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A Computational Approach to Predict the Molecular Drug Targets Against *Candida glabrata*

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ABSTRACT

Non- albicans Candida (NAC) species are responsible for 35-65% of all candidaemias in the general population and are associated with a high rate of morbidity and mortality (about 15% to 35%). The availability of few commercially used antifungal drugs against candidiasis and rapid emergences of antibiotic resistance among NAC species has significantly contributed to their increased global outbreak. Green tea is known for its multi-beneficial effects including antimicrobial potential against Candida. The present study investigated the molecular drug targets of green tea phytocompounds against inhibition of ergosterol biosynthesis in *Candida glabrata* using *in silico* tools.The molecular interaction was studied between ligands and essential proteins participating in ergosterol biosynthesis in *C. glabrata* using autodockvina software. The protein validation and homology modeling estimation were determined by the SWISS MODEL workspace. The Drug likeness study of all the test ligands was performed using SwissADME, while the toxicity of test compounds was analyzed using the admetSAR 2.0 version.The *in silico* analyses identified Rutin, Chlorogenic acid, Coumaroylquinic acid, Quercetin, Epigallocatechingallate as the potent phytocompounds with significant molecular binding with Erg 6, Erg 27, Erg 8, Erg 7, Erg 24 respectively. The ADMET data suggested an absence of the CYP2 inhibitors indicating the metabolism of all the tested drug candidates in the intestine and liver.The present study highlighted the possible drug targets of green tea phytocompounds against ergosterol biosynthesis protein in *C. glabrata*. It is pertinent that the current study has provided preliminary breakthroughs which could lead to exploring their avenues in potent drug development against NAC species.

KEY WORDS: AUTODOCKVINA, CANDIDA, EGCG, ERGOSTEROL, RUTIN.

INTRODUCTION

Over the last decade, the fungal infections associated with the non-albicans Candida species have become a global cause of concern for health professionals (Sardi et al. 2013). Candidiasis is a common fungal infection caused by yeasts from the genus Candida. The disease is associated with a diverse range of infections including mucosal, cutaneous, subcutaneous, and systemic mycoses. Candidiasis which was once considered to be majorly caused by *C. albicans*, other non- albicans Candida (NAC) species have been recognised to be primary pathogens associated with increase incidences of Candidiasis. Epidemiological studies have shown that NAC species are responsible for 35-65% of all candidaemias in the general population (Presterl et al. 2007; Arendrup, 2014; Ahmed et al. 2020).The most common NAC species include *C. parapsilosis* (20-40% of all Candida species), *C. tropicalis* (10-30%), *C. krusei* (10-35%), *C. glabrata* (5-40%), *C. auris* (5%), *C. lusitaniae* (2-8%), and *C. guilliermondii* (1-5%). Other rare NAC species, are *C. rugosa*, *C. kefyr*, *C. stellatoidea*, *C. norvegensis* and *C. famata* (≤1% of Candida infection) (Du et al. 2020).

These NAC species are also identified to be associated with a high rate of morbidity and mortality (about 15% to 35%) particularly in individuals who are immunocompromised like organ transplant recipients, HIV patients, and patients under chemotherapy (Krcmery and Barnes 2002;Bitar 2014; Rudramurthy et al. 2017; Du et al. 2020). A progressive shift in NAC species infection has been linked with indiscriminate use of antibiotics, severe immunosuppressants in immune-compromised such as HIV, cancer or organ transplant patients.The studies have reported that several NAC spp. are inherently resistant to common antifungal drugs and have demonstrated acquired/cross-resistance against antifungals like triazoles (Du et al. 2020).

Indeed, with the availability of a few antifungal drugs commercially used in the treatment of candidiasis and rapid emergences of toxic side effects as well as antibiotic resistance among NAC species, the increased outbreak of NAC associated fungal infection are becoming a global

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threat (Magill et al. 2006; Pfaller and Diekema 2007; Oberoi et al. 2012; Deorukhkar et al. 2014; Chowdhary et al. 2014; Du et al. 2020). Green tea known for its multi-factorial health properties has been scientifically recognised as a possible antifungal drug representative that could along with standard chemotherapeutics enhance the efficacy of the general treatment approach. There is plethora of scientific evidence highlighting the antifungal potential of green tea catechins against *Candida albicans* and identified potent drug candidate's targeting key enzymes participating in ergosterol biosynthesis (Hirasawa and Takada 2004; Anand et al. 2015; Musial et al. 2020; Huang et al. 2020). As an urgent need to explore alternative potent drug candidates for the development of novel medication against NAC infection, the present study attempts to investigate the inhibitory potential of green tea phytocompounds against ergosterol biosynthesis in *C. glabrata* using in silico tools.

