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Computational Drug-Likeness Studies of Selected Thiosemicarbazones: A Sustainable Approach for Drug Designing †

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Abstract: Drug intake, its absorption in the body, removal, and various side effects are factors considered when designing the drugs. Here, the in silico tools act as virtual shortcuts, assisting in the prediction of several important physicochemical properties like polar surface area (PSA), molecular weight, and molecular flexibility, etc., to evaluate probable drug leads as potential drug candidates. These tools also play a vital role in the prediction of the bioactivity score of probable drug leads against various human receptors. This paper presents a virtual combinatorial library of selected thiosemicarbazones (TSCs) and their metal complexes. Different properties like bioactivity score, physicochemical, distribution, absorption, excretion, metabolism, and toxicity (ADMET) parameters were assessed. By using ChemDraw Ultra 12.0, the structures of ligands and complexes were drawn and downloaded in PDB format. Physicochemical parameters were calculated using online softwares viz. Molinspiration and SwissADME, and ADMET properties were calculated using admetSAR (2.0). Molecular docking was performed using PyRx Python Prescription 0.8. with Janus Kinase and Transforming Growth Factor Beta (Tgf-β). Janus Kinase and Tgf-β are some cytokines involved in cell development, proliferation, and cell death. Three important TSCs, i.e., salicyldehyde thiosemicarbazone, acenaphthenequinone thiosemicarbazone, 2-chloronicotinic thiosemicarbazone, and their virtually designed complexes exhibited appreciable in silico results. Most ligands and complexes had good bioactivity values against all the biological targets.

Keywords: thiosemicarbazones; in silico studies; bioactivity score; molecular docking; sustainability

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1. Introduction

TSCs have a significant position among Schiff-based ligands because of the presence of various donor atoms and their potential to modify their denticity. Structure–activity relationship studies have shown that a bulky group attached to the terminal nitrogen of the TSCs moiety improves the pharmacological activity [1,2]. Their activity is attributed to their ability to inhibit DNA biosynthesis, probably by blocking base replication, binding to the nitrogen bases of DNA, blocking the enzyme ribonucleotide diphosphate reductase, or causing DNA strands damage through oxidative rupture [3]. Various investigations have focused on transition metal ion complexes of TSCs [4]. These complexes exhibited a variety

of biological applications, such as anticancer [5], antibacterial, antiviral and antifungal activities [6]. An increasing number of studies have focused on heterocyclic TSC complexes. TSCs are thiourea derivatives, and their biological properties are influenced by the parent aldehyde or ketone [7]. They also exhibit second-order nonlinear optical properties used in optical frequency conversion [8] and optical parameter oscillators [9]. TSCs may provide a wide range of coordination modes when used as ligands [10]. The ability to chelate metal is a promising strategy for developing anticancer drugs due to the high demand for essential metals in neoplastic cells for growth and proliferation [11]. Schiff base ligands derived from TSCs and their complexes have gained significant attention due to their medicinal properties [12]. Ni(II) and Fe(III) complexes using S-methyl-thiosemicarbazone of 2-hydroxy-R-benzaldehyde were tested against different cell lines. The Ni-substituted chelates exhibited improved cytotoxicity against K562 and ECV304, whereas Fe displayed strong cytotoxicity against K562 [13]. Activity alterations have been noticed when structural modifications were made in the reacting aldehyde and ketone moiety, the coordinating sites of the thione group, and the position of the isoquinoline/pyridine moiety in α-N heterocyclic TSCs. N-4 substituted TSCs exhibited increased activity against a variety of cancerous cell lines. Due to their poor water solubility, their effectiveness in vivo is limited and requires structural modifications [14]. Ionic and neutral copper bis(thiosemicarbazone) complexes with different substituents have been tested, and it has been observed that bis copper chelates derived from glyoxalbis(4-methyl-4-phenyl-3-thiosemicarbazone) were active against various cancer cell lines and also inhibited DNA synthesis [15].

