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Original Article

SYNTHESIS, ANTICANCER AND ANTITUBERCULOSIS STUDIES FOR [1-(4-CHLOROPHENYL) CYCLOPROPYL] (PIPERAZINE-YL) METHANONE DERIVATES

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ABSTRACT

Objective: Synthesis, anticancer and antituberculosis studies for 1-(4-Chlorophenyl) cyclopropyl] (piperazin-1-yl) methanone derivates **3a-j**

Methods: A series of new [1-(4-Chlorophenyl) cyclopropyl] (piperazin-1-yl) methanone derivates were synthesized using reductive amination method in presence of sodium triacetoxyborohydride to yield piperzine derivatives **3a-j**. The structures of all newly synthesized compounds have been characterised by elemental analysis and spectral studies.

Results: Five selected compounds have been screened for *invitro* anticancer activity against human breast cancer cell line MDA-MB-435 at 10, 20, 40 and 80 µG/mL concentration using sulforhodamine B assay method. and Two compounds **3a** and **3c** have shown *in vitro* anticancer activity.

Five selected compounds have been screened for anti-tuberculosis activity using Middlebrook 7H-9 broth and standard strain of M. tb h37Rv. Three compounds **3a, 3b** and **3c** have shown significant antituberculosis

Conclusion: Synthesis of [1-(4-Chlorophenyl) cyclopropyl] (piperazin-1-yl) methanone derivates **3a-j** simple and convenient method. Some of the tested compounds have exhibited significant antituberculosis and anticancer activity. Compound **3c** showed both antituberculosis and anticancer activity.

Keywords: Piperazine, Aldehydes, Cyclopropane, Antituberculosis, Anticancer.

INTRODUCTION

Disubstituted piperazines exhibit wide range of biological properties as reported in the literature. In the last decade, a number of piperazine derivatives have been synthesized and evaluated for their cytotoxic activity [1-6]. Additional clinical drug development studies of the piperazine compounds in small-animal models by the US National Cancer Institute (NCI) demonstrated that these targets had the ability to suppress experimental tumours.

As a result of the study for the lead compounds, It has been reported that inhibitory action was observed against colon, prostate, breast, lung and immune cell tumours in many indole carrying small anti cancer molecules [7]. In addition, piperazines have been found to posses several biological activities [8-11] including antituberculosis activity [12]. The polarity of nitrogen atoms of piperazine ring enhances favourable interaction with bio macromolecules and thus confers the biological activity [13-14]. Thus, based on these observations in the literature, the present study was initiated with aim of identifying the structural requirements of piperazines in terms of anticancer and antitubercular activity.

MATERIALS AND METHODS

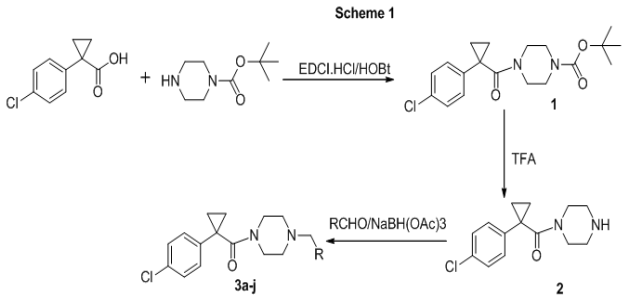
Chemistry

All the chemicals and solvents used in this work were of analytical reagent grade (anhydrous) and purchased from Sigma-Aldrich. All the IR spectra were recorded on Bruker alpha FTIR spectrophotometer, ^{1}H NMR spectra were measured on Bruker AV 400MHZ using $CDCl_3$ and DMSO as solvent. Chemical shifts are expressed in δ ppm.

Elemental Analysis was performed on an Elementar Vario EL elemental analyzer. Satisfactory C, H, N analyses were obtained for all the compounds. All the reactions were followed and checked by TLC (silica coated on alumina) using ethylacetate-pet ether (3:7) and further purification was done by column chromatography using 60-120 mesh silica gel.

