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Synthesis, characterization, PASS prediction, molecular docking and ADME study of benzo[*b*]thiophen-5-amine based biologically active Schiff bases

Raksha V Zala[a], Chandresh S Vaya*[a,b] & Rakesh Jani[a,c]

[a] Department of Chemistry, Kamani Science College and Prataprai Arts College, Amreli 365 601, Gujarat, India
[b] GMB Polytechnic, Rajula 365 560, Gujarat, India
[c] Lalan Science College, Bhuj 370 001, Gujarat, India
E-mail: c.s.vaya2011@gmail.com

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Adopting the potentiality of benzo[*b*]thiophene moiety and Schiff base compounds, a series of Schiff base compounds namely, 2-{[(1-benzothiophen-5-yl)imino]methyl}phenol *i.e.* **5a**, 3-{[(1-benzothiophen-5-yl)imino]methyl}benzene-1,2-diol *i.e.* **5b**, 2-{[(1-benzothiophen-5-yl)imino]methyl}-6-methoxyphenol *i.e.* **5c**, 2-{[(1-benzothiophen-5-yl)imino]methyl}-5-methoxyphenol *i.e.* **5d**, 2-{[(1-benzothiophen-5-yl)imino]methyl}-4-nitrophenol *i.e.* **5e** and 2-{[(1-benzothiophen-5-yl)imino]methyl}-4-chlorophenol *i.e.* **5f** have been synthesized in good yields and characterized by FT-IR, ^{1}H and ^{13}C NMR, and mass spectroscopy. Biological activity has been checked after performing antimicrobial and antifungal activity studies of synthesized compounds using the Minimum Inhibitory Concentration (MIC) determination technique. Computational studies like PASS (Prediction of Activity Spectra for Substances) prediction, molecular docking, and an ADME (Absorption, Distribution, Metabolism, Excretion) study have been performed to gain insight into the synthesized molecules' *in silico* properties.

Keywords: ADME, Antimicrobial Activity, Antifungal activity, Benzo[*b*]thiophen-5-amine, Molecular docking, PASS prediction, Schiff base

In the class of sulfur heterocycles, benzo[b]thiophene is one of the important pharmacophores of some bioactive molecules and because of the same reason, it has fascinated much interest in it[1,2]. A broad range of biological/pharmacological activities displayed by derivatives of benzo[*b*]thiophenes like anti-inflammatory, analgesics[3], anti-fungal[4], enzyme inhibitors[5], anti-cancer[6], anti-tubercular[7], anticonvulsant agents[8], anti-diabetic[9], estrogen receptor modulating[10], and many other activities. A Few benzo[*b*]thiophene-based compounds such as mobam, benocyclidine, sertaconazole, zileuton, and raloxifene are available in the market. Mobam, a benzo[*b*]thiophene consists compound used for the protection of crop[11]. Benocyclidine substance is a psychoactive that is a potent and selective psychostimulant and dopamine reuptake inhibitor (DRI)[12]. Sertaconazole is used to treat skin infections as an anti-fungal cream such as on athlete's foot (tinea pedis)[13]. Zileuton is a benzo[*b*]thiophene derivative an inhibitor of 5-lipoxygenase[14]. Raloxifene a class of compounds known as selective estrogen receptor modulators (SERMs) that exhibit estrogen agonist-like actions on bone tissues and serum lipids while displaying potent estrogen antagonist properties in the breast and uterus was approved by the U.S. Food and Drug Administration (FDA) for the prevention and treatment of osteoporosis in postmenopausal women[15-17]. Now, Schiff base compounds are the imine or azomethine (–C=N–) functional group carrying compounds produced from condensation reactions between carbonyl compounds with primary amines and were first reported by Hugo Schiff[18–20] having gained importance in medicinal and pharmaceutical fields due to a broad spectrum of biological activities like anti-inflammatory[21], analgesic[22], antimicrobial[23], anticonvulsant[24], antitubercular[25], anticancer[26], antioxidant[27], anthelmintic[28], and so forth. Schiff base compounds possess nitrogen atom which may be involved in the formation of a hydrogen bond with the active centers of cell constituents and interferes with normal cell processes[29,30]. So, on consideration of the importance of benzo[*b*]thiophene moiety and Schiff base compounds an effort has been made to synthesize Schiff base compounds from benzo[*b*]thiophene derivative and its various studies like PASS prediction, molecular docking, and

ADME study were performed to obtain it's *in silico* properties.

