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A SYNTHESIS OF IMIDAZOLE-BASED CARBOTHIOAMIDES VIA CONDENSATION FOR THEIR PHARMACOLOGICAL EVALUATION

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ABSTRACT

The current research work indicates the novel imidazole carbothioamide derivatives (5a–5e) as promising heterocycles with varied biological activities and suitable for drug discovery aimed at developing novel antimicrobial therapeutics. This is carried out through a combination of techniques and strategies, including synthesis, characterisations, bioactive testing, molecular modelling, and prediction of ADME and toxicity parameters. These novel scaffolds have excellent potential as useful candidates for overcoming microbial resistance because they have strong inhibitory effects on clinically important microorganisms like *Salmonella typhimurium*, *Escherichia coli*, *Bacillus megaterium*, *Staphylococcus aureus*, and *Aspergillus niger*. In addition, these scaffolds have good binding properties with the human topoisomerase IIα–DNA–etoposide, which makes it possible to suggest an interesting mechanism of action and study their anticancer activity. From an academic perspective, the current research advances the field of medicinal chemistry by identifying innovative biologically active derivatives derived from imidazole and carbothoamide moieties. From a practical standpoint, it may yield significant insights into the advancement of safe and effective antimicrobial pharmaceuticals. It is highly recommended that future studies of the promising findings focus on creating new compounds by improving SAR and studying how they stop enzymes from working, as well as doing pharmacology studies in living things.

Keywords: Carbothioamide Scaffolds Synthesis, Pharmacological Activity, Cellular Level Cytotoxicity, *In Silico* Molecular Docking Study, Pro-Tox, Anti-Bacterial Activity

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INTRODUCTION

Carbothioamide was initially prepared during the 19th century, and its analogues were quickly found to exhibit a potent role in the pharmacophore industry for drug discovery.[1,2] Carbothioamide and imidazole scaffolds have been emphasised in the recent research on antimicrobial, antibacterial and antifungal studies. A series of novel phenylthiourea derivatives was indicated to have an inhibitory effect on the *Staphylococcus* and *Aspergillus* strains at low MIC.s[2] In addition, complex thiourea hybrids are sub-mu/mg/L potent against resistant *S. aureus, B. subtilis*, and *P. aeruginosa.*[2] Complementarily, imidazole heterocycles are also common drug motifs: the five-member electron-rich ring is easy to bind to enzymes and receptors, and imidazole-based drugs have extensive bioactivities.[3a] Imidazole cores are found in a lot of antifungal agents and antibacterial leads. It is observed in reviews that several imidazole derivatives have been created with strong antibacterial and antifungal actions.[3b] Indeed, when imidazole moiety-bearing hybrid molecules are reported, they have been found to increase their antibacterial effect.[2,3] Collectively, these developments demonstrate that thiourea and imidazole chemotypes also have room to continue their exploration to find new antimicrobial agents.

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The necessity of new antimicrobials and antifungals is explained by the tendency of resistance around the globe. Antimicrobial resistance has become one of the leading global health problems. Most current studies indicate that already millions of infections and deaths are linked to drug-resistant bacteria, and the number of people affected by them will skyrocket by 2050 unless new drugs are developed.[4] Similarly, there is the increasing antifungal resistance: e.g., another fungal pathogen, *Candida auris,* is spreading in hospitals, and the majority of its strains are also resistant to all three major antifungal classes. *C. auris* is a problematic fungus to the extent that it is declared a critical fungal pathogen by the WHO[5]. These tendencies indicate significant gaps: most popular antibiotics and azole antifungals are becoming less effective, and there are acute requirements for new scaffolds with new mechanisms of action. To overcome resistance, a molecular hybridisation strategy was adopted by combining carbothioamide and imidazole moieties to create dual-action compounds with synergistic effects. The present work directly aligns with SDG-3: Good health and Well-Being. The present study aimed to design and synthesise novel carbothioamide–imidazole hybrid compounds (5a–5e) through molecular hybridisation and evaluate them for antimicrobial activity using MIC against Gram-positive, Gram-negative bacteria, and pathogenic yeasts. Cytotoxicity was assessed using *Schizosaccharomyces pombe,* and molecular docking studies against human topoisomerase IIα (PDB ID: 5GWK) were performed to explore possible mechanisms, while in silico analyses using SwissADME and ProTox-3.0 predicted pharmacokinetic and toxicity profiles, providing a comprehensive evaluation of the compounds.[6,7]

EXPERIMENTAL

Material and Methods

The synthesised compounds were initially assessed for purity by melting point determination using the open capillary method. Structural characterisation was performed using IR spectroscopy (4000–400 cm^{-1}, KBr pellet), ^1H NMR (400 MHz, DMSO-d_6, TMS as reference), and mass spectrometry (GC-MS and LC/MS). The percentage purity, along with progress in the reaction, was further confirmed by TLC with UV detection.

