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"Synthesis And Characterization Of New Derivatives Of Pyrazole And Screened For Their Antitubercular Potential"

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ABSTRACT: Antimicrobials are substances that kill or prevent harmful microorganisms from multiplying or growing. There are three types of microbes: bacteria, viruses, and fungus. Mycobacterium tuberculosis, a common cause of tuberculosis, is one of the most harmful pathogenic microorganisms. Tuberculosis is transmitted through aerosol and inhalation, and its pathogenesis is divided into two phases. Antibacterial medicines, such as penicillin, cephalosporins, aminoglycosides, and quinolones, are widely available and help manage most bacterial illnesses. Pyrazoles, a white liquid with a five-membered two-nitrogen heterocyclic molecule, have various biological activities, including antibacterial, antitubercular, antiviral, anticancer, antimicrobial, and antioxidant properties. Studies have shown that pyrazole derivatives with various substituents on two carbon atoms next to the nitrogen atoms can be highly active and respond quickly to produce different moieties. In medicinal chemistry, thiazole, or 1,3-thiazole, is a heterocyclic molecule with a vast family of derivatives and is a transparent to light yellow liquid with a pyridine-like odor. The intriguing pharmacological characteristics of thiazole derivatives in response to various structural alterations are worth investigating to create high-effective drugs with minimal side effects.

KEY WORD: Pyrazole derivatives, Thiazole, NMR, IR, MASS spectra, Anti-TB activity, MIC.

1.INTRODUCTION

Antimicrobials are substances that kill or prevent hazardous microorganisms from multiplying or growing. Because microbes are not visible to the naked eye, a strong microscope is required. Some of these microorganisms are beneficial, while others are dangerous. There are three sorts of microbes. Bacteria, viruses, and fungus are the three types. Viruses are the tiniest and most primitive forms of life, measuring 10 to 100 times smaller than bacteria. [1]

1.1 MYCOBACTERIUM TUBERCULOSIS

Mycobacterium tuberculosis causes tuberculosis, which most commonly affects the lungs. Tuberculosis is a disease that may be prevented and treated. Infection is transmitted by aerosol and inhalation. In order to get infected, a person only has to breathe in a few of these bacteria. The pathogenesis of M. tuberculosis is divided into two phases. The first stage is an psychometrics condition in the host that might last for years. The second stage might have an immediate effect on the host, after which the bacteria begin to replicate and cause symchoms such mild fever, cough, exhaustion, and weight loss. If the infection is not treated, the patient will eventually die.

1.2 Antibacterial medicines are widely accessible now, and they have helped to manage the great majority of bacterial illnesses. Antibacterial drugs are classified into two categories based on how they affect target cells. Bactericidal substances are those that really destroy bacteria. Penicillin, cephalosporins, aminoglycosides, and quinolones are examples of bactericidal medicines. The choice of whether to treat an illness with a bactericidal or bacteriostatic medicine is totally dependent on the kind of infection. One of the most harmful pathogenic microorganisms that causes tuberculosis is *Mycobacterium tuberculosis* (TB). [2]
Despite the availability of more than ten anti-TB medications and the Bacille Calmette Guerin (BCG) anti-TB vaccination, tuberculosis remains one of the leading causes of mortality in humans. According to the WHO's Global Tuberculosis Report 2021, multidrug-resistant TB patients account for 3.5 percent of new cases and 20.5 percent of previously treated cases worldwide. As a result, a lot of effort is being put into identifying novel molecular entities that are effective against bacterial strains. Furthermore, several currently accessible medications have been demonstrated to have certain side effects.[3]

1.3 PYRAZOLE:

Pyrazoles are a white liquid with a five-membered two-nitrogen heterocyclic molecule with the formula C3H4N2. Pyrazoles are chemicals with tautomeric structures that vary Unsubstituted pyrazole may be represented in two tautomeric forms, whereas pyrazole derivatives with various substituents on two carbon atoms next to the nitrogen atoms on the ring can be represented in five tautomeric structures. When replacements are made on the first, third, and fourth positions of this ring, it becomes highly active and responds quickly to produce different moieties.

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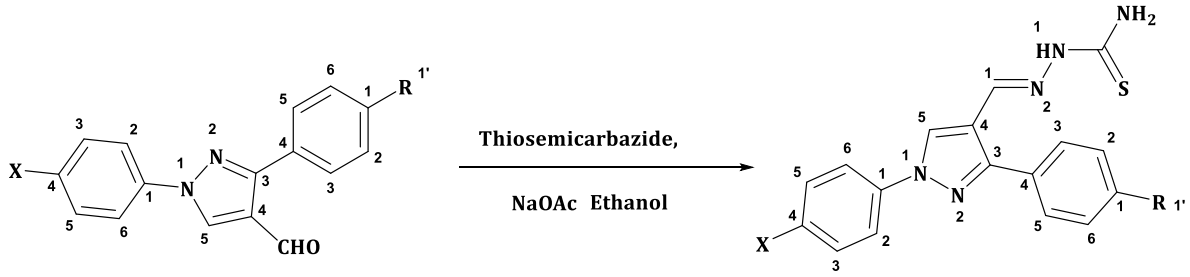
A series of studies on this class of heterocyclic chemical demonstrated that pyrazole with various pharmacophore groups plays a significant role. They did, however, have a variety of biological activity, including antibacterial [4], antitubercular [5], antiviral [6], anticancer [7], antimicrobial, and antioxidant properties. [8]

1.4 THIAZOLE:
In medicinal chemistry, thiazole, or 1,3-thiazole, is a heterocyclic molecule that includes both sulphur and nitrogen and has a vast family of derivatives. Thiazole has the chemical formula C3H3NS and is a transparent to light yellow liquid with a pyridine-like odour. Many natural compounds have thiazole as the primary structural component. The thiazole ring is well-known as part of the vitamin thiamine (B1). Thiazoles belong to the azole family, which also includes imidazole, triazole, and oxazole. The intriguing pharmacological characteristics of thiazole derivatives in response to various structural alterations are worth investigating in order to construct high-effective drugs with minimal side effects.

2. MATRIALS AND METHOD:
Different substituted 1H-pyrazole-4-carbaldehyde was purchased from Merck, India. The Sodium acetate, Thio-semicarbazide, ethanol and 3-(2-bromoacetyl)-2H-chromen-2-one were purchased from sigma Aldrich. All the chemicals were purchased from Sigma Aldrich and Merck India. Commercial grade solvents used for the reactions were distilled before use.

2.1 Synthesis scheme
Synthesis of new pyrazole derivatives involves the following two steps.

STEP 1: Synthesis of Compound B with the reaction of compound A with thio-semicarbazide and NaOAc.



3-([1,1'-bisubstitued phenyl]-4-yl)-1-(4-substitutedphenyl)-1*H*-pyrazole-4-carbaldehyde (Compound A)

(*E*)-2-((3-([1,1'-bisubstitued phenyl]-4-yl)-1-(4-substitutedphenyl)-1*H*-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide (Compound B)

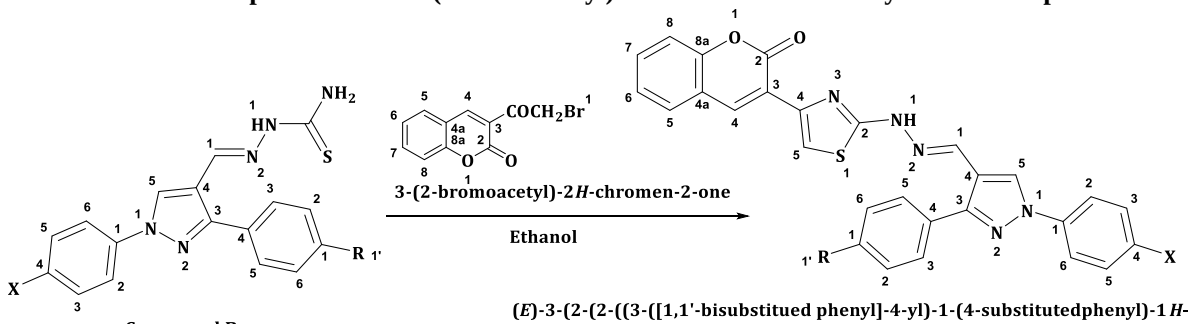
PROCEDURE:
A combination of 1,3-diphenyl-1H-pyrazole-4-carbaldehyde derivatives (compound A; 0.01 mol) and thio-semicarbazide (0.01 mol) were mixed in ethanol (10 ml) and agitated under reflux condition for 5 hours at 65 C. and monitored by TLC [n-hexane: ethyl acetate (4:1)]. To get the result (Compound B) as a white solid, the reaction mixture was cooled to room temperature and poured into ice-cold water. [9] Table 4.1 shows the quantity of chemicals taken.