Experimental Section

Reagents and Solutions

Experiment work starts with the preparation of Schiff bases. All purchased chemicals were of analytical grade and used as received without further purification. Aldehydes and amine were obtained from TCI and Zeta Respectively.

Apparatus

The determinations of melting points were performed using capillary with paraffin oil and are uncorrected. Infrared spectra were recorded on the Shimdzu-8400 spectrophotometer and expressed in cm^{-1}. Mass spectra (MS) were determined using Waters spectrometers. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 as solvent on Bruker magnetic resonance spectrometer at 400 MHz and 100 MHz respectively. Measurements were conducted using the δ (ppm) scale.

General procedure for the synthesis of Schiff bases

The reaction mixture of benzo[*b*]thiophen-5-amine (0.002mol) and 2-hydroxybenzaldehyde / 2,3-dihydroxy benzaldehyde / 2-hydroxy-3-methoxybenzaldehyde / 2-hydroxy-4-methoxybenzaldehyde / 2-hydroxy-5-nitrobenzaldehyde / 2-hydroxy-5-chlorobenzaldehyde (0.002 mol) was prepared by using methanol as solvent with catalytic amount of glacial acetic acid. The reaction mixture was refluxed with constant stirring at 64°C for 2 h. Schiff bases were obtained by cooling the reacting mixture overnight at room temperature. The product was isolated, dried, and recrystallized using hot methanol. The homogeneity of compounds was checked by TLC and they were characterized by infrared, ^{1}H and ^{13}C NMR and mass spectroscopy.

Antimicrobial and Antifungal Activity

Antimicrobial and Antifungal activities of synthesized Schiff bases were carried out by using the Minimum inhibitory concentration (MIC) determination technique using suspended N Broth in sterile double distilled water as a media. The antibacterial activity of the compounds has been tested against S. aureus (Gram-positive bacteria), and E. coli (Gram-negative bacteria), and antifungal activity was carried out against Rhizopus spp. and A. niger. MIC was determined by using a serial dilution technique in liquid media containing varying concentrations of tested compounds from 50, 100, 250, 500, and 1000 ppm. All equipment and culture media used during the process were sterile.

PASS Prediction

PASS (Prediction of Activity Spectra for Substances) prediction online web tool (http://www.way2drug.com/) is used for the prediction of biological activity spectra of organic molecules based on their structural formula which is applied to substances that have the probability to be "drug-like". PASS prediction result of a compound is designated as Probable to be active (Pa) and Probable to be inactive (Pi)[31].

Molecular docking study

In the present investigation, 3 proteins namely carbonic anhydrase (PDB ID: 6LUX), fungal protein (PDB ID: 4M8B) and Complement factor D (PDB ID: 5NB7) have been taken for molecular docking studies and the crystallographic structures of proteins were retrieved from protein database website (www.rcsb.org).

Protein and ligand preparation

During the preparation of the protein, water molecules, inhibitors, and metal ions were deleted from the protein to obtain a clean protein. Then polar-only hydrogen was added and assigned Kollmann charge using the autodock tool and then converted to pdbqt format from pdb format by using the Open Babel tool. The ligands were drawn using ChemDraw Pro 12.0 and then converted into pdbqt format by using the Open Babel tool. AutoDock 4.2 tools were used for docking purposes and during the docking process, a maximum of 10 conformers were considered for each compound[32].

