Biological Forum – An International Journal **15(5): 1795-1801(2023)**

ISSN No. (Print): 0975-1130
ISSN No. (Online): 2249-3239

Synthesis, Molecular Docking and Cytotoxic Activity of Some Novel Semicarbazone Derivatives

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(Received: 15 March 2023; Revised: 10 April 2023; Accepted: 20 April 2023; Published: 15 May 2023)
(Published by Research Trend)

ABSTRACT: Semicarbazone derivatives have gained significant attention in medicinal chemistry due to their diverse biological activities, including anticancer properties. In this study, we report the synthesis of novel semicarbazone derivatives using a simple and efficient condensation reaction between semicarbazide and various substituted aldehydes or ketones. The synthesized compounds were characterized using spectroscopic techniques such as NMR, and mass spectrometry to confirm their structural integrity. Molecular docking studies were conducted to assess the binding affinity of these derivatives with key cancer-associated protein targets. The docking results revealed strong interactions with active site residues, suggesting their potential as anticancer agents. Furthermore, the cytotoxic activity of the synthesized compounds was evaluated against selected cancer cell lines. Several derivatives exhibited significant cytotoxicity, with IC_{50} values comparable to standard anticancer drugs. The findings highlight the potential of these novel semicarbazone derivatives as promising candidates for anticancer drug development.

Keywords: Semicarbazone derivatives, synthesis, molecular docking, cytotoxicity, anticancer activity.

INTRODUCTION

Cancer remains one of the leading causes of mortality worldwide, necessitating the continuous development of novel therapeutic agents (Kummar, 2010). Traditional chemotherapeutic drugs, while effective, are often associated with severe side effects and the emergence of drug resistance (Nikolaou *et al.*, 2018). Therefore, the search for new anticancer agents with enhanced efficacy and reduced toxicity is of paramount importance (Cragg *et al.*, 2009). Among various classes of bioactive molecules, semicarbazone derivatives have emerged as promising candidates due to their diverse pharmacological activities, including anticancer, antioxidant, antimicrobial, anticonvulsant, and anti-inflammatory properties (Pal *et al.*, 2022). These derivatives have gained significant attention in drug discovery owing to their ability to interact with biological macromolecules and inhibit critical pathways involved in cancer progression (Neidle and Thurston 2005).

Semicarbazones are organic compounds characterized by the presence of a semicarbazide (-NH-CONH-NH_2) functional group, which imparts unique physicochemical properties and biological activity (Neidle and Thurston, 2005). They are typically synthesized by the condensation of semicarbazide with aldehydes or ketones (Conant and Bartlett 1932). The structural flexibility of semicarbazones allows them to interact with various biological targets, including enzymes and receptors, making them valuable scaffolds for drug development (Malki *et al.*, 2001).

The pharmacological relevance of semicarbazones is primarily attributed to their ability to chelate metal ions, form hydrogen bonds, and exhibit redox activity (Petrasheuskaya *et al.*, 2022). These properties contribute to their cytotoxic effects by inducing oxidative stress, disrupting cellular homeostasis, and triggering apoptotic pathways in cancer cells (Arfin *et al.*, 2021). Moreover, molecular modifications of semicarbazone derivatives can enhance their selectivity, stability, and bioavailability, further improving their therapeutic potential (Rodrigues *et al.*, 2021).

Molecular docking is a widely used computational technique in modern drug discovery that predicts the binding affinity and interaction of small molecules with target proteins (Pinzi and Rastelli 2019). This approach provides valuable insights into the structural and functional aspects of drug-target interactions, facilitating the rational design of potent and selective inhibitors (Huggins *et al.*, 2012). Molecular docking studies help in identifying potential binding sites, elucidating key molecular interactions, and optimizing lead compounds for enhanced bioactivity (Chen *et al.*, 2020).