Synthesis of 1-(4-Chlorophenyl) cyclopropyl] (piperazin-1-yl) methanone derivatives (3a-j)

1-(4-Chlorophenyl) cyclopropyl] (piperazin-1-yl) methanone (1.0 eq) was dissolved in dry THF (10 mL). The solution was stirred for 10 min at ambient temperature. Then added substituted aldehydes (1.1 eq), followed by sodium triacetoxyborohydride (1.4 eq) and glacial acetic acid (1.5 eq). The reaction mixture was heated at 65-70^{0}C for 12-14 hr. The completion of reaction was monitored by TLC. The reaction mixture was diluted with ethyl acetate, the organic layer was washed with 10% sodium bicarbonate, followed by water, and brine solution and dried over anhydrous sodium sulphate. The organic layer was evaporated under reduced pressure and the crude reaction mixture was purified by column chromatography using 60-120 mesh silica gel and 20% ethyl acetate in hexane. The series of reactions carried out have been depicted in **scheme 1**.



Scheme 1: Synthesis of piperazine methanone derivatives 3a-j.

1. *t-Butyl 4-(1-(4-Chlorophenyl) cyclopropanecarbonyl) piperazine-1-carboxylate (1)*

1-(4-Chlorophenyl) cyclopropanecarboxylic acid (2.00 g, 0.0102 mol) was dissolved in dry tetrahydrofuran (20 mL). The solution

was stirred for 10 min at ambient temperature. 1-Ethyl-3-(3-dimethyllaminopropyl)carbodiimide hydrochloride (2.15 g, 0.01122 mol) was added, followed by 1-hydroxybenzotriazole (1.718 g, 0.01122 mol) and *N*,*N*-diisopropylethylamine (3.955 g,0.0305 mol). The reaction mixture was stirred for 20 min at ambient temperature, and then it was cooled to 0°C. Boc-piperazine (*tert*-butyl piperazine-1-carboxylate) (1.894 g, 0.0102 mol) was added portion-wise to the reaction mixture and stirring was continued for 6 h at ambient temperature.

The completion of the reaction was monitored by TLC. The reaction mixture was diluted with ethyl acetate (25 mL) and washed with sodium bicarbonate (10%, 25 mL) followed by water (15 mL) and brine (15 mL) and dried over sodium sulphate (5.0 g) and evaporate under reduced pressure. The crude reaction mixture was purified by column chromatography using silica gel and 10% ethyl acetate in hexane to get 3.4 g of t-butyl 4-(1-(4-chlorophenyl) cyclopropanecarbonyl) piperazine-1-carboxylate (1).

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 365.2**;** ^{1}H NMR: (400 MHz, DMSO-d_6): δ 7.40 (d, *J* = 2.0 Hz, 2H), 7.17 (d, *J* = 3.0 Hz, 2H), 3.63 (m, 2H), 2.96 (m, 2H), 1.37 (q, 2H), 1.18 (q, 2H); 1.2 (s, 9H), IR (KBr) ν (cm^{-1}):1646 (C=O); Elemental analysis: Calculated (%) for $C_{14}H_{17}ClN_2O$:C 62.54, H 6.91, N 7.68; Found: C 62.55, H 6.94, N 7.62

2. ***[1-(4-Chlorophenyl)cyclopropyl](piperazin-1-yl)methanone (2)***

Compound **1** (3.4 g, 0.00934 mol) was dissolved in dry Dichloromethane (20 mL) and the reaction mixture was cooled to o to 5^{0}C. Trifluoroacetic acid (3.19 g, 0.028 mol,3.0 eq) was added slowly to the cooled reaction mixture and stirred for 6 h at ambient temperature. The completion of the reaction was monitoring by TLC.

The reaction mixture was evaporated under reduced pressure and it was dissolved in Dichloromethane (30 mL). Organic layer was washed with water (15 mL), brine (15 mL) and dried over sodium sulphate (6 g).