MATERIAL AND METHODS

In the present in silico study, we selected 15 phytocompounds present in green tea based on their reported antimicrobial activity against *Candida* spp. These phytocompouds were used as ligands for docking with the ergosterol biosynthesis proteins. Autodockvina(version is 1.1.2) tool was used for assessing the molecular interaction based on binding energies. As a positive control, we used azoles (Fluconazole, Itraconazole, and ketoconazole) and Amphotericin B in molecular docking analysis.The code of SMILES for all the aforementioned green tea phytocompounds and positive controls was procured from the online chemical database PubChem (https://pubchem.ncbi.nlm.nih.gov/) (Cheng et al. 2002; Diana et al. 2014).

Table1a. Green tea Phytocompounds used as ligands

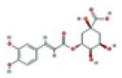
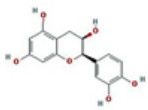
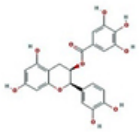
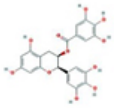
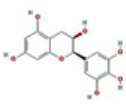
S.No.	Phytocompounds	PUBCHEM ID	SMILES code	2-D Structure
1.	2,5-Dimethyl1-4-hydroxy-3-(2H)-furanone	14259114	OCC1OC(OC2=C(C)OC(C2=O)C)C(C(C1O)O)O	
2.	B-ionone	26955	CC(=O)C=CC1=C(C)CCCC1(C)C	
3.	Chlorogenic acid	348159	O=C(OC1CC(O)(CC(C1O)O)C(=O)O)C=Cc1ccc(c(c1)O)O	
4.	Coumaroylquinic acid	53420248	O=C(OC1CC(O)(CC(C1O)O)C(=O)O)C=Cc1ccc(cc1)O	
5.	Dihydroactinidiolide	27029	O=C1C=C2C(O1)(C)CCCC2(C)C	
6.	Epicatechin	1203	Oc1cc2OC(c3ccc(c(c3)O)O)C(Cc2c(c1)O)O	
7	Epicatechin gallate	367141	Oc1cc(O)c2c(c1)OC(C(C2)OC(=O)c1cc(O)c(c(c1)O)O)c1ccc(c(c1)O)O	
8.	Epigallocatechin gallate	65064	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C(=C3)O)O)O)OC(=O)C4=CC(=C(C(=C4)O)O)O	
9.	Epigallocatechin	1249	Oc1cc2OC(c3cc(O)c(c(c3)O)O)C(Cc2c(c1)O)O	

Table1b. Green tea Phytocompounds used as ligands

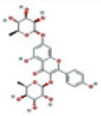
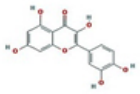
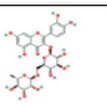
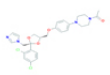
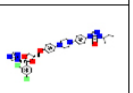
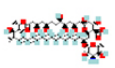
S.No.	Phytocompounds	PUBCHEM ID	SMILES code	2-D Structure
1.	Gallic acid	370	OC(=O)c1cc(O)c(c(c1)O)O	
2.	Kaempferitrin	12305415	Oc1ccc(cc1)c1oc2cc(OC3OC(C)C(C(C3O)O)O)cc(c2c(=O)c1OC1OC(C)C(C(C1O)O)O)O	
3.	Myricetin	5281672	Oc1cc(O)c2c(c1)oc(c(c2=O)O)c1cc(O)c(c(c1)O)O	
4.	Pyrazine	9261	n1ccncc1	
5.	Quercetin	5280343	Oc1cc(O)c2c(c1)oc(c(c2=O)O)c1ccc(c(c1)O)O	
6.	Rutin	5280805	CC1C(C(C(C(C(O1)OCC2C(C(C(C(O2)OC3=C(OC4=CC(=CC(=C4C3=O)O)O)C5=CC(=C(C(=C5)O)O)O)O)O)O)O)O)O)O	