General Procedure

Synthesis of chalcones (3a–3e)

The target compounds imidazole chalcones (3a-3e) were synthesised via the condensation of chlorobutyl-substituted carboxaldoimidazole with the corresponding aryl aldehydes in the presence of 20% NaOH. The reaction completed with a good yield of 77% and 87 °C melting point. The elemental analysis results were in close agreement with the theoretical values. Calculated %: C 64.04; H 6.02; N 8.79; $C_{17}H_{19}ClN_2O_2$; Found %: C 64.06; H 6.03; N 8.80. IR (cm^{-1}): 2968 (CH); 2865 (CH); 3060 (CH); 1558 (C=C); 1166 (CH); 751 (CH); 1220 (CN); 1515 (C=N); 3415 (NH); 1600 (NH); 1653 (C=O); 1459 (vinyl); 728 (C-Cl); 1250 (ether). ^1H NMR δ/ppm: 0.9 (3H, t, CH_3); 1.2-1.3 (2H, m, CH_2); 1.5-1.6 (2H, m, CH_2); 2.6 (2H, t, CH_2); 12.8 (1H, s, NH); 7.4 (1H, d, Vinylic H) 7.6 (1H, d, Vinylic H); 7.1 (2H, d, Aromatic H); 8.0 (2H, d Aromatic H); 3.8 (3H, s, Methoxy H). Mass (m/z): 320.

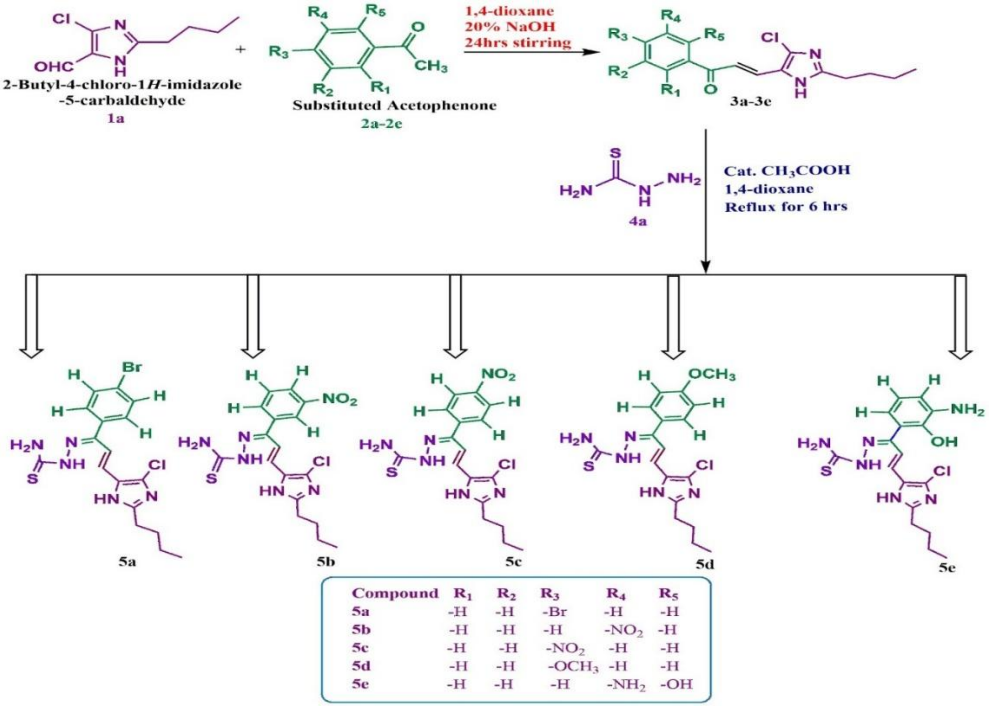
Synthesis of carbothioamide derivatives (5a-5e)

Novel imidazolyl carbothioamide derivatives (5a–5e) was synthesised via the condensation of imidazole chalcone with thiosemicarbazide in HAc and 1,4-dioxane. The complete synthesis of carbothioamides (5a–5e) is outlined in Scheme-1.

