynthase isoform of exo-1,3-beta-glucanase whose PDB ID:4M80, was downloaded from the Protein Data Bank (PDB) and prepared for docking. It seems to have one 399-amino-acid-residue protein chain (A) with molecular weight 45.69 KD (Fig. 1). The input files were prepared with AutoDock Tools (ADT) 1.5.6. Molecules of water, HET atoms, as well as ions have all been completely removed. The polar hydrogen atoms have been given Kollman charges (Shreen *et al.*, 2021).

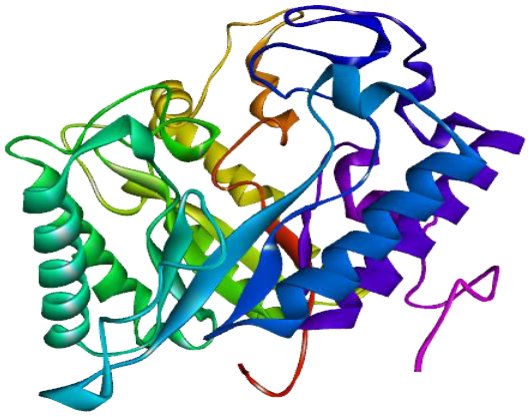


Fig. 1: 3D picture of exo-1,3-beta-glucanase enzymatic protein (PDB ID: 4M80).

Selection and preparation of ligand molecules:

For selection of ligand molecules, we used target-based ligand selection approach. LEA3D-CNRS (https://chemoinfo.ipmc.cnrs.fr/LEA3D/index.html) was used for selecting ligand structure. PubChem was used to obtain 3D structures of the most prevalent organosulfur compounds and flavonoids found in garlic. There was total 32 molecules which were used in this study along with two reference compounds (Table 1). The Ligands were imported into AutoDock Tools in the 'Sybyl mol2' format and handled with the 'Ligand' option, which corrects the torsion tree, non-polar hydrogens, charges, and atom kinds. With all the structure further ADME prediction were carried out by using SWISS ADME to filter all phytochemical compounds based on Lipinski rule of five (Rouf *et al.*, 2020).

Molecular Docking investigation:

Molecular docking analysis performed with target like 4M80 by using PyRx virtual screening tool (Padmni *et al.*, 2020; Sarkar, 2021). This tool used Auto Dock as docking algorithm. Here first we uploaded prepared protein structure as macromolecule and then one by one all selected bioactive compounds (ligand). Software first minimized ligand energy and then converted it into Auto Dock ligand format (pdbqt). Finally started blind docking after covering entire protein structure under grid box to screen best fitted bioactive compounds based on energy value. Each simulation was conducted roughly ten times, resulting in ten docked conformations. The least energy configurations were deemed to be the highest binding conformations as a result of this. Employing Discovery Studio software, the intra - molecular interactions such as hydrogen bonds, van der Waals, and hydrophobic interactions with that specific bioactive compounds have been clearly analyzed (Alghmadi *et al.*, 2021).

Results and Discussion

The 4M80 (exo-1,3-beta-glucanase enzymatic protein) is a ~399 amino acid long glucanase enzyme of 45.69 kD, the crystal structure with a resolution of 1.85 Å has been elucidated here. *In-silico* molecular analysis was performed on a variety of bioactive compounds. Various physicochemical parameters such as donors or acceptors of hydrogen bond, number of flexible bonds, molecular mass, and others were often

Table 1: Phytocompounds (Ligand) selected for the study with their compound name, PubChem ID and molecular formula

S. No.	Name of the Phytochemicals	Molecular formula	PubChem ID
1	Quinine	$C_{20}H_{24}N_2O_2$	3034034
2	Cannabidiol	$C_{21}H_{30}O_2$	644019
3	Hesperidin	$C_{28}H_{34}O_{15}$	10621
4	Rhoifolin	$C_{27}H_{30}O_{14}$	5282150
5	Pectolinarin	$C_{29}H_{34}O_{15}$	168849
6	Morin	$C_{15}H_{10}O_7$	5281670
7	Epigallocatechingallate	$C_{22}H_{18}O_{11}$	65064
8	Herbacetin	$C_{15}H_{10}O_7$	5280544
9	Ethyl cholate	$C_{26}H_{44}O_5$	6452096
10	Kaempferol	$C_{15}H_{10}O_6$	5280863
11	Tangeretin	$C_{20}H_{20}O_7$	68077
12	Chalcone	$C_{15}H_{12}O$	637760
13	Nobiletin	$C_{21}H_{22}O_8$	72344
14	Bis (3, 5, 5-trimethylhexyl) phthalate	$C_{26}H_{42}O_4$	34277
15	6-gingerol	$C_{17}H_{26}O_4$	442793
16	6-shogaol	$C_{17}H_{24}O_3$	5281794
17	Hydroxychloroquine	$C_{18}H_{26}ClN_3O$	3652
18	Myristicin	$C_{11}H_{12}O_3$	4276
19	Eugenol	C10H12O2	3314
20	Sinigrin	$C_{10}H_{16}KNO_9S_2$	23682211
21	Xanthoangelol	$C_{25}H_{28}O_4$	643007
22	Savinin	$C_{20}H_{16}O_6$	5281867
23	Pristimerin	$C_{30}H_{40}O_4$	159516
24	Apigenin	$C_{15}H_{10}O_5$	5280443
25	Curcumin	$C_{21}H_{20}O_6$	969516
26	Cryptotanshinone	$C_{19}H_{20}O_3$	160254
27	Broussochalcone A	$C_{20}H_{20}O_5$	6438825
28	Epigallocatechin	$C_{15}H_{14}O_7$	72277
29	Baicalein	$C_{15}H_{10}O_5$	5281605
30	Ellagic acid	$C_{14}H_6O_8$	5281855
31	Cinnamamide	C_9H_9NO	5273472
32	6,8-Diprenylgenistein	$C_{25}H_{26}O_5$	480783
33	Rhamnazin 3-O-rutinoside	$C_{29}H_{34}O_{16}$	5464499
34	Fluconazole	$C_{13}H_{12}F_2N_6O$	3365

used to anticipate and grade drug compliance (Nag *et al.*, 2021). The "Lipinski rule of five" was checked for all of these compounds. The results are summarized in Table 2.

The protein (4M80) interactions with a specified ligand library were explored, predicted, and understood using the molecular docking technique, which was also utilised to illustrate the likely binding. The binding energy and interaction residues of analogues docked with receptors (4M80) using the PyRx virtual screening tool, which employed Autodock 4.2.1, are shown in Table 3. In Figs. 2-35, all 3D and 2D diagrams of the corresponding ligand with protein (4M80) are shown.

Mucormycosis seems to be a very uncommon illness. Mucor fungus, that is widely formed naturally, vegetation, compost, including deteriorating fruits and veggies, causes disease (Wu *et al.*, 2020; Garg *et al.*, 2021). It damages the sinus, the central nervous system, and the pulmonary tissues, although it can be fatal in diabetics or persons who are extremely immunocompromised, including cancer victims as

Table 2: Lipinski rule related information of selected phytocompounds studied along with reference compound Hydroxychloroquine and Fluconazole. Given emphasis on molecular weight, number of hydrogen bond donor as well as acceptor, along with Log Po/w and Log S value of the phytocompounds