ADME study

Swiss ADME-based molecular sketcher drawing tool ChemAxon's Marvin JS was used to submit the molecules[33]. Swiss ADME is a free web tool that predicts whether a compound has the potential to be drug-like by checking its various properties and filters of the submitted compound which includes absorption, distribution, metabolism and excretion parameters such as log P value, human gastrointestinal absorption (HIA), water solubility, along with pharmacokinetic properties such as molar mass, hydrogen donor, hydrogen acceptor, and topological polar surface area (TPSA), *etc*.

Physical and Spectral Data

2-{[(1-Benzothiophen-5-yl)imino]methyl}phenol, 5a: Colour: Yellow. Yield 82%. m.p.132°C. Mol. Wt.

253.2. FT-IR (KBr): 1155, 1192, (υ C=N) 1664, (υ Ar C-H) 3057, (υ O-H) 3238 cm^{-1}; ^1H NMR(400 MHz, DMSO-d_6): δ 6.98-8.06 (m, 9H, Ar-H), 9.04 (s, 1H, HC=N), 13.27 (s, 1H, Ar-OH); ^{13}C (100 MHz, DMSO-d_6): δ 116.43, 117.08, 118.79, 119.60, 119.86, 123.86, 124.65, 129.46, 133.01, 133.62, 138.15, 140.90, 145.42, 160.80, 163; Mass spectra (ESI-MS): *m/z* 254.2 $[M-H]^+$.

3-{[(1-Benzothiophen-5-yl)imino]methyl}benzene-1,2-diol, 5b: Colour: Red. Yield 87%. m.p.158°C. Mol. Wt. 269.2. FT-IR (KBr): 1255, 1275, (υ C=N) 1630,(υ Ar C-H) 3098, (υ O-H) 3468 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 6.79-8.09 (m, 8H, Ar-H), 9.03 (s, 1H, HC=N), 12.69 (s, 2H, Ar-OH); ^{13}C (100 MHz, DMSO-d_6): δ 116.29, 118.83, 119.23, 119.37, 119.97, 123.17, 123.91, 124.65, 129.50, 138.06, 140.92, 145.35, 146.15, 149.82, 164.03; Mass spectra (ESI-MS): *m/z* 270.2 $[M-H]^+$.

2-{[(1-Benzothiophen-5-yl)imino]methyl}-6-methoxyphenol, 5c: Colour: Orange. Yield 92.58%. m.p.128°C. Mol. Wt. 283.1. FT-IR (KBr): 1213, 1255, (υ C=N) 1612, (υ Ar C-H) 3001, (υ O-H) 3067 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.84 (s, 3H, CH_3) 6.91-8.09 (m, 8H, Ar-H), 9.06 (s, 1H, HC=N), 13.35 (s, 1H, Ar-OH); ^{13}C (100 MHz, DMSO-d_6): δ 56.34(Ar-OCH_3), 115.96, 116.40, 118.78, 119.08, 119.78, 123.92, 124.35, 124.66, 129.52, 138.15, 140.92, 145.29, 148.40, 151.01, 163.80; Mass spectra (ESI-MS): *m/z* 284.1 $[M-H]^+$.

2-{[(1-Benzothiophen-5-yl)imino]methyl}-5-methoxyphenol, 5d: Colour: Light green. Yield 74.5%. m.p.122°C. Mol. Wt. 283.1. FT-IR (KBr): (υ C-N) 1211, 1242, (υ C=N) 1614, (υ Ar C-H) 2978, (υ O-H) 3098 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.82 (s, 3H, CH_3), 6.52-8.28 (m, 8H, Ar-H), 8.96 (s, 1H, HC=N), 13.77 (s, 1H, Ar-OH); ^{13}C (100 MHz, DMSO-d_6): δ 55.93(Ar-OCH_3), 101.33, 107.26, 113.57, 116.04, 118.71, 123.84, 124.60, 129.38, 134.51, 137.62, 140.94, 145.33, 162.81, 163.57, 164.05; Mass spectra (ESI-MS): *m/z* 284.1 $[M-H]^+$.