Spectral Analysis of 4-bromophenyl-3-(2-n-butyl-4-chloro-1H-imidazol-5-l)allylidene)hydrazine-1-carbothioamide (5a)

Brown powder, yield 90%, Melting point: 110-115°C, MW: 439, Calculated %: C 46.32; H 4.34; Br 18.13; Cl 8.04; N 15.89; S 7.27%. $C_{17}H_{19}BrClN_5OS$ Found %: C 46.31; H 4.35; Br 18.11; Cl 8.06; N 15.91; S 7.26 %. *FT-IR (cm^{-1}):* 2957 (CH); 2857 (CH); 1440 (CH); 3205 (CH); 1640 (C=C); 1172 (CH); 792 (CH); 1595 (CN); 1546 (C=N); 3574 (NH); 1511 (NH); 1401 (C=C Vinyl); 747 (CBr); 697 (CCl). *Proton NMR δ/ppm:* 0.89-1.29 (3H, t, CH_3), 1.31-1.39 (2H, q, CH), 1.63-1.71 (2H, q, CH_2), 2.65-2.69 (2H, t, CH_2), 7.12-7.13 and 8.01-8.03 (4H, dd, aromatic H), 7.40-7.65 (2H, d, vinyl H), 3.37 (2H, s, NH_2) 10.03 (1H, s, NH), 12.80 (1H, s, imidazole H). *Mass (m/z):* (M^+) 440.8 Approaches and process.

Characterised via proton NMR, Fourier Transform-Infrared, and Mass spectra of novel carbothioamides (5a-5e) have been shown in Supplementary Material 1. The biological evaluation of novel carbothioamides (5a–5e), as presented in Supplementary Material 2, includes *in vitro* cell viability and cytotoxicity assays against *S. pombe* cells, antibacterial and antifungal activity studies, in silico molecular docking analysis, as well as assessment of ADME and toxicity parameters in *Homo sapiens*.



Compound	R_1	R_2	R_3	R_4	R_5
5a	-H	-H	-Br	-H	-H
5b	-H	-H	-H	$-NO_2$	-H
5c	-H	-H	$-NO_2$	-H	-H
5d	-H	-H	$-OCH_3$	-H	-H
5e	-H	-H	-H	$-NH_2$	-OH

Scheme-1: General reaction of synthesised carbothioamide derivative compounds (5a-5e).

RESULTS AND DISCUSSION

Chemistry

The n-butyl chain present in 5a-5e was confirmed by the existence of a triplet signal of methyl protons (-CH_3) in ^{1}H NMR spectra at 0.899-1.298 ppm. Methylene protons exhibiting pentet signal of the n-butyl chain (-CH_2-CH_3) were found at 1.316-1.391 ppm, pentet signal is assigned to methylene protons next to 1st methylene group (-CH_2-CH_2-CH_3) at 1.635-1.710 ppm, triplet signal assigned to methylene protons attached to the imidazole moiety (-CH_2-CH_2-CH_2-CH_3) existed at 2.659-2.697 ppm. Aromatic protons resonated in the range of 7.120-8.036 ppm, and vinyl protons (-CH=CH-) resonated as doublets at 7.404-7.652 ppm. Separate singlets corresponding to protons associated with the carbothioamide and imidazole, i.e. -NH and -NH_2 at 10.003 to 12.89 ppm respectively, and a singlet signal was observed due to -NH_2 of carbothioamide existed at 3.377 ppm, also a singlet signal of -OCH_3 proton appeared at 3.877, and additional singlets of -OH at 7.001 ppm and -NH_2 at 5.001 ppm were seen in the substituted analogue. ^{1}H NMR spectra of the synthesised compounds (5a-5e) are shown in Supplementary material 3. FT-IR (cm^{-1}) spectra of all derivatives showed typical absorptions of aliphatic -CH stretching (2955-2857), aromatic CH stretching (3055), C=C aromatic ring skeletal (16022), carbothioamide group NH stretching (3531-3300), C=N stretching (1650-1430), CN stretching (1559-1560), NH bending (1524-1400) and C=C vinyl (1422). The methoxy substituent of (5d) exhibited Symmetric stretching at 1228 cm^{-1}. Symmetric stretching of the nitro NO_2 substituent of 5b and 5c is found at 1341. Specific to the substituent, OH stretching in hydroxy derivatives (5e) at ~3500, and amino derivatives (5e) at ~3300-3500 were observed, CCl stretching in chloro derivatives (5a-5e) at ~698-701. FT-IR spectra of the synthesised compounds (5a-5e) are represented in Supplementary material 4. The molecular ion peaks (M^+) in mass spectra of all compounds correspond to their molecular formulas (e.g., m/z 440.8 for 5a, 406.9 for 5b/5c, 391.9 for 5d, 392.9 for 5e) and are evidence of the proposed structures. Mass spectra of the synthesised compounds (5a-5e) have been represented in Supplementary Material 5.