The crude reaction mixture obtained was purified by column chromatography using silica gel and 3% methanol in Dichloromethane to get 1.8 g of purified [1-(4-chlorophenyl) cyclopropyl] (piperazin-1-yl)methanone (**2**). LC-MS (ESI, Positive): m/z: $[M+H]^+$: 265.2**;** ^{1}H NMR: (400 MHz, DMSO-d_6): δ 9.32 (s, 1H, NH), 7.40 (d, *J* = 2.0 Hz, 2H), 7.17 (d, *J* = 3.0 Hz, 2H), 3.63 (m, 2H), 2.96 (m, 2H), 1.37 (q, 2H), 1.18 (q, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 169.9, 139.9, 131.3, 129.1 127.5 42.6, 28.89 15.7 (2C); IR (KBr) ν (cm^{-1}): 2970 (N-H), 1646 (C=O); IR (KBr) ν (cm^{-1}): 1646 (C=O); Elemental analysis: Calculated for $C_{14}H_{17}ClN_2O$:C 63.51,H 6.47 N, 10.58; Found: C, 63.53 H 6.46, N 10.57.

3. General procedure preparation of methanone derivates (3a-j).

Compound **2** (0.5 g, 0.00188 mol) was dissolved in dry THF solvent (10mL). The solution was stirred for 10 min at ambient temperature. Substituted aldehydes(0.0020 mol) was added, followed by sodium triacetoxyborohydride (0.557g,0.002632 mol) and Glacial acetic acid (0.169 g,0.00282 mol).

The reaction mixture was heated at 65-70^{0}C for 12-14 hr. The completion of reaction was monitored by TLC. The reaction mixture was diluted with ethyl acetate, the organic layer was washed with 10% sodium bicarbonate solution followed by water, brine and dried over anhydrous sodium sulphate. The organic layer was evaporated under reduced pressure and the crude reaction mixture was purified by column chromatography using 60-120 mesh silica gel and 3% methanol in dichloromethane.

3.1. 4-((1H-indol-3-yl) methyl) piperazin-1-yl)(1-(4Chlorophenyl) cyclopropyl)methanone (3a)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 394.9; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.92 (bs, 1H, NH), 7.59-7.58 (d, *J* = 6.4 Hz, 1H), 7.35-7.33 (m, 3H), 7.19-7.13(m, 3H),7.08-6.96(m, 1H) 3.60-3.33 (m, 6H), 2.31-1.91(m, 4H), 1.27-1.25 (m, 2H), 1.16-1.14 (m, 2H), 1.18 (q, *J* = 5.0 Hz, 2H); IR (KBr) ν(cm^{-1}): 3266 (N-H),817 (C-Cl); Elemental analysis: Calculated (%) for $C_{23}H_{24}ClN_3O$:C 70.13, H 6.14, N 10.64; Found: C 70.15, H 6.12, N 10.50.

3.2. 1-(4-Chlorophenyl) cyclopropyl) (4-(pyridin-3-ylmethyl) piperazin-1-yl)methanone (3b)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 356.8; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.50-8.48 (dd, *J* = 4.4 Hz, 2H), 7.38-7.35 (m, 2H), 7.30-7.28 (d, *J* = 6.0 Hz, 2H), 7.18-7.15(m, 2H) 3.47 (s, 2H), 3.45-3.38 (m, 4H), 3.34-2.30 (m, 4H)1.31-1.28 (m, 2H), 1.18-1.15 (m, 2H). IR (KBr) ν(cm^{-1}): 1718 (C=O), 760 (C-Cl) Elemental analysis: Calculated (%) for $C_{20}H_{22}ClN_3O$: C 67.50, H 6.23, N 11.81; Found: C 67.52, H 6.22, N 11.78.