Table 2. Positive controls used in molecular docking study

S.No.	Inhibitors (antibiotics/drugs)		PUBCHEM ID	SMILES CODE	2-D Structure
1	Azoles	Fluconazole	3365	C1=CC(=C(C=C1F)F)C(CN2C=NC=N2)(CN3C=NC=N3)O	
		Ketoconazole	236076	CC(=O)N1CCN(CC1)C2=CC=C(C=C2)OCC3COC(O3)(CN4C=CN=C4)C5=C(C=C(C=C5)Cl)Cl	
		Itraconazole	55283	CCC(C)N1C(=O)N(C=N1)C2=CC=C(C=C2)N3CCN(CC3)C4=CC=C(C=C4)OCC5COC(O5)(CN6C=NC=N6)C7=C(C=C(C=C7)Cl)Cl	
2	Amphotericin B		5280965	CC1C=CC=CC=CC=CC=CC=CC(CC2C(C(CC(O2)(CC(CC(C(CCC(CC(CC(=O)OC(C(C1O)C)C)O)O)O)O)O)O)O)C(=O)OC3C(C(C(C(O3)C)O)N)O	

The 2-D structures of the test ligands were retrieved by converting the SMILES code (.smiles format) into PDB (.pdb) format using chemical interconversion software Open Babel (v 2.3.1). The Drug Likeness reports of all the test ligands were prepared by submitting individual SMILES code for each drug to SwissADME. The toxicity of test compounds was analyzed using the admetSAR 2.0 version (Cheng et al. 2002; Diana et al. 2014).

The 3-D structure of all the proteins participating in the ergosterol biosynthesis was retrieved in PDB format (Table 3) using the PHYRE program (Kelly 2009). The amino acid sequences of ERG proteins in FASTA format were obtained from NCBI [https://www.ncbi.nlm.nih.gov/]. The 3D-protein homology models were generated from the SWISS-MODEL workspace.The protein homology models were validated through a Ramachandran plot created in the SWISS-MODEL workspace.The Molecular interactions were studied for the ERG proteins and the selected phytocompounds as well as positive controls using Autodockvina software. The autodocking tool generated the binding energies of molecular interaction between all the green tea phytocompounds and respective PDB proteins of ergosterol biosynthesis (Waterhouse et al. 2018).

RESULTS AND DISCUSSION

***In silico* docking analysis:** The *in silico* analysis demonstrated significant molecular interaction between ligands (Tables 1) Positive controls (Table 2) and the docked

ERG proteins(Table 3). Among the 15 phytocompounds tested, Rutin and ERG 6 showed the most stable molecular interaction with the least binding energy of -10.80 kcal, compared to the positive control antifungal drugs. It is considered that least the docking energy, the higher will be the binding affinity of a compound with the target protein. Hence, Rutin demonstrated the best interaction among all the investigated green tea phytocompounds.

Table 3. Enzymes involved in ergosterol biosynthesis in *Candida glabrata*

S.No.	Gene	Protein	Amino acid Sequence Length
1.	ERG1	Squalene epoxidase (Erg1)	206
2.	ERG2	C-8 sterol isomerise (Erg2)	224
3.	ERG3	C-5 sterol desaturase (Erg3)	364
4.	ERG4	C-24(28) sterol reductase (Erg4)	468
5.	ERG 5	C-22 sterol denaturase (Erg5)	364
6.	ERG6	Sterol 24-C methyltransferase (Erg6)	372
7.	ERG7	Lanosterol synthase (Erg7)	733
8.	ERG8	Phosphomevalonate kinase (Erg8)	445
9.	ERG9	Squalene synthase (Erg 9)	443
10.	ERG 10	Acetyl coA C-acetyltransferase (Erg10)	398
11.	ERG11	Lanosterol 14-α- demethylase (Erg11)	533
12.	ERG12	Mevalonate kinase (Erg12)	430
13.	ERG 13	3-Hydroxy-3-methylglutaryl-coA (HMG-coA) synthase	281
14.	ERG20	Farnesyl pyrophosphate Synthetase (Erg20)	351
15.	ERG 24	Sterol C-14 reducaase (Erg24)	437
16.	ERG25	C-4 methyl sterol oxidase (Erg25)	308
17.	ERG26	C-3 Sterol dehydogenase (Erg26)	350
18.	ERG27	3- keto sterol reductase (Erg27)	348

Table 4. Protein validation and homology modeling estimation by SWISS MODEL workspace.