Pharmacological Application

In Vitro* Cell Viability and Cytotoxicity Assay against *Schizosaccharomyces Pombe

The synthesised carbothioamide derivative heterocyclic moieties have been assessed using in vitro cytotoxicity against *S. Pombe* cells (5a–5e). Potency is influenced by various functional group types and amounts of produced carbothioamide derivative heterocyclic moieties (5a-5e). Compared to chemicals 5a and 5b (4-Br and 3-NO_2), compounds 5c, 5d, and 5e (4-NO_2, 4-OCH_3, and 2-OH, 3-NH_2) are shown to be exceptionally poisonous. Synthesised carbothioamide derivative heterocyclic moieties (5a–5e) have an in vitro cytotoxicity potency comparable to that of the common medication ciprofloxacin. Because the chemicals are poisonous, many *S. Pombe* cells are destroyed within 17 to 20 hours of treatment. The synthesised compound's cytotoxicity order is ciprofloxacin > 5c > 5e > 5d >5b > 5a > DMSO > untreated cell. Table-1 illustrates the influence of synthesised carbothioamide derivative heterocyclic moieties (5a–5e) on the proportion of *S. Pombe* cells that survive at various concentrations (µM), with an error uncertainty of ± 5%.

Table-1: Proves Effect of Synthesised Carbothioamide Derivative Heterocyclic Moieties (5a-5e) on the Percentage of *S. Pombe* Cells that Live at Varied Concentrations (µM), Plus an Error Uncertainty of ± 5%

Concentration (µM)	20	40	60	80	100
Compounds	% Viability				
Ciprofloxacin	68 ± 1	65 ± 2	62 ± 1	59 ± 3	54 ± 2
DMSO	96 ± 2				
Untreated cell	98 ± 1				
5a	96 ± 2	93 ± 3	88 ± 2	86 ± 1	82 ± 3
5b	90 ± 2	87 ± 1	84 ± 2	81 ± 3	79 ± 2
5c	70 ± 3	65 ± 2	64 ± 1	60 ± 2	58 ± 1
5d	85 ± 1	83 ± 3	81 ± 3	78 ± 4	75 ± 3
5e	77 ± 2	74 ± 1	71 ± 3	69 ± 2	66 ± 1

Antibacterial Activity

As microorganisms show resistance to antibacterial treatments, in vitro antibacterial investigations against various bacterial cultures and the identification and development of novel antibacterial agents are essential to modern research.[8, 9] Bacterial species, namely Gram(+ve) positive *B. megaterium* and *S. aureus* and Gram(–ve) *S. typhimurim* and *E. coli*, were used to test the synthesised carbothioamide derivative compounds (5a–5e). The range of substances' minimum inhibitory concentration (MIC) values is 13–24 µg/mL. MIC values for every drug and the ciprofloxacin standard used in the tests are shown in Fig.-2.[10] Compared to other synthetic compounds, compounds 5c, 5d and 5e exhibit good antimicrobial activity against bacteria because compound 5a contains bromo functional groups on the *p* position of the aromatic ring, while compound 5b contains meta position of phenyl ring -NO_2 functional groups.[11]