S. No.	Phytochemicals	Molecular Weight (g/mol)	No. of H bond donor	No. of H bond acceptor	Log $P_{o/w}$	Log S	Lipinski Rule violation
1	Quinine	356.67	1	4	1.40	-1.73	0
2	Cannabidiol	350.75	2	2	4.83	-5.61	1
3	Hesperidin	610.56	8	15	-0.72	-3.28	3
4	Rhoifolin	346.42	0	5	3.38	-4.43	0
5	Pectolinarin	622.57	7	15	-0.43	-3.74	3
6	Morin	319.37	5	7	-0.93	-0.48	0
7	Epigallocatechin gallate	482.66	8	11	-0.92	-1.49	2
8	Herbacetin	319.37	5	7	-0.72	-1.02	0
9	Ethyl cholate	436.62	3	5	3.52	-3.86	0
10	Kaempferol	286.24	4	6	1.70	-3.31	0
11	Tangeretin	404.62	0	7	1.30	-2.37	0
12	Chalcone	234.46	0	1	3.78	-4.22	0
13	Nobiletin	436.66	0	8	1.00	-2.22	0
14	Bis (3, 5, 5-trimethylhexyl) phthalate	418.61	0	4	6.48	-6.90	1
15	6-gingerol	322.61	2	4	2.88	-2.80	0
16	6-shogaol	305.60	1	3	3.65	-3.63	0
17	Hydroxychloroquine	364.09	2	4	1.33	-0.97	0
18	Myristicin	210.35	0	3	1.17	-1.70	0
19	Eugenol	183.35	1	2	1.75	-2.20	0
20	Sinigrin	372.48	4	10	-1.10	-0.64	0
21	Xanthoangelol	433.81	3	4	4.50	-5.24	0
22	Savinin	378.54	0	5	1.03	-1.64	0
23	Pristimerin	464.64	1	4	5.57	-6.54	1
24	Apigenin	291.40	3	5	0.36	-1.45	0
25	Curcumin	398.62	2	6	2.56	-2.92	0
26	Cryptotanshinone	300.39	0	3	2.96	-3.04	0
27	Broussochalcone A	370.61	4	5	2.46	-3.56	0
28	Epigallocatechin	324.41	6	7	-0.72	-0.92	1
29	Baicalein	291.40	3	5	0.46	-1.80	0
30	Ellagic acid	312.27	4	8	-0.47	-1.09	0
31	Cinnamamide	164.31	1	1	1.65	-2.03	0
32	6,8-Diprenylgenistein	443.76	3	5	3.48	-4.37	0
33	Polygalacin	638.57	8	16	-0.34	-3.74	3
34	Fluconazole	306.26	1	7	0.88	-2.17	0

well as AIDS sufferers (Das *et al.*, 2021). Clinicians suspect that use of corticosteroids, a life-saving treatment for both comorbidities and acute Covid-19 sufferers, may be causing mucormycosis, since it has a fifty per cent overall casualty rate (Ricciutelli *et al.*, 2021). Steroids able to improve/prevent several of the impairment that could really occur only when innate immune system kicks into gear to combat the coronavirus by reducing symptoms of asthma (Verma *et al.*, 2021). However, in both diabetes as well as non-diabetic Covid-19 sufferers, they lower defence as

Table 3: Molecular docking study with various phytochemicals used and their interaction study with 4M80. Interaction energy, interaction residues as well as number of hydrogen bond involved in interaction also depicted

S. No.	Name of the Phytochemicals	Interacting residues	Interaction energy Kcal/mol	No of H Bonds in interaction	Fig. No.
1	Quinine	Trp 360, Val 361, Ala 290, Gly 359, Gly 291, His 252, Asp 251, Trp 131, Ile 15, Val 250, Asn 288, Val 249, Tyr 10, Gly 358	-7.64	2	2
2	Cannabidiol	Pro 222, Trp 131, Asn 288, Val 289, Val 250, Asp 251, Ile 225, Val 248, Val 223, Trp 287, Tyr 10	-7.96	2	3
	Hesperidin	Trp 131, Arg 92, Phe 24, Leu 116, Phe 80, Leu 120, Val 91, Leu 20, Ile 95, Asp 133, Ala 119, Ile 132, Val 130, Pro 94	-10.47	2	4
4	Rhoifolin	Gly 22, His 70, Trp 74, Trp 71, Phe 24, Tyr 115, Ala 119, Ile 75, Trp 122, Phe 80, Ile 91, Leu 20, Gly 21, Val 25	-9.73	1	5
5	Pectolinarin	Asp 251, Asp 227, His 252, Val 289, Asn 288, Ile 225, Val 249, Trp 287, Trp 235, His 286	-10.38	2	6
6	Morin	His 254, Trp 293, Tyr 255, Trp 363, Val 361, Asn 19, Ala 290, His 253	-7.64	2	7
7	Epigallocatechin gallate	His 252, Thr 357, Ala 281, Glu 284, His 286, Gly 358, Trp 287, Val 289, Val 250, Val 249	-9.30	2	8
8	Herbacetin	Gly 59, Lys 60, Thr 55, Ala 62, Leu 64, Gln 68, Leu 67, Ile 66, Trp 54, Leu 58, Arg 65, Val 109, Glu 61	-7.24	2	9
9	Ethyl cholate	Val 249, His 252, Thr 357, Ala 281, Glu 284, His 286,	-7.14	2	10

		Gly 358, Trp 287, Val 289, Val 250			
10	Kaempferol	Ala 281, Tyr 356, Lys 282, Valk 14, Glu 355, Gly 359, Phe 354, Ala 353, Asn 288, Gly 358	-7.86	2	11
11	Tangeretin	Val 91, Ile 185, Tyr 10, Ile 224, Phe 90, Val 249, Asp 251, Val 289, Gly 291, Glu 188, Arg 92, Asp 133, Ile 93, Ile 132, Val 130, Gly 186	-8.58	3	12
12	Chalcone	His 252, Thr 357, Ala 281, Glu 284, His 286, Gly 358, Trp 287, Val 289, Val 250, Val 249	-6.68	2	13
13	Nobiletin	His 252, Thr 357, Ala 281, Glu 284, His 286, Gly 358, Trp 287, Val 289, Val 250, Val 249	-8.93	2	14
14	Bis (3, 5, 5-trimethylhexyl) phthalate	Asp 251, Asp 227, His 252, Val 289, Asn 288, Ile 225, Val 249, Trp 287, Trp 235, His 286, Asp 227, Asp 251	-8.24	2	15
15	6-gingerol	Ala 281, Lys 282, Glu 284, Asn 236, Ser 285, Asp 280, Trp 279	-8.07	1	16
16	6-shogaol	Phe 354, Ile 15, Val 14, Val 289, Asn 288, Thr 357	-7.49	1	17
17	Hydroxychloroquine	Ala 290, Gly 359, Gly 291, His 252, Asp 251, Trp 131, Ile 15, Val 250, Asn 288, Val 249, Tyr 10, Gly 358, Val 361, Trp 360	-8.49	2	18
18	Myristicin	Trp 277, Trp 279, Asp 280, Lys 282, Asn 288, Glu 284, Thr 357, Phe 232, Lys 2983, Gly 278	-6.51	2	19
19	Eugenol	Thr 379, Phe 384, Trp 360, Leu 88, Leu 86, Val 18, Phe 362, Trp 365, Ser 364, Ser 374, Thr 377, Leu 378, Gln 376	-6.94	3	20
20	Sinigrin	Gly 278, Trp 279,	-8.21	2	21

		Thr 357, Tyr 356, Ala 281, Glu 284, Lys 283, Asp 280			
21	Xanthoangelol	His 252, Thr 357, Ala 281, Glu 284, His 286, Gly 358, Trp 287, Val 289, Val 250, Val 249	-9.05	2	22
22	Savinin	Ile 83, Ile 93, Arg 92, Val 130, Trp 131, Phe 90, Ile 128, Phe 80, Val 18, Arg 129, Leu 20	-8.62	2	23
23	Pristimerin	Ile 187, Asp 251, Pro 222, Val 249, Trp 131, Tyr 10, Gly 186, His 226, Leu 189, Glu 188, Val 223, Ile 225	-6.31	2	24
24	Apigenin	His 252, Thr 357, Ala 281, Glu 284, His 286, Gly 358, Trp 287, Val 289, Val 250, Val 249	-7.82	2	25
25	Curcumin	Ala 281, Tyr 356, Lys 282, Val 14, Glu 355, Gly 359, Phe 354, Ala 353, Asn 288, Gly 358	-8.65	2	26
26	Cryptotanshinone	Gly 359, Val 289, Val 361, Ser 292, Trp 360, His 252, His 254, Phe 354	-7.21	2	27
27	Broussochalcone A	Trp 131, Arg 92, Phe 24, Leu 116, Phe 80, Leu 120, Val 91, Leu 20, Ile 95, Asp 133, Ala 119, Ile 132, Val 130, Pro 94	-8.50	2	28
28	Epigallocatechin	Ala 281, Tyr 356, Lys 282, Val 14, Glu 355, Gly 359, Phe 354, Ala 353, Asn 288, Gly 358	-7.80	2	29
29	Baicalein	His 254, Trp 293, Tyr 255, Trp 363, Val 361, Asn 19, Ala 290, His 253	-7.50	2	30
30	Ellagic acid	Tyr 97, Trp 98, Gly 96. Ala 99, Tyr 175, Ile 95, Val 113, Ile 171, Thr 170, Val 167, Gln 110	-7.74	1	31
31	Cinnamamide	Val 91, Ile 185, Tyr 10, Ile 224,	-6.48	3	32

