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Synthesis, Biological Evaluation and Molecular Docking of Novel Benzothiazol-2-ylcarbamodithioates as Potential Antifungals

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ABSTRACT: A series of novel carbamodithioates with benzothiazole scaffold have been synthesized and evaluated for their antifungal activity against various phytopathogenic fungi. Compound **17** has inflicted best fungitoxicity (ED_{50}=45µg/ml)against *Ustilago tritici.* To understand the enzyme-inhibitor interactions, molecular modelling studies were performed to dock the compounds. The experimental results of antifungal potential were also supported by molecular docking of compounds and log P values in the active site of CYP51.

Keywords: Antifungal; Benzothiazoles; Carbamodithioates; Docking; log P; Phytopathogenic fungi.

INTRODUCTION

Organic carbamodithioates are the most heavily used organic fungicides in terms of tonnage [1]and plays pivotal role in agriculture[2] and as other bioactive agents[3-23]. They are used for treatment of seeds, soil, foliar and post-harvest diseases affecting several types of crops [2]. More and more studies are made towards modifying this moiety, because of little resistance developed towards these carbamodithioates, multisite mode of action, low mammalian toxicity [10], high efficiency in controlling various plant pathogenic fungi[10], and high resistance developed towards azole fungicides[24]. Thousands of derivatives have been developed and majority of them contains contain only simple alkyl substituents[25] on S side of carbamodithioates. So, functionalization of the backbone of carbamodithioate is a developing area in chemistry[26].

On the other hand, benzothiazole is active scaffold possesses broad spectrum of biological activities like antibacterial [26], anti-inflammatory [27], antifungal[28], antitubercular [29], antitumor[30] and antioxidant [31]. It is also present in a range of commercially available antifungal compounds for agriculture use[32].

Derivatization of known pesticides to produce new potent molecular moieties continuous to be fruitful area of development [2]and this derivatization by combining them with other bioactive leads to give more potent molecules still seems an unexplored area. In an effort to develop new antifungalagents, we were interested in combining benzothiazoles with carbamodithioates. Therefore, in thepresent study, a series of benzothiazol-2-ylcarbamodithioates have been synthesized and evaluated for their antifungal activities against various phytopathogenic fungi viz. *Dreschlera oryzae* (brown leaf spot of rice), *Puccinia striiformis* (yellow rust of wheat), *Puccinia triticina* (brown rust of wheat), *Pyricularia grisea* (blast of rice) , *Ustilago hordei* (covered smut of barley) and *Ustilago tritici* (loose smut of wheat). In addition, Molecular docking study is used to predict the affinity of the molecule to their target enzyme and thus, activity of the molecule along with log P values that insight about water solubility and the favourable hydrophilic or hydrophobic interaction of the molecule with the fungal spores.

EXPERIMENTAL

Chemistry

Melting points were determined on electrical melting point apparatus and are uncorrected. Purity of the compounds was checked by TLC. The IR spectra were recorded on a Perkin Elmer FT-IR spectrometer using KBr disc. The NMR spectra

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were recorded on a Bruker Avance II 400 MHz spectrometer in DMSO with TMS as internal standard. Mass spectra were recorded on Perkin Elmer Clarus 500 Mass Spectrometer. Solvents used were purified by simple distillation. Docking studies were made by using the software package ArgusLab 4.0.1[36]. Log P values were calculated online using Molinspiration Cheminformatics Softwares [37].

General procedure for the synthesis of potassium benzo[d]thiazol-2-ylcarbamodithioate (11-15)

A solution of benzothiazol-2-amine (0.001 mol) and 20N potassium hydroxide in DMSO (10ml), was treated with carbon disulfide(0.002 mol) and stirred continuously on ice bath for 1 hr at 0 °C. The completion of reaction was confirmed by disappearance of benzothiazol-2-amine spot on TLC plate (dichloromethane/ EtOAc 10:1). The reaction mixture was placed undisturbed for few days and the product formed was recrystallized from methanol.