3.3. 1-(4-Chlorophenyl) cyclopropyl) (4-(quinolin-6-ylmethyl) piperazin-1-yl)methanone (3c)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 406.9; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.95-8.93(m,1H) 8.86-8.85 (m, 1H), 8.49-8.47 (m,1H) 7.77-7.4 (m, 2H), 7.35-7.30 (m, 2H), 7.29-7.27(m, 1H) 7.21-7.15(m, 2H), 3.62 (s, 2H), 3.45-3.38 (m, 4H), 3.34-2.30(m, 4H)1.30-1.27 (m, 2H), 1.17-1.14 (m, 2H). Elemental analysis: Calculated (%) for $C_{24}H_{24}ClN_3O$: C 71.01, H 5.96, N 10.35; Found: C 71.10, H 6.01,N 10.41.

3.4. 4-((1H-imidazol-2-yl) methyl) piperazin-1-yl) (1-(4-chlorophenyl) cyclopropyl) methanone (3d)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 345.8; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.5 (bs, 1H), 7.55 (s,1H),7.38-7.31(m, 2H) 7.19-7.15 (m, 2H), 6.92(s, 1H)3.46(s, 2H)3.45-3.38(m, 4H) 2.40-2.24 (m, 4H), 1.31-1.28 (m, 2H), 1.18-1.15 (m, 2H). IR (KBr) ν(cm^{-1}): 1699 (C=O),773 (C-Cl); 3338 (N-H); Elemental analysis: Calculated (%) for $C_{18}H_{21}ClN_4O$: C 62.69, H 6.14, N 16.25; Found: C 62.71, H 6.16, N 16.31.

3.5. 1-(4-Chlorophenyl) cyclopropyl) (4- ((5-nitrothiazol-2-yl) methyl) piperazin-1-yl)methanone (3e)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 406.1; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.01-8.00 (d, *J* = 4.4 Hz, 1H), 7.38-7.35 (d, *J* = 8.8 Hz, 2H), 7.18-7.16 (d, *J* =8.8 Hz, 2H), 7.09-7.08 (d, *J* =4.0 Hz, 1H),3.74 (s, 2H), 3.45-3.38(m, 4H) 2.40-2.24 (m, 4H), 1.32-1.29 (m, 2H), 1.18-1.15 (m, 2H). ^{13}C NMR (400 MHz,CDCl3): δ 169.30, 153.65, 147.72, 139.97, 130.75, 130.15, 128.64, 127.11,125.68, 56.08, 51.99, 28.68, 15.8, Elemental analysis: Calculated (%) for $C_{19}H_{20}ClN_3O_3S$: C 53.13, H 4.71, N 13.77; Found: C 53.18, H 4.70, N 13.73.

3.6. 1-(4-Chlorophenyl)cyclopropyl) (4-((6-methylpyridin-2-yl) methyl) piperazin-1-yl)methanone (3f)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 370.8; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.63-7.59 (m, 1H), 7.37-7.34 (d, *J* = 8.4 Hz, 2H), 7.19-7.14 (m, 3H), 7.10-7.08 (m, 1H), 3.74 (s, 2H), 3.49-3.40(m, 4H), 2.36 (s, 3H) 2.33-2.19 (m, 4H), 1.30-1.27 (m, 2H), 1.17-1.14 (m, 2H). 13C NMR (400 MHz,DMSO-d_6): δ 169.65, 157.52, 140.44, 137.18, 131.12, 129.03, 127.51, 212.84, 120.12, 63.94, 52.70, 29.10, 24.43, 15.75.IR (KBr) ν(cm^{-1}): 1698 (C=O),779 (C-Cl); Elemental analysis: Calculated (%) for $C_{21}H_{24}ClN_3O$: C 68.19, H 6.54, N 11.36; Found: C, 68.21, H 6.50, N 11.31.