S.No.	Gene	Template	Sequence identity (%)	Ramachandran favoured regions (%)	Ramachandran outliers (%)	Q-mean score	Mol probity score
1.	ERG1	6c6n.1.A	39.30	94.09	1.48	-2.39	2.04
2.	ERG2	5hk1.1.A	30.54	94.13	1.11	-3.49	1.85
3.	ERG3	6sny.1.A	31.03	100	0.00	0.05	0.50
4.	ERG4	4fgs.1.A	21.49	85.98	4.44	-6.29	2.32
5.	ERG6	3mgg.1.A	18.22	92.52	0.79	-3.87	1.96
6.	ERG7	1w6k.1.A	39.61	93.64	1.11	-2.03	1.76
7.	ERG8	3k17.1.A	20.17	82.49	5.03	-7.5	2.49
8.	ERG 9	3vj9.1.A	48.65	97.37	0.58	-2.37	1.20
9.	ERG 10	5xyj.1.a	81.11	97.72	0.25	0.81	1.17
10.	ERG11	5jlc.1.A	100	96.48	0.20	-0.34	1.24
11.	ERG12	2r3v.1.A	36.67	93.32	1.87	-2.29	2.39
12.	ERG 13	2p8u.1.A	46.77	91.79	0.95	-4.13	2.09
13.	ERG20	4dem.1.A	46.33	96.37	0.29	-0.59	1.49
14.	ERG 24	4quv.2.A	36.74	92.86	2.62	-4.97	2.26
15.	ERG25	1rh5.1.A	26.09	97.44	0.00	-0.09	1.52
16.	ERG26	3lu1.1.A	20.45	90.61	1.88	-3.94	2.43
17.	ERG27	4quv.2.A	31.26	90.40	3.51	-5.63	1.98

Among other ligands, Chlorogenic acid, Coumaroylquinic acid, quercetin, *Epigallocatechin gallate* (EGCG) showed favorable molecular interaction with identified drug targets viz., Erg 6, Erg 27, Erg 8, Erg 7, Erg 24, respectively in ergosterol biosynthesis in *C. glabrata*. These findings are in agreement with our previous *in silico* investigation in which we highlighted the inhibitory effect of green tea phytocompounds like chlorogenic acid, EGCG, kaempferitrin against *Candida albicans* (Anand et al. 2015; Anand et al. 2021).

Table 5. Binding energies of molecular interaction between ligands and ERG proteins

¬¬¬¬Green tea Phytocompounds	Ergosterol Biosynthesis (ERG) proteins																	
	Erg 1	Erg 2	Erg 3	Erg 4	Erg 5	Erg 6	Erg 7	Erg 8	Erg 9	Erg 10	Erg 11	Erg 12	Erg 13	Erg 20	Erg 24	Erg 25	Erg 26	Erg 27
Gallic acid	-6.8	-7.8	-5.6	-6.5	-7.9	-6.7	-6.7	-6.6	-6.3	-5.6	-6	-6	-6.4	-6.1	-7.2	-6.4	-6.3	-7.2
Epicatechin	-6.8	-7.9	-6.6	-6.8	-7	-7.4	-7.9	-7.2	-6.9	-5.7	-6.5	-6.8	-7.3	-5.9	-7.5	-6.5	-6.8	-7.8
Dihydroactinidiolide	-6.8	-8.6	-7	-7.6	-7.9	-7.4	-7.9	-7.3	-6.9	-5.7	-6.5	-6.3	-7.4	-5.9	-7.5	-6.1	-6.9	-7.8
Pyrazine	-4.1	-4.5	-3.9	-3.8	-4.5	-4	-3.9	-4.3	-3.6	-3.3	-3.7	-4.1	-3.7	-4.1	-4	-3.8	-3.6	-3.9
Chlorogenic acid	-8.7	-8.9	-8.1	-8.8	-8.9	-9.3	-9.5	-8.6	-7.9	-7.7	-7.8	-7.1	-9	-9.2	-9.3	-7.8	-8.4	-9.4
Coumaroylquinic acid	-8.9	-8.7	-8.5	-7.4	-9.2	-9.2	-9.6	-10.1	-7.8	-7.2	-8.6	-7.4	-8.6	-9.3	-9.7	-7.6	-8.8	-9.6
Quercetin	-7.6	-7.8	-7.8	-8.1	-8.8	-8.6	-9.8	-8.9	-8.9	-7	-7.8	-7.8	-7.8	-8.1	-9	-8.8	-8.7	-7.6
Epigallatecatechin	-8.3	-7.9	-7.3	-7.4	-7.8	-8.5	-8.7	-6.9	-7.6	-6.3	-7	-6.2	-7.6	-8.1	-7.9	-6.7	-8.6	-6.9
Epigallocatechin gallate	-8.5	-8.5	-7.5	-8.9	-8.5	-10.5	-4.5	-9.8	-9.1	-8	-10	-7.9	-8.7	-8.6	-10.3	-8.4	-9.1	-8.8
Myricetin	-8.6	-9	-7.6	-7.8	-9.1	-9.1	-9.6	-9.7	-8.8	-7	-8.4	-7.6	-8.7	-7.8	-9.7	-8	-9.3	-8.9
β-ionone	-6.7	-7.2	-6.9	-7.9	-7.2	-7.2	-8.2	-7.2	-7.3	-5.3	-7.1	-6.5	-7.1	-6.3	-7.1	-7.2	-6.7	-8.3
Epicatechingallate	-9.1	-10.1	-9.1	-9.1	-10.1	-10.8	-8.2	-8.2	-9.3	-7.9	-8.7	-9.1	-9.3	-10	-10.9	-8.5	-8.6	-8.2
Kaempferitrin	-11.2	-9.5	-9.5	-10.6	-9.5	-12	-7.7	-9.3	-10.1	-7.9	-9.4	-8.9	-9.9	-8.5	-12	-9.2	-10.7	-9.1
Rutin	-8.2	-8.6	-9.3	-10.1	-8.8	-10.8	-4.4	-8.6	-10.8	-7.6	-10.5	-9.5	-9.1	-8.2	-11.4	-8	-9.2	-8.5
2, 5- Dimethyl-4-hydroxy-3- (2H) – furanone	-5.5	-7	-4.8	-5.5	-7	-6.2	-5.4	-5.5	-5.2	-4.7	-5	-5.4	-5.5	-5.5	-5.8	-5.1	-5.1	-5.3