2. Materials and Methods

Using ChemDraw Ultra 12.0, the structures of ligands and complexes were drawn and downloaded in PDB format. Physicochemical parameters were calculated using online softwares viz. Molinspiration and SwissADME, and ADMET properties were computed using admetSAR (2.0). PyRx Python Prescription 0.8 was used to perform molecular docking.

3. Results and Discussion

3.1. Combinatorial Library of Selected TSCs

Virtual screening of 12 TSCs was performed to assess their drug likeliness, bioactivity scores and ADMET properties. The TSCs of substituted aldehydes and ketones were selected for the activity as they are associated with promising medicinal importance. For substitution, both electron-withdrawing and electron-donating groups were considered. The common names and molecular formulas of the complexes are given in Table 1.

Table 1. Common names of the selected TSC ligands for virtual screening.

S. No.	Chemical Formula	Name of the Ligand
1	$C_6H_{11}N_3OS$	Acetyl-acetone thiosemicarbazone
2	$C_8H_9N_3S$	Benzaldehyde thiosemicarbazone
3	$C_9H_{11}N_3O_2S$	Vanillin thiosemicarbazone
4	$C_8H_7Cl_2N_3S$	2,4-dichlorobenzaldehyde thiosemicarbazone
5	$C_8H_7Cl_2N_3S$	2,6-dichlorobenzaldehyde thiosemicarbazone
6	$C_{10}H_{14}N_4S$	4-(dimethylamine) benzaldehyde thiosemicarbazone

Table 1. *Cont.*

S. No.	Chemical Formula	Name of the Ligand
7	$C_9H_{11}N_3S$	Acetophenone thiosemicarbazone
8	$C_{10}H_{10}N_4S$	Indole-3-carboxaldehyde thiosemicarbazone
9	$C_2H_5N_3S$	Formaldehyde thiosemicarbazone
10	$C_8H_9N_3OS$ (L_1)	Salicylaldehydethiosemicarbazone
11	$C_{13}H_7N_3OS$ (L_2)	Acenaphthenequinonethiosemicarbazone
12	$C_7H_7ClN_4OS$ (L_3)	2-chloronicotinic acid thiosemicarbazone

3.1.1. Pharmacokinetic Parameters

Using the Molinspiration and SwissADME softwares, the pharmacokinetic characteristics of the produced TSC ligands and their metal complexes were determined. Many properties, like molecular weight, clogP, TPSA, number of hydrogen bond donors/acceptors, etc., were determined to evaluate the compounds' potential as lead candidates. Lipinski's filter was used to evaluate the compounds' bioavailability. According to Lipinski's rule of five, a molecule having a molecular weight of less than 500 is more likely to be an oral medication [16]. The odds of an obeying candidate being an orally active medicine are higher, although the regulations do not specifically look into metabolism. According to Molinspiration software, the results for salicylaldehyde thiosemicarbazone, acenaphthenequinone thiosemicarbazone, 2-chloronicotinic thiosemicarbazone, and their metal complexes, the Lipinski's filter showed that maximum complexes had fewer than two violations, suggesting that they may potentially be lead compounds. Complexes' higher molecular weight brought on the majority of violations. The partition coefficient (cLogP) determines the compound hydrophilicity, which results in poor absorption and permeation [17]. The value of clogP should not exceed 5.0, and all the complexes had clogP values that were smaller than 4.15, suggesting high oral bioavailability (Table 2). Increased invasion speed has been linked to low polar surface area (PSA) [18]. High PSA levels have been shown to have a deleterious impact on intestinal absorption [19]. A significant consideration when administering medication orally in the absence of active passage is membrane permeability. The PSA was determined using a formula used in an earlier study [20]. The ligands and majority of complexes' TPSA, which was under 140 $Å^2$, and the proportion of donor/acceptor atoms for hydrogen bonds were similarly within the range [21].

