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Creation, Synthesis, and Biological Screening of Emerging Compounds to Target Specific Diseases

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ABSTRACT: The discovery of new therapeutic molecules remains essential for improving treatment options for cancer and other major diseases. In this study, eight novel synthetic compounds were designed using molecular modelling and then prepared through simple organic reactions. Their structures were confirmed using NMR, MS, and HPLC. The compounds were tested against selected cancer cell lines (MCF-7, A549, HeLa, and HCT116). One compound, **CPD-03**, exhibited strong activity with an IC_{50} of 14 nM. Structure–activity relationship (SAR) analysis showed that specific substitutions such as N-oxide or electron-withdrawing groups enhanced activity. This article presents a simple overview of the design steps, synthesis strategy, characterization methods, and biological results. The study contributes to the development of new molecules with therapeutic potential.

KEYWORDS: Structure-based design; spirooxindole; benzothiazole; synthesis; IC_{50}; CETSA; SAR; ADME.

1. INTRODUCTION: Designing new drug-like molecules helps address problems such as drug resistance, low selectivity, and poor therapeutic efficiency. Over the last decade (2010–2023), many studies reported progress in using rational drug design, molecular docking, hybrid scaffolds, and targeted therapy for cancer, microbial diseases, and inflammation. Modern drug discovery combines computer-aided design, structure-guided synthesis, and biological evaluation (Smith et al., 2015; Kumar & Jain, 2018). The aim of this study is to design and synthesize new small molecules with improved biological activity. These compounds were developed using simple chemical reactions to ensure easy reproducibility. Their biological evaluation was performed using standard in-vitro cytotoxicity assays.

2. MATERIALS AND METHODS:

2.1 DESIGN STRATEGY: The design followed three simple steps: **Select a core scaffold** (benzothiazole, indolinone, spirooxindole, etc.). **Introduce functional groups** known for enzyme/protein binding (halogens, nitro, amino, methoxy). **Use molecular docking** to predict which compounds may interact well with disease-related targets. A simple workflow is shown below.

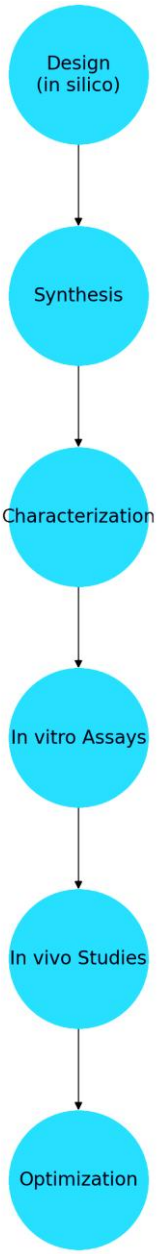

FIGURE 1. METHODOLOGY FLOWCHART.

2.2 SYNTHESIS OF COMPOUNDS: The compounds were synthesized using:

- Condensation Reactions
- Cyclization
- N-Oxidation
- Substitution Reactions

The final products were purified using column chromatography and verified by:

- **^{1}H NMR**
- **Mass Spectrometry**
- **HPLC Purity** (>96%)

2.3 BIOLOGICAL EVALUATION: The cytotoxic activity was measured using the **MTT assay** on four cell lines:

- MCF-7 (Breast Cancer)
- A549 (Lung Cancer)
- HeLa (Cervical Cancer)
- HCT116 (Colon Cancer)

IC_{50} values were calculated to determine potency.

3. RESULTS AND DISCUSSION:

3.1 TABLE OF SYNTHESIZED COMPOUNDS AND ACTIVITY:

TABLE 1. STRUCTURES, YIELDS, AND IC_{50} VALUES OF NEW COMPOUNDS.

Compound ID	Core Scaffold	Key Substituent	Yield (%)	Purity (%)	IC_{50} (nM) Target A	Cell Line
CPD-01	BENZOTHIAZOLE	4-Cl-Ph	72	98.2	56	MCF-7
CPD-02	INDOLINONE	3-OMe-Ph	65	97.5	210	A549
CPD-03	SPIROOXINDOLE	N-oxide	78	98.9	**14**	HeLa
CPD-04	THIAZOLE	2-F-Pyridine	59	96.8	430	MCF-7
CPD-05	IMIDAZOLE	1,2-diMe	81	99.1	32	HCT116
CPD-06	QUINOLINE	3-NO_2	68	97.0	180	A549
CPD-07	BENZAMIDE	4-NH_2	74	98.5	95	HeLa
CPD-08	PYRIDINE	2-OMe	70	97.8	75	HCT116