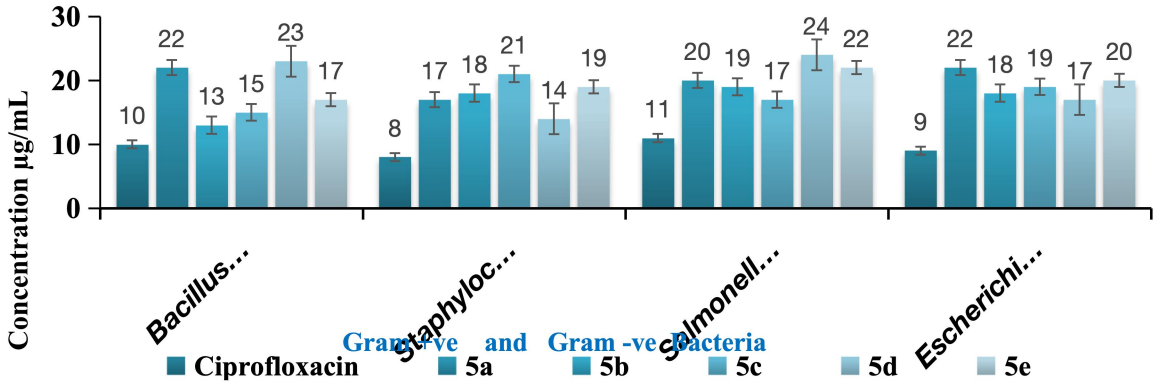


Fig.-1: Minimum Inhibitory Concentration Value of Carbothioamide Derivative Heterocyclic Substances (5a–5e) against *B. megaterium*, *S. aureus*, *S. typhimurium*, and *E. coli*. The variance of three repetitions ± 5% is Represented by Error Bars.

Antifungal Activity

Antifungal efficacy against *Aspergillus niger* is strongly indicated by evaluated inhibition zones, which range from 10 mm to 23 mm. Larger clear zones around test materials in disk diffusion assays are linked to higher antifungal potency; these patterns are consistent with results seen in related studies. On *A. niger*, for example, stronger drugs showed inhibitory zones of at least 14 mm, while typical antifungal extracts showed zones of about 12 mm. In a different situation, silver nanoparticles showed inhibitory zones against fungal strains of up to 14 mm. Zone-of-inhibition statistics show that samples with diameters of 10–15 mm have modest antifungal activity, while samples with zones of 18 mm or more show high inhibitory effectiveness against *Aspergillus niger*.

Interestingly, drugs that produce inhibition zones of 22–23 mm are highly intriguing leads that should be investigated further and even given priority in the drug development process. Disk-diffusion classification frameworks, such as those described in CLSI recommendations, frequently classify zones larger than 17 mm as susceptible and those less than 10 mm as resistant for a variety of bacterial agents. In general, these frameworks align with this comprehension.[12]

Universal inhibition zones usually indicate better antifungal efficacy and enhanced sensitivity, which is the same interpretive notion, even if antifungal-specific zones of inhibition are less frequently described. Synthesised compounds (5a-5e), antifungal properties in comparison to the common medication ciprofloxacin are represented in Fig.-2: ciprofloxacin > 5c > 5e > 5d >5b > 5a is the order of the synthesised compounds (5a–5e) in terms of their potency against *A. niger*.

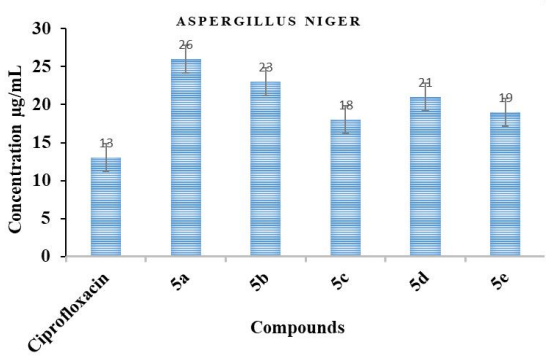


Fig.-2: Anti-Fungal Activity of Synthesised Carbothioamide Derivative Moieties (5a-5e) Compared with Standard Drug Ciprofloxacin[10]