Table 6. Binding energies of molecular interaction of positive controls and ERG proteins

Inhibitors (antibiotics/drugs)		Targetreceptor	Binding energy
Azoles	Fluconazole	ERG11	-7.62
		ERG 5	-8.24
	Ketoconazole	ERG 5	-11.93
	Itraconazole		-11.69
Amphotericin B		ERG	-12.97

Table 7. Most favorable docking poses for the molecular interaction between green tea ligands and ERG proteins.

S.No.	Most significant molecular bindings	Most favourable docking poses
1	ERG 27 and Chlorogenic acid	ALA 108, PHE 244, ASN 18, SER 17,GLY 14,LYS 48, ARG 44
2	ERG 6 and Rutin	TRY 84, SER 95, GLY 251, LEU 344, ASN 284, TRY 288,PHE 318, ARG 314
3	ERG8 and Coumaroylquinic acid	ALA151, SER 150, LYS 191, ALA 377, GLY 148,SER 149, THR 145, LEU 147, GLY 146, LYS 144, PHE 84, PRO 269
4	ERG 7 and Quercetin	TYR 91, HIS 226, GLY 377, TRP 583, TYR 703, PHE 695
5	ERG 24 and EGCG	ASP 136, GLU 145, TRP 205, TRP 233, MET 230

The Ramachandran plot depicted structural stability and showed confirmation of residues in the favorable region (Figure 1; Table 4). A Ramachandran phi-psi plot for all ERG proteins revealed 82.49% to 100.00% of residues are in the allowed region (light gray), and only 0.00% to 4.44% lay in the disallowed region (white). The above analysis of the predicted structure provides supporting evidence that the predicted 3D structure of ERG protein is of good quality.The protein models of ERG proteins showed local similarity to the crystal structures of target templates (Table 4). The Q mean value of protein models was reliable as depicted in the estimated Figure 2. Based on the binding scores, rutin interacted with ERG 6 at the amino acid residues TRY-84, SER-95, GLY-251, ASN-284, TRY-288, ARG-314, PHE-318, and LEU-344 with the least binding energy of -10.80 kcal (Figure 3, Table 5, Table 6, Table 7) (Gao et al. 2020; Anand et al. 2021).