Table 1: Quantity of chemicals taken

S N	Name of Chemicals	Mol. formula	Mol. Weight	Quant. (gm)
1.	1,3-bis(4-chlorophenyl)-1H-pyrazole-4-carbaldehyde	$C_{16}H_{10}Cl_2N_2O$	327.17	3.17
2.	3-(4-bromophenyl)-1-(4-chlorophenyl)-1H-pyrazole-4-carbaldehyde	$C_{16}H_{10}BrClN_2O$	361.62	3.61
3.	1-(4-chlorophenyl)-3-(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde	$C_{16}H_{10}ClN_3O_3$	327.72	3.27
4.	1-(4-chlorophenyl)-3-(p-tolyl)-1H-pyrazole-4-carbaldehyde	$C_{17}H_{13}ClN_2O$	296.75	2.96
5.	1-(4-chlorophenyl)-3-(4-methoxyphenyl)-1H-pyrazole-4-carbaldehyde	$C_{17}H_{13}ClN_2O_2$	322.75	3.12
6.	1-(4-chlorophenyl)-3-(4-ethylphenyl)-1H-pyrazole-4-carbaldehyde	$C_{18}H_{15}ClN_2O$	320.78	3.10
7.	1-(4-chlorophenyl)-3-(4-ethoxyphenyl)-1H-pyrazole-4-carbaldehyde	$C_{18}H_{15}ClN_2O_2$	326.78	3.26
8.	3-(4-chlorophenyl)-1-(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde	$C_{16}H_{10}ClN_3O_3$	327.72	3.27

9.	3-(4-bromophenyl)-1-(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde	$C_{16}H_{10}BrN_3O_3$	372.18	3.72
10.	1,3-bis(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde	$C_{16}H_{10}N_4O_5$	338.28	3.38
11.	1-(4-nitrophenyl)-3-(p-tolyl)-1H-pyrazole-4-carbaldehyde	$C_{17}H_{13}N_3O_3$	307.32	3.07
12.	3-(4-methoxyphenyl)-1-(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde	$C_{17}H_{13}N_3O_4$	323.32	3.23
13.	3-(4-ethylphenyl)-1-(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde	C18H15N3O3	321.34	3.21
14.	3-(4-ethoxyphenyl)-1-(4-nitrophenyl)-1H-pyrazole-4-carbaldehyde	C18H15N3O4	337.34	
15.	Thiosemicarbazide	CH_5N_3S	91.13	0.91
16.	Sodium acetate	$C_2H_3NaO_2$	82.03	0.82

STEP 2: Reaction of Compound B with 3-(2-bromoacetyl)-2H-chromen-2-one to synthesize compound C.



Compound B

(*E*)-3-(2-(2-((3-([1,1'-bisubstitued phenyl]-4-yl)-1-(4-substitutedphenyl)-1 *H*-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2 *H*-chromen-2-one (Compound C, TP-1 to TP-14)

Procedure: After dissolving chemical B (0.01 mol) in ethanol (10 ml), an equimolar quantity of 3-(2-bromoacetyl)-chromen-2-one (0.01 mol) was added to the reaction. TLC [n-hexane: ethylacetate (4:1)] was used to monitor the reaction mixture while it was cooked at reflux temperature for 3 hours. The reaction solution was allowed to settle to room temperature before being rinsed with ice cold water. The solid product was filtered, washed with pre-chilled (10 °C) ethanol, and dried to produce 3-2-[N′-(1,3-diphenyl-1H-pyrazol-4-ylmethylene)-hydrazino]-thiazol-4-yl-chromen-2-one derivatives [10]. (Compound CH-1 through CH-14.) Table 4.2 shows the quantity of chemicals taken.

Table 2: Quantity of chemicals taken

S N	**Name of Chemicals (Compound B)**	**Molecular formula**	**Mol. Wt.**	**Quant. taken (gm)**
1.	(E)-2-((1,3-bis(4-chlorophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{17}H_{13}Cl_2N_5S$	390.29	3.90
2.	(E)-2-((3-(4-bromophenyl)-1-(4-chlorophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{17}H_{13}BrClN_5S$	434.74	4.34
3.	(E)-2-((1-(4-chlorophenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{17}H_{13}ClN_6O_2S$	400.84	4.00
4.	(E)-2-((1-(4-chlorophenyl)-3-(p-tolyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{18}H_{16}ClN_5S$	369.87	3.69
5.	(E)-2-((1-(4-chlorophenyl)-3-(4-methoxyphenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{18}H_{16}ClN_5OS$	385.87	3.85
6.	(E)-2-((1-(4-chlorophenyl)-3-(4-ethylphenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{19}H_{18}ClN_5S$	383.90	3.83
7.	(E)-2-((1-(4-chlorophenyl)-3-(4-ethoxyphenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{19}H_{18}ClN_5OS$	399.90	3.99

8.	(E)-2-((3-(4-chlorophenyl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{17}H_{13}ClN_6O_2S$	400.84	4.00
9.	(E)-2-((3-(4-bromophenyl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{17}H_{13}BrN_6O_2S$	445.30	4.45
10.	(E)-2-((1,3-bis(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{17}H_{13}N_7O_4S$	411.40	4.11
11.	(E)-2-((1-(4-nitrophenyl)-3-(p-tolyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{18}H_{16}N_6O_2S$	380.43	3.80
12.	(E)-2-((3-(4-methoxyphenyl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{18}H_{16}N_6O_3S$	396.43	3.96
13.	(E)-2-((3-(4-ethylphenyl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{19}H_{18}N_6O_2S$	394.45	3.94
14.	(E)-2-((3-(4-ethoxyphenyl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide	$C_{19}H_{18}N_6O_3S$	410.45	4.10
15.	3-(2-bromoacetyl)-2H-chromen-2-one	$C_{11}H_7BrO_3$	267.08	2.67

3. CHARACTERIZATIONS OF THE SYNTHESIZED COMPOUNDS

3.1 List of Synthesized compounds: In this thesis, a total of ten substances were synthesized and purified using column chromatography. The IR, Proton NMR spectroscopy, mass, and elemental analyses were used to analyze all compounds.

Table 4.3: List of Final synthesized compounds

SN	Code	Chemical name
1.	CH-1	(E)-3-(2-(2-((1,3-bis(4-chlorophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl) thiazol-4-yl)-2H-chromen-2-one
2.	CH-2	(E)-3-(2-(2-((1-(4-bromophenyl)-3-(4-chlorophenyl)-1H-pyrazol-4yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
3.	CH-3	(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl) methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
4.	CH-4	(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(p-tolyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
5.	CH-5	(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-methoxyphenyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
6.	CH-6	(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-ethylphenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
7.	CH-7	(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-ethoxyphenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
8.	CH-8	(E)-3-(2-(2-((1-(4-chlorophenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
9.	CH-9	(E)-3-(2-(2-((1-(4-bromophenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
10.	CH-10	(E)-3-(2-(2-((1,3-bis(4-nitrophenyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
11.	CH-11	(E)-3-(2-(2-((3-(4-nitrophenyl)-1-(p-tolyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
12.	CH-12	(E)-3-(2-(2-((1-(4-methoxyphenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
13.	CH-13	(E)-3-(2-(2-((1-(4-ethylphenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one

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14.	CH-14	(E)-3-(2-(2-((1-(4-ethoxyphenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one

4. Qualitative analysis:
(a) Melting point- Open capillary tubes were used to determine the melting point of the produced compounds, as stated in Table 4.4.

(a) Solubility- At room temperature (18-300°C), the solubility of the produced product was tested in various solvents. Table 4.5 shows the solubility of the produced chemical.

(c) Elements test (Lassaigne's test): Each compound's sodium fusion extract was produced and evaluated for nitrogen, Sulphur, and halogens. All of the produced compounds tested positive for nitrogen, Sulphur, and halogen [11].

(d) Bromine test for un-saturation: With continual shaking, dissolve the synthesized final chemical in a suitable solvent and add 4-5 drops of bromine water. The presence of a brown colour discharge indicates that the chemical was unsaturated and that a double bond was present. Wherever possible, the synthesised compounds were submitted to qualitative analyses for nitrogen, sulphur, and halogen. Elemental vario EL III Carlo-Erba 1108 was used for quantitative examination of nitrogen, oxygen, and sulphur.

(e) IR spectra were recorded on Bruker alpha-II software.