Potassium (6-bromobenzo[d]thiazol-2-yl)carbamodithioate (11)

Orange crystals; Yield (58.8%); mp 236°C; TLC (dichloromethane); MS: m/z: 342.94 $[M]^+$,344.34 $[M+2]^+$; IR (KBr):3394, 2995, 1592, 1049, 996 cm^{-1};^{1}H NMR (D_2O, 400 MHz): δ 5.2 (1H, s, NH), δ 7.4-8.5 (3H, m, Ar C-H); ^{13}C NMR 117.0, 118.8, 124.1, 128.7, 132.8, 152.2, 174.5, 196.1.

Potassium (6-chlorobenzo[d]thiazol-2-yl)carbamodithioate (12)

Yellow crystals; Yield (60%); mp 182°C; TLC (petroleum ether/EtOAc 10:1); MS: m/z: 297.34 $[M]^+$, 299.40 $[M+2]^+$; IR (KBr): 3433, 3002, 1595, 1057, 986 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ 5.3 (1H, s, NH), δ 7.1-7.7 (3H, m, Ar C-H); ^{13}C NMR 118.3, 121.2, 125.8, 129.8, 132.3, 151.3, 174.5, 196.1.

Potassium (5-chloro-6-fluorobenzo[d]thiazol-2-yl)carbamodithioate (13)

Brown crystals; Yield (64%); mp 223°C; TLC (dichloromethane/EtOAc 10:1); MS: m/z: 315.34 $[M]^+$, 317.58 $[M+2]^+$; IR (KBr): 3468, 3006, 1597, 1060, 988 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ 5.4 (1H, s, NH), δ 7.5-8.2 (2H, m, Ar C-H); ^{13}C NMR 109.4, 117.4, 122.7,129.7, 146,159.8, 174.5, 196.1.

Potassium (6-fluorobenzo[d]thiazol-2-yl)carbamodithioate (14)

White crystals; Yield (53%); mp 195°C; TLC (dichloromethane/EtOAc 10:1); MS: m/z: 281.39 $[M]^+$; IR (KBr): 3430, 3004, 1597, 1078, 990 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ 5.1 (1H, s, NH), δ 7.2-7.8 (3H, m, Ar C-H); ^{13}C NMR 108.0, 113.9, 117.8, 131.6, 148.8, 158.5, 174.5, 196.1.

Potassium (6-nitrobenzo[d]thiazol-2-yl) carbamodithioate (15)

Orange crystals; Yield (65%); mp 248°C; TLC (dichloromethane/EtOAc 10:1); MS: m/z: 308.30 $[M]^+$; IR (KBr): 3463, 2998, 1594, 1056, 987 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz): δ 5.1 (1H, s, NH), δ 7.8-8.5 (3H, m, Ar C-H); ^{13}C NMR 117.3, 119.1, 121.3, 131.3, 144.3, 159.3, 174.5, 196.1.

General procedure for the synthesis butyl/ethyl (benzo[d]thiazol-2-yl)carbamodithioates (16-25)

Butyl iodide/ ethyl iodide (0.001 moles) was added drop wise to potassium (benzo[d]thiazol-2-yl)carbamodithioate (0.0005 moles) and reaction mixture was stirred for 1 hour at 0°C. The completion of reaction was monitored by TLC in dichloromethane/EtOAc (10:1). Then the reaction mixture was poured into ice cold water and the solid obtained was filtered. The product was purified on silica gel column chromatography (ethyl acetate:n-hexane 3:7) and crystallized from methanol to give a series of carbamoditioates **16-20**. None of the investigated compounds have been reported in earlier publications.

Butyl (6-bromobenzo[d]thiazol-2-yl) carbamodithioate (16)

Yellow crystals; Yield (78%); mp 252°C; TLC (dichromethane/EtOAc 10:1); MS: m/z: 361.20$[M]^+$, 363.26 $[M+2]^+$;IR (KBr): 3391, 2955, 1592, 1049, 994 cm^{-1}; ^{1}H NMR (CDCl3, 400 MHz) δ: 0.96 (3H, t, $-CH_3$), δ: 1.2 (2H, sext, $-CH_2$), δ: 1.4 (2H, quint, $-CH_2$), δ: 3.2 (2H, t, $-CH_2$), δ: 5.1 (1H, s, -NH), δ: 6.9-7.6 (3H, m, Ar -CH); ^{13}C NMR 13.8, 21.3, 32.0, 35.2, 117.0, 118.8, 124.1, 128.7, 132.8, 152.2, 174.5, 199.9.