Figure 1A: Ramachandran plot of Erg3

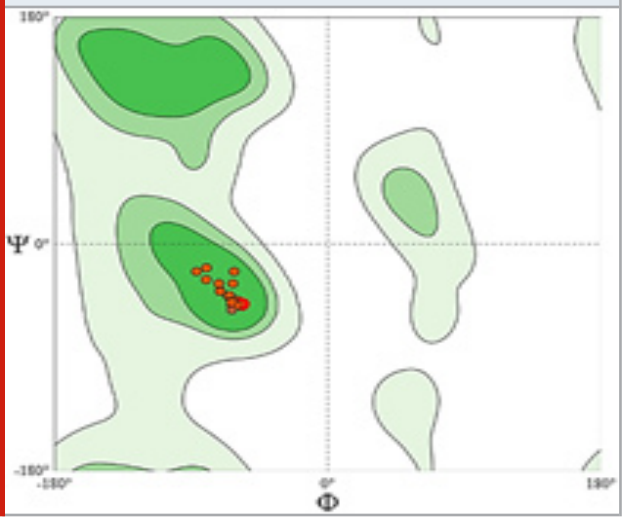


Figure 1B: Ramachandran plot of Erg9

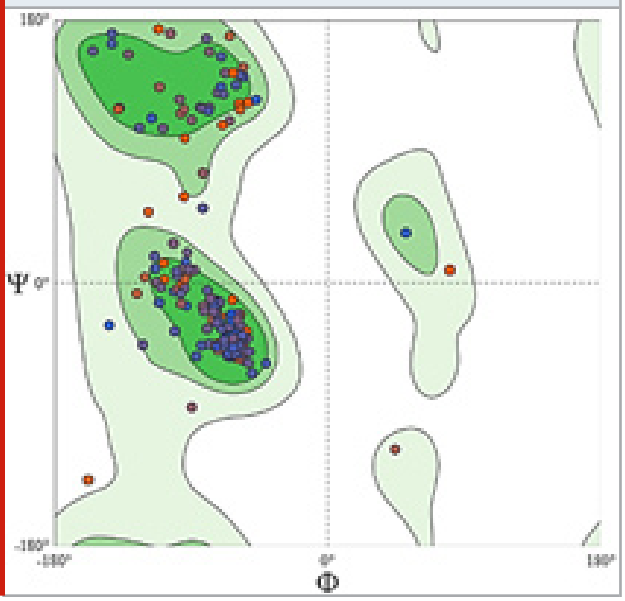


Figure 1C: Ramachandran plot of Erg 25

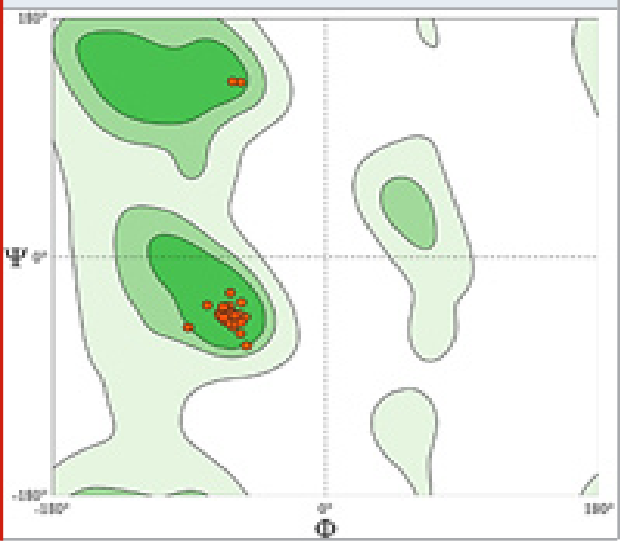


Figure 1D: Ramachandran plot of Erg 27

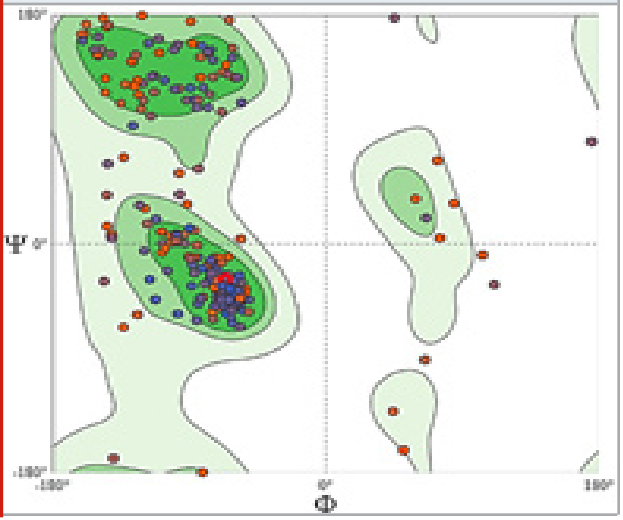
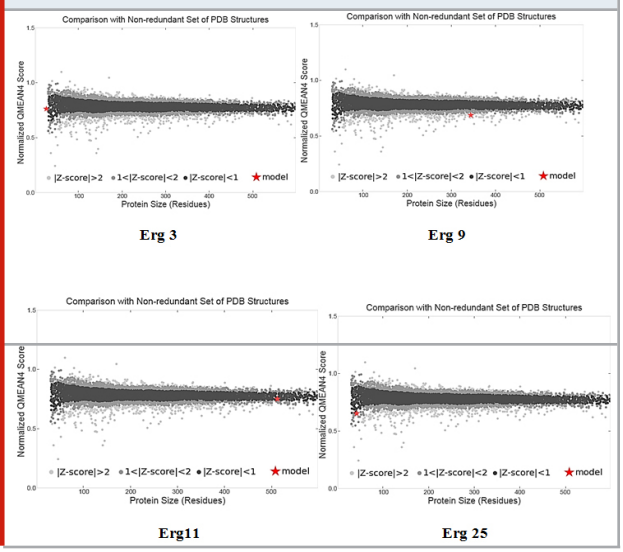