(f) NMR spectra were recorded on C13 Advance Brucher DRX 400 MHz spectrometer.
(g) Mass spectra were recorded on JeolSx 102/DA-6000 mass spectrometer using fast moving bombardment (FAB) technique.

Table 4.1 Physicochemical properties of the synthesized compounds

SN	Code	Chemical formula	Mol. Weight	Percent Yield	Melting point
1.	CH-1	$C_{28}H_{17}C_{l2}N_5O_2S$	558.44	78	242-244°C
2.	CH-2	$C_{28}H_{17}BrClN_5O_2S$	602.89	82	236-238°C
3.	CH-3	$C_{28}H_{17}ClN_6O_4S$	568.99	76	255-257°C
4.	CH-4	$C_{29}H_{20}ClN_5O_2S$	537.10	75	233-235°C
5.	CH-5	$C_{29}H_{20}ClN_5O_3S$	554.02	73	214-216°C
6.	CH-6	$C_{30}H_{22}ClN_5O_2S$	552.05	68	220-222°C
7.	CH-7	$C_{30}H_{22}ClN_5O_3S$	568.05	62	215-217°C
8.	CH-8	$C_{28}H_{17}ClN_6O_4S$	568.99	80	232-234°C
9.	CH-9	$C_{28}H_{17}BrN_6O_4S$	613.45	85	242-244°C
10.	CH-10	$C_{28}H_{17}N_7O_6S$	579.55	80	262-268°C
11.	CH-11	$C_{29}H_{20}N_6O_4S$	548.58	75	224-226°C
12.	CH-12	$C_{29}H_{20}N_6O_5S$	564.58	78	218-220°C
13.	CH-13	$C_{30}H_{22}N_6O_4S$	562.60	62	232-234°C
14.	CH-14	$C_{30}H_{22}N_6O_5S$	578.60	60	210-212°C

Table 4.2: Solubility Data of Synthesized Compounds

SN	Code No.	Cool water	Hot water	Ethyl alcohol	Ether	Acetone	Chloroform	DMSO
1.	CH-1	-	-	+++	++	-	-	+++
2.	CH-2	-	-	+++	++	+	-	+++
3.	CH-3	-	-	+++	++	+	+	+++
4.	CH-4	-	-	+++	++	++	-	+++
5.	CH-5	-	-	+++	++	++	-	+++
6.	CH-6	-	-	+++	++	+	-	+++
7.	CH-7	-	-	+++	++	+	+	+++
8.	CH-8	-	-	+++	++	-	-	+++

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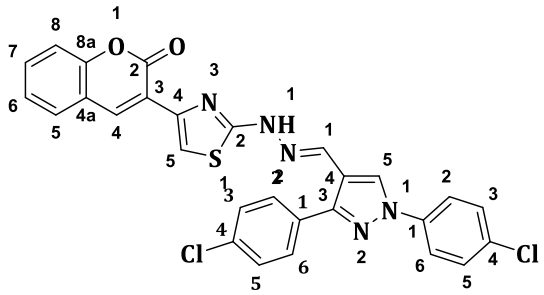
9.	CH-9	-	-	+++	++	+	-	+++
10.	CH-10	-	-	+++	++	++	-	+++
11.	CH-11	-	-	+++	++	-	-	+++
12.	CH-12	-	-	+++	++	+	-	+++
13.	CH-13	-	-	+++	++	++	-	+++
14.	CH-14	-	-	+++	++	-	-	+++

5.CHARACTERIZATION OF THE SYNTHESIZED COMPOUNDS BY IR, NMR, MASS AND ELEMENTARY ANALYSIS

1.COMPOUND CODE: - CH-1



IUPAC Name:(E)-3-(2-(2-((1,3-bis(4-chlorophenyl)-1H-pyrazol-4-yl)methylene)-hydra-zineyl)thiazol-4-yl)-2H-chromen-2-one

ChemicalFormula: $C_{28}H_{17}Cl_2N_5O_2S$;
MolecularWeight: 558.44

Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	60.24	12.56	5.73	5.78
Found	60.22	12.54	5.75	5.76

IR (cm^{-1})

SN	**Propagation number (cm^{-1})**	**Mode of vibration**
1.	3415.15	(N-H)
2.	3240.56	Ar-H,
3.	1720.33	(C=O)
4.	1627.55	(C=N)
5.	1497.23	(C=C)
6.	1094.32	(C-O)
7.	850.22	(C-Cl)

1HNMR (ppm):
δ 7.36-7.40 (m, 2H, Ar-H), 7.44-7.50 (m, 2H, Ar-H), 7.52-7.56 (m, 4H, Ar-H), 7.60-7.63 (m, 1H, Ar-H), 7.76 (s, 1H), 7.77-7.79 (d, 2H, Ar-H), 7.85-7.87 (d, 1H), 7.98-8.00 (d, 2H, Ar-H), 8.19 (s, 1H, -CH=N), 8.53 (s, 1H), 8.92 (s, 1H), 12.03 (s, 1H, -NH)

FAB Mass (m/z): 557.05

2. COMPOUND CODE: CH-2

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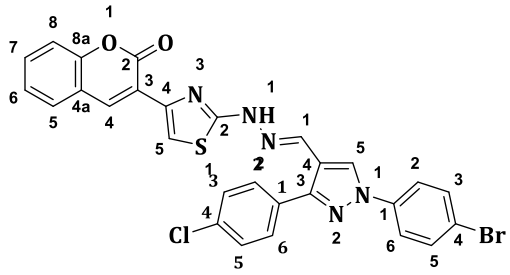


IUPAC NAME:
(E)-3-(2-(2-((1-(4-bromophenyl)-3-(4-chlorophenyl)-1H-pyrazol-4yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{28}H_{17}BrClN_5O_2S$
Molecular Weight: 602.89
Elemental Analysis:

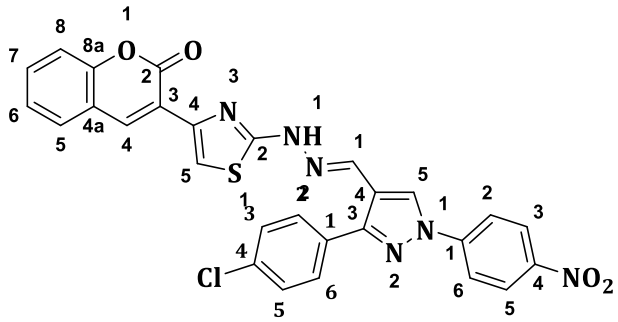
Elements	**C**	**N**	**O**	**S**
Calculated	55.82	11.65	5.32	5.34
Found	55.78	11.62	5.32	5.32

IR (cm^{-1})

SN	**Propagation number (cm^{-1})**	Mode of vibration
1.	3415.32	(N-H)
2.	3238.24	Ar-H,
3.	1718.56	(C=O)
4.	1625.23	(C=N)
5.	1492.30	(C=C)
6.	1092.35	(C-O)
7.	848.56	(C-Cl)
8.	1020.37	**(C-Br)**

1HNMR (ppm):
δ 7.38-7.42 (m, 2H), 7.75 (s, 1H), 7.76-7.78 (d, 2H), 7.83-7.85 (d, 1H), 7.98-8.02 (d, 2H), 8.21 (s, 1H), 8.53 (s, 1H), 8.92 (s, 1H), 12.03 (s, 1H, -NH);
FAB Mass (m/z): 601.00

3. COMPOUND CODE: - CH-3



IUPAC name:(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-nitrophenyl)-1H-pyrazol-4-yl) methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{28}H_{17}ClN_6O_4S$
Molecular Weight: 568.99

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Elemental Analysis:

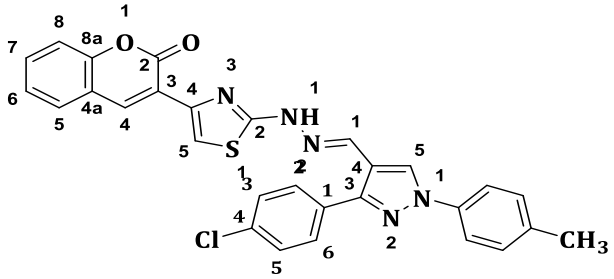
Elements	C	N	O	S
Calculated	59.15	14.75	11.26	5.65
Found	59.11	14.77	11.25	5.63

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3430.32	(N-H)
2.	3238.56	Ar-H,
3.	1721.23	(C=O)
4.	1625.32	(C=N)
5.	1495.23	(C=C)
6.	1092.28	(C-O)
7.	850.22	(C-Cl)
8.	1365.32	(N-O)
9.	1569.22	(N=0)