In the context of semicarbazone derivatives, molecular docking studies can be instrumental in understanding their mechanism of action against cancer-related proteins such as kinases, topoisomerases, and proteasomes (Naseer *et al.*, 2022; Verma *et al.*, 2022). By predicting the binding conformation and affinity of these compounds, molecular docking enables the selection of promising candidates for further in vitro

and in vivo evaluation (Honarparvar *et al.*, 2014). The integration of computational modeling with experimental validation accelerates the drug development process and enhances the likelihood of discovering novel anticancer agents (Basith *et al.*, 2017; Mousa, 2026; Pathade *et al*., 2023).

The present research aims to synthesize, characterize, and evaluate the molecular docking and cytotoxic activity of novel semicarbazone derivatives. The development of semicarbazone-based anticancer agents holds significant promise in addressing the limitations of existing chemotherapeutics. By combining synthetic chemistry, computational modeling, and biological evaluation, this research aims to contribute valuable knowledge to the field of medicinal chemistry and oncology. The findings from this study will provide a foundation for further optimization and preclinical studies, paving the way for the potential development of novel anticancer drugs.

MATERIAL AND METHODS

All the melting points reported in the dissertation progress report were determined by open capillary tube method and are uncorrected. The synthesis and analytical studies of the compounds were carried out using laboratory grade and analytical grade reagents as the case may be standard procedure or reported method were followed with or without modification appropriately as and when required. Elemental analysis (C, H and N) was undertaken with a Perkin-Elmer model 240C analyzer, and all analyses were consistent with theoretical values (within 0.4 %) unless indicated. ^{1}H NMR spectra were recorded on the Bruker DPX-400 instrument at 400 MHz. The ^{1}H chemical shifts are reported as parts per million (ppm) downfield from TMS (Me_4Si). The LC mass spectra of the compounds were recorded on Shimadzu 8201PC spectrometer. The homogeneity of the compounds was monitored by ascending thin-layer chromatography (TLC) on silica gel G (Merck)-coated aluminum plates, visualized by iodine vapor.

Synthetic procedure for compound (1). In Step 1 involves the synthesis of 4-methoxybenzohydrazide (1) from 4-methoxyaniline. This is achieved via diazotization followed by the reaction with glacial acetic acid (GAA). In a round-bottom flask, dissolve 4-methoxyaniline (1 eq.) in glacial acetic acid and maintain the temperature between 0–5°C. Prepare a cold aqueous solution of sodium nitrite (1.1 eq.) in a separate RBF. Slowly add the sodium nitrite solution to the flask containing 4-methoxyaniline under continuous stirring, maintaining the temperature 0°C. After 15–30 minutes, gently warm the reaction mixture to room temperature while stirring. The diazonium salt reacts with the acetic acid, forming 4-methoxybenzohydrazide. Dilute the reaction mixture with cold water to precipitate the product and collect the solid by vacuum filtration and wash with water to remove residual impurities and obtain pure 4-methoxybenzohydrazide (1).

Synthetic procedure for compound (2). Step 2 involves the synthesis of compound 2 from 4-methoxybenzohydrazide (1) through reaction with hydrazine hydrate ($NH_2NH_2 \cdot H_2O$). In a clean, dry round-bottom flask, dissolve 4-methoxybenzohydrazide (1) (1 eq.) in ethanol:water (10:1). Added an excess of hydrazine hydrate ($NH_2NH_2 \cdot H_2O$) (3 eq.) to the flask under stirring. Heat the reaction mixture at 80 °C for 6 hours, stir continuously to ensure uniform heating and stirring. Check the progress of the reaction periodically using TLC, after completion cool the reaction mixture to room temperature. concentrate the mixture under reduced pressure to remove the solvent and precipitate the product by adding cold water filter the solid and wash with cold water to remove impurities.

4-(4-methoxyphenyl) semicarbazide (2): yield: 91%; M.P.: 212-215°C; R_f: 0.45 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.71 (s, 3H, OCH_3), 1.24 (s, 1H, NH), 7.14 (s, 1H, NH), 3.63 (s, 2H, NH_2), 6.07-7.99 (m, 4H, Ar-H); LCMS (ESI): calcd. for $C_8H_{11}N_3O_2$ $[M+H]^+$: 181.1932, found: 182.5265. Elemental analysis: C, 53.03; H, 6.12; N, 23.19.