		Phe 90, Val 249, Asp 251, Val 289, Gly 291, Glu 188, Arg 92, Asp 133, Ile 93, Ile 132, Val 130, Gly 186			
32	6,8-Diprenylgenistein	Gly 186, asp 133, Val 130, Ile 95, Ile 171, Tyr 175, Leu 120, Val 184, Leu 134, Glu 188, Ile 187, Leu 116, Trp 131, Ile 93	-7.98	2	33
33	Rhamnazin 3-O-rutinoside	Asp 251, Asp 277, His 252, Val 289, Asn 288, Ile 225, Val 249, Trp 287, His 286, Trp 235	-10.54	2	34
34	Fluconazole	His 252, Thr 357, Ala 281, Glu 284, His 286, Gly 358, Trp 287, Val 289, Val 250, Val 249	-7.57	2	35

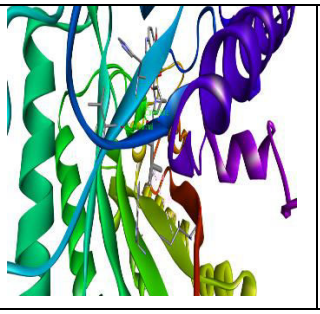
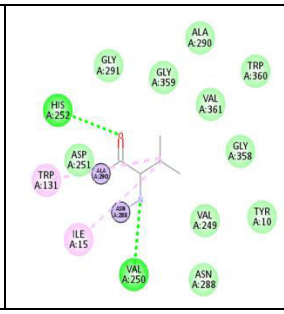



Fig. 2: 3D and 2D interaction between 4M80 and Quinine.

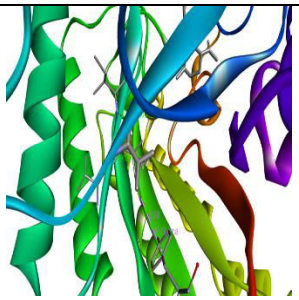
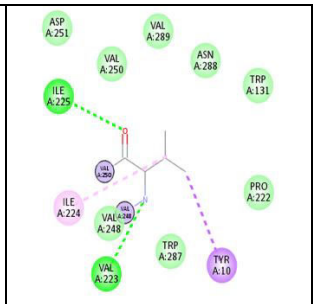



Fig. 3: 3D and 2D interaction between 4M80 and Cannabidiol.

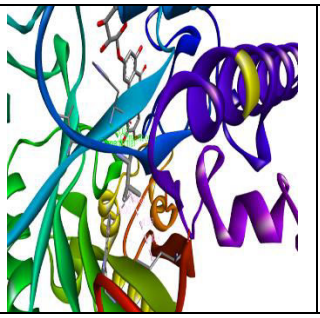
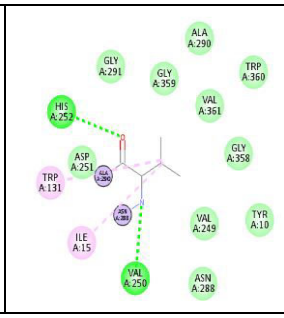



Fig. 4: 3D and 2D interaction between 4M80 and Hesperidin.

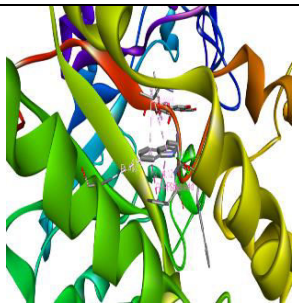
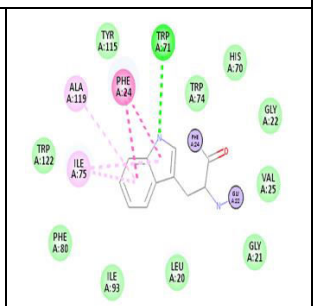



Fig. 5: 3D and 2D interaction between 4M80 and Rhoifolin.

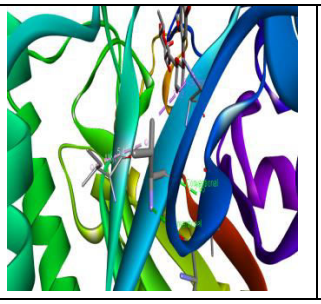
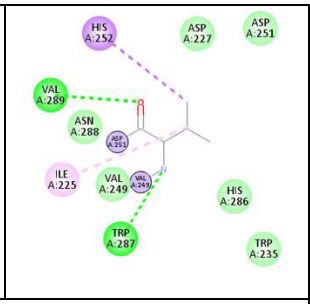



Fig. 6: 3D and 2D interaction between 4M80 and Pectolinarin.

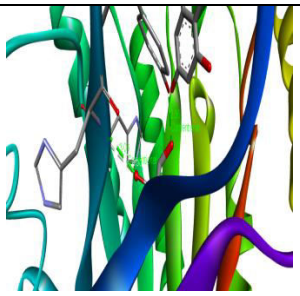
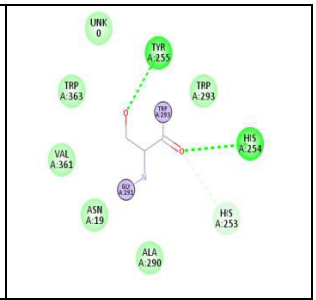



Fig. 7: 3D and 2D interaction between 4M80 and Morin.

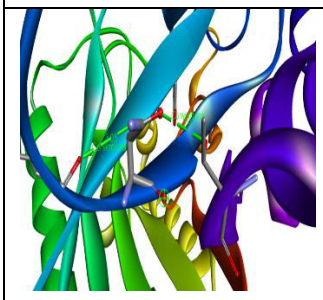
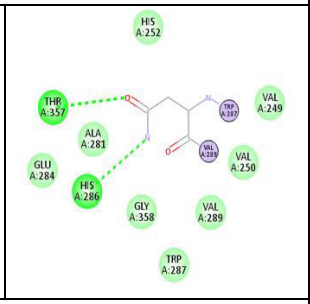



Fig. 8: 3D and 2D interaction between 4M80 and Epigallocatechin gallate.

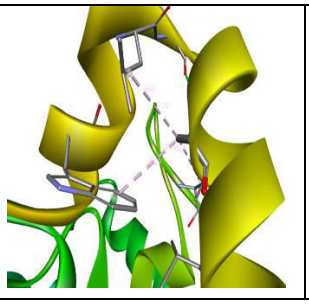
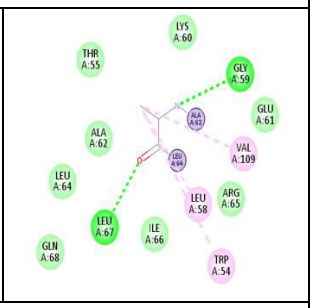



Fig. 9: 3D and 2D interaction between 4M80 and Herbacetin.

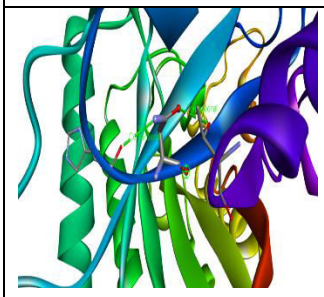
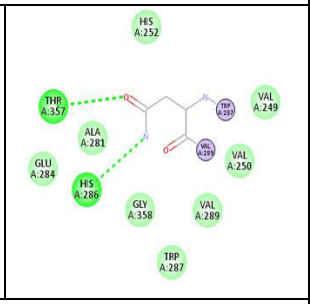



Fig. 10: 3D and 2D interaction between 4M80 and Ethyl cholate.

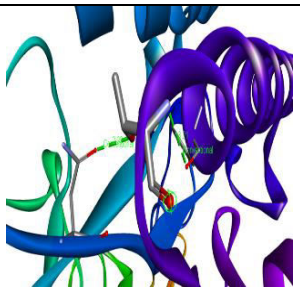
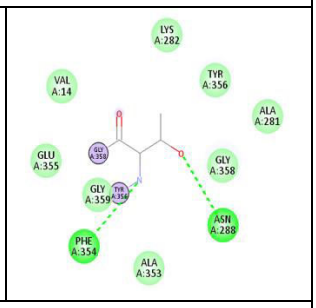



Fig. 11: 3D and 2D interaction between 4M80 and Kaempferol.