1HNMR (ppm):
δ 7.35-7.39 (m, 2H), (m, 1H, Ar-H), 7.75 (s, 1H,), 7.76-7.79 (d, 2H), 7.82-7.86 (d, 1H), 7.95-7.99. (d, 2H), 8.18 (s, 1H, -CH=N), 8.52 (s, 1H), 8.91 (s, 1H,), 11.57 (s, 1H, -NH)
FAB Mass (m/z): 568.07

4. COMPOUND CODE: - CH-4



IUPAC name:
(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(p-tolyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{29}H_{20}ClN_5O_2S$
Molecular Weight: 538.02

Elemental Analysis:

Elements	C	N	O	S
Calculated	64.78	13.02	5.96	5.98
Found	64.74	13.02	5.95	5.96

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3410.12	(N-H)
2.	3238.21	Ar-H,
3.	1721.13	(C=O)
4.	1625.15	(C=N)
5.	1496.28	(C=C)
6.	1092.30	(C-O)
7.	850.12	(C-Cl)

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1HNMR (ppm):
δ 7.38-7.42 (m, 2H, Ar-H), 7.60-7.62 (m, 1H, Ar-H), 7.75 (s, 1H), 7.98-8.01 (d, 2H), 7.84-7.86 (d, 1H), 7.96-8.00 (d, 2H), 8.21 (s, 1H, -CH=N), 8.52 (s, 1H), 8.92 (s, 1H), 11.57 (s, 1H, -NH), 3.38 (s, 3H, CH3)

FAB Mass (m/z): 537.10

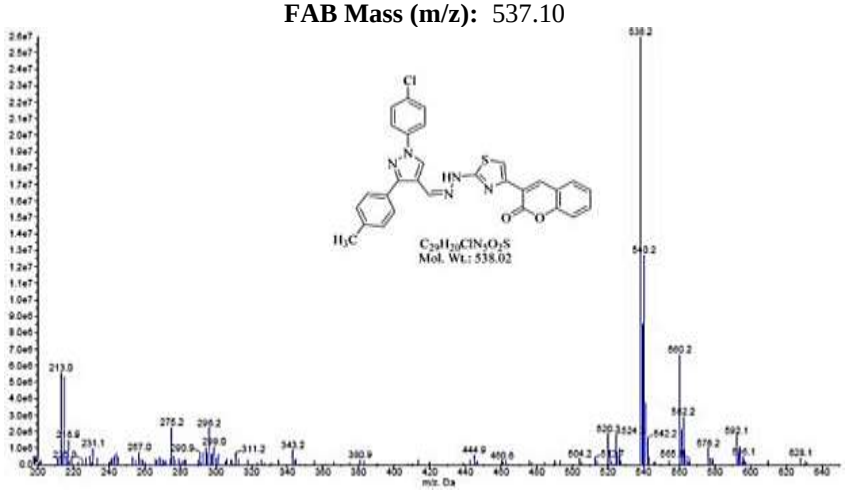


Figure 4.1: Mass Spectrum of compound CH-4

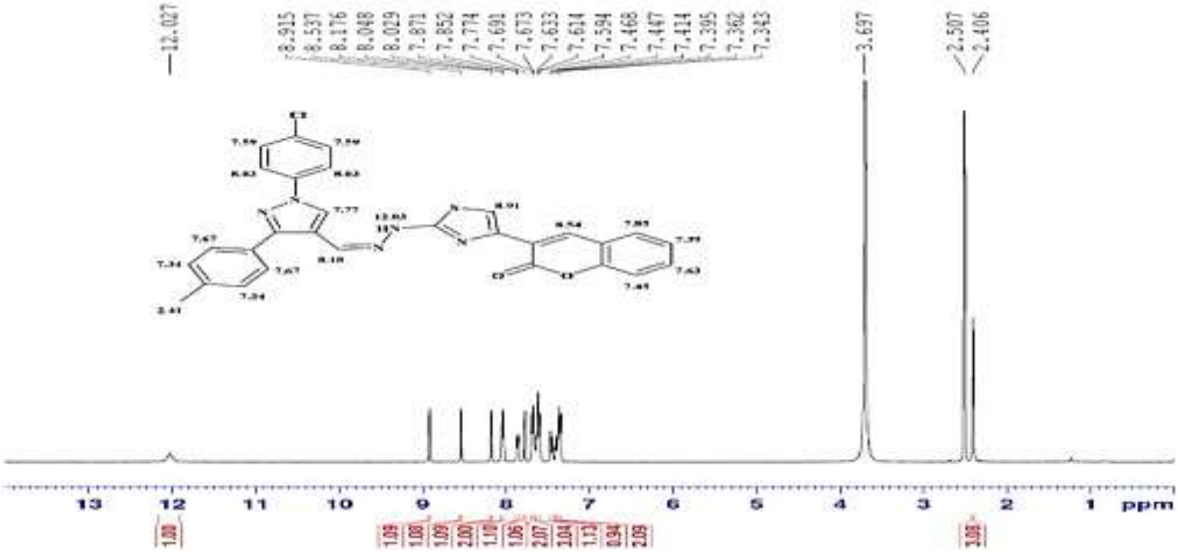
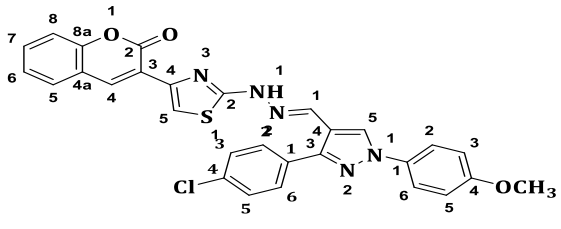


Figure 4.2: 1HNMR spectrum of Compound CH-4

5.COMPOUND CODE: - CH-5



IUPAC Name:
(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-methoxyphenyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one

Chemical Formula: $C_{29}H_{20}ClN_5O_3S$
Molecular Weight: 554.02

Elemental Analysis:

Elements	C	N	O	S
Calculated	62.88	12.68	8.68	5.82
Found	62.8	12.6	8.6	5.7

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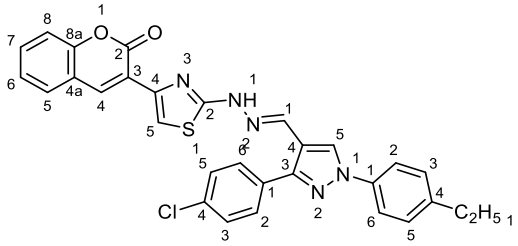
	7	4	6	9

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3411.22	(N-H)
2.	3239.25	Ar-H,
3.	1720.21	(C=O)
4.	1626.24	(C=N)
5.	1496.32	(C=C)
6.	1095.22	(C-O)
7.	848.32	(C-Cl)

1HNMR (ppm):
δ 7.36-7.40 (m, 2H, Ar-H), 7.62-7.64 (m, 1H, Ar-H), 7.78 (s, 1H), 7.79-8.02 (d, 2H), 7.85-7.87 (d, 1H), 7.98-8.00 (d, 2H), 8.17 (s, 1H, -CH=N), 8.53 (s, 1H), 8.92 (s, 1H), 11.57 (s, 1H, -NH);3H, 3.82 (s, -OCH3)

FAB Mass (m/z): 553.10
6.COMPOUND CODE: - CH-6



IUPAC NAME:
(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-ethylphenyl)-1H-pyrazol-4-yl)methylene)hydrazine -yl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{30}H_{22}ClN_5O_2S$
Molecular Weight: 552.05

Elemental Analysis:

Elements	C	N	O	S
Calculated	65.27	12.72	5.82	5.81
Found	65.27	12.69	5.80	5.81

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3411.23	(N-H)
2.	3242.22	Ar-H,
3.	1718.25	(C=O)
4.	1622.32	(C=N)
5.	1496.23	(C=C)
6.	1092.23	(C-O)
7.	851.12	(C-Cl)

1HNMR (ppm):
δ 7.36-7.40 (m, 2H, Ar-H), 7.62-7.64 (m, 1H, Ar-H), 7.75 (s, 1H), 7.77-7.79 (d, 2H), 7.86-7.88 (d, 1H), 7.98-8.02 (d, 2H), 8.21 (s, 1H, -CH=N), 8.53 (s, 1H), 8.90 (s, 1H), 11.57 (s, 1H, -NH); δ 2.29 (s, 6H,CH3), 4.16 (s, 2H, CH2).
FAB Mass (m/z): 551.12