General synthetic procedure for compound 3(a-l). This procedure describes the synthesis of 1-(diphenylmethylene)-4-(4-methoxyphenyl)semicarbazide derivatives **3a-3l** through the reaction of various substituted benzophenones with 4-(4-methoxyphenyl)semicarbazide (2). In a clean, dry round-bottom flask, substituted benzophenone and 4-(4-methoxyphenyl) semicarbazide (2) in a 1:1 molar dissolve both compounds in ethanol. Add 1-2 drops of glacial acetic acid to catalyse the reaction and attach the flask to a reflux condenser and heat the mixture at 80°C under reflux for 12 h. During the reaction, the semicarbazide group reacts with the carbonyl group to form the semicarbazone (C=N). Check the progress of the reaction by TLC and after completion of the reaction, cool the reaction mixture to room temperature, evaporate the solvent under reduced pressure to obtain the crude product dilute with water formed precipitates collect it by vacuum filtration and purify with column chromatography to afford final compounds 3(a-l).

1-(diphenylmethylene)-4-(4-methoxyphenyl)semicarbazide (**3a**): yield: 63%; M.P.: 171-174 °C; R_f: 0.47 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.78 (s, 3H, OCH_3), 1.37 (s, 1H, NH), 7.17 (s, 1H, NH), 6.07-7.99 (m, 14H, Ar-H); LCMS (ESI): calcd. for $C_{21}H_{19}N_3O_2$ $[M+H]^+$: 345.3946, found: 346.4585. Elemental analysis: C, 73.03; H, 5.54; N, 12.17.

(*E*)-4-(4-methoxyphenyl)-1-(phenyl(o-tolyl)methylene)semicarbazide (**3b**): yield: 66%; M.P.: 167-170 °C; R_f: 0.49 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 2.77 (s, 1H, NH), 7.17 (s, 1H, NH), 2.50 (s, 3H, CH_3), 6.50-7.99 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{22}H_{21}N_3O_2$ $[M+H]^+$: 359.4261, found: 360.6643. Elemental analysis: C, 73.52; H, 5.89; N, 11.69.

(*E*)-4-(4-methoxyphenyl)-1-(phenyl(m-tolyl)methylene)semicarbazide (**3c**): yield: 68%; M.P.: 181-185 °C; R_f: 0.44 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H,

OCH_3), 3.61 (s, 1H, NH), 6.92 (s, 1H, NH), 2.34 (s, 3H, CH_3), 6.50-8.09 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{22}H_{21}N_3O_2$ $[M+H]^+$: 359.4261, found: 360.3243. Elemental analysis: C, 73.52; H, 5.89; N, 11.69.

(*E*)-4-(4-methoxyphenyl)-1-(phenyl(p-tolyl)methylene)semicarbazide (**3d**): yield: 66%; M.P.: 167-170 °C; R_f: 0.48 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.82 (s, 3H, OCH_3), 3.52 (s, 1H, NH), 6.87 (s, 1H, NH), 2.14 (s, 3H, CH_3), 6.50-8.00 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{22}H_{21}N_3O_2$ $[M+H]^+$: 359.4282, found: 360.1742. Elemental analysis: C, 73.52; H, 5.89; N, 11.69.

(*E*)-1-((3,4-dimethylphenyl)(phenyl)methylene)-4-(4-methoxyphenyl)semicarbazide (**3e**): yield: 71%; M.P.: 182-186 °C; R_f: 0.51 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 3.51 (s, 1H, NH), 5.94 (s, 1H, NH), 2.35 (s, 6H, CH_3, CH_3), 6.50-8.09 (m, 12H, Ar-H); LCMS (ESI): calcd. for $C_{23}H_{23}N_3O_2$ $[M+H]^+$: 373.4564, found: 374.1845. Elemental analysis: C, 73.97; H, 6.21; N, 11.25.