Chemical substances known as Pan Assay Interference Compounds (PAINS) are responsible for false positives in high-throughput screening (HTS). PAINS often exhibited non-specific reactions with several biological targets before selectively disrupting the desired target [22]. According to data from the SwissADME analysis (Table 3), the PAIN warning for most complexes was 1, meaning there is little possibility that these complexes would produce biological activity for incorrect reasons. Through SwissADME, another significant element, fractional Csp^3, was also estimated. The odds of the chemical being successful in a clinical setting improve by adding sp^3 characters. To determine the complexes' drug-likeness, $FCsp^3$ was computed. The lead candidate will perform better if $FCsp^3$ is higher [23]. The ability to synthesize a molecule is a significant factor in drug design since occasionally compounds developed by computer software cannot be produced so. Typically, the top candidates are evaluated using standards like drug likeness or expected activity [24]. Swiss ADME also predicted the synthetic accessibility of the complexes, and it was found that most of them had accessibility scores between 2 and 5, indicating that they can be easily prepared.

Table 2. Pharmacokinetic parameters of the selected TSCs and metal complexes.

S. No.	Compound	Volume	TPSA	MW	M Log p	nOHNH	nON	nRB
1	$C_6H_{11}N_3OS$	156.35	67.48	173.24	0.02	3	4	4
2	$C_8H_9N_3S$	158.86	50.41	179.25	1.88	3	3	3
3	$C_9H_{11}N_3O_2S$	192.42	79.88	225.27	1.22	4	5	4
4	$C_8H_7Cl_2N_3S$	185.93	50.41	248.14	3.17	3	3	3
5	$C_8H_7Cl_2N_3S$	185.93	50.41	248.14	3.14	3	3	3
6	$C_{10}H_{14}N_4S$	284.76	53.65	222.32	1.99	3	4	4
7	$C_9H_{11}N_3S$	175.42	50.41	193.28	1.80	3	3	3
8	$C_{10}H_{10}N_4S$	187.83	66.20	218.28	2.03	4	4	3
9	$C_2H_5N_3S$	87.76	50.41	103.15	0.23	3	3	2
10	$C_8H_9N_3OS$ (L_1)	166.87	70.64	195.25	1.82	4	4	3
11	$C_{13}H_7N_3OS$ (L_2)	210.99	67.48	255.30	2.48	3	4	2
12	$C_7H_7ClN_4OS$ (L_3)	176.25	83.53	230.68	0.51	4	5	3
13	$[Fe(L_1)_2]SO_4$	428.39	201.43	617.30	−1.44	8	14	4
14	$[Co(L_1)_2]Cl_2$	398.10	123.03	524.37	2.61	8	8	4
15	$[Cu(L_1)_2]SO_4$	409.58	175.64	554.13	0.18	8	12	4
16	$[Zn(L_1)_2]SO_4$	409.58	175.64	555.98	0.90	8	12	4
17	$[Fe(L_2)_2]SO_4$	497.87	169.33	666.54	1.38	6	12	2
18	$[Co(L_2)_2]Cl_2$	486.38	116.72	644.48	4.09	6	8	2
19	$[Cu(L_2)_2]SO_4$	497.87	169.33	674.25	1.66	6	12	2
20	$[Zn(L_2)_2]SO_4$	497.87	169.33	676.09	2.38	6	12	2
21	$[Fe(L_3)_2]SO_4$	428.39	201.43	617.30	−1.44	8	14	4
22	$[Co(L_3)_2]Cl_2$	416.91	148.82	595.23	1.27	8	10	4
23	$[Cu(L_3)_2]SO_4$	428.39	201.43	625.00	−1.16	8	14	4
24	$[Zn(L_3)_2]SO_4$	428.39	201.43	626.85	−0.44	8	14	4

TPSA = topological polar surface area; Log p = logarithm of the partition coefficient of a compound between n-octanol and water; MW = molecular weight; OHNH = number hydrogen bond donors; ON = number hydrogen bond acceptors; nRB = number of rotatable bonds.