2-{[(1-Benzothiophen-5-yl)imino]methyl}-4-nitrophenol, 5e: Colour: Light brown. Yield 70.2%. m.p.160°C. Mol. Wt. 298.2. FT-IR (KBr): (υ C-N) 1200, 1257, (υ C=N) 1618, (υ O-H) 3103 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 6.71-8.70 (m, 8H, Ar-H), 9.05 (s, 1H, HC=N), 14.41 (s, 1H, Ar-OH); ^{13}C (100 MHz, DMSO-d_6): δ 116.82, 118.43, 118.86, 119.15, 124.13, 124.63, 128.81, 128.85, 129.88, 138.86, 139.51, 140.86, 143.78, 161.69, 167.52; Mass spectra (ESI-MS): *m/z* 299.2 $[M-H]^+$.

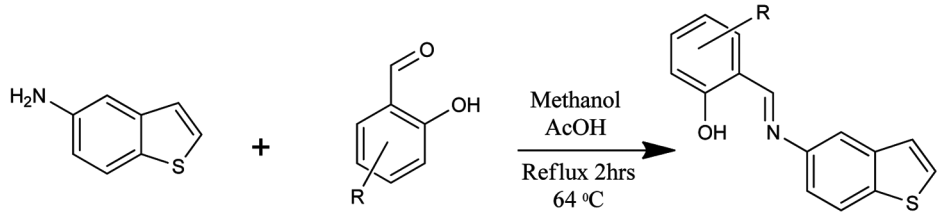
2-{[(1-Benzothiophen-5-yl)imino]methyl}-4-chlorophenol, 5f: Colour: Cream. Yield 60.1%. m.p.168°C. Mol. Wt. 287.1. FT-IR (KBr): (υ C-N) 1188, 1277, (υ C=N) 1616, (υ O-H) 3072 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.01-8.10 (m, 8H, Ar-H), 9.08 (s, 1H, HC=N), 13.15 (s, 1H, Ar-OH); ^{13}C (100 MHz, DMSO-d_6): δ 116.61, 118.70, 119.09, 121.16, 123.03, 123.96, 124.66, 129.62, 131.44, 133.08, 138.43, 140.88, 145.25, 159.38, 162.10; Mass spectra (ESI-MS): *m/z* 288.1 $[M-H]^+$.

Results and Discussion

Synthesis and Characterization of Compounds

The Schiff base compounds were synthesized by condensation reaction as shown in Scheme 1. The structures of all the compounds were established based on the FT-IR, mass, ^1H NMR, and ^{13}C NMR spectral data. All synthesized compounds were soluble in methanol and Dimethyl sulfoxide (DMSO).

IR spectra of six Schiff bases observed at 1612-1665 cm^{-1} strong band suggest (HC=N) vibration of the azomethine group. The hydroxyl group (O-H) vibration occurred in the range 3066-3468 cm^{-1}. The C-Cl stretching vibration appeared at 700 cm^{-1}. υ(C-NO_2) appeared in the 1340 & 1527 cm^{-1} region in the



Benzo[b]thiophen-5-amine 2-hydroxybenzaldehyde Schiff bases

(a) R=H (b) R=3-OH (c) R=3-OMe (d) R=4-OMe (e) R=5-NO2 (f) R=5-Cl

Scheme 1 — Synthesis of Schiff bases **5a-f**

5e spectrum. Aromatic υ(C-H) stretching at 3098-3001 cm^{-1} and the (C=C) stretching vibrations of Schiff bases are strongly observed at 1577 cm^{-1}, 1554 cm^{-1}, 1568 cm^{-1}, 1570 cm^{-1}, 1562 cm^{-1} and 1577 cm^{-1} respectively in **5a-f** proved existence of aromatic rings. The mass spectra showed molecular ion peaks at m/z 254.2, 270.2, 284.1, 284.1, 299.2, and 288.1 corresponding to molecular weights of the **5a-f** respectively. In the ^{1}H NMR spectra of Schiff bases, the chemical shift of aromatic protons is observed as multi signals within the range from δ 6.52-8.70. A sharp singlet is observed for Schiff bases within the δ 8.96-9.08 region of the spectrum corresponding to the azomethine group proton. The methoxy group of compounds was shown singlet at about δ 3.81-3.83. The signal in the region δ 12.68-14.40 was assigned to –OH group protons in the compounds.