(*E*)-1-((4-ethylphenyl)(phenyl)methylene)-4-(4-methoxyphenyl)semicarbazide (**3f**): yield: 65%; M.P.: 171-177 °C; R_f: 0.61 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 3.47 (s, 1H, NH), 5.96 (s, 1H, NH), 1.33 (t, 3H, CH_3), 2.66 (q, 2H, CH_2), 6.50-8.00 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{23}H_{23}N_3O_2$ $[M+H]^+$: 373.4591, found: 374.1844. Elemental analysis: C, 73.97; H, 6.21; N, 11.25.

(*E*)-1-((4-isopropylphenyl)(phenyl)methylene)-4-(4-methoxyphenyl)semicarbazide (**3g**): yield: 73%; M.P.: 166-169 °C; R_f: 0.47 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.82 (s, 3H, OCH_3), 3.67 (s, 1H, NH), 6.33 (s, 1H, NH), 1.35 (d, 3H, $2CH_3$), 3.13 – 3.03 (m, 1H, CH), 6.50-8.00 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{24}H_{25}N_3O_2$ $[M+H]^+$: 387.4741, found: 388.2045. Elemental analysis: C, 74.39; H, 6.50; N, 10.84.

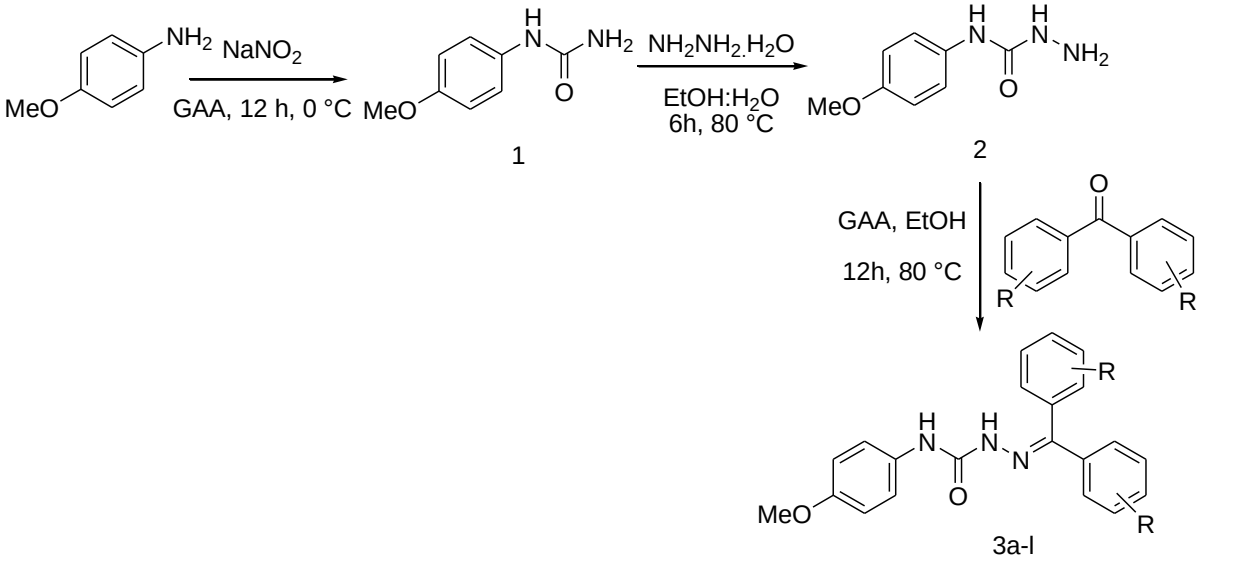
(*E*)-1-((4-tert-butylphenyl)(phenyl)methylene)-4-(4-methoxyphenyl)semicarbazide (**3h**): yield: 67%; M.P.: 149-154 °C; R_f: 0.53 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 3.42 (s, 1H, NH), 6.03 (s, 1H, NH), 1.38 (s, 9H, CH_3), 6.50-8.59 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{25}H_{27}N_3O_2$ $[M+H]^+$: 401.5031, found: 402.2 121. Elemental analysis: C, 74.79; H, 6.78; N, 10.47.