In silico Molecular Docking Study

The synthesised compounds are significant inhibitors of Human topoisomerase II alpha (TOP2A) enzymes, and docking analysis was used to determine the structural basis of their interactions with TOP2A. The synthesised compound's binding affinity (5d) is close to that of etoposide, a well-known inhibitor of topoisomerase II. Inhibitory efficacy against topoisomerase I has already been documented in the literature for structurally equivalent drugs[13, 14]. The synthesised carbothioamide derivatives (5a–5e) show excellent binding interactions with human topoisomerase II alpha (TOP2A, PDB ID: 5GWK), suggesting their potential as enzyme inhibitors, according to molecular docking research. All of the drugs exhibited considerable interaction potential, while having slightly lower binding affinities (−9.1 to −10.5 kcal/mol) than the conventional medication etoposide (−12.2 kcal/mol). Compound 5c, which was stabilised by several H-Bonds, hydrophobic interactions, and van der Waals forces, showed the highest binding affinity (−10.5 kcal/mol) among them, indicating robust complex formation with TOP2A. While compound 5b demonstrated a moderate affinity (−9.5 kcal/mol), compounds 5e and 5d also demonstrated significant binding energies (−10.3 and −10.0 kcal/mol, respectively), with a variety of interactions, including hydrogen bonding and π-based interactions. These results indicate that compounds 5b–5e possess promising inhibitory potential against TOP2A, with compound 5c emerging as the most effective candidate, comparable to the standard inhibitor in terms of binding interactions. Molecular docking 2D and 3D poses of synthesised carbothioamide moieties (5a-5e) are represented in supplementary material 6.

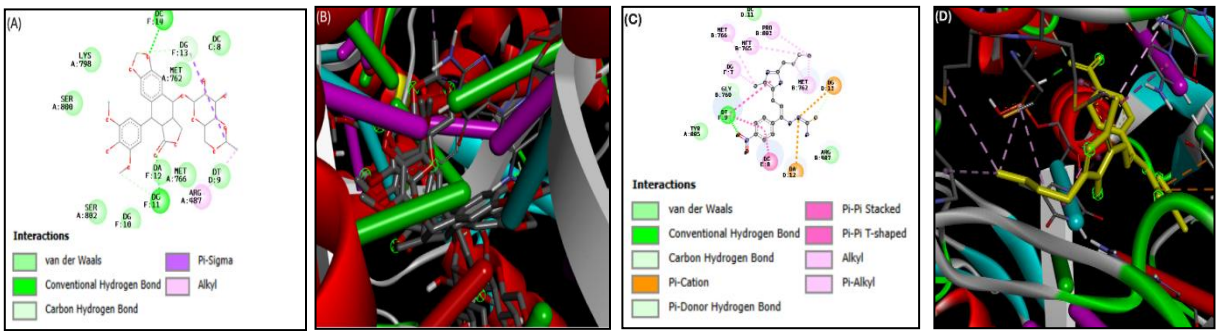


Fig.-3: Docking Poses of Compound 5c and Etoposide Drug with Human Topoisomerase II Alpha (TOP2A). (A) 2D Docking Pose (B) 3D Docking Pose (C) 2D Docking Pose of Compound 5c, (D) 3D Docking Pose of Compound 5c

Table-2: Conventional Hydrogen-Bonding Interactions between the Synthesised Compounds (5a-5e) and Human Topoisomerase II Alpha (TOP2A), Compared with Standard Etoposide

Compounds	Docking Score (Kcal/mol)	Amino Acid Interaction Residues	Conventional Hydrogen Bonds
Etoposide	-12.2	SER A:802, SER A:800, MET A:762, ARG A:487, MET A:766	DC F:11, DC F:14
5a	-9.1	-	-
5b	-9.5	GLY B:615, GLY B:617, THR B:618, TYR A:805, HIS B:758, LYS B:614, SER B:756, ASP B:832, ARG A:740, GLU A: 741, PHE A: 807, ILE A:787, ARG A:804, LYS A:743	LYS B:614
5c	-10.5	GLY B:760, MET B:766, MET B:765, PRO B:802, MET B:762, ARG B: 487, TYR A:805	DT F:9
5d	-10.0	ARG B:487, GLY B:760, MET B: 762, MET B: 766	DT F:9
5e	-10.3	TYR B:805, GLY A:760, SER A:763, MET A:766, MET A:762	DT D:9, ARG A:487