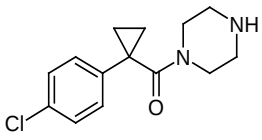
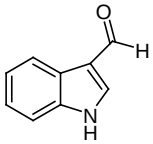
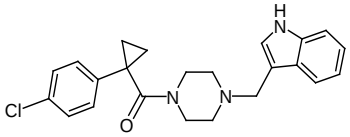
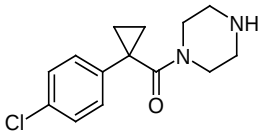
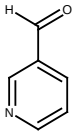
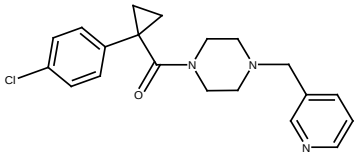
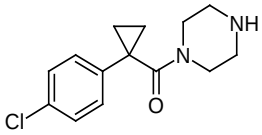
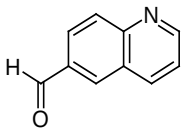
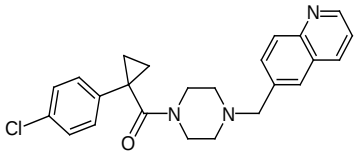
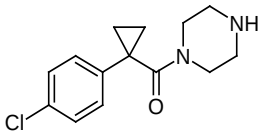
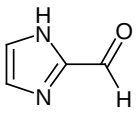
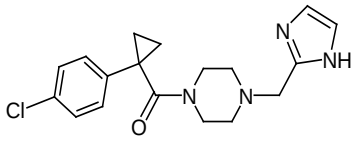
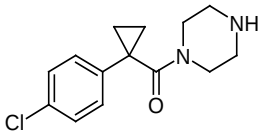
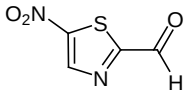
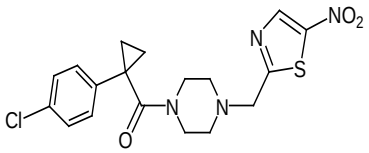
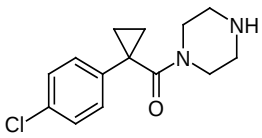
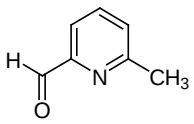
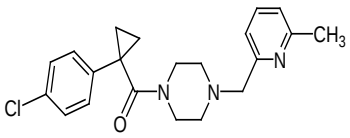
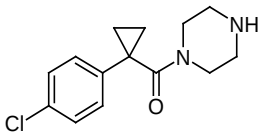
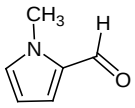
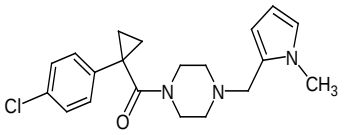
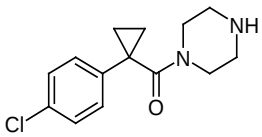
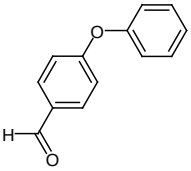
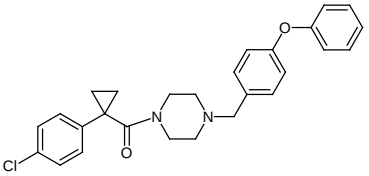
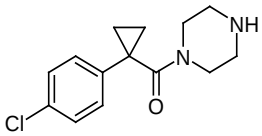
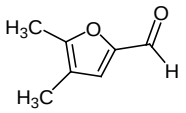
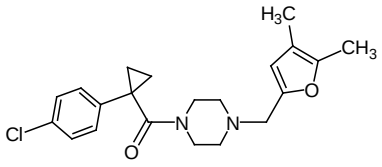
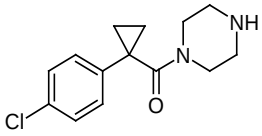
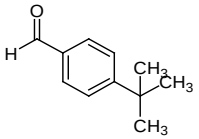
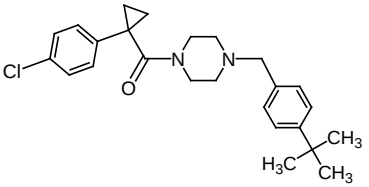
3.7. 1-(4-Chlorophenyl)cyclopropyl)(4-((1-methyl-1H-pyrrol-2-yl) methyl) piperazin-1-yl)methanone (3g)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 358.8; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.38-7.35 (m, 2H), 7.20-7.14 (m, 2H), 6.64-6.63 (m, 1H), 5.84-5.83 (m, 2H), 3.54 (s, 2H), 3.46-3.39 (m, 4H), 3.34 (s, 3H) 2.23-2.11 (m, 4H), 1.29-1.26 (m, 2H), 1.18-1.14 (m, 2H). IR (KBr) ν(cm^{-1}): 1714 (C=O),779 (C-Cl); Elemental analysis: Calculated (%) for $C_{20}H_{24}ClN_3O$: C 67.12, H 6.76, N 11.74; Found: C 67.11, H 6.72, N 11.71.