Butyl (6-chlorobenzo[d]thiazol-2-yl) carbamodithioate (17)

Light yellow crystals; Yield (63%); mp 195°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 316.34

$[M]^+$, 318.45 $[M+2]^+$; IR (KBr): 3433, 2956, 1595, 1057, 985 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 0.98 (3 H, t, $-CH_3$), δ: 1.4 (2H, sext, $-CH_2$), δ: 1.7 (2H, quint, $-CH_2$), δ: 3.3 (2H, t, $-CH_2$), δ: 5.1 (1H, s, -NH), δ: 7.2-7.7 (3H, m, Ar -CH); ^{13}C NMR 13.8, 21.3, 32.0, 35.2, 118.3, 121.2, 125.8, 129.8, 132.3, 151.3, 174.5, 199.9.

butyl (5-chloro-6-fluorobenzo[d]thiazol-2-yl) carbamodithioate (18)

Light brown crystals; Yield (42%); mp 230°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 333.26 $[M]^+$, 335.16 $[M+2]^+$; IR (KBr): 3468, 2959, 1595, 1060, 988 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 0.97 (3 H, t, $-CH_3$), δ: 1.4 (2H, sext, $-CH_2$), δ: 1.7 (2H, quint, $-CH_2$), δ: 3.2 (2H, t, $-CH_2$), δ: 5.0 (1H, s, -NH), δ: 6.8-7.7 (3H, m, Ar -CH); ^{13}C NMR 13.8, 21.3, 32.0, 35.2, 109.4, 117.4, 122.7, 129.7, 146.0, 159.8, 174.5, 199.9.

butyl (6-fluorobenzo[d]thiazol-2-yl) carbamodithioate (19)

Light green crystals; Yield (60%); mp 110°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 300 $[M]^+$; IR (KBr): 3430, 2985, 1592, 1073, 994 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 0.97 (3 H, t, $-CH_3$), δ: 1.4 (2H, sext, $-CH_2$), δ: 1.7 (2H, quint, $-CH_2$), δ: 3.3 (2H, t, $-CH_2$), δ: 5.1 (1H, s, -NH), δ: 7.1-7.8 (3H, m, Ar -CH); ^{13}C NMR 13.8, 21.3, 32.0, 35.2, 108.0, 113.9, 117.8, 131.6, 148.8, 158.5, 174.5, 199.9.

butyl (6-nitrobenzo[d]thiazol-2-yl) carbamodithioate (20)

Yellow crystals; Yield (68%); mp 220°C; TLC (dichloromethane/EtOAc 10:1Mass (ESI): 326.19 $[M]^+$; IR (KBr): 3463, 2967, 1595, 1057, 987 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 0.98 (3H, t, $-CH_3$), δ: 1.4 (2H, sext, $-CH_2$), δ: 1.7 (2H, quin, $-CH_3$), δ: 3.3 (2H, t, $-CH_2$), δ: 5.3 (1H, s, -NH), δ: 7.9-8.5 (3H, m, Ar -CH); ^{13}C NMR 13.8, 21.3, 32.0, 35.2, 117.3, 119.1, 121.3, 131.3, 144.3, 159.3, 174.5, 199.9.

Ethyl (6-bromobenzo[d]thiazol-2-yl) carbamodithioate (21)

Brown crystals; Yield (76%); mp 282°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 333.67 $[M]^+$, 335.23 $[M+2]^+$; IR (KBr): 3360, 2953, 1585, 1058, 980 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 1.3 (3H, t, $-CH_3$), δ: 3.4 (2H, q, $-CH_2$), δ: 5.1 (1H, s, -NH), δ: 7.1-7.5 (3H, m, Ar -CH); ^{13}C NMR 13.9, 31.3, 117.0, 118.8, 124.1, 128.7, 132.8, 152.2, 174.5, 198.9.