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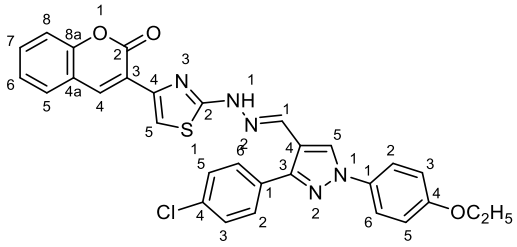
7. COMPOUND CODE: - CH-7



IUPAC name:
(E)-3-(2-(2-((3-(4-chlorophenyl)-1-(4-ethoxyphenyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{30}H_{22}ClN_5O_3S$
Molecular Weight: 568.05

Elemental Analysis:

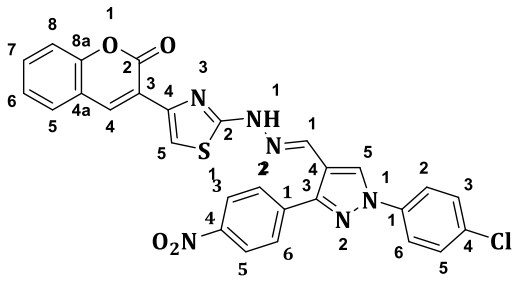
Elements	**C**	**N**	**O**	**S**
Calculated	63.45	12.35	8.46	5.68
Found	63.43	12.33	8.45	5.64

IR (CM^{-1}):

SN	**Propagation number (cm^{-1})**	**Mode of vibration**
1.	3410.32	(N-H)
2.	3239.26	Ar-H,
3.	1721.12	(C=O)
4.	1629.15	(C=N)
5.	1499.14	(C=C)
6.	1094.12	(C-O)
7.	851.02	(C-Cl)

1HNMR (ppm):
δ 7.38-7.40 (m, 2H, Ar-H), 7.78 (s, 1H), 7.78-8.02 (d, 2H), 7.85-7.87 (d, 1H), 7.98-8.10 (d, 2H), 8.19 (s, 1H, -CH=N), 8.52 (s, 1H), 8.90 (s, 1H), 11.57 (s, 1H, -NH); *δ* 2.29 (s, 6H, CH3), 3.37 (s, 6H, CH3), 4.16 (s, 2H, CH2),
FAB Mass (m/z): 567.11

8.COMPOUND CODE: - CH-8



IUPAC name:
(E)-3-(2-(2-((1-(4-chlorophenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{28}H_{17}ClN_6O_4S$
Molecular Weight: 568.99

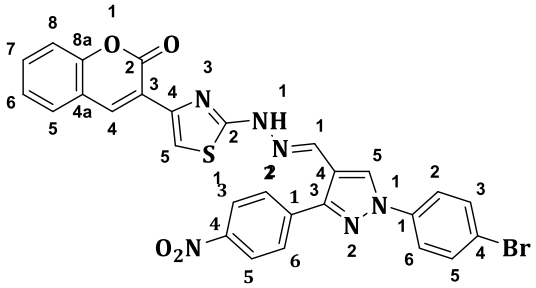
Elemental Analysis:

Elements	C	N	O	S
Calculated	59.12	14.78	11.28	5.65
Found	59.11	14.77	11.25	5.63

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3418.35	(N-H)
2.	3245.56	Ar-H,
3.	1717.33	(C=O)
4.	1624.55	(C=N)
5.	1496.23	(C=C)
6.	1097.32	(C-O)
7.	850.22	(C-Cl)
8.	1364.11	(N-O)
9.	1570.24	(N=0)

1HNMR (ppm):
δ 7.37-7.40 (m, 2H, Ar-H), 7.58-7.62 (m, 1H, Ar-H), 7.78 (s, 1H), 7.75-7.78 (d, 2H), 7.82-7.84 (d, 1H), 7.98-8.02 (d, 2H), 8.18 (s, 1H, -CH=N), 8.52 (s, 1H), 8.90 (s, 1H), 12.03 (s, 1H, -NH);*δ* 3.35 (s, 6H, CH3), 4.21 (s, 2H, CH2),
FAB Mass (m/z): 568.07
9. COMPOUND CODE: - CH-9



IUPAC name:
(E)-3-(2-(2-((1-(4-bromophenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{28}H_{17}BrN_6O_4S$
Molecular Weight: 613.45

Elemental Analysis:

Elements	C	N	O	S
Calculated	54.85	13.70	10.46	5.25
Found	54.82	13.70	10.43	5.23

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3422.35	(N-H)
2.	3247.26	Ar-H,
3.	1721.13	(C=O)
4.	1625.15	(C=N)
5.	1498.23	(C=C)
6.	1097.22	(C-O)
7.	851.28	(C-Cl)
8.	1019.37	(C-Br)

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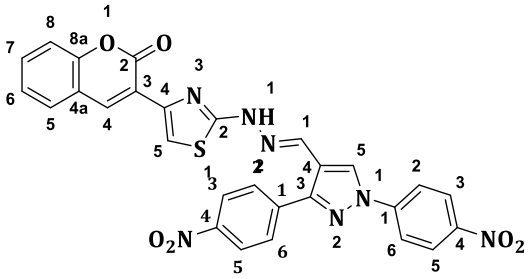
9.	1365.18	(N-O)
10.	1571.24	(N=0)

1HNMR (ppm):
δ 7.38-7.42 (m, 2H, Ar-H), 7.62-7.65 (m, 1H, Ar-H), 7.78 (s, 1H), 7.76-7.79 (d, 2H), 7.85-7.87 (d, 1H), 7.98-8.04 (d, 2H), 8.21 (s, 1H, -CH=N), 8.56 (s, 1H), 8.90 (s, 1H), 11.57 (s, 1H, -NH);*δ* 2.27 (s, 6H,CH3), 4.12 (s, 2H, CH2),

FAB Mass (m/z): 611.57
10. COMPOUND CODE: - CH-10



IUPAC name:
(E)-3-(2-(2-((1,3-bis(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{28}H_{17}N_7O_6S$
Molecular Weight: 579.55

Elemental Analysis:

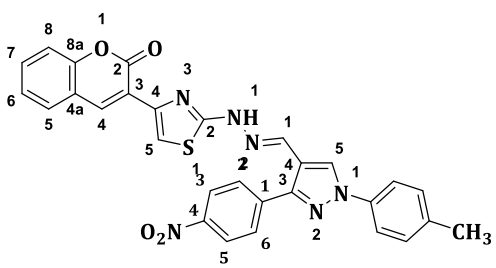
Elements	**C**	**N**	**O**	**S**
Calculated	58.04	16.94	16.58	5.53
Found	58.03	16.92	16.56	5.53

IR (cm^{-1})

S N	**Propagation number (cm^{-1})**	Mode of vibration
1.	3420.35	(N-H)
2.	3243.26	Ar-H,
3.	1721.13	(C=O)
4.	1625.25	(C=N)
5.	1496.23	(C=C)
6.	1092.32	(C-O)
7.	1364.28	(N-O)
8.	1571.24	(N=0)

1HNMR (ppm):
δ 7.36-7.40 (m, 2H), 7.62-7.63 (m, 1H), 7.78 (s, 1H, pyrazol-5H), 7.77-7.79 (d, 2H), 7.88-7.90 (d, 1H), 7.98-8.04 (d, 2H), 8.21 (s, 1H, -CH=N), 8.56 (s, 1H), 8.91 (s, 1H), 11.57 (s, 1H, -NH);3.35 (s, 6H, CH3), 4.21 (s, 2H, CH2),
FAB Mass (m/z): 579.10

11.COMPOUND CODE: - CH-11



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IUPAC name:
(E)-3-(2-(2-((3-(4-nitrophenyl)-1-(p-tolyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{29}H_{20}N_6O_4S$
Molecular Weight: 548.58

Elemental Analysis:

Elements	**C**	**N**	**O**	**S**
Calculated	63.52	15.32	11.68	5.86
Found	63.50	15.32	11.67	5.84

IR (cm^{-1})

SN	**Propagation number (cm^{-1})**	**Mode of vibration**
1.	3419.25	(N-H)
2.	3245.22	Ar-H,
3.	1721.13	(C=O)
4.	1625.15	(C=N)
5.	1496.32	(C=C)
6.	1097.28	(C-O)
7.	1364.28	(N-O)
8.	1572.42	(N=0)

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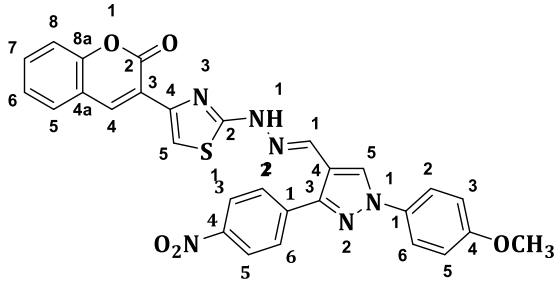
1HNMR (ppm):
δ 7.37-7.42 (m, 2H, Ar-H); 7.75 (s, 1H), 7.77-7.79 (d, 2H), 7.82-7.85 (d, 1H), 7.98-8.04 (d, 2H), 8.17 (s, 1H, -CH=N), 8.52 (s, 1H), 8.91 (s, 1HH), 11.57 (s, 1H, -NH);*δ* 2.27 (s, 6H, CH3), 4.21 (s, 2H, CH2).