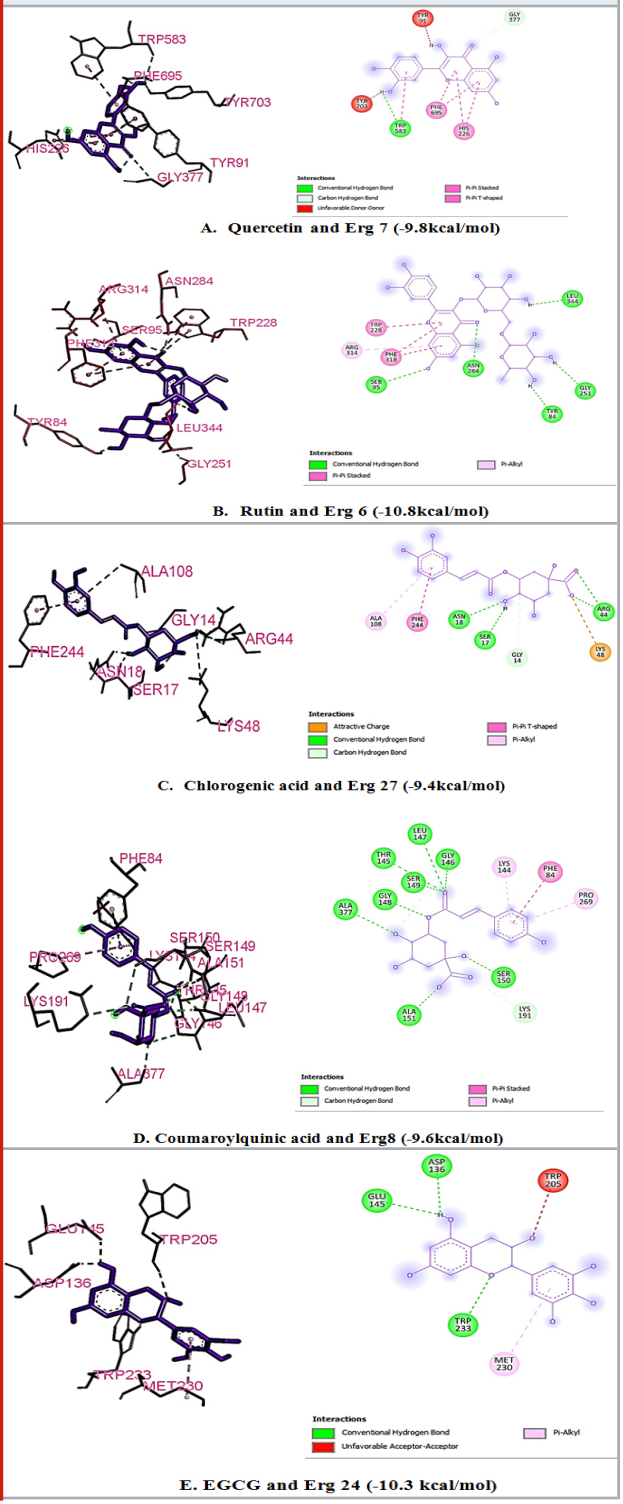
Figure 2: Q mean Z-score value of ERG proteins



Mammalian metabolism and toxicity of all the proposed green tea phytocompounds as potent antifungal drug agents were tested through ADMET analysis. The ADMET analysis depicted that out of 15 ligands, 13 compounds are non-toxic and obeyed Lipinski's rule of five. The drug likeliness report determined that Kaempferitrin, rutin, and EGCG are toxic as they have violated two to three rules from Lipinski's rule of five. Their toxicity level could restrict its application as a potent candidate for antifungal agents; however, before their therapeutic application, the dose regime of these drugs is necessary to be considered and analyzed for the drug toxicity. The solubility, dissolution, and GI permeability of any drug are essential parameters to be determined before their associated medical effect can be induced. These factors are rate-limiting steps for pre-formulation interpretations in drug development (Shekhawat and Pokharkar, 2017; Mitra et al. 2021). In our study, Dihydroactinidiolide and B-ionone, epicatechin, Epigallocatechin, gallic acid, pyrazine, and Quercetin demonstrated high GI absorption, while other ligands were observed to be considerably soluble (Gao et al. 2020; Anand et al. 2021).