Ethyl (6-chlorobenzo[d]thiazol-2-yl) carbamodithioate (22)

Light green crystals; Yield (64%); mp 178°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 287.13 $[M]^+$, 289.15$[M+2]^+$; IR (KBr): 3368, 2960, 1587, 1054, 984 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 1.2 (3 H, t, $-CH_3$), δ: 3.1 (2H, q, $-CH_2$), δ: 5.0 (1H, s, -NH), δ: 7.2-7.7 (3H, m, Ar -CH); ^{13}C NMR 13.9, 31.3, 1118.3, 121.2, 125.8, 129.8, 132.3, 151.7, 174.5, 199.9.

Ethyl (5-chloro-6-fluorobenzo[d]thiazol-2-yl)carbamodithioate (23)

Light yellow crystals; Yield (45%); mp 218°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 305.31 $[M]^+$, 307.01 $[M+2]^+$; IR (KBr): 3365, 2966, 1595, 1056, 981cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 1.6 (3 H, t, $-CH_3$), δ: 3.1 (2H, q, $-CH_2$), δ: 5.3 (1H, s, -NH), δ: 6.6-7.5 (3H, m, Ar -CH); ^{13}C NMR 13.9, 31.3, 109.4, 117.4, 122.7, 129.7, 146.0, 159.8, 174.7, 199.9.

Ethyl (6-fluorobenzo[d]thiazol-2-yl) carbamodithioate (24)

Light green crystals; Yield (75%); mp 232°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 271.23 $[M]^+$; IR (KBr): 3372, 2970, 1589, 1058, 985 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 1.3 (3 H, t, $-CH_3$), δ: 3.1 (2H, q, $-CH_2$), δ: 5.4 (1H, s, -NH), δ: 7.1-7.8 (3H, m, Ar -CH); ^{13}C NMR 13.9, 31.3, 108.0, 113.9, 117.8, 131.6, 149.5, 158.5, 174.5, 199.9.

Ethyl (6-nitrobenzo[d]thiazol-2-yl) carbamodithioate (25)

Yellow crystals; Yield (65%); mp 278°C; TLC (dichloromethane/EtOAc 10:1); Mass (ESI): 298.55$[M]^+$; IR (KBr): 3367, 2968, 1585, 1055, 981 cm^{-1}; ^1H NMR (CDCl3, 400 MHz) δ: 1.4 (3 H, t, $-CH_3$), δ: 3.1 (2H, q, $-CH_2$), δ: 4.9 (1H, s, -NH), δ: 8.0-8.6 (3H, m, Ar -CH); ^{13}C NMR 13.9, 31.3, 117.3, 119.1, 121.3, 131.3, 144.2, 159.3, 174.5, 199.9.

Antifungal activity assay

A spore germination inhibition technique[38] was employed *in vitro* to evaluate the antifungal activity of synthesized compounds. Activities of the compounds were tested against *D. oryzae, P. grisea, P. striiformis, P. triticina, U. hordei,* and *U. tritici.* Stock solution of the test compounds and standard fungicides Bavistin (Methyl-2-benzimidazole-2-yl carbamate), Vitavax (5,6-

dihydro-2-methyl-1,4-oxathiin-3-carboxamide) and Tilt (1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole) were prepared by dissolving each chemical (20 mg) in 1 ml of Tween 20 (Polyoxyethylene sorbitan monolaurate) and volume was made to 10 ml with sterilized distilled water. Stock solutions of 2000 µg/ml, prepared on active ingredient basis were kept in refrigerator till further use. Serial dilutions were done according to the need to 1000, 500, 250, 100, 50, 25 and 10 µg/ml respectively.

Spore suspension was made by adding sterilized distilled water to the fresh spores of respective fungi. Suspension was filtered through three layers of sterilized cheese cloth in order to remove mycelial particles under aseptic conditions. Haemocytometer was used to form standardized spore suspension (1×10^6spores/ml). Small droplets (0.02 ml) of test solution and spore suspension in equal amount were seeded in the cavity of the cavity slides. These slides were placed in Petri plates lined with moist filter paper and were incubated. The numbers of spores germinated were counted and per cent spore germination inhibition was calculated.