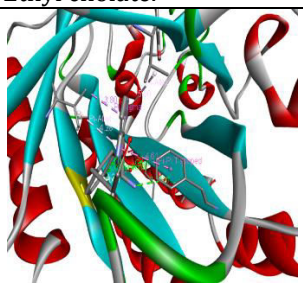
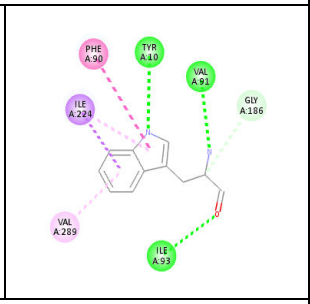



Fig. 12: 3D and 2D interaction between 4M80 and Tangeretin.

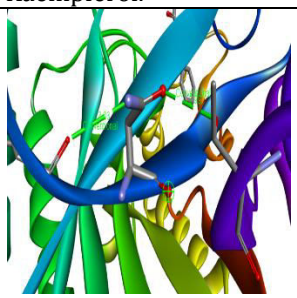
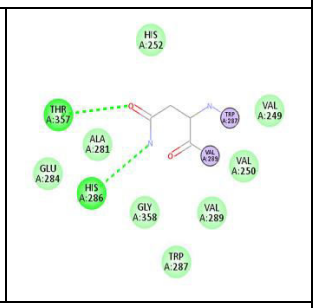



Fig. 13: 3D and 2D interaction between 4M80 and Chalcone.

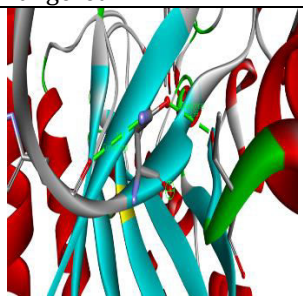
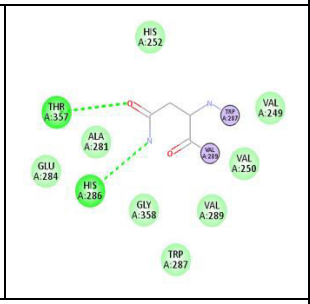



Fig. 14: 3D and 2D interaction between 4M80 and Nobiletin.

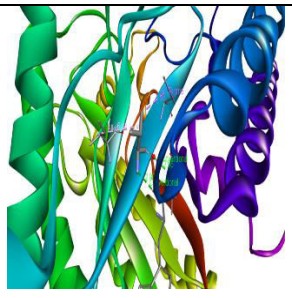
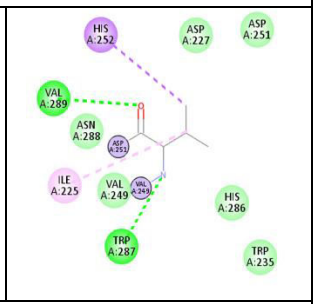



Fig. 15: 3D and 2D interaction between 4M80 and Bis (3,5,5-trimethylhexyl) phthalate.

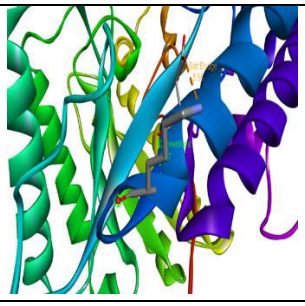
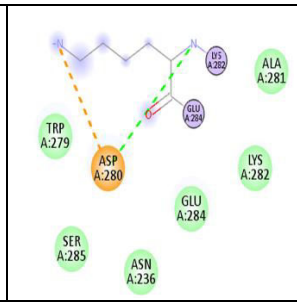



Fig. 16: 3D and 2D interaction between 4M80 and 6-gingerol.

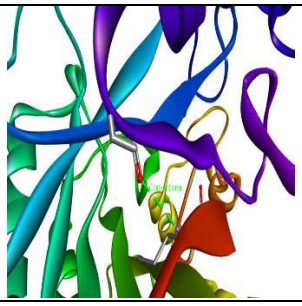
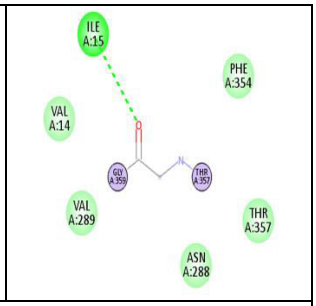



Fig. 17: 3D and 2D interaction between 4M80 and 6-shogaol.

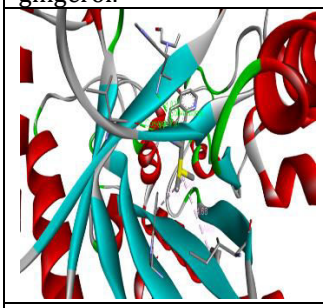
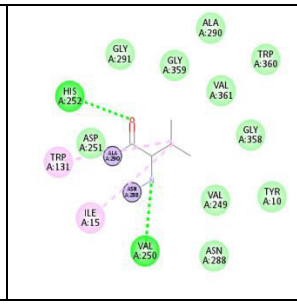



Fig. 18: 3D and 2D interaction between 4M80 and Hydroxychloroquine.

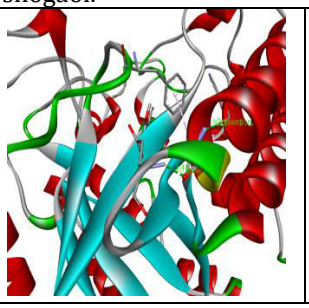
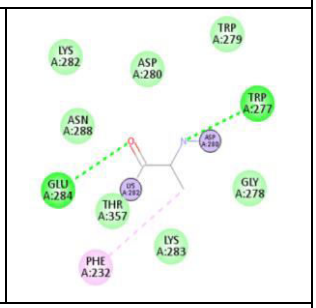



Fig. 19: 3D and 2D interaction between 4M80 and Myristicin.

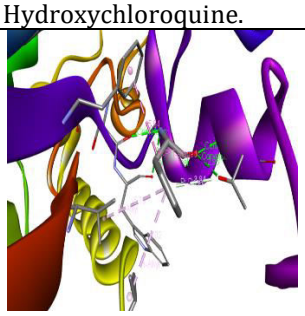
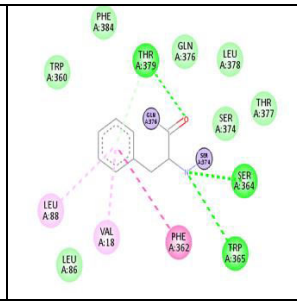



Fig. 20: 3D and 2D interaction between 4M80 and Eugenol.

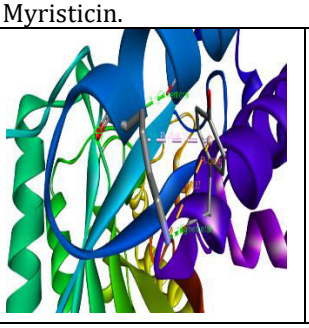
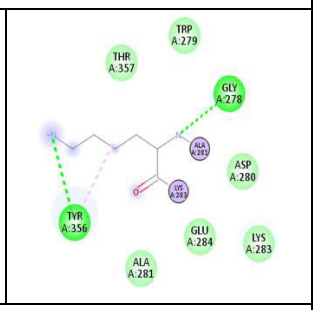



Fig. 21: 3D and 2D interaction between 4M80 and Sinigrin.

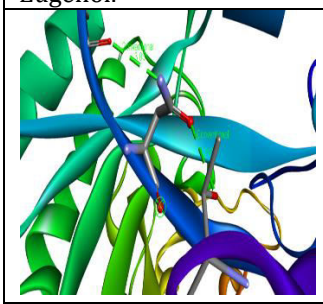
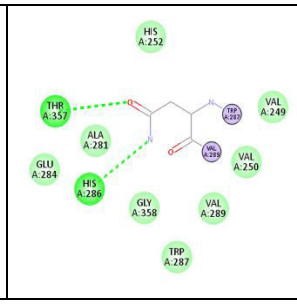



Fig. 22: 3D and 2D interaction between 4M80 and Xanthoangelol.