Concerning drug potency, the ability of drugs to cross blood-brain barriers (BBB) is estimated. The present study estimated and indicated poor membrane permeation properties of all the tested 13 ligands except Dihydroactinidiolide and B-ionone (Table 8). CYP2 are the family of drug-metabolizing subsets that are involved in the biotransformation of drugs, xenobiotics. The ADMET data suggested an absence of the CYP2 inhibitors indicating metabolism of all drug candidates in the intestine and liver (Table 8) (Tran 2011; Palleri et al. 2013).The Bioavailability score which is an integral part of the pharmacokinetics paradigm was evaluated less than a standard score of 0.55 for chlorogenic acid, EGCG, kaempferitrin, and rutin and thus depicted their poor bioavailability (Martin 2005). The co-existence of CYP3A4 and Pgp at the same site acts synergistically to reduce the bioavailability of the drug (Mohamed and El-Kadi 2012). Recent studies have also reported poor bioavalibility of Rutin, EGCG, however novel identified transporter system in human can regulate the increase the bioavailibilty of EGCG (Ishii et al. 2019; Fatima et al. 2020).

Figure 3: Molecular Docking images of interaction via in silico study.



A. Quercetin and Erg 7 (-9.8kcal/mol)

B. Rutin and Erg 6 (-10.8kcal/mol)

C. Chlorogenic acid and Erg 27 (-9.4kcal/mol)

D. Coumaroylquinic acid and Erg8 (-9.6kcal/mol)

E. EGCG and Erg 24 (-10.3 kcal/mol)

Table 8. Drug likeliness report of green tea phytocompounds.

Molecule	MLOGP	ESOL Class	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Lipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score	Leadlikeness #violations
2,5-Dimethyll-4-hydroxy-3-(2H)-furanone	-2.71	Very soluble	Low	No	Yes	No	No	No	No	No	0	1	0	0	0	0.56	0
B-ionone	2.94	Soluble	High	Yes	No	No	No	No	No	No	0	0	0	0	2	0.55	1
Chlorogenic acid	-1.05	Very soluble	Low	No	No	No	No	No	No	No	1	1	1	1	2	0.11	1
Coumaroylquinic acid	-0.54	Very soluble	Low	No	No	No	No	No	No	No	0	1	1	1	0	0.56	0
Dihydroactinidiolide	2.37	Soluble	High	Yes	No	No	No	No	No	No	0	0	0	0	1	0.55	1
Epicatechin	0.24	Soluble	High	No	Yes	No	No	No	No	No	0	0	0	0	0	0.55	0
Epicatechin gallate	0.05	Soluble	Low	No	No	No	No	No	No	No	1	0	1	1	2	0.55	1
Epigallocatechin gallate	-0.44	Soluble	Low	No	No	No	No	No	No	No	2	0	1	1	3	0.17	1
Epigallocatechin	-0.29	Soluble	High	No	No	No	No	No	No	No	1	0	0	0	1	0.55	0
Gallic acid	-0.16	Very soluble	High	No	No	No	No	No	No	Yes	0	2	0	0	1	0.56	1
Kaempferitrin	-2.69	Soluble	Low	No	Yes	No	No	No	No	No	3	4	1	1	3	0.17	1
Myricetin	-1.08	Soluble	Low	No	No	Yes	No	No	No	Yes	1	0	1	1	2	0.55	0
Pyrazine	-0.92	Very soluble	High	No	No	No	No	No	No	No	0	3	0	0	2	0.55	1
Quercetin	-0.56	Soluble	High	No	No	Yes	No	No	Yes	Yes	0	0	0	0	0	0.55	0
Rutin	-3.89	Soluble	Low	No	Yes	No	No	No	No	No	3	4	1	1	4	0.17	1

CONCLUSION

The findings of the present study highlights the antifungal drug targets of green tea phytocompounds against inhibition of ergosterol biosynthesis in *Candida glabrata*. Rutin, Chlorogenic acid, Coumaroylquinic acid, quercetin, EGCG were screened as the most active green tea phytocompounds with Erg 6, Erg 7, Erg 8, Erg 24, and Erg 27 in ergosterol biosynthesis pathway as their possible drug targets. The poor bioavailability of rutin, chlorogenic acid, and EGCG is a limiting factor and needs further investigation to enhance their bioavailability. The current study is a preliminary analysis that needs to test *in vitro* to explore the future avenues of potent drug development against NAC species.

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