Molecular docking

Compounds were built using the builder tool kit of the software package ArgusLab 4.0.1 and geometry was optimized using semi-empirical quantum mechanical method PM_3.Lanosterol 14a-demethylase (PDB ID 2VKU) was downloaded from protein data bank [39]and the active site of the enzyme was located. The molecule to be docked in the active site of the protein was pasted in the work space carrying the structure of the enzyme. The docking programme implements an efficient grid based docking algorithm which approximates an exhaustive search within the free volume of the binding site cavity. The conformational space was explored by the geometry optimization of the flexible ligand (rings were treated as rigid) in combination with the incremental construction of the ligand torsions. Thus, docking occured between the flexible ligand parts of the compound and enzyme.

RESULTS AND DISCUSSION

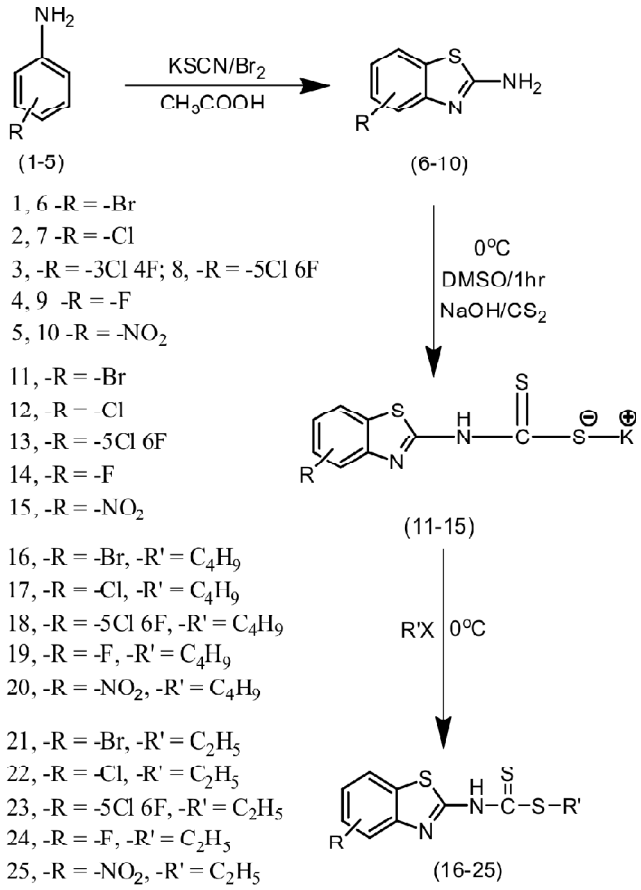
Chemistry

The Benzothiazol-2-amines(**6-10)**were first prepared by bromo-cyclisation of substituted anilines according to the method given in the literature [33,34]. The synthetic route of the synthesis is outlined in **Scheme 1**. Further, the desired benzothiazol-2-ylcarbamodithioates were prepared by reaction of benzothiazol-2-amines **(6-10)** with carbon disulfide in presence of potassium hydroxide to give potassium(benzo[d]thiazol-2-yl)carbamodithioates (**11-15**), that on alkylation gave the respective butyl (benzo[d]thiazol-2-yl)carbamodithioates (**16-20**) and ethyl (benzo[d]thiazol-2-yl)carbamodithioates (**21-25**).All the synthesized carbamodithioates **11-25** were characterized by ^{1}H NMR, ^{13}C NMR, IR and Mass spectral studies.