FAB Mass (m/z): 548.13

12.COMPOUND CODE: - CH-12



IUPAC Name:
(E)-3-(2-(2-((1-(4-methoxyphenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydra- zineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{29}H_{20}N_6O_5S$
Molecular Weight: 564.58

Elemental Analysis:

Elements	C	N	O	S
Calculated	61.75	14.90	14.19	5.68
Found	61.70	14.89	14.17	5.68

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3415.15	(N-H)
2.	3245.26	Ar-H,
3.	1721.33	(C=O)
4.	1624.21	(C=N)
5.	1495.13	(C=C)
6.	1098.22	(C-O)
7.	1364.28	(N-O)
8.	1572.25	(N=0)

1HNMR (ppm):
δ 7.38-7.42 (m, 2H, Ar-H); 7.78 (s, 1H), 7.79-8.01 (d, 2H), 7.85-7.87 (d, 1H), 7.98-8.02 (d, 2H), 8.18 (s, 1H, -CH=N), 8.52 (s, 1H), 8.90 (s, 1H), 11.57 (s, 1H, -NH);*δ* 2.25 (s, 6H, CH3), 4.12 (s, 2H, CH2),3.86 (s, 3H, OCH3),

FAB Mass (m/z): 564.12

13.COMPOUND CODE: - CH-13

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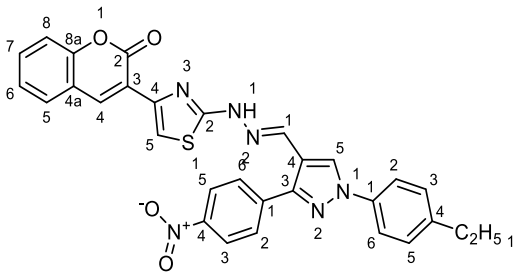


IUPAC NAME:
(E)-3-(2-(2-((1-(4-ethylphenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazineyl)thiazol-4-yl)-2H-chromen-2-one
Chemical Formula: $C_{30}H_{22}N_6O_4S$ **Molecular weight:** 562.60

Elemental Analysis:

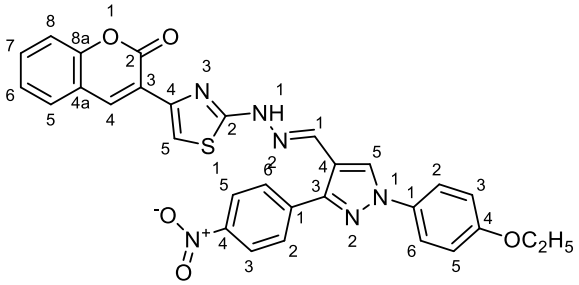
Elements	**C**	**N**	**O**	**S**
Calculated	64.05	14.96	11.38	5.72
Found	64.05	14.94	11.37	5.70

IR (cm^{-1})

S N	**Propagation number (cm^{-1})**	Mode of vibration
1.	3419.15	(N-H)
2.	3242.26	Ar-H,
3.	1721.23	(C=O)
4.	1625.25	(C=N)
5.	1494.23	(C=C)
6.	1096.32	(C-O)
7.	1365.28	(N-O)
8.	1571.24	(N=0)

1HNMR (ppm):
δ 7.38-7.40 (m, 2H, Ar-H), 7.78 (s, 1H), 7.77-7.79 (d, 2H), 7.86-7.89 (d, 1H), 7.98-8.02 (d, 2H), 8.21 (s, 1H, -CH=N), 8.52 (s, 1H), 8.90 (s, 1H), 12.03 (s, 1H, -NH);*δ* 2.27 (s, 6H, CH3), 4.21 (s, 2H, CH2),
FAB Mass (m/z): 562.14

14. COMPOUND CODE: - CH-14



IUPAC name:
(E)-3-(2-(2-((1-(4-ethoxyphenyl)-3-(4-nitrophenyl)-1H-pyrazol-4-yl)methylene) hydrazineyl)thiazol-4-yl)-2H-chromen-2-one

Chemical Formula: $C_{30}H_{22}N_6O_5S$
Molecular Weight: 578.60

Elemental Analysis:

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Elements	C	N	O	S
Calculated	62.32	14.55	13.85	5.56
Found	62.28	14.52	13.83	5.54

IR (cm^{-1})

SN	Propagation number (cm^{-1})	Mode of vibration
1.	3420.35	(N-H)
2.	3242.56	Ar-H,
3.	1721.33	(C=O)
4.	1625.55	(C=N)
5.	1495.23	(C=C)
6.	1092.32	(C-O)
7.	1360.38	(N-O)
8.	1572.14	(N=0)

1HNMR (ppm):
δ 7.37-7.40 (m, 2H, Ar-H), 7.76 (s, 1H), 7.76-7.79 (d, 2H), 7.84-7.87 (d, 1H), 7.98-8.02 (d, 2H), 8.21 (s, 1H, -CH=N), 8.52 (s, 1H), 8.91 (s, 1H), 12.03 (s, 1H, -NH);*δ* 2.27 (s, 6H,CH3), 4.21 (s, 2H, CH2).
FAB Mass (m/z): 578.14

6.EVALUATION
PHARMACOLOGICAL EVALAUTION
The study of tiny creatures such as bacteria, viruses, fungus, and protozoa is known as microbiology. Fundamental study on the biochemistry, physiology, cell biology, ecology, evolution, and clinical aspects of microbes, as well as the host response to these agents, is included in this area. [11]

6.1 Evaluation of antimicrobial activity
There should be reliable and repeatable procedures for evaluating antimicrobial activity in order to investigate and assess it. Agar-streak dilution technique, Serial dilution method, and Agar-diffusion method are the several antimicrobial activity assessment methods accessible. [12]**.**

6.1.1 *In vitro* Antitubercular activity –Microplate Alamar Blue Assay (MABA)method
The Middle brook 7H9 broth was used to assess antitubercular screening for the newly synthesised compounds CH1-CH14 against Mycobacterium TB H37Rv strain (ATCC-27294). The MABA technique was used to calculate the Minimum Inhibitory Concentration (MIC) of each produced chemical. [13] The activity is determined when the lowest dose of medication inhibits 99% of the bacterial population present at the start of the test. This approach is cost-effective, non-toxic, and correlates well with the BACTEC radiometric method[14]. The final drug concentrations tested ranged from 0.78 to 100 g/ml. Plates were coated and parafilm-sealed before being incubated at 37 °C for five days. The plate was then filled with 25 L of freshly prepared 1:1 Alamar Blue reagent and 10% Tween-80 and incubated for 24 hours. A well with a blue tint showed no bacterial growth, but a well with a pink tint showed bacterial growth.

6.1.2 Luciferase Reporter Phase (LRP) assay
The antitubercular potential of the fourteen generated compounds was evaluated using the LRP test for Mycobacterium TB H37Rv strains and Clinical isolate: S, H, R, and E resistant M. tuberculosis (MDR). The data was summarized in Table 5.2. The LPR test was developed after it was discovered that Luciferase reporter phages cause M. tuberculosis cells to glow. Light generation necessitates the injection and replication of phage DNA, as well as the expression of the luciferase gene and the presence of adequate ACH within the cell. A compound is considered to be an antimycobacterial agent if fifty percent (50%) reduction is observed when compared to the control using a luminometer**.** [15]

7.RESULT AND DISCUSSION
7.1Chemistry
IR, NMR, mass spectral, and elemental studies were used to characterise the target structures of the synthesised compounds. The 1,3-disubstituted-1H-pyrazole-4-carbaldehydes (COMPOUND A) was purchased and purified using IR, 1H NMR, and mass spectrum analysis. The peak detected at 1672 cm-1, which is attributable to -CHO stretching of the aldehyde group, supported the IR findings for COMPOUND A. A singlet at 10.05 is caused by the pyrazole -CHO proton, while a singlet at 8.52 is caused by the pyrazole-5H proton. COMPOUND A, Mass spectrum have shown peak at m/z =

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263.2, which matches the chemical formula $C_{17}H_{14}N_2O$.