(*E*)-4-(4-methoxyphenyl)-1-((4-methoxyphenyl)(phenyl)methylene)semicarbazide (**3i**): yield: 71%; M.P.: 164-168 °C; R_f: 0.48 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 3.39 (s, 1H, NH), 7.48 (s, 1H, NH), 3.84 (s, 3H, OCH_3), 6.50-8.00 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{22}H_{21}N_3O_3$ $[M+H]^+$: 375.4246, found: 376.1635. Elemental analysis: C, 70.38; H, 5.64; N, 11.19.

(*E*)-1-((4-chlorophenyl)(4-hydroxyphenyl)methylene)-4-(4-methoxyphenyl) semicarbazide (**3j**): yield: 68%; M.P.: 172-175 °C; R_f: 0.46 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 3.06 (s, 1H, NH), 6.30 (s, 1H, NH), 5.13 (s, 1H, OH), 6.50-8.00 (m, 12H, Ar-H)); LCMS (ESI): calcd. for $C_{21}H_{18}ClN_3O_3$ $[M+H]^+$: 395.8464, found: 396.1163. Elemental analysis: C, 63.72; H, 4.58; N, 10.62.

(*E*)-1-((4-fluorophenyl)(phenyl)methylene)-4-(4-methoxyphenyl)semicarbazide (**3k**): yield: 69%; M.P.: 165-169 °C; R_f: 0.54 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 3.50 (s, 1H, NH), 6.31 (s, 1H, NH), 6.50-8.59 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{21}H_{18}FN_3O_2$ $[M+H]^+$: 363.3875, found: 364.1465. Elemental analysis: C, 69.41; H, 4.99; N, 11.56.

(*E*)-4-(4-methoxyphenyl)-1-(phenyl(4-(trifluoromethyl)phenyl)methylene)semicarbazide (**3l**): yield: 66%; M.P.: 172-176 °C; R_f: 0.45 (silica gel, 50% EtOAc/Hexane); ^{1}H-NMR (400 $CDCl_3$, TMS): δ 3.81 (s, 3H, OCH_3), 3.46 (s, 1H, NH), 6.88 (s, 1H, NH), 6.50-8.59 (m, 13H, Ar-H); LCMS (ESI): calcd. for $C_{22}H_{18}F_3N_3O_2$ $[M+H]^+$: 413.3965, found: 414.1551. Elemental analysis: C, 63.92; H, 4.39; N, 10.16.



***In vitro* Anticancer activity.** The anticancer activity of the synthesized compounds was evaluated against four cancerous cell lines; human breast (MCF-7), cervical cancer (C33A), oral (KB) and prostrate (DU-145) using (SRB) colorimetric assay. Doxorubicin was included in the experiments as reference cytotoxic compounds for all the tested cell lines. The results were expressed as median growth inhibitory concentration (IC_{50}) values, which represent the concentration of a drug that is required for 50% inhibition of cell growth after 48 h of incubation, compared to untreated controls (Sibuh *et al*., 2021; El-Etrawy and Sherbiny *et al.*, 2021).

***In Silico* Likeness.** In-silico study of synthesized compounds (**3a-3h**) was performed for prediction of ADME properties. Polar surface area (TPSA) and molecular volume were calculated online using Swiss ADME tool (da Silva Filho *et al*., 2019; Stolarczyk *et al*., 2021; Punia *et al*., 2022).

Molecular Docking Study. The molecular docking studies of the synthesized peptides was performed on Windows 10 (64-bit) operating systems with 64 GB RAM and AMD Ryzen 9 5950X 16-Core Processor 3.40 GHz. Autodock tools, Autodock Vina, PyRx, Pymol and Maestro Visualiser tools were used.