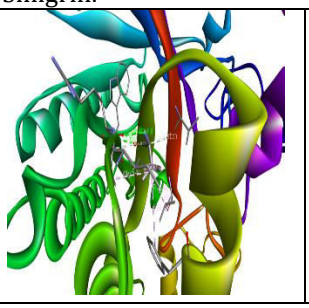
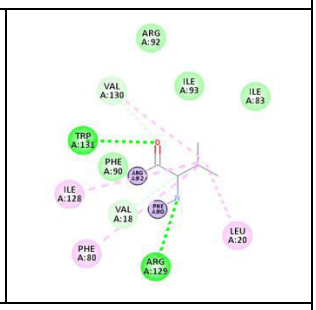



Fig. 23: 3D and 2D interaction between 4M80 and Savinin.

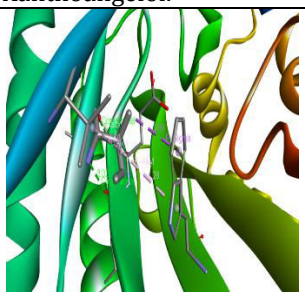
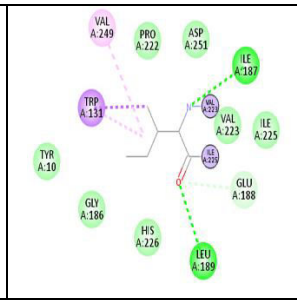



Fig. 24: 3D and 2D interaction between 4M80 and Pristimerin.

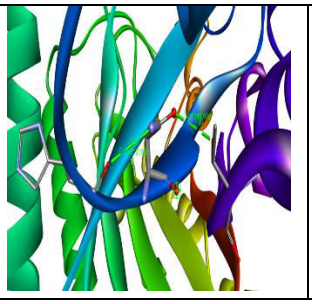
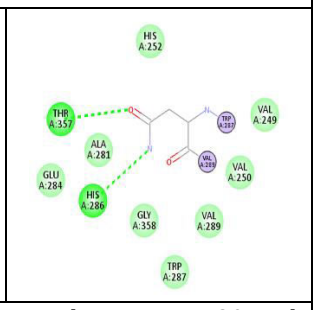



Fig. 25: 3D and 2D interaction between 4M80 and Apigenin.

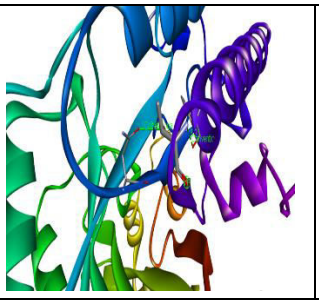
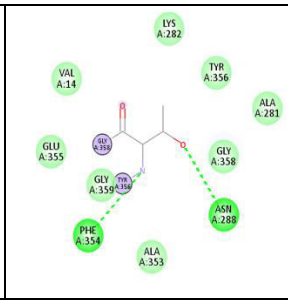



Fig. 26: 3D and 2D interaction between 4M80 and Curcumin.

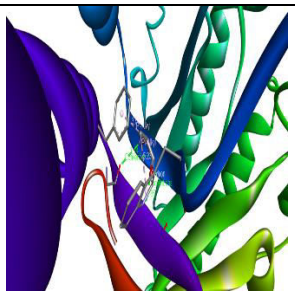
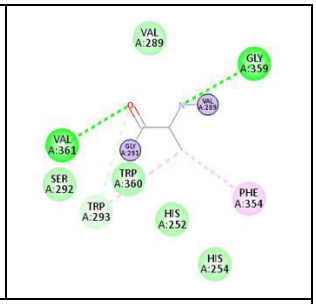



Fig. 27: 3D and 2D interaction between 4M80 and Cryptotanshinone.

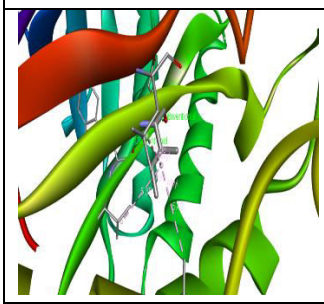
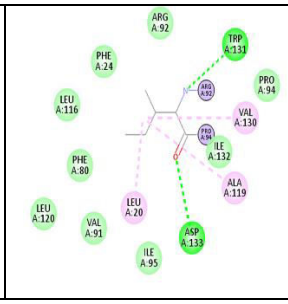



Fig. 28: 3D and 2D interaction between 4M80 and Broussochalcone A.

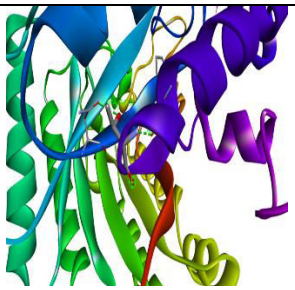
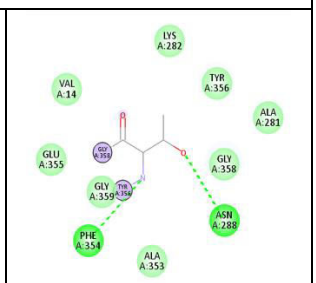



Fig. 29: 3D and 2D interaction between 4M80 and Epigallocatechin.

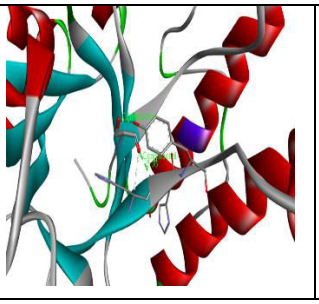
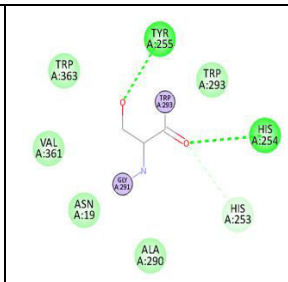



Fig. 30: 3D and 2D interaction between 4M80 and Baicalein.

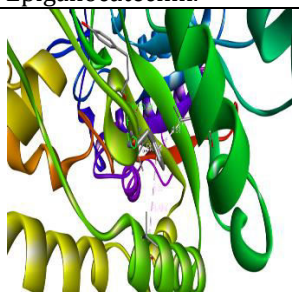
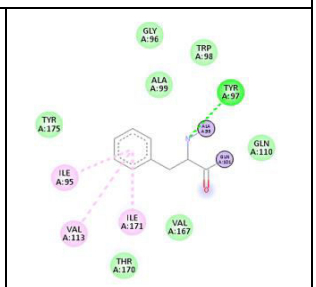



Fig. 31: 3D and 2D interaction between 4M80 and Ellagic acid.

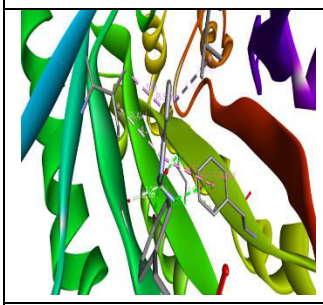
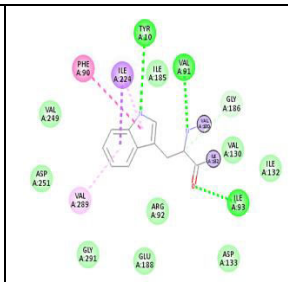



Fig. 32: 3D and 2D interaction between 4M80 and Cinnamamide.

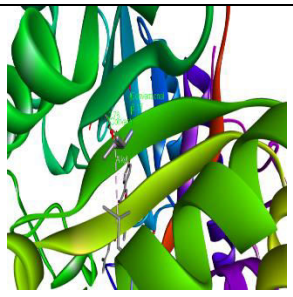
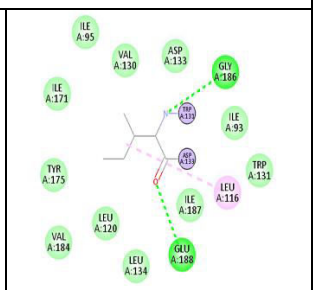



Fig. 33: 3D and 2D interaction between 4M80 and 6,8-Diprenylgenistein.