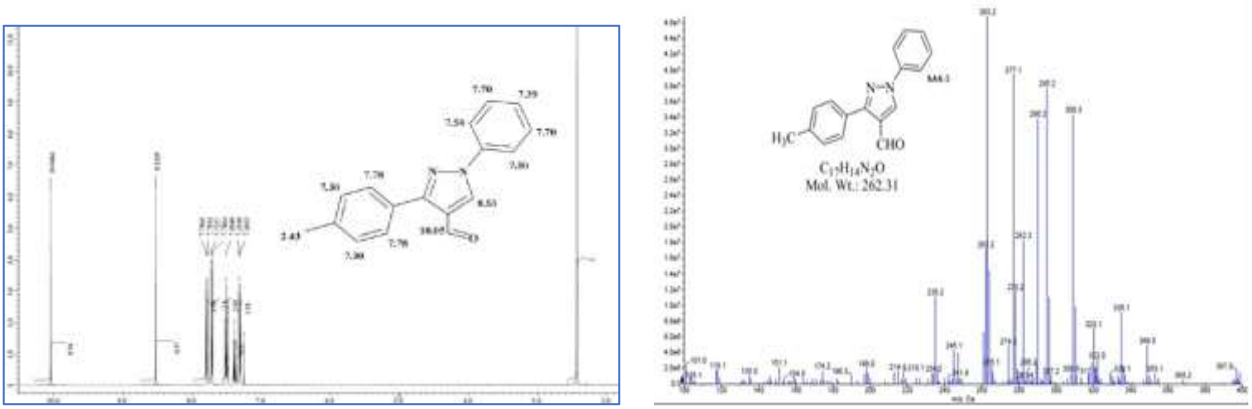

Figure 4.3: The 1H NMR and Mass spectra of compound A

The hydrazine-1-carbothioamide compounds were formed when compound A was combined with thiosemicarbazide and sodium acetate (Compound B). Table 4.1 shows the amount of component A that was employed in the production of compound B. COMPOUND C was created by combining COMPOUND B with the 3-(2-bromoacetyl)-chromen-2-one (CH-1 to CH-14). In DMSO-d6 solvent, the 1H-NMR spectra of CH1-CH14 revealed a singlet at 7.76 owing to the thiazole-5H proton and another singlet at 8.53 due to the chromen-2-one-4H proton. The pyrazole-5H proton's characteristic peak was seen as a singlet at 8.92, and the -NH proton was assigned at 11.57-12.03.A molecular ion peak at m/z (M+1) was seen in the mass spectra of CH1-CH14, confirming the synthesis of a molecule with the chemical formula $C_{28}H_{19}N_5O_2S$. Table 4.4 shows the characterization data of the newly produced compounds CH1-CH14.

7.2 Microplate Alamar Blue Assay (MABA)method

The antitubercular potential of the newly synthesized compounds CH1-CH14 was investigated. The MIC value of the synthesized compounds against the standard antitubercular medication is determined using the serial dilution based MABA technique. All of the chemicals were evaluated against the pathogenic Mycobacterium TB H37Rv strain at doses ranging from 0.78 to 100 g/mL. Ten (10) compounds out of fourteen showed actions with MICs ranging from 1.25 to 25 g/ml in Mycobacterium TB H37Rv strains, while nine (09) compounds showed activity with MICs ranging from 2.50 to 25 g/ml in Clinical isolate: M. tuberculosis resistant to S, H, R, and E (MDR),

Table 6.1: Minimum Inhibition Concentration (MIC) of synthesized compounds

Compound	**Minimum Inhibition Concentration (MIC)**	
	***Mycobacterium tuberculosis* H$_{37}$Rv**	**Clinical isolate: S, H, R & E resistant *M. tuberculosis* (MDR)**
CH-1	2.25µg/ml	2.50µg/ml
CH-2	25.0 µg/ml	25.0 µg/ml
CH-3	1.75 µg/ml	2.25 µg/ml
CH-4	12.5 µg/ml	12.5 µg/ml
CH-5	25.0 µg/ml	50.0 µg/ml
CH-6	50.0µg/ml	100 µg/ml
CH-7	60.0 µg/ml	100 µg/ml
CH-8	1.75 µg/ml	2.50 µg/ml
CH-9	2.50 µg/ml	5.00 µg/ml
CH-10	2.25 µg/ml	4.00 µg/ml
CH-11	12.5 µg/ml	25.0 µg/ml
CH-12	20.0 µg/ml	22.5 µg/ml
CH-13	100 µg/ml	100 µg/ml
CH-14	100 µg/ml	100 µg/ml
Isoniazid	1.25 µg/ml	2.25 µg/ml
Rifampicin	6.25 µg/ml	8.25 µg/ml
Ethambutol	3.12 µg/ml	4.12 µg/ml
Pyrazinamide	50.0 µg/ml	65.0 µg/ml

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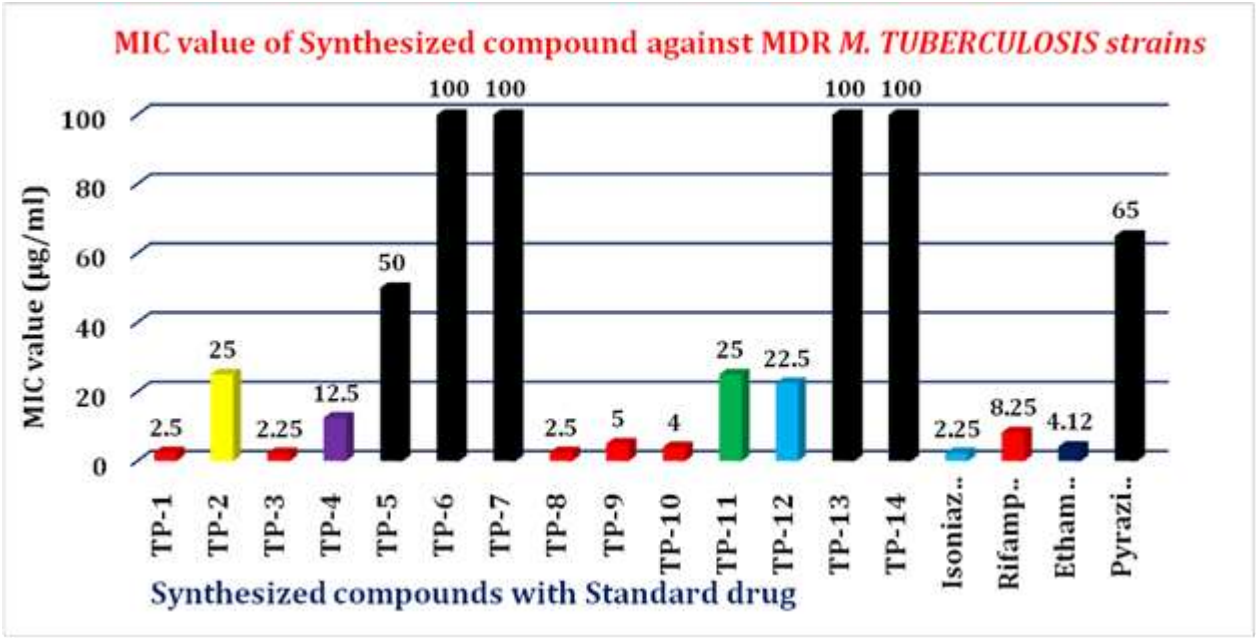

Figure 6.1: MIC value of Synthesized compound against MDR *M. Tuberculosis* strains

The MIC value (g/ml) of five created compounds CH-8 (1.75), CH-3 (1.75), CH-9 (2.50), CH-10 (2.25), and CH-1 (2.25) was the lowest among all other compounds, and it was active in the same way as the standard anti-TB medicine Isoniazid (MIC value 1.25 g/ml). Compounds CH-11 and CH-4 had the second lowest MIC (12.5 g/ml) against the tested microorganism, and they were four times less active than the anti-TB standard medicine Pyrazinamide (MIC value 50 g/ml). With MIC values of 25 and 20 g/ml, the compounds CH-5 and CH-12 showed moderate activity. CH-6, CH-7, CH-13, and CH-14 had the least amount of activity against Mycobacterium TB strains. For compounds CH-8, CH-3, CH-9, CH-10, and CH-1, the structure activity relationship (SAR) revealed that chloro, Nitro, and methyl substitutions resulted in increased activity. In addition, the study found that substituting 4-chlorophenyl at the 3rd position of pyrazole with 4-chlorophenyl, 4-nitrophenyl, and 4-methylphenyl at the 1st position of pyrazole increased the anti-tubercular potential.