The crystallographic 3D structure of E. coli thymidylate Synthase complexed with an anticancer drug ZD1694 (PDB ID: 2KCE) was accessed from Protein Data Bank. The resolution of the XRD structure of pdb (2KCE) is 2.20 Å. The structure of PDB complexes was downloaded from RCSB database and protein preparation was carried out using the Autodock Wizard by deleting attached water molecules, bound heteroatoms/ligand, adding polar hydrogens, kollman charges, spreading charge equally over all atoms and checking for missing atoms on residues. The PDB files were then converted to the PDBQT format for executing the next step (Rutenber and Stroud 1996; Jackman and Calvert 1995; Garg *et al*., 2010; Rolta *et al*., 2022).

The 2D structures were drawn by Chemdraw and converted into 3D format. The ligands were minimized by MMFF94 Force Field and converted to PDBQT format by openbabel in PyRx tool.

For carrying out docking between prepared receptors and ligands, grid was generating by taking the center on attached ligand. The grid dimensions for PDB ID: 2KCE was number of points as 25, 25, 25 in X,Y,Z direction 14.1, 13.6, 34.4 with default spacing.

RESULTS AND DISCUSSION

Step 1 involves the synthesis of 4-methoxybenzohydrazide (1) from 4-methoxyaniline. Step 2 involves the synthesis of compound 2 from 4-methoxybenzohydrazide (1) through reaction with hydrazine hydrate ($NH_2NH_2 \cdot H_2O$). Final steps the synthesis of 1-(diphenylmethylene)-4-(4-methoxyphenyl) semicarbazide derivatives 3(a-l) through the reaction of various substituted benzophenones with 4-(4-methoxyphenyl)semicarbazide (2). The reaction was monitored by TLC and melting point. The structures of the compounds were confirmed by IR, NMR and Mass spectrometry. The purity of compounds was established by elemental analysis (Atyam *et al*., 2010).

In vitro anticancer activity of various compounds against four cancer cell lines: DU 145 (prostate cancer), MCF7 (breast cancer), C33A (cervical cancer), and KB (oral epidermoid carcinoma). The activity is quantified by the IC50 values (the concentration of a compound required to inhibit 50% of cell growth), expressed in µg/ml. Lower IC_{50} values indicate higher potency. Compound **3h** and **3l** found most potent overall, with IC_{50} values of 0.8 µg/ml (DU 145), 1.8 µg/ml (MCF7), 2.8 µg/ml (C33A), and 2.1 µg/ml (KB), for **3l** found IC_{50} values of 1.1 µg/ml (DU 145), 1.2 µg/ml (MCF7), 1.8 µg/ml (C33A), and 1.1 µg/ml (KB).

Table 1: *In vitro* anticancer activity of Compounds (3a-3l).

Compound	IC_{50} (µg/ml)			
	DU 145	MCF7	C33A	KB
3a	14.8	23.9	21.6	15.2
3b	3.5	1.9	1.2	3.0
3c	20.1	27.8	24.4	22.1
3d	9.2	4.8	3.1	3.6
3e	5.4	4.9	3.1	5.9
3f	23.2	32.4	19.8	22.8
3g	10.5	5.7	4.6	4.9
3h	0.8	1.2	1.8	1.1
3i	13.3	23.9	16.8	11.8
3j	2.7	3.4	3.5	5.9
3k	15.8	23.4	21.7	15.6
3l	1.1	1.3	3.1	1.5
Doxorubicin	2.4	1.0	1.6	1.4

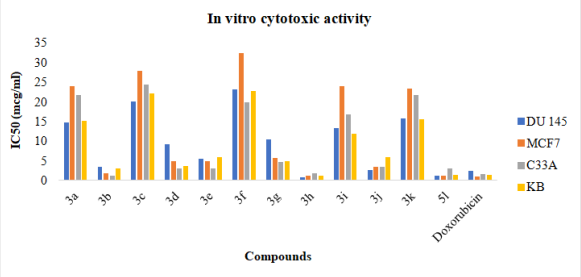


Fig. 1. *In vitro* anticancer activity of Compounds (3a-3l).