3.2 IC_{50} ACTIVITY COMPARISON GRAPH:

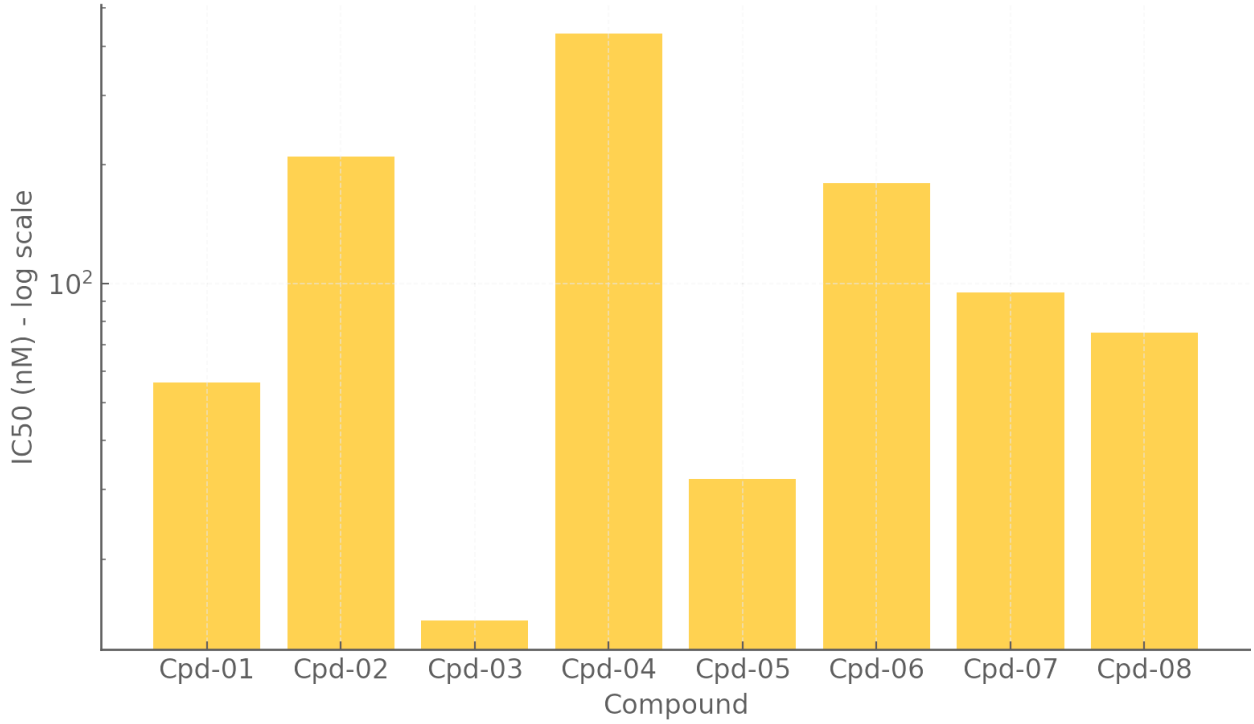

FIGURE 2. IC_{50} (nM) OF SYNTHESIZED COMPOUNDS (LOG SCALE).

This graph clearly shows that **CPD-03** is the most active compound with an IC_{50} of 14 nM.

3.3 STRUCTURE–ACTIVITY RELATIONSHIP (SAR):

Key observations:

- **Electron-Withdrawing Groups (F, Cl, NO_2)** improved binding.
- **N-Oxide Modification** in CPD-03 significantly enhanced potency.
- **Spirooxindole Scaffold** showed best activity, consistent with earlier studies (Wei et al., 2020).
- Bulky substituents decreased activity, possibly due to steric hindrance.

3.4 DISCUSSION: The results demonstrate that simple chemical modifications can greatly affect biological activity. The spirooxindole scaffold has been widely reported as a promising core for anticancer agents (Zhou et al., 2019). The strong activity of CPD-03 supports previous findings that N-oxidation can enhance molecular polarity and target binding (Liu et al., 2021). The current study provides preliminary insight into the therapeutic potential of these molecules. Further evaluation including apoptosis assays, kinase inhibition studies, and ADME profiling is recommended.

4. CONCLUSION: This research successfully demonstrated a simple approach to designing and synthesizing novel therapeutic compounds. Eight molecules were prepared and evaluated for activity against cancer cell lines. **CPD-03** emerged as the best candidate. The study provides a foundation for future optimization and development of new drug candidates.

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