ADME Parameter

The SwissADME result has revealed several variables, such as the number of distinct atom types, molecular refractivity, the partition coefficient of n-octanol and water (log Po/w), the topological surface area of Polar (TPSA), the permeability of the BBB, bioavailability score, and H bond acceptors and donor molecules. High permeability and bioavailability are indicated by the TPSA values for the synthesised molecule, which range from 111.18 to 157.43 Å2. Synthesised compounds fall outside of the typical range of lipophilicity values when the log Po/w value, or lipophilicity value, is less than 5 or between 2.72 and 4.31. The molar solubility (log S) of the synthesized compounds (5a–5e) showed that they were all fairly soluble in water. As a result of their high GI absorption, synthesized carbothioamide derivatives (5a–5e) are substantially absorbed in the gastrointestinal system. Any drug can penetrate the blood-brain barrier. We also demonstrated an ADME analysis using admetSAR, another online platform, because the SwissADME online platform does not offer accurate results for gastrointestinal (GI) absorption and BBB permeability[15]. Another important criterion for assessing a compound's drug-likeness is the Lipinski rule, also referred to as the rule of five (Ro5). Based on the compounds' high in vivo bioavailability, it appropriately evaluates how drug-like they are. The Lipinski rule, also referred to as the rule of five, is not consistently violated by the compounds. Consequently, it suggests that substances have oral activity. Table-3 and supplementary material 7 show the ADME values of the synthesized carbothioamide heterocyclic derivative moieties (5a–5e). Figure-4 displays a BOILED-Egg model representation of synthetic carbothioamide heterocyclic derivative scaffolds (5a–5e).

Toxicity Parameters of Compounds (5a-5e) in Homo Sapiens

ProTox-II's in silico toxicity evaluation of carbothioamide derivatives (5a–5e) showed different but similar toxicological profiles throughout the series. With LD_{20} values of 270 mg/kg, compounds 5a, 5b,

5d, and 5e showed moderate toxicity and were classified in toxicity class 3, whereas compound 5c showed comparatively lesser toxicity and was classified in toxicity class 4.

Table-3: ADME Parameters of Synthesized Carbothioamide Derivative Moieties (5a-5e)

Mol. Wt. (g/mol)	440.79	406.89	406.89	391.92	392.91
Rotatable bonds	8	9	9	9	8
H-bond acceptors	2	4	4	3	3
H-bond donors	3	3	3	3	5
MR	111.86	112.98	112.98	110.65	110.59
TPSA (Aº)	111.18	157.00	157.00	120.41	157.43
Consensus Log P	4.31	2.92	2.92	3.67	2.72
ESOL Solubility (mg/ml)	-5.56	-4.72	-4.72	-4.73	-4.17
GI Absorption	High	LOW	LOW	High	LOW
Blood-brain permeant	NO	NO	NO	NO	NO
P-gp substrate	NO	NO	NO	NO	NO
Lipinski violations	YES	YES	YES	YES	YES
Muegge violations	NO	NO	NO	YES	NO
PAINS alerts	0	0	0	0	1
Leadlikeness	NO	NO	NO	NO	NO

All predictions had an accuracy of 23%. The majority of compounds had similar negative effects, such as neurotoxicity, respiratory toxicity, immunotoxicity, disruption of the blood–brain barrier, and nutritional toxicity, according to toxicity radar analysis.

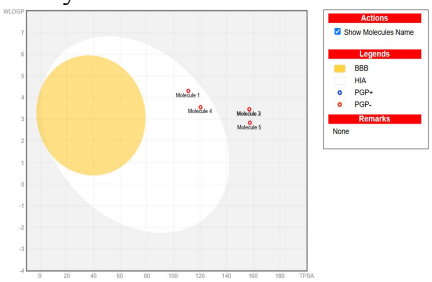


Fig.-4: Boiled-Egg Classical Diagram of Synthesized Carbothioamide Heterocyclic Derivative Moieties (5a-5e)

Some derivatives also displayed hepatotoxicity (5a, 5d, 5e), nephrotoxicity, carcinogenicity, and mutagenicity (5b, 5c, 5e), and ecotoxicity (5a, 5d). Tox21 nuclear receptor activation and responses to stress pathways were consistently shown to be activated ($p > 0.7$), indicating potential disruptions to biological circuits. Cytochrome P450 enzymes, including CYP2C9 and CYP2D6, were identified as important targets by metabolic prediction, suggesting possible involvement in hepatic metabolism. Interestingly, all of the drugs showed moderate structural similarity (~33–36%) to human topoisomerase II alpha (PDB ID: 5GWK), indicating a shared biological interaction mechanism.