The molecular properties of the synthesized semicarbazone derivatives (3a–3l) were analyzed using key drug-likeness parameters, including molecular weight, rotatable bonds, hydrogen bond interactions, topological polar surface area (TPSA), lipophilicity (Log P), gastrointestinal (GI) absorption, and Lipinski's rule of five compliance (Zafar *et al*., 2020). Most compounds exhibit favorable drug-like properties, with good oral bioavailability (high GI absorption), moderate lipophilicity, and adherence to Lipinski's rule. Compounds **3h** and **3l**, despite slightly higher molecular weights and one Lipinski violation, may still be promising candidates due to their strong cytotoxic activity.

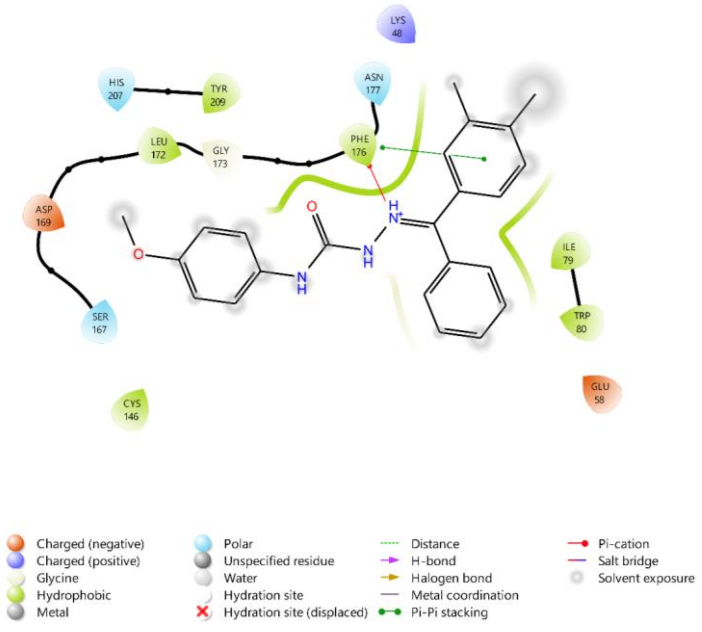
Table 2: *In silico* Drug Likeness and absorption.

Comp	Molecular weight	Num. rotatable bonds	Num. H-bond acceptors	Num. H-bond donors	TPSA (Å^2)	Log Po/w (iLOGP)	GI Absorption	Lipinski
3a	345.3	7	3	2	62.72	3.53	High	0
3b	359.4	7	3	2	62.72	3.38	High	0
3c	359.4	7	3	2	62.72	3.79	High	0
3d	359.4	7	3	2	62.72	3.75	High	0
3e	373.4	7	3	2	62.72	3.93	High	0
3f	373.4	8	3	2	62.72	4.07	High	0
3g	387.4	8	3	2	62.72	4.19	High	1
3h	401.5	8	3	2	62.72	4.29	High	1
3i	375.4	8	4	2	71.95	3.82	High	0
3j	395.8	7	4	3	82.95	3.41	High	0
3k	363.3	7	4	2	62.72	3.60	High	0
3l	413.3	8	6	2	62.72	3.70	High	1

Compounds **3h, 3e**, and **3b** show the strongest binding affinity, suggesting they are promising lead molecules for further development. Hydrophobic interactions with ILE79, PHE176, CYS146, and LEU172 play a significant role in binding stability. Overall, the docking results suggest that these semicarbazone derivatives could be potential anticancer agents, with some performing comparably or even better than doxorubicin.

Table 3: Molecular Docking Study Results of PDB Id: 2KCE.