Table 3. Drug-likeness of the selected TSCs and metal complexes.

S. No.	Compound	Physiochemical Properties		Medicinal Feasibility	
		FRACTION Csp^3	Molar Refractivity	PAINS	Synthetic Accessibility
1	$C_6H_{11}N_3OS$	0.50	48.14	0 alert	2.92
2	$C_8H_9N_3S$	0.00	53.20	0 alert	2.17
3	$C_9H_{11}N_3O_2S$	0.11	61.72	1 alert	2.24
4	$C_8H_7Cl_2N_3S$	0.00	63.22	0 alert	2.43
5	$C_8H_7Cl_2N_3S$	0.00	63.22	0 alert	2.39
6	$C_{10}H_{14}N_4S$	0.20	67.41	0 alert	2.17
7	$C_9H_{11}N_3S$	0.11	58.01	0 alert	2.13
8	$C_{10}H_{10}N_4S$	0.00	65.06	0 alert	2.12
9	$C_2H_5N_3S$	0.00	28.71	0 alert	2.83
10	$C_8H_9N_3OS$ (L_1)	0.00	55.22	1 alert	2.21
11	$C_{13}H_7N_3OS$ (L_2)	0.00	73.98	1 alert	2.68
12	$C_7H_7ClN_4OS$ (L_3)	0.00	57.58	0 alert	2.28
13	$[Fe(L_1)_2]SO_4$	0.25	131.03	1 alert	5.70
14	$[Co(L_1)_2]Cl_2$	0.25	131.61	1 alert	5.59
15	$[Cu(L_1)_2]SO_4$	0.25	131.03	1 alert	5.60
16	$[Zn(L_1)_2]SO_4$	0.25	131.03	1 alert	5.55
17	$[Fe(L_2)_2]SO_4$	0.15	168.55	0 alert	6.56
18	$[Co(L_2)_2]Cl_2$	0.15	169.12	0 alert	6.48
19	$[Cu(L_2)_2]SO_4$	0.15	168.55	0 alert	6.45
20	$[Zn(L_2)_2]SO_4$	0.15	168.55	0 alert	6.44
21	$[Fe(L_3)_2]SO_4$	0.29	134.92	0 alert	5.90
22	$[Co(L_3)_2]Cl_2$	0.29	135.49	0 alert	5.76
23	$[Cu(L_3)_2]SO_4$	0.29	134.92	0 alert	5.83
24	$[Zn(L_3)_2]SO_4$	0.29	134.92	0 alert	5.82

3.1.2. ADMET Properties

Since experimental evaluation is a time-consuming and expensive procedure, computational algorithms that can isolate and filter ADMET features have been applied. By

using admetSAR, the ADMET characteristics of the ligand and complexes were determined (Table 4). The majority of an oral drug's absorption occurs in the gut, and a good medicinal compound should be capable of being absorbed by the gut. The positive value of all the complexes indicated their absorption in the bloodstream because human intestinal absorption (HIA) measures a drug compound's capacity to be absorbed by the gut. Almost all the ligands and complexes had positive blood–brain barrier (BBB) values, indicating they had appropriate brain penetration characteristics. Human epithelial cancer cell line Caco-2 is frequently utilized as a model for how the human digestive tract absorbs medicines and other substances. Caco-2 favorable test findings suggest excellent permeability. For several transcellular routes and metabolic transformations of test chemicals, Caco-2 cells produce transporters, phase II conjugation enzymes, and efflux proteins [25].

Table 4. ADMET properties of the selected TSCs and metal complexes.