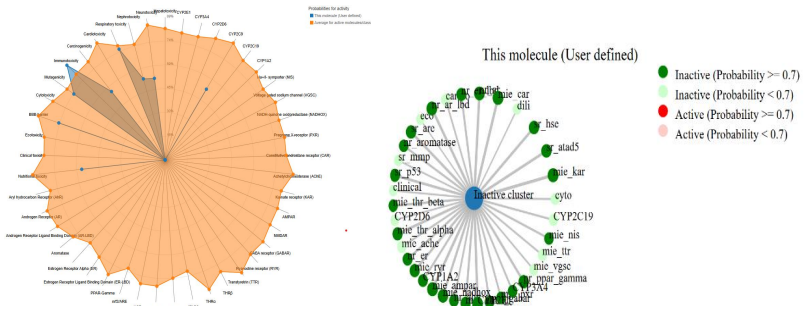


Fig.-5: Diagram of Toxicity Radar Chart of Carbothioamide Scaffold 5c

As shown in Supplementary Material 8 and figures, compound 5c exhibited a relatively favourable toxicity profile among the series, as evidenced by its higher LD_2^1 and fewer toxic alerts. This is further

supported by toxicity radar clustering and comparative analysis with standard compounds. These results show that compound 5c is a comparatively safer candidate for additional pharmacological research, even though the majority of derivatives show moderate toxicity risks (Fig.-6).

Table-4: Predicted Toxicological Properties of Carbothioamide Scaffold (5c) via Pro Tox-II

Target	Classification	Prediction	Probability	PredictedLD_{50} (mg/kg)	Toxicity Class
Hepatotoxicity	Organ toxicity	Inactive	0.52		
Cardiotoxicity	Organ toxicity	Inactive	0.68		
Cytotoxicity	Toxicity endpoint	Inactive	0.61		
Ecotoxicity	Toxicity endpoint	Inactive	0.51		
Clinical toxicity	Toxicity endpoint	Inactive	0.59	700 mg/kg	IV

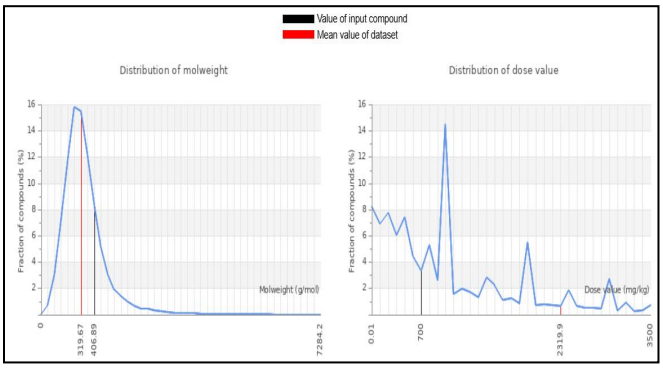


Fig.-6: Toxicity Evaluation Between the Standard Compound and the Synthesised Scaffold (5c)

CONCLUSION

New carbothioamide–imidazole compounds (5a–5e) with promising biological potential were effectively synthesised and studied. The substances demonstrated considerable inhibition against *S. pombe* and *Aspergillus niger*, as well as notable cytotoxic, antibacterial, and antifungal properties. Effective interaction with human topoisomerase II alpha (TOP2A) was validated by molecular docking and binding studies; compound 5c demonstrated the excellent affinity towards binding and the best score in docking, equivalent to standard medicines. Positive pharmacokinetic characteristics were revealed by the ADME study. These compounds are promising prospects for additional anticancer drug research since the presence of electron-withdrawing groups increased biological activity, aiming to promote good health and well-being.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

The present work is related to *SDG-3: Good Health and Well-Being*. All the authors contributed significantly to this manuscript, participated in reviewing/editing and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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