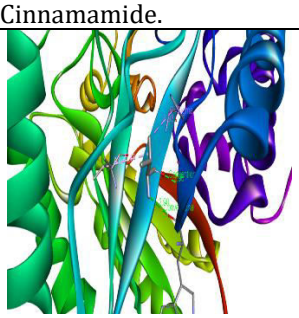
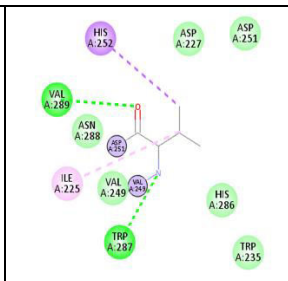



Fig. 34: 3D and 2D interaction between 4M80 and Rhamnazin 3-O-rutinoside.

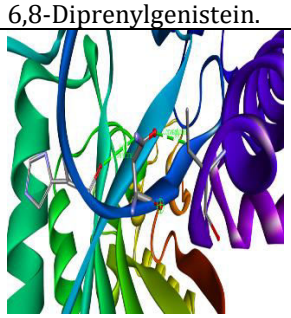
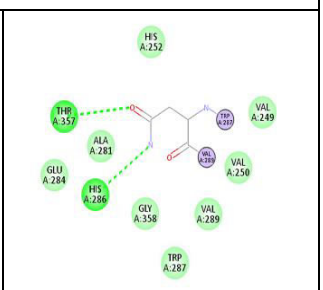
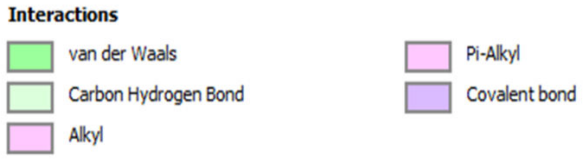



Fig. 35: 3D and 2D interaction between 4M80 and Fluconazole

	**NOTE:** Colour in the 2D interaction in all picture indicates respective bonds involved in interaction bwtween 4M80 and ligands.

well as raise hyperglycemia (Nag *et al.*, 2021). Mucormycosis can cause the jaw bone and possibly the eye to be lost (Garg *et al.*, 2021). According to experts, a variety of therapies may be required. This encompasses the use of antifungal medicine, as well as insulin sensitivity and the evacuation of any necrotic tissue as soon as possible. Traditional healing was being used as a substitute for a range of ailments by individuals around the globe (Mahmoud *et al.*, 2020). The number of bioactive elements in many therapeutic plants makes them capable of fighting black fungus assault (Akella *et al.*, 2020). The current study investigates how various phytocompounds might be used to suppress the growth and spread of black fungus sickness among COVID-19 victims in India and overseas by using molecular docking strategy.

Phytochemicals are produced by plants to help them resist diseases caused by fungi, bacteria, and plant viruses, as well as to be ingested by insects and other animals (Araki *et al.*, 2020). As part of our drug discovery effort, we investigated 32 phytochemicals from medicinal herbs, as well as two conventional drugs, that have been reported to have fungal antagonistic effect. Every one of the phytocompounds investigated have been shown to exhibit antifungal activity *in vitro*. The 4M80 protein of the Black fungus has been found to have inhibitory properties. Within fungi, 1,3-beta-glucan synthase seems to be a glucosyltransferase group of enzyme that produces beta-glucan. It is a therapeutic candidate for fungal medications called as 1,3-Beta-glucan synthase antagonists, that included caspofungin in acetate form, an antifungal antibiotic, and echinocandins, which would include anidulafungin as well as micafungin, an antifungal treatment used to manage *Candida* infections (Prem *et al.*, 2021). Molecular docking using molecular dynamics modelling appears to be the most famous and frequently used approaches for analysing the relationship underlying ligand-protein complexes at the atomic level (Pinku *et al.*, 2022). Using such approach, breakthrough antagonists targeting disease-causing therapeutic potential could always be developed. Among the 32-phytochemical utilized, we found rhamnazin 3-rutinoside related to the flavonoid-3-O-glycosides variety of chemicals, was the very best interacting phytomolecule, having most negative interacting -10.54 Kcal/mol (Table 3, Fig. 34). These are polyphenol with a flavonoid group at C3-position that is O-glycosidically bonded to a sugar monomer. Fruits were found to contain rhamnazin 3-rutinoside, although it has not been measured. As a result, rhamnazin 3-rutinoside could be used as a marker for those kinds of foodstuffs' ingestion. According to a review of the literature, just only few reports on Rhamnazin 3-rutinoside have indeed been released. Rhamnazin 3-rutinoside was shown to have anti-infective capabilities, such as antivirus, fungicidal, anti-angiogenic, anti-tumorigenic, as well as antiproliferative bio-properties, in addition to being antioxidants (Seema *et al.*, 2020). Hesperidin which was found second best interacting chemical (-10.47 Kcal/mol), is abundant in citrus fruits including lemon, orange, lemon, and grapefruit (Table3, Fig. 4). Both prophylactic and therapeutic doses of hesperidin are generally very safe. Various researches have shown that systemically hesperidin treatment should help with a range of disorders, namely coronary heart disease, hyperglycemia, Alzheimer's disease, even malignancy (Namisha *et al.*, 2020). Hesperidin has been shown to have antibacterial properties in recent investigations. Even though detailed mechanism underlying their

antibacterial activities remain unknown, various hypotheses have been suggested, including recruitment of the innate immunity, biological membranes rupture, including inhibition with enzyme production (Eman *et al.*, 2021). Pectolinarin the third ranked molecule found to have interacting energy -10.38 Kcal/mol (Table 3, Fig. 6). Along with its occurrence in many therapeutic plants, pectolinarin, that corresponds to the flavone subgroup, had also attracted much interest. Pectolinarin has proven to be a useful pharmacological component, with oxidative, anti-inflammatory, hypoglycaemic, and anticancer properties that have been tested *in vitro* experiments (Taïbi *et al.*, 2021). Because of its antioxidant properties, it may be beneficial in the fight against black fungus disease. Interacting energy -9.73 Kcal/mol was exhibited by molecule named Rhoifolin (Table 3, Fig. 5). Rhoifolin is indeed a flavone discovered from the *Boehmeria nivea* plant. These are natural antioxidants with a flavonoid group at the C7-position that is O-glycosidically bonded to a molecule of glucose (Mohamed *et al.*, 2021). Epigallocatechin gallate is a kind of catechin that is made up of the combination of epigallocatechin plus gallic acid. Epigallocatechin gallate is a natural antioxidant which might adequately defend cells from oxidative stress – induced (Aguila *et al.*, 2021). In our study we found interaction energy for this compound was -9.30 Kcal/mol (Table 3, Fig 8). Other phytochemical, named as Xanthoangelol was found to have quite higher interaction energy i.e., -9.05 Kcal/mol (Table 3, Fig. 22). The chalcone plus isoprene groups of Xanthoangelol forms a periodic design. Potent antioxidant behavior, hypertension action, anti-inflammatory function, plus virucidal were only ever a few of the healing powers of xanthoangelol (Aguila *et al.*, 2021). Furthermore, while having antimicrobial effect towards Gram-positive organisms, xanthoangelol's bioactivity has yet to be proven. Citrus peels contain a flavonoid called nobiletin**.** Although nobiletin, a potential vegetables phytochemical taken from citrus fruits, having recently been shown to decrease ovarian cancerous cells (Zhao *et al.*, 2022). It exhibited interaction energy -8.93 Kcal/mol (Table 3, Fig. 14). Sinigrin seems to be a glucosinolate identified in the *Brassicaceae* plant family, and it falls to the glucosides class and showed interaction potential as -8.21 Kcal/mol (Table 3, Fig. 21). Despite generating harm, savinin, a lignan, suppressed tumour necrosis factor (TNF) production and T cell growth produced by concanavalin (Con A) in RAW264.7 cells after treatment with lipopolysaccharide (Oubella *et al.*, 2021). This savinin found to have interaction potential as -8.62 Kcal/mol (Table 3, Fig. 23). Curcumin is just a diarylheptanoid that includes the likes of phenolic pigments known as curcuminoids (Aguila *et al.*, 2021). It exhibited potential binding energy as -8.65Kcal/mol (Table 3, Fig. 26). Another flavonoid component 6,8-Diprenylgenistein has been discovered in the *Lupinusmutabilis* plants (Mohamed *et al.*, 2021). It exhibited interaction energy – 7.98 Kcal/mol (Table 3, Fig. 33). Antimicrob and antibacterial properties of 6,8-diprenylgenistein have been discovered. Other molecule, in endometriosis, cryptotanshinone suppresses the E6 receptor of the human papillomavirus (HPV) that promote the level of the p53 as well as p21 genes (Das *et al.*, 2021). Cryptotanshinone is very much a biocide that has a wide spectrum of action towards gram-positive pathogens (Oubella *et al.*, 2021). It depicted interaction energy value -7.21 Kcal/mol (Table 3, Fig. 27). Cryptotanshinone was utilised as an anti-cancer drug to suppress tumorigenesis by decreasing cyclin D1 transcription while increasing cyclin A1 as well as cyclin B1 translation (Das *et al.*, 2021). Cinnamamide is an unsaturated carboxylic acid that can be found in a variety of crops and showed interaction potential towards 4M80 as -6.48 Kcal/mol (Table 3, Fig. 32). All other molecules which were found equally potential to antagonised towards 1M17 are presented in Table 2 and Figures 2-34. More interestingly, the antimalarial drug hydroxychloroquine was already suggested like a therapy against coronavirus infection which has been used in this study as one of the control molecules (Govindarasu *et al.*, 2021). It showed