S. No.	Compound	HIA	Caco-2	BBB	HOB
1	$C_6H_{11}N_3OS$	(+) 0.9342	(−) 0.6104	(+) 0.9793	(+) 0.6857
2	$C_8H_9N_3S$	(+) 0.9692	(+) 0.9335	(−) 0.9828	(+) 0.8000
3	$C_9H_{11}N_3O_2S$	(+) 0.9785	(+) 0.7591	(+) 0.9731	(+) 0.6286
4	$C_8H_7Cl_2N_3S$	(+) 0.9694	(+) 0.8509	(+) 0.9773	(+) 0.7000
5	$C_8H_7Cl_2N_3S$	(+) 0.9694	(+) 0.9434	(+) 0.9773	(+) 0.8857
6	$C_{10}H_{14}N_4S$	(+) 0.9700	(+) 0.8595	(+) 0.9775	(+) 0.6857
7	$C_9H_{11}N_3S$	(+) 0.9948	(+) 0.8765	(+) 0.9844	(+) 0.7429
8	$C_{10}H_{10}N_4S$	(+) 0.9729	(+) 0.7011	(+) 0.9729	(+) 0.6571
9	$C_2H_5N_3S$	(+) 0.9014	(+) 6085	(+) 0.9844	(+) 0.7286
10	$C_8H_9N_3OS$ (L_1)	(+) 0.9698	(+) 0.8413	(+) 0.9732	(+) 0.7571
11	$C_{13}H_7N_3OS$ (L_2)	(+) 0.9921	(+) 0.6885	(+) 0.9749	(+) 0.7143
12	$C_7H_7ClN_4OS$ (L_3)	(+) 0.9910	(+) 0.5565	(+) 0.9748	(+) 0.8571
13	$[Fe(L_1)_2]SO_4$	(+) 0.9562	(−) 0.7028	(+) 0.9704	(+) 0.5857
14	$[Co(L_1)_2]Cl_2$	(+) 0.9605	(−) 0.6077	(+) 0.9730	(+) 0.6571
15	$[Cu(L_1)_2]SO_4$	(+) 0.9562	(−) 0.7028	(+) 0.9704	(+) 0.5143
16	$[Zn(L_1)_2]SO_4$	(+) 0.9562	(−) 0.7028	(+) 0.9704	(+) 0.6143
17	$[Fe(L_2)_2]SO_4$	(+) 0.9829	(−) 0.7916	(+) 0.9689	(+) 0.5429
18	$[Co(L_2)_2]Cl_2$	(+) 0.9847	(−) 0.7685	(+) 0.9729	(+) 0.6000
19	$[Cu(L_2)_2]SO_4$	(+) 0.9829	(−) 0.7916	(+) 0.9689	(−) 0.5000
20	$[Zn(L_2)_2]SO_4$	(+) 0.9829	(−) 0.7916	(+) 0.9689	(+) 0.6286
21	$[Fe(L_3)_2]SO_4$	(+) 0.9463	(−) 0.7818	(+) 0.9688	(+) 0.6000
22	$[Co(L_3)_2]Cl_2$	(+) 0.9515	(−) 0.7468	(+) 0.9722	(+) 0.6143
23	$[Cu(L_3)_2]SO_4$	(+) 0.9463	(−) 0.7818	(+) 0.9688	(−) 0.5000
24	$[Zn(L_3)_2]SO_4$	(+) 0.9463	(−) 0.7818	(+) 0.9688	(+) 0.5714

HIA = human intestinal absorption; Caco-2 = cell permeability; BBB = blood–brain barrier; HOB = human oral bioavailability.