In the ^{13}C NMR δ 56.34 in **5c** and δ 55.93 in **5d** value belong to methoxy carbon. All values between δ 100-170 region belong to alkene (C=C) and aromatic carbons.

Antimicrobial and Antifungal Activity

All the above-synthesized compounds along with standard Sertaconazole were screened for antimicrobial activity by using MIC determination technique. The results showed that among the synthesized Schiff bases only **5b** had the lowest value of MIC among all organisms on testing. **5f** has been found very effective against Gram-positive bacteria S. Aureus. **5a** and **5e** have been found very effective against Gram-negative bacteria E. coli. **5c** is moderately active against both gram-positive and gram-negative bacteria. In the fungal studies, **5b** exhibited effective antifungal activity against Rhizopus spp. and A. Niger. Comparison between synthesized compounds along with standard are represented in Fig. 1.

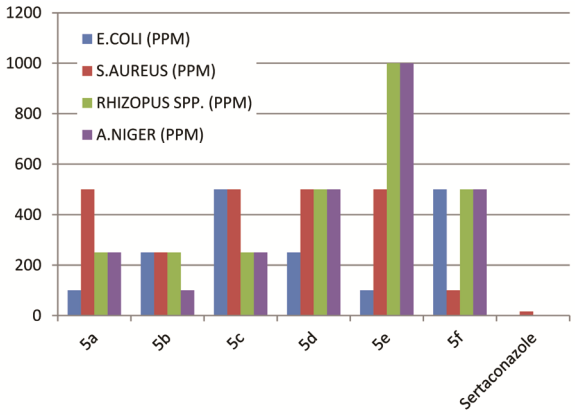


Fig. 1 — Comparison in MIC values of synthesized Schiff bases

PASS prediction

PASS prediction of synthesized compounds (**5a-f**) along with the standard sertaconazole were carried out. From this prediction set of antibacterial, antifungal, and complement factor D inhibitor results are shown in Table 1. The predicted results showed that new derivatives (**5a-f**) have a Pa range (0.232-0.342) for antibacterial, Pa range (0.265-0.300) for antifungal, and Pa range (0.530-0.702) for complement factor D inhibitor. While on comparison sertaconazole have Pa 0.431 as per Table 1. From this prediction study we may conclude that the new derivatives have less antifungal activity than sertaconazole with **5f** has high predicted antifungal activity among synthesized compounds.

Molecular Docking Study

The molecular docking analysis results showed that all the molecules exhibited good binding energies for (**5a-f**) compounds compared to standard Sertaconazole for three different proteins namely Carbonic anhydrase **(PDB ID**: **6LUX)**, Complement factor D **(PDB ID**: **5NB7)** and Fungal protein **(PDB ID**: **4M8B)** as per Table 2 and shows comparatively good docking energy values.

ADME study

Some of the physicochemical factors and pharmacokinetic signifiers were calculated through the online web tool SwissADME[33].

Physicochemical properties

For the design of new pharmacological compounds, physicochemical properties understanding is necessary. The Drug-likeness profile can be evaluated through these parameters of the molecule such as molecular weight, TPSA, number of heavy atoms, HBA (Hydrogen bond acceptor), HBD (Hydrogen bond donor), rotatable bonds, and molar refractivity. These parameters were calculated for compounds (**5a-f**) and Sertaconazole as per Table 3.