quite higher potentiality towards target (4M80) as -8.49 Kcal/mol. Of course, many other molecules used in this research also found to have more significant higher binding energy than hydroxychloroquine. Another potential drug named fluconazole, also used in this study is basically a drug which fight against many fungi and having antibiotic potentiality (Surunarayana *et al.*, 2021). This drug was found to have interaction potential towards 4M80 as -7.57 Kcal/mol, which was quite lower than many phytochemicals studied in this study. As a result, it was hypothesized that when -glucan synthase binds to various phytochemicals, it closes, causing a repressor in the enzyme that prevents further catalytic reaction, reducing the pathogenic potential as well as propagation of black fungus further into host organism.

In India, an outbreak of black fungus recently formed (Oubella *et al.*, 2021). Molecular docking would be a commonly adopted machine learning approach for biorecognition research that seeks to anticipate the binding mechanism as well as propensity of a combination produced by two or more respective components with defined structures (Das *et al.*, 2021). Protein-ligand docking would be an essential part of molecular docking along with its clinical applications in contemporary structure-based pharmaceutical research. Right place plus affinity anticipation represents two cornerstones of an effective docking research (Zhao *et al.*, 2022). In terms of docking precision, ranking accurateness, and time wastage, each software seems to have its unique set of benefits and downsides, thus a comprehensive review cannot be established (Eman *et al.*, 2021). The mistrust in having scored algorithms' competence to provide correct binding affinity which would be a key constraint of molecular docking. This would be attributed to the reason that certain molecular geometry parameters, such as covalent bonding effect and thermodynamic parameters, are difficult to anticipate precisely (Sarkar *et al.*, 2021). In signalling pathways, the interactions among physiologically important biomolecules, polypeptide, nucleotides, sugars, and triglycerides are crucial (Das *et al.*, 2021). Due to its capacity to anticipate the receptor - interacting of novel molecular ligands towards the correct target binding domain, molecular docking is among the most commonly utilised strategies in structure-based medicinal chemistry (Eman *et al.*, 2021). The dramatic rise of resistant pathogens to traditional antibiotics has caused major alarm in the prevention and cure (Pinku *et al.*, 2022). Many studies and research are being conducted in order to uncover possible answers to these issues. Phytoconstituents were shown to exhibit antibacterial activity towards antibiotic susceptibility infections through a variety of ways (Akella *et al.*, 2020). The molecular basis of many polyphenols remained unknown, however, it could be influenced by the active pharmaceutical ingredient quality of the product(Prem*et al.*, 2021). In light of these findings, phytochemicals could be considered a useful reservoir of biologically active molecules exhibiting antibacterial activity. Taking into consideration the antimicrobial characteristics of herbal supplements, we focused in this study on a number of phytochemical constituents that might be hopeful as adequate pharmacological agents in the management of Mucormycosis sickness. More *in vivo* and *in vitro* prototype investigations, on the other hand, may lay the foundation for these molecules to be used in medication development.

Conclusion

Mucormycosis had suddenly decimated numerous Indian states. Millions of recuperating victims with impaired immune systems are being left in the shadow of the COVID-19 outbreak presently sweeping India. Mucormycosis, a truly horrible fungus, was indeed reaping the benefits. Since the start of time, seedlings have been used as a traditional remedy. The molecular docking of different phytochemicals against the -glucan synthase protein (4M80) was discovered in this work. We observed that rhamnazin 3-rutinoside, which belongs to the flavonoid-3-O-glycosides family of compounds, would have been the highest

interacting phytomolecule, with the highest negative relating -10.54 Kcal/mol. Hesperidin, the second-best interacting chemical, had to have an interacting energy of -10.47 Kcal/mol, while pectolinarin, the third ranked molecule, do have an interacting energy of -10.38 Kcal/mol. Hesperidin, nabiximols, pectolinarin, epigallocatechin gallate, and rhoifolin displayed lower binding free energies towards 4M80 protein of SARS-CoV-2, according to our findings. The antimalarial medication hydroxychloroquine had a potentiality of -8.49 Kcal/mol towards target (4M80). Fluconazole is a drug that has been discovered to have a -7.57 Kcal/mol interaction potential with 4M80. This research, which focused to forecast the repressive activities of plant-derived substances which thus deliberately address 4M80 proteins, revealed a myriad of things, such as whether the pharmaceutical seemed to have a significantly higher posture and complex formation than hydroxychloroquine and the antibiotic fluconazole. Furthermore, the botanicals' in-silico drug likeness employing ADMET analysis revealed considerable medicinal qualities. As a consequence, the current study could create a basis for much future investigations into the phytocompounds' efficacy towards the treatment of mucormycosis. More *in vivo* and clinical prototype investigations, on the other hand, may open the path for these molecules to be used in medication development.

Acknowledgements

The authors gratefully acknowledge the support provided by Principal and Vice Principal Maharaj to carry out this research. Authors are also grateful to all faculty members in the Department of Microbiology, Ramakrishna Mission Vidyamandira.

References

Águila ID, Mendiola MA, Pradhan S, Sinha C, Torres EL. (2021) Synthesis, characterization, in vitro cytotoxic activity and molecular docking of dinuclear gold(I) complexes with terephthalaldehyde bis(thiosemicarbazones). Polyhedron 210: 115498.

Akella M and Malla R. (2020) Molecular modeling and in vitro study on pyrocatechol as potential pharmacophore of CD151 inhibitor. J Molec Graphics Modelling 100: 107681.

Alghamdi HA, Attique SA, Yan W, Arooj A, Albulym O, Zhu D, Bilal M and Nawaz MZ. (2021) Repurposing the inhibitors of COVID-19 key proteins through molecular docking approach, Process Biochem. 110: 216-222.

Amani M, Shokati E, Entezami K, Khorrami S, Jazayeri MH and Safari E. (2021) The immunomodulatory effects of low molecular weight garlic protein in crosstalk between peripheral blood mononuclear cells and colon cancer cells. Process Biochem. 108: 161-168.

Araki M, Kanda N, Iwata H, Sagae Y, Masuda K and Okuno Y. (2020) Identification of a new class of non-electrophilic TRPA1 agonists by a structure-based virtual screening approach. Bioorg Med Chem Lett. 30 (11): 127142.

Chen YT, Chen YA, Lee CH, Wu JT, Cheng KC and Hsieh CW. (2020) A strategy for promoting γ-glutamyltransferase activity and enzymatic synthesis of S-allyl-(L)-cysteine in aged garlic via high hydrostatic pressure pretreatments. Food Chem. 316: 126347.

Das A, Kumar S, Persoons L, Daelemans D, Schols D, Alici H, Tahtaci H and Karki SS. (2021) Synthesis, in silico ADME, molecular docking and in vitro cytotoxicity evaluation of stilbene linked 1,2,3-triazoles. Heliyon 7(1): e05893.

Das A, Roy A, Mandal A, Mondal HA, Hess D, Kundu P and Das S. (2021) Inhibition of *Bemisia tabaci* vectored, GroEL mediated transmission of tomato leaf curl New Delhi virus by garlic leaf lectin (*Allium sativum* leaf agglutinin). Virus Res. 300: 198443.