3.1.3. Bioactivity Score

By using the Molinspiration Cheminformatics program, bioactivity score prediction was further assessed with GPCR ligands, kinase inhibitors, ion channel modulators, enzyme inhibitors, protease inhibitors, and nuclear receptor ligands. G-protein-coupled receptors (GPCRs) are also called heptahelical receptors, serpentine receptors, and seven-pass transmembrane domain receptors [26]. Ion channels are modulated by drugs known as channel

modulators or ion channel modulators. They consist of channel openers and blockers [27]. An enzyme inhibitor known as a protein kinase inhibitor prevents one or more protein kinases from working. Protein kinases are enzymes that modify a protein's function by adding a phosphate (PO_4^{3-}) group to it. In molecular biology, nuclear receptors are defined as a group of proteins that are present in cells and are in charge of regulating the expression of particular genes, which in turn regulate the metabolism, homeostasis, and growth of the organism [28]. Table 5 shows the bioactivity ratings for each suggested complex. Generally, the possibility that the molecule under research will be active increases as the bioactivity score increases. Therefore, a molecule with a bioactivity score of more than 0.0 is likely to exhibit significant biological activities, whilst scores between −5.0 and 0.0 are predicted to be moderately active, and scores below −5.0 are assumed to be inert. Most of the ligands and complexes exhibited good bioactivity scores against all the biological targets.

Table 5. The bioactivity scores of the selected TSCs and metal complexes.

S. No.	Compound	Parameters of Bioactivity Score					
		GPCR Ligand	Ion Channel Modulator	Kinase Inhibitor	Nuclear Receptor Ligand	Protease Inhibitor	Enzyme Inhibitor
1	$C_6H_{11}N_3OS$	−2.60	−1.86	−3.10	−2.98	−1.88	−1.04
2	$C_8H_9N_3S$	−2.85	−1.59	−1.86	−2.42	−1.60	−0.91
3	$C_9H_{11}N_3O_2S$	−1.51	−1.25	−1.30	−1.67	−1.26	−0.59
4	$C_8H_7Cl_2N_3S$	−1.72	−1.35	−1.53	−2.08	−1.40	−0.77
5	$C_8H_7Cl_2N_3S$	−1.62	−1.30	−1.55	−2.01	−1.33	−0.71
6	$C_{10}H_{14}N_4S$	−1.48	−1.21	−1.24	−1.70	−1.17	−0.62
7	$C_9H_{11}N_3S$	−1.83	−1.42	−1.93	−1.96	−1.22	−0.70
8	$C_{10}H_{10}N_4S$	−1.14	−1.04	−1.04	−1.66	−1.07	−0.41
9	$C_2H_5N_3S$	−4.01	−3.94	−3.96	−4.07	−3.74	−3.72
10	$C_8H_9N_3OS$ (L_1)	−1.79	−1.55	−1.63	−1.99	−1.33	−0.74
11	$C_{13}H_7N_3OS$ (L_2)	−0.94	−0.94	−0.96	−1.21	−1.02	−0.43
12	$C_7H_7ClN_4OS$ (L_3)	−1.41	−0.69	−1.24	−1.79	−1.04	−0.46
13	$[Fe(L_1)_2]SO_4$	0.21	−0.04	−0.05	−0.07	0.18	0.11
14	$[Co(L_1)_2]Cl_2$	0.06	−0.03	−0.04	−0.07	0.05	0.01
15	$[Cu(L_1)_2]SO_4$	0.16	−0.04	−0.05	−0.07	0.18	0.16
16	$[Zn(L_1)_2]SO_4$	0.16	−0.04	−0.05	−0.07	0.18	0.23
17	$[Fe(L_2)_2]SO_4$	0.11	−0.47	−0.33	−0.38	0.06	−0.10
18	$[Co(L_2)_2]Cl_2$	0.04	−0.24	−0.20	−0.25	−0.05	−0.11
19	$[Cu(L_2)_2]SO_4$	0.07	−0.47	−0.33	−0.38	0.06	−0.12
20	$[Zn(L_2)_2]SO_4$	0.07	−0.47	−0.33	−0.38	0.06	−0.06
21	$[Fe(L_3)_2]SO_4$	0.25	0.12	0.04	−0.14	0.20	0.22
22	$[Co(L_3)_2]Cl_2$	0.12	0.15	0.06	−0.15	0.08	0.05
23	$[Cu(L_3)_2]SO_4$	0.20	0.12	0.04	−0.14	0.20	0.19
24	$[Zn(L_3)_2]SO_4$	0.20	0.12	0.04	−0.14	0.20	0.26