The drug-likeness profiles were also calculated based on Lipinski, (LogP ≤ 5; MW ≤ 500; HBA ≤ 10 and HBD ≤ 5), Ghose (160 ≤ MW ≤ 480; -0.4 ≤ WLogP ≤ 5.6; 40 ≤ MR ≤ 130 and 20 ≤ atoms ≤ 70), Veber (rotatable bonds ≤ 10 and TPSA ≤ 140), Egan (WLogP ≤ 5.88 and TPSA ≤ 131.6) and Muegge (200 ≤ MW ≤ 600; -2 ≤ XLogP ≤ 5; number of aromatic rings ≤ 7; number of heteroatoms > 1; number of rotatable bonds ≤ 15; HBA ≤ 10 and HBD ≤ 5) rules along with the prediction of bioactivity score. The

Table 1 — PASS prediction results of Schiff bases

Compd	Antibacterial		Antifungal		Complement factor D inhibitor	
	Pa	Pi	Pa	Pi	Pa	Pi
5a	0.287	0.065	0.275	0.093	0.702	0.018
5b	0.298	0.061	0.289	0.086	0.670	0.024
5c	0.258	0.079	0.265	0.098	0.547	0.053
5d	0.274	0.070	0.286	0.087	0.562	0.049
5e	0.342	0.045	0.294	0.083	0.530	0.059
5f	0.232	0.094	0.300	0.081	0.694	0.020
Sertaconazole	–	–	0.431	0.043	–	–

Table 2 — Molecular docking study

Compd	Docking energies (Kcal/mol)		
	PDB ID: 6LUX	PDB ID: 5NB7	PDB ID: 4M8B
5a	–6.5	–6.8	–8.1
5b	–6.1	–7.7	–8.2
5c	–6.2	–7.2	–7.9
5d	–5.4	–7.1	–7.8
5e	–7.7	–8.8	–9.6
5f	–7.2	–7.8	–8.7
Sertaconazole	–7.9	–8.6	–8.7

Table 3 — Physicochemical properties of compounds

Compd	Mol. Wt.	No. Heavy Atom	HBA	HBD	RB	Fraction Csp3	MR	TPSA Å^2
5a	253.32	18	2	1	2	0	77.54	60.83
5b	269.32	19	3	2	2	0	79.57	81.06
5c	283.34	20	3	1	3	0.06	84.04	70.06
5d	283.34	20	3	1	3	0.06	84.04	70.06
5e	298.32	21	4	1	3	0	86.37	106.65
5f	287.76	19	2	1	2	0	82.55	60.83
Sertaconazole	515.84	33	3	1	6	0.08	136.23	75.52

Table 4 — Drug likeness, bioactivity and synthetic accessibility score of compounds

Compd	Lipinski violations	Ghose violations	Veber violations	Egan violations	Muegge violations	Bio availability Score	Synthetic Accessibility
5a	0	0	0	0	0	0.55	2.44
5b	0	0	0	0	0	0.55	2.55
5c	0	0	0	0	0	0.55	2.61
5d	0	0	0	0	0	0.55	2.6
5e	0	0	0	0	0	0.55	2.62
5f	0	0	0	0	0	0.55	2.49
Sertaconazole	2	3	0	1	1	0.17	4.16

prediction results of these compounds showed that all the five rules were obeyed by them with a bioactivity score of 0.55 while sertaconazole had few violations with a bioactivity score of 0.17 (Table 4). Further, synthetic accessibility of the (**5a-f**) was assessed to quantify the complexity of the molecular structure. The results showed that the compounds do not have complex synthetic routes based on their score in the range of 2.44-2.62 while standard sertaconazole has 4.16 as per Table 4.

ADME Properties

For the molecules, nonaqueous solubility was calculated by using the consensus log Po/w from mean predicted lipophilicity values. As per the model, if consensus log Po/w values are more negative then the molecule is more soluble. From the results it is clear that molecules (**5a-f**) were not soluble in a non-aqueous medium (Table 5) and to predict the aqueous solubility log S scale was used: if log S < −10 - poorly soluble, < −6 - moderately soluble, < −4 - soluble, <

−2 - very soluble, and < 0 highly soluble. Based on this predictive model, compounds (**5a-f**) are moderately water-soluble while sertaconazole is predicted to be poorly water-soluble (Table 5).