Bioactivity

In vitro antifungal activities of all the synthesised compounds from **6-25** were evaluated against six phytopathogenic fungi *viz.D. oryzae, P. striiformis, P. triticina, P. grisea, U. hordei,and U. tritici* by spore germination inhibition technique. The results are summarized in **Table 1,** in terms of ED_{50} values that represents effective dose at which 50 percent spore germination inhibition has occurred. These data are the mean of three replicate tests performed with each antifungal compound. The spore germination in control was 100 percent. Most of the compounds had shown moderate results against all the test fungi, with number of carbamodithioates showing remarkable effects on antifungal activities. Especially, against *U. tritici,* compound **17** was found to be the most potent with ED_{50} value of 45mg/ml that is comparable to standard. Additionally, compounds **6**, **7**, **8** and **14** exhibited promising results against *U. tritici* withED_{50} values of less than 100 mg/ml. Against *P. striiformis* also, all the compounds were found to be active with compound **22** to be most active with ED_{50} value of 80mg/ml along with moderate activity of less than 200 mg/ml by compounds **7, 8, 12, 15, 21** and **25** whereas, against *U. hordei* only compound **6** had shown the moderate results.

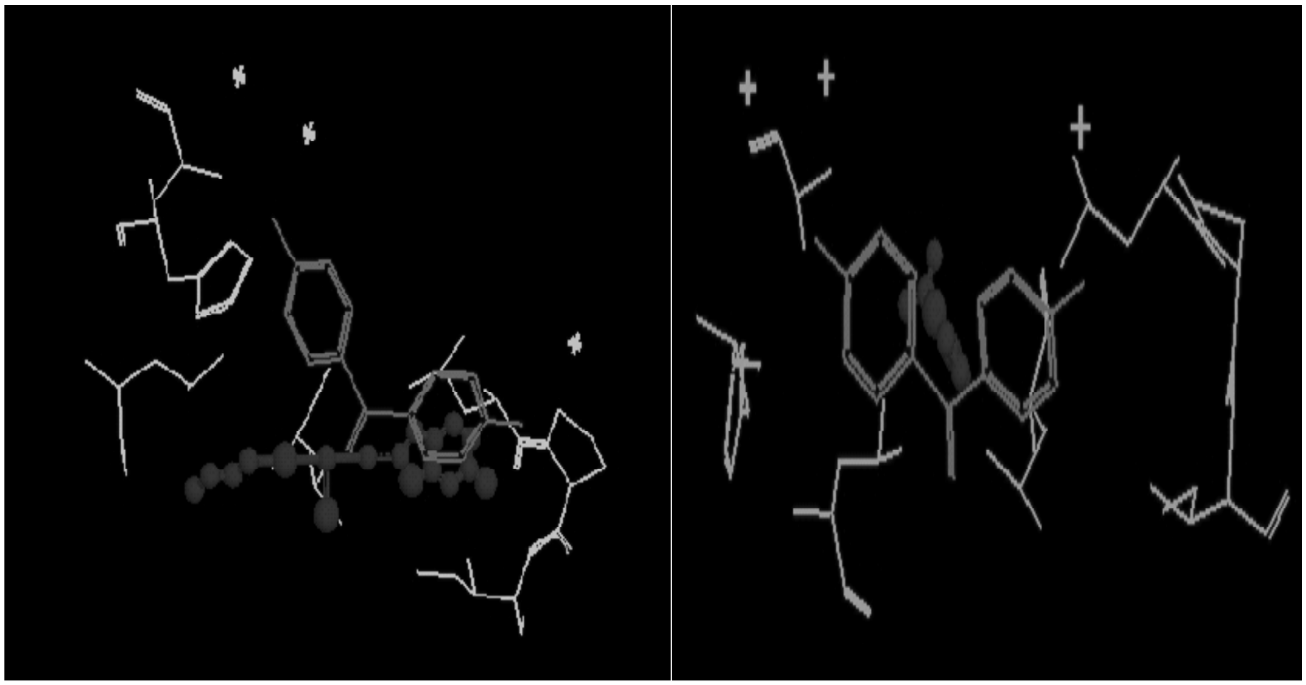
To gain more understanding on the potency of the synthesized compounds, we proceeded to examine the interaction of the compounds with lanosterol 14a-demethylase CYP-51 (PDB ID 2VKU)[35]. For this purpose, molecular docking of these compounds in the active site of the enzyme was performed, using ArgusLab 4.0.1. The calculated free energies of binding were used as the parameter for the selection of the cluster of