3.2. Molecular Docking Studies

Target proteins and ligands were docked with PyRx (Python Prescription 0.8). PyRx is a computational drug discovery software used to virtually screen compound libraries against potential therapeutic targets. Docking was performed with two proteins. Janus Kinase and Tgf-β are cytokines that are crucial in cell growth, proliferation, and apoptosis [29–31]. The binding energy values were taken from the nine ligands and protein molecule poses where the chosen pose displayed a zero RMSD value. A greater negative number from the perspective of binding stability denotes a stronger binding affinity for a protein receptor. Higher binding affinities demonstrated that ligands suit the active site of proteins the best [32,33]. It was found that the affinity of the binding of TGFβ increased towards L2 in

the coordinated Fe(II) complex, showing a binding energy of −8.4 kJ/mol. The binding affinity of Co(II) and Cu(II) complexes toward Janus Kinase was high, particularly upon coordination with L3, exhibiting a binding energy of −7.5 and −7.4 kJ/mol, respectively. The docking results are summarized in Table 6.

Table 6. Predicted binding energies (kJ/mol) of the selected TSCs and metal complexes.

S. No.	Chemical Formula	Binding Energy (kJ/mol) Against Target Protein	
		Transforming Growth Factor Beta	Janus Kinase
1.	$C_6H_{11}N_3OS$	−5.1	−5.3
2.	$C_8H_9N_3S$	−6.2	−6.2
3.	$C_9H_{11}N_3O_2S$	−6.2	−6.6
4.	$C_8H_7Cl_2N_3S$	−6.6	−6.4
5.	$C_8H_7Cl_2N_3S$	−6.3	−6.7
6.	$C_{10}H_{14}N_4S$	−6.1	−6.3
7.	$C_9H_{11}N_3S$	−6.5	−6.3
8.	$C_{10}H_{10}N_4S$	−7.0	−7.0
9.	$C_2H_5N_3S$	−4.1	−3.9
10.	$C_8H_9N_3OS$ (L_1)	−6.1	−6.3
11.	$C_{13}H_7N_3OS(L_2)$	−7.8	−8.5
12.	$C_7H_7ClN_40S(L_3)$	−6.1	−6.3
13.	$[Fe(L_1)_2]SO_4$	−6.5	−7.8
14.	$[Co(L_1)_2]Cl_2$	−6.3	−6.1
15.	$[Cu(L_1)_2]SO_4$	−6.3	−6.7
16.	$[Zn(L_1)_2]SO_4$	−6.3	−6.3
17.	$[Fe(L_2)_2]SO_4$	−8.4	−7.6
18.	$[Co(L_2)_2]Cl_2$	−6.3	−6.2
19.	$[Cu(L_2)_2]SO_4$	−5.1	−7.1
20.	$[Zn(L_2)_2]SO_4$	−6.2	−6.2
21.	$[Fe(L_3)_2]SO_4$	−6.2	−6.2
22.	$[Co(L_3)_2]Cl_2$	−6.5	−7.5
23.	$[Cu(L_3)_2]SO_4$	−7.0	−7.4
24.	$[Zn(L_3)_2]SO_4$	−6.3	−6.1

4. Conclusions

The paper has also highlighted the significance of virtual screening and computational drug designing, which is cost- and time-effective. Although TSC complexes have received considerable attention for their pharmaceutical utility, the complexes exhibit some undesirable properties like poor water solubility, which makes them unfavorable to cross cell membranes. Studies involving structure–activity relationship (SAR) and quantitative structure–activity relationship (QSAR) must be undertaken to gain insight into the influence of structural modification upon activity.

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