Eman YA, Elserwy WS, El-Mansy MF, Serry AM, Salem AM, Abdou AM, Abdelrahman BA, Elsayed KH and Abd Elaziz MR. (2021) Angiokinase inhibition of VEGFR-2, PDGFR and FGFR and cell growth inhibition in lung cancer: Design, synthesis, biological evaluation and molecular docking of novel azaheterocyclic coumarin derivatives. Bioorg Med Chem Lett. 48: 128258.

Garg D, Muthu V, Sehgal IS, Ramachandran R, Kaur H, Bhalla A, Puri GD, Chakrabarti A and Agarwal R. (2021) Coronavirus disease (Covid-19) associated mucormycosis (CAM): Case report and systematic review of literature. Mycopathol. 186: 289-298.

Govindarasu M, Ganeshan S, Ansari MA, Mohammad N, Alomary, Yahya SA, Saad A, Mazen A, Govindasamy R, Muthu T and Manju V. (2021) In silico modeling and molecular docking insights of kaempferitrin for colon

cancer-related molecular targets. J Saudi Chem Soc. 25(9): 101319.

Mahmoud AA, Abdelrahman AHM, Hussien TA, Badr EAA, Mohamed TA, El-Seedi HR, Pare PW, Efferth T and Hegazy MF. (2020) In silico drug discovery of major metabolites from spices as SARS-CoV-2 main protease inhibitors. Comput Biol Med. 126: 104046.

Mirzavandi F, Mollahosseini M, Abargouei AS, Makiabadi E and Khosravi HM. (2020) Effects of garlic supplementation on serum inflammatory markers: A systematic review and meta-analysis of randomized controlled trials. Diabetes Metabol Synd Clin Res Rev. 14(5): 1153-1161.

Mohamed BE, Hala FR, Seham AI, Amira KF, El-Tahawy MMT and Doha MB. (2021) Assessment of anti-hemolytic, cytotoxicity, antioxidant activities and molecular docking study based on thienopyrazole scaffold as pharmacophore. J Molec Struct. 1240: 130602.

Mondal A, Banerjee S, Bose S, Mazumder S, Haber RA, Farzaei MH and Bishayee A. (2021) Garlic constituents for cancer prevention and therapy: From phytochemistry to novel formulations. Pharmacol Res. 175(7): 105837.

Moosavian SP, Arab A, Paknahad Z and Moradi S. (2020) The effects of garlic supplementation on oxidative stress markers: A systematic review and meta-analysis of randomized controlled trials. Complem Ther Med. 50: 102385.

Nag A, Paul S, Banerjee R and Kundu R. (2021) In silico study of some selective phytochemicals against a hypothetical SARS-CoV-2 spike RBD using molecular docking tools. Comput Biol Med. 137: 104818.

Namisha S, Mehanathan M, Ashish P and Manoj P. (2020) Genomics approaches to synthesize plant-based biomolecules for therapeutic applications to combat SARS-CoV-2. Genomics 112(6):, 4322-4331.

Oubella A, El Mansouri AE, Fawzi M, Bimoussa A, Laamari Y, Auhmani A, Morjani H, Robert A, Riahi A and Youssef AIM. (2021) Thiazolidinone-linked1,2,3-triazoles with monoterpenic skeleton as new potential anticancer agents: Design, synthesis and molecular docking studies. Bioorgc Chem. 115: 105184.

Padmini R, Maheshwari VU, Saravanan P, Lee KW, Razia M, Mona SA, Ravindran B, Mohamed SE, Young OK, Hyungsuk K, Hak-Jae K. (2020) Identification of novel bioactive molecules from garlic bulbs: A special effort to determine the anticancer potential against lung cancer with targeted drugs. Saudi J Biol Sci. 27 (12): 3274-3289.

Pinku H, Pal U, Paladhi P, Dutta S, Paul P, Pal S, Das D, Ganguly A, Dutta I, Mandal S, Ray A and Ghosh S. (2022) Evaluation of potency of the selected bioactive molecules from Indian medicinal plants with MPro of SARS-CoV-2 through in silico analysis. J Ayurveda Integ Med. 13: 100449.

Prem PK, Atul KS, Kumari SP, Mohd S, Sanjay G and Shashank K. (2021) Phytochemicals present in Indian ginseng possess potential to inhibit SARS-CoV-2 virulence: A molecular docking and MD simulation study. Microb Pathogen. 157: 104954.

Ricciutelli M, Nzekoue FK, Caprioli G, Sagratini G, Alesi A, Vici G and Polzonetti V. (2020) Study of the effect of marination treatment on garlic bioactive compounds through an innovative HPLC-DAD-MS method for alliin and curcuminoids analysis. LWT-Food Sci Technol. 131: 109788.

Rouf R, Uddin SJ, Sarker DK, Islam MT, Ali ES, Shilpi JA, Nahar L, Tiralongo E and Sarker SD. (2020) Antiviral potential of garlic (*Allium sativum*) and its organosulfur compounds: A systematic update of pre-clinical and clinical data. Trends Food Sci Technol. 104: 219-234.

Sangouni AA, Azar MRMH and Alizadeh M. (2020) Effects of garlic powder supplementation on insulin resistance, oxidative stress, and body composition in patients with non-alcoholic fatty liver disease: A randomized controlled clinical trial. Complem Ther Med. 51: 102428.

Sarkar D. (2021) Molecular docking study to identify potent fungal metabolites as inhibitors against SARS-CoV-2 main protease enzyme. Int J Pharm Bio Sci. 12(2): 78-85.

Seema AK, Santhosh KN, Veena R, Velusamy P and Periyar SS and Thirumurthy M. (2020) Computational evaluation of major components from plant essential oils as potent inhibitors of SARS-CoV-2 spike protein, J Molec Struct. 1221: 128823.

Sharma AD and Kaur I. (2021) Targeting β-glucan synthase for Mucormycosis “The 'black fungus” maiming Covid patients in India: computational insights. J Drug Delivery Therapeut. 11(3-S): 9-14.

Shereen ST, Ahmed Fahim JR, Khayrya A, Youssif Amin MN, Hossam MH Abdel-Aziz, Alexander OB, Jörn P, Usama RA and Ashraf NEH. (2021) Cytotoxic potential of *Allium sativum* L. roots and their green synthesized nanoparticles supported with metabolomics and molecular docking analyses. South African J Bot. 142: 131-139.

Suryanarayana K, Robert AR, Kerru N, Pooventhiran T, Thomas R, Maddila, S and Jonnalagadda SB. (2021) Design, synthesis, anticancer activity and molecular docking analysis of novel dinitrophenylpyrazole bearing 1,2,3-triazoles. J Molec Struct. 1243: 130865.

Taïbi N, Balas QAA, Bekari N, Talhi O, Jabal GAA, Benali

Y, Ameraoui R, Hadjadj M, Taïbi A, Boutaiba ZM, Abou-Mustapha M, Khammar F, Dergal F, Hassaine R, Boukenna L, Bachari K and Soares Silva AM. (2021) Molecular docking and dynamic studies of a potential therapeutic target inhibiting glyoxalase system: Metabolic action of the 3, 3 '- [3- (5-chloro-2-hydroxyphenyl) -3-oxopropane-1, 1-diyl] - Bis-4-hydroxycoumarin leads overexpression of the intracellular level of methylglyoxal and induction of a pro-apoptotic phenomenon in a hepatocellular carcinoma model. Chem Biol Interaction 345: 109511.

Verma AK, Kumar V, Singh S, Goswami BC, Camps I, Sekar A, Yoon S and Lee KW. (2021) Repurposing potential of Ayurvedic medicinal plants derived active principles against SARS-CoV-2 associated target proteins revealed by molecular docking, molecular dynamics and MM-PBSA studies. Biomed Pharmacother 137: 111356.

Wu C, Liu Y, Yang Y, Zhang P, Zhong W, Wang Y and Wang Q. (2020) Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. Acta Pharmaceut Sinica B 10: 766-788.

Zhang Y, Liu X, Ruan J, Zhuang X, Zhang X and Li Z. (2020) Phytochemicals of garlic: Promising candidates for cancer therapy. Biomed Pharmacother. 123: 109730.

Zhao L, Xiao S, Jiang S, Jin Y, Fang W and Wang Z. (2022) Detailed structural investigation of Crizotinib and the exploration of its antitumor potential by DFT calculations and molecular docking. J Molec Struct. 1248: 131530.