Scheme 1: Structures of the investigated compound

docking pose to be evaluated, in which the binding mode of the lowest energy structure located in the top docking cluster **Table 2**. The similar pattern of the bioactivity was followed against all the fungi, which are in accordance with estimated free energy values of all the test compounds. The compounds with higher negative free energy values of nearly -9.0 K cal/mol were found to be more active than the one with comparatively lesser negative free energy values. The lowest ED_{50} value of the compound **17** is inconsonance with the highest negative free energy value of the docking studies.Energy minimized conformation of compound **17, 22** and the standard compoundsVitavax and Tilt docked in the active site of the enzyme is shown in Figure **1**, the compound gets concealed in the interior of the enzyme and the selected pose of **17** had an estimated free energy of binding of -9.631 kcal/mol that is comparatively more negative than free binding energy of standard compound Vitavax against *U. tritici* (-6.601 kcal/mol).

In order to analyse the structure activity relationship of the compounds, the value of logarithm of partition coefficient (log P) was determined. These values are reported in Table **2.** The low ED_{50} value of compound **22** against *P. striiformis,* thathas free energy of binding of -8.295



Compound 17

Standard (Vitavax)

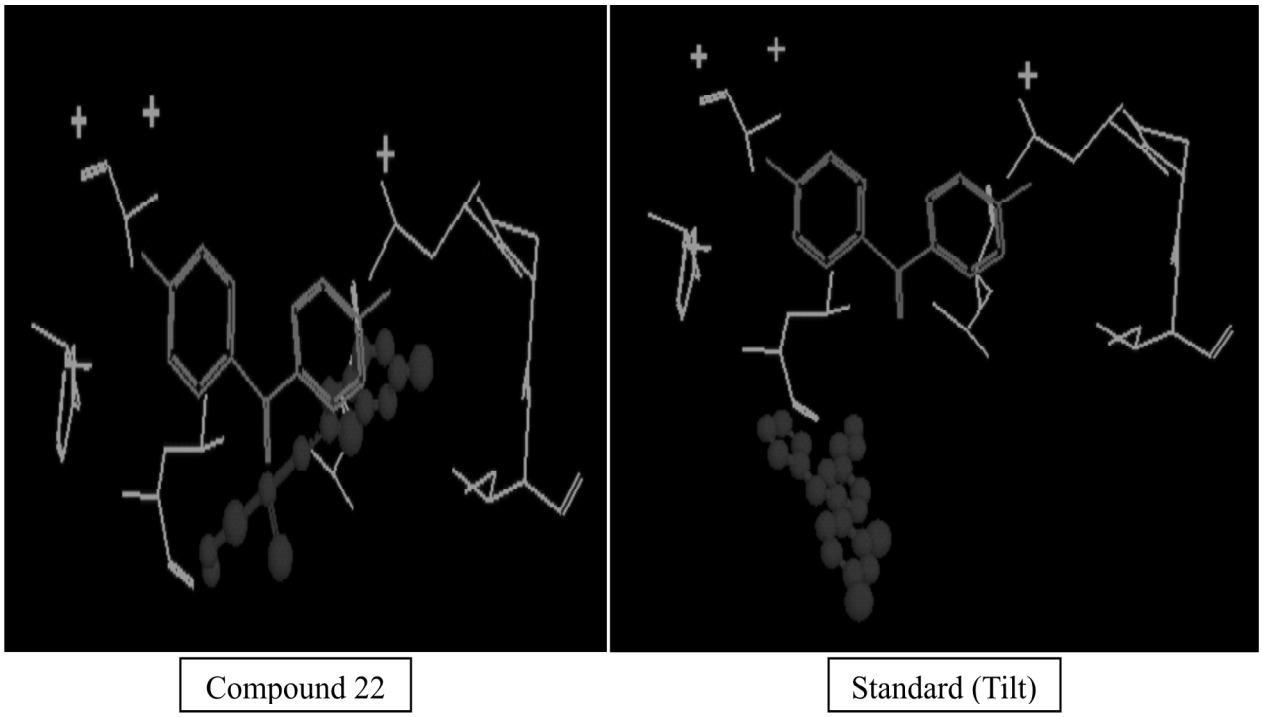


Figure 1: The docking poses of active compounds along with standards shown in blue