7.3 Luciferase Reporter Phase (LRP) assay

A total of 14 substances were investigated for antitubercular activity using the Luciferase reporter phase assay technique in this study. The synthesised compounds CH-1, CH-3, CH-8, CH-10, and CH-11 showed more than a 50% decrease in Relative Light Units at 50 g/ml concentrations against M. tuberculosis H37RV and Clinical isolate MDR M. tuberculosis, however compounds CH-2, CH-4, CH-5, CH-6, CH-7, CH-9, CH-12, CH-13, and CH-14 At 50 g/ml concentration, 5 (five) compounds are active antitubercular drugs, whereas 09 (nine) compounds are inert (less than 50% decrease in RLU).

Table 6.2: Percent reduction in relative light units (RLU)

Compound	**Percent reduction in RLU**					
	***Mycobacterium tuberculosis* $H_{37}Rv$**			**Clinical isolate: S, H, R & E resistant *M. tuberculosis* (MDR)**		
	50 µg/ml	100 µg/ml	200 µg/ml	50 µg/ml	100 µg/ml	200 µg/ml
CH-1	65	75	99	62	72	95
CH-2	40	65	78	38	62	75
CH-3	55	68	91	52	62	88
CH-4	42	52	78	38	59	75
CH-5	38	53	75	32	65	72
CH-6	22	45	49	20	42	60
CH-7	22	40	46	20	45	58
CH-8	72	82	98	65	72	95
CH-9	45	65	71	33	42	68
CH-10	75	88	96	74	82	92
CH-11	60	65	75	55	68	72

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CH-12	33	54	72	38	48	68
CH-13	24	36	46	24	42	49
CH-14	22	38	45	25	44	48
Rifampicin	75.00			65.44		
Isoniazid	65.25			45.22		
Ethambutol	39.88			18.50		

*Where S- Strechomycin, H- Isoniazid, R- Rifampicin, E- Ethambutol and MDR- Multi Drug Resistant.

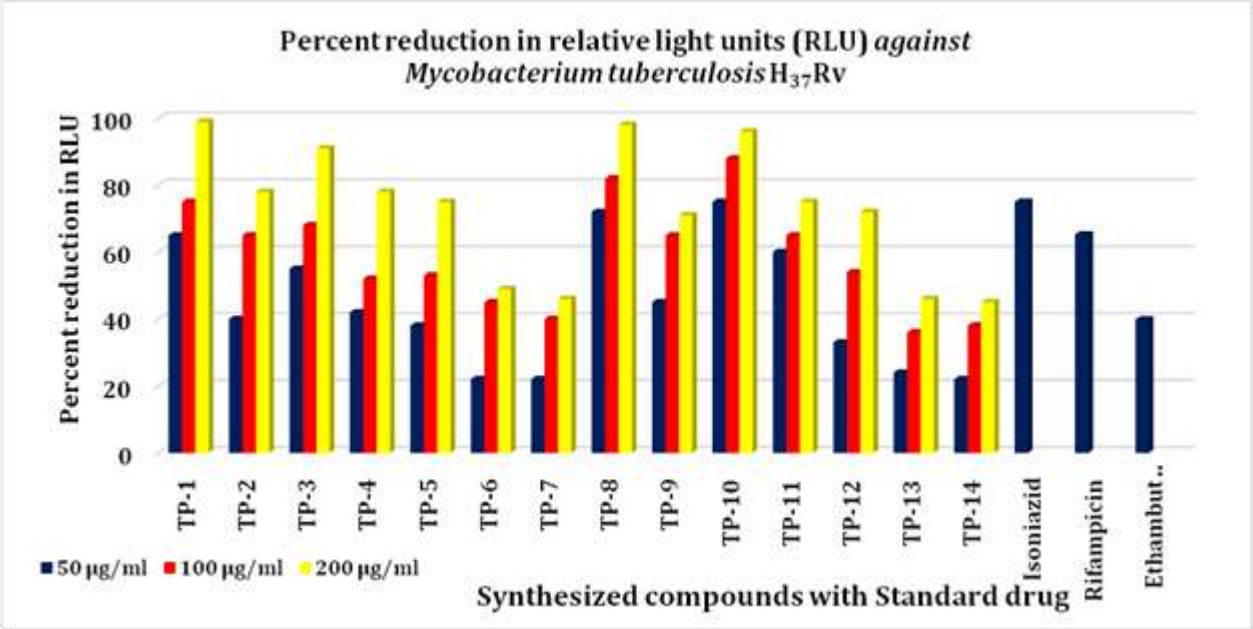

Figure 6.3: Percent reduction in relative light units (RLU) *against Mycobacterium tuberculosis* $H_{37}Rv$

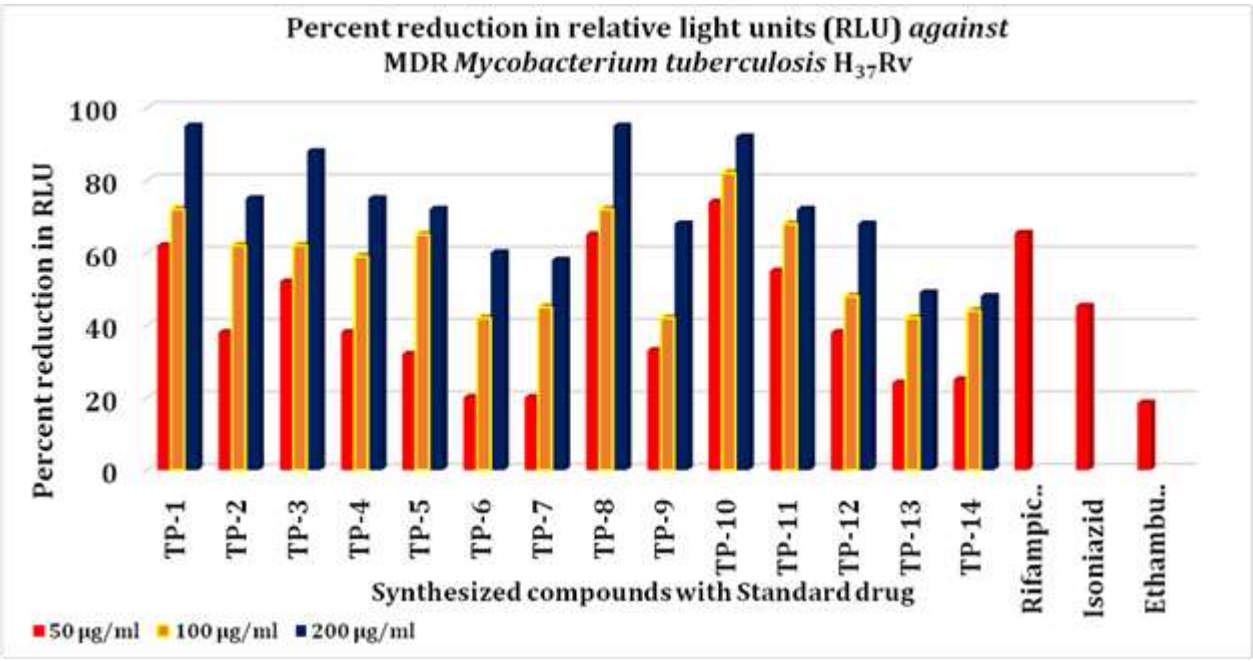

Figure 6.4: Percent reduction in relative light units (RLU) *against* MDR *Mycobacterium tuberculosis* $H_{37}Rv$

However, at a concentration of 100 g/ml, the synthesised compounds CH-6, CH-7, CH-13, and CH-14 showed a reduction in Relative Light Units of less than 50%, and out of the fourteen (14) compounds, ten (CH-1, CH-2, CH-3, CH-4, CH-5, CH-8, CH-9, CH-10, CH-11, and CH-12) showed potent anti-tubercular activity. In this series, the four compounds (CH-6, CH-7, CH-13, and CH-14) are the least active. After further examination, molecular modification of the present series of pyrazole containing thiazole compounds may be beneficial as an antitubercular drug.

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SUMMARY AND CONCLUSION

Medicinal chemistry is concerned with the discovery and development of novel drugs to cure ailments. The majority of the discipline's activities are focused on developing novel natural or synthetic organic molecules. Heterocyclic nucleus containing moieties make up a significant component of these organic compounds. New antitubercular drugs are being developed using thiazole-based pyrazole derivatives. Several papers in the literature mentioned the antibacterial, antimalarial, antitubercular, anticancer, anti-inflammatory, antidepressant, and antihistaminic properties of thiazole and pyrazoline. Pyrazole derivatives are known to have antibacterial properties.

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