Human gastrointestinal absorption measurement from this predictive result showed that all the derivatives (**5a-f**) have high and sertaconazole has low HIA absorption. Brain blood barrier (BBB) permeant parameters suggest that compounds **5b, 5e,** and sertaconazole have no BBB permeant while compounds **5a, 5c, 5d, and 5f** are blood-brain permeants which suggest there may be the possibility of causing harmful toxicants in the brain and bloodstream when metabolized as per Table 6. From the model, the skin permeability can predict and identify potential drugs for oral and transdermal administration. As per the model if a molecule has more negative log Kp value then the molecule is said to be less skin permeant. Based on this model all the compounds and sertaconazole were found to be the least skin permeable (Table 6).

Table 5 — Predicted absorption parameters of compounds

Compd	Consensus Log Po/w	Consensus Log S	Solubility class
5a	3.75	–4.87	Moderate
5b	3.38	–4.64	Moderate
5c	3.76	–4.97	Moderate
5d	3.81	–4.97	Moderate
5e	3.03	–5.08	Moderate
5f	4.29	–5.47	Moderate
Sertaconazole	6.38	–8.9	Poorly soluble

Table 6 — Predicted distribution parameters of compounds

Compd	GI absorption	BBB permeant	Log Kp (cm/s)
5a	High	Yes	–5.08
5b	High	No	–5.44
5c	High	Yes	–5.29
5d	High	Yes	–5.29
5e	High	No	–5.49
5f	High	Yes	–4.85
Sertaconazole	Low	No	–4.27

The permeability glycoprotein (P-gp) is an important protein that has a significant role in drug absorption and disposition. Hence, the compounds (**5a-f**) and sertaconazole were evaluated to determine whether the compound can act as a substrate or an inhibitor of P-gp, and results revealed that all compounds are found to be non-substrates of P-gp except sertaconazole compound. Molecule interaction with cytochrome P450 (CYP) enzymes is essential because these isoenzymes are involved in drug elimination through metabolic transformation. Inhibition of these isoenzymes may result in unwanted adverse side effects by lowering the solubility and the accumulation of the drug or its metabolites. Prediction reveals that the compounds (**5a-f**) act as a noninhibitor for CYP2D6 whereas acts as inhibitors of CYP2C19, CYP2C9, and CYP1A2 (except **5e**) (Table 7). Due to the inhibition of these enzymes, the newly synthesized compounds and sertaconazole may cause drug interactions and adverse effects due to less purification and accumulation of the drug[34].

Conclusions

In this research article, we have synthesized Schiff bases of Benzo[*b*]thiophene-5-amine with different derivatives of 2-hydroxybenzaldehyde to obtain **5a-f** compounds. By use of various spectral and physicochemical methods, their characterization has been confirmed. PASS prediction study revealed that compounds may act as antibacterial, antifungal, and complement factor D inhibitor agents among the plethora of predicted activity. A Molecular docking study shows good binding energies compared to standard compound sertaconazole. ADME, the study evaluates its drug-likeliness properties and suggests a few drawbacks as per the model. *In vitro*, the antibacterial and antifungal activity of synthesized compounds were investigated and were found to be active antimicrobial and antifungal. Comparison with *in vitro* results showed that new compounds have less probability to be more active antifungal activity than standard drug sertaconazole. In addition, between

Table 7 — Predicted metabolism parameters of compounds

Compd	P-gp	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor
5a	No	Yes	Yes	Yes	No	No
5b	No	Yes	Yes	Yes	No	Yes
5c	No	Yes	Yes	Yes	No	Yes
5d	No	Yes	Yes	Yes	No	Yes
5e	No	No	Yes	Yes	No	No
5f	No	Yes	Yes	Yes	No	No
Sertaconazole	Yes	Yes	Yes	Yes	Yes	Yes

synthesized compounds **5b** compound has the lowest value of MIC amongst all organisms on comparison.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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