Table 1
Antifungal activity of Benzothiazol-2-ylcarbamodithioates (in terms of ED_{50} values expressed in mg/ml)

Compd	*ED_{50} values (mg/ml)*					
	D. oryzae	*P. striiformis*	*P. triticina*	*P. grisea*	*U. hordei*	*U. tritici*
6	480	150	350	240	140	80
7	400	200	480	230	300	90
8	320	200	450	250	580	85
9	350	450	510	330	210	350
10	250	450	980	250	250	300
11	760	950	450	355	600	400
12	600	180	550	420	680	950
13	600	990	850	300	185	850
14	450	980	755	350	150	90
15	860	130	659	400	850	900
16	750	900	⋆	280	140	150
17	650	350	355	250	280	45
18	450	300	380	240	370	180
19	560	950	550	300	450	190
20	750	980	⋆	480	500	250
21	860	120	800	450	680	280
22	800	80	450	245	345	280
23	750	900	850	400	580	185
24	800	300	350	350	490	190
25	850	200	400	240	350	600
Bavistin*	45	-	-	-	-	-
Tilt**	-	35	8	20	-	-
Vitavax***	-	-	-	-	15	8

⋆Indicates ED_{50}values more than 1000 mg/ml.
*Standard fungicide against *D. oryzae*.
**Standard fungicide against *P. striiformis, P. triticina* and*P. grisea*.
*** Standard fungicide against *U. hordei*and *U. tritici*.

Table 2
The docking score and log P values of Benzothiazol-2-ylcarbamodithioate derivatives.

Compd	*Docking score (K cal / mol)*	*Log P*
6	-9.077	2.763
7	-9.368	2.632
8	-9.229	2.723
9	-8.561	2.117
10	-7.029	1.913
11	-7.602	0.919
12	-7.634	0.788
13	-7.710	0.879
14	-7.178	0.273
15	-7.147	0.069
16	-9.171	5.506
17	-9.631	5.375
18	-9.603	5.467
19	-9.185	4.861
20	-8.947	4.656
21	-8.679	4.445
22	-8.295	4.313
23	-8.421	4.405
24	-7.908	3.799
25	-7.667	3.594
Bavistin	-6.601	1.457
Tilt	-8.182	3.639
Vitavax	-6.413	0.338

K cal/mol, had comparatively lower log P value.The lipophillicity estimated by log P (octanol/water partition coefficient) varies between 0.069 and 5.476. But the ED_{50} valuesrevealed that high lipophilicity favours the fungitoxicity in most of the cases. The low ED_{50} values of carbamodithioate salts are in accordance with lower log P values against most of the fungi with the exception of compound **14** that had shown appreciable fungitoxicity. Collectively, thetotal antifungal effects are in resonance with the docking score and log P values.

CONCLUSION

In the present work, the synthesized novel benzothiazol-2-ylcarbamodithioates exhibited good antifungal activity against the phytopathogenic fungi. Compound **17** had shown the best antifungal potential against *U. tritici* with ED_{50} value of 45µg/ml followed by compound **22** against *P. striiformis* with ED_{50} value of 80 µg/ml. The activities of the compounds were supported by molecular docking studies carried out to understand enzyme-inhibitor interactions. Higher log P values are found to be more favourable for fungitoxicity of all the test fungi. Compound **17** showed the best enzyme inhibitor interaction. Higher lipophilicity which favoured the fungitoxic effects against *U. tritici* was owing to higher molecular weight moiety at S-end of carbamodithioate that made the molecule more lipophillic and the presence of chloro group on benzothiazole ring favoured the results. Hence, the chlorobenzo[d]thiazol-2-ylcarbamodithioates with heavier groups on S-side of carbamodithioate can be explored as substrates for synthesis of better fungicidal agent used against *U. tritici* and *P. striiformis*.

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