Comp. No.	Hydrophobic Interactions	H-bond	Binding Affinity
3a	CYS146, LEU143, ALA263, VAL262, LEU172, PHE176, ILE79, TRP83	-	-9
3b	PHE176, ILE79, TPR80, LEU172, CYS146, TYR209, VAL262	-	-9.5
3c	ILE79, TRP80, LEU143, CYS146, TRP83, LEU172, PHE176, VAL262	SER167	-9.4
3d	TRY209, VAL262, LEU172, PHE176, TRP80, ILE79, CYS146, LEU143	-	-9.4
3e	LEU172, TYR209, PHE176, ILE79, TRP80, CYS146	-	**-9.6**
3f	TYR209, ILE79, TRP80, PHE176, LEU172, CYS146	HIS207	-9.3
3g	ALA263, VAL262, PHE176, ILE796, LEU172, TRP83, CYS146, LEU143	-	-9.5
3h	ILE79, LEU172, PHE176, VAL262, ALA263, TRP83, CYS146, LEU143	-	**-9.9**
3i	ILE79, TRP80, TYR209, CYS146, LEU172, PHE176	HIS207	-9.1
3j	ALA263, VAL262, LEU172, ILE79, PHE176, CYS146, TRP83, LEU143	ASN177	-9.5
3k	ILE79, TRP80, CYS146, LEU143, LEU172, TYR209, VAL262, PHE176	-	-9.2
3l	ILE79, TRP80, TYR209, CYS146, LEU172, PHE176, VAL262	HIS207	-9.5
Doxorubicin	ILE79, ASP169, LEU172, CYS146, TRP83, LEU143, ARG21, TRP80, ASN177, GLY173, GLU58, HIS147, PHE62, PHE176, LYS259, ALA260, VAL262	-	-9.3



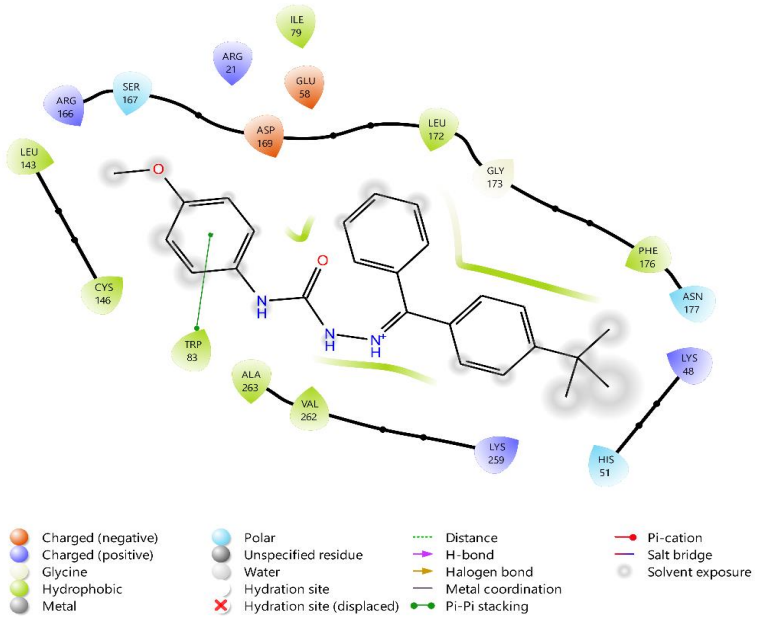


Fig. 2. Binding Pattern of Synthesized compounds (3e and 3h) against 2KCE.

CONCLUSIONS

The study suggests that compounds **3h** and **3l** exhibit the most promising cytotoxic activity against all tested cancer cell lines, making them potential lead molecules for further anticancer drug development. Compounds **3b**, **3d**, **3e**, and **3j** also demonstrate good activity, warranting further investigation.

FUTURE SCOPE

The synthesis of novel semicarbazone derivatives has gained significant attention due to their potential biological activities. Molecular docking studies help in understanding their binding interactions with target proteins. Evaluating their cytotoxic activity is crucial for drug development, offering promising insights for anticancer therapy with improved efficacy and selectivity.

Acknowledgement. The authors are thankful to Bhupal Nobles' University, Udaipur for providing laboratory facilities.
Conflict of Interest. None.

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How to cite this article: Shivani Dhariwal and Hemendra Pratap Singh (2023). Synthesis, Molecular Docking and Cytotoxic Activity of Some Novel Semicarbazone Derivatives. *Biological Forum – An International Journal*, *15*(5): 1795-1801.