3.8. 4-(4-Phenoxybenzyl) piperazin-1-yl)(1-(4-Chlorophenyl) cyclopropyl)methanone (3h)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 447.1; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.50-8.48 (dd, *J* = 4.4 Hz,1.4Hz 2H), 7.38-7.35 (m, 2H), 7.30-7.28 (d, *J* = 6.0 Hz, 6H), 7.18-7.15(m, 5H), 7.00-6.95 (2m, H) 3.49 (s, 2H), 3.47-3.40 (m, 4H), 3.36-2.32 (m, 4H)1.32-1.29 (m, 2H), 1.19-1.16 (m, 2H).Elemental analysis: Calculated (%) for $C_{27}H_{27}ClN_2O_2$: C 72.55, H 6.09, N 6.27; Found: C 72.61, H 6.29, N 6.12.

Table 1: Synthesis of piperazine methanone derivatives 3a-j

Compound No.	piperazine scaffold	aromatic aldehydes	piperazine derivatives	% Yield
3a				80
3b				65
3c				74
3d				63
3e				75
3f				81
3g				75
3h				80
3i				75
3j				79

3.9. 1-(4-Chlorophenyl) cyclopropyl) (4-((4,5-dimethylfuran-2-yl) methyl)piperazin-1-yl)methanone (3i):

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 373.8; ^1H NMR (400 MHz, DMSO-d_6): δ 7.39-7.34 (m, 2H), 7.19-7.14 (m, 2H), 5.59 (s, 1H), 3.6 (s, 2H), 3.46-3.39 (m, 4H), 2.23-2.11 (m, 4H), 2.10 (s, 3H)1.92 (s, 3H), 1.19-1.15 (m, 2H).

^{13}C NMR (400 MHz, DMSO-d_6): δ 169.62, 148.62, 146.59, 140.44, 131.13, 129.01, 127.54, 114.39, 112.51, 54.30, 52.06, 29.10, 15.68, IR

(KBr) ν(cm^{-1}): 1710 (C=O); Elemental analysis: Calculated (%) for $C_{21}H_{25}ClN_2O_2$: C 67.64, H 6.76, N 7.51; Found: C 67.68, H 6.72 N 7.52.

3.10. 1-(4-Chlorophenyl) cyclopropyl) (4-((1,3-dimethyl-1H-pyrazol-4 yl) methyl)piperazin-1-yl)methanone (3j)

LC-MS (ESI, Positive): m/z: $[M+H]^+$: 373.8; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.31 (s, 1H),7.39-7.35 (m,2H) 7.20-7.14 (m, 2H), 3.69 (s, 2H), 3.46-3.39 (m, 4H),3.18 (s, 3H), 2.35 (s,3H), 2.23-2.11 (m, 4H), 1.19-1.15 (m, 2H).

IR (KBr) ν(cm^{-1}):779 (C-Cl) Elemental analysis: Calculated (%) for $C_{20}H_{25}ClN_4O$: C 64.42, H 6.76, N 15.02; Found: C 64.48, H 6.78, N 15.08.

Anticancer activity

Five selected compounds have been screened for *invitro* anticancer activity against human breast cancer cell line MDA-MB-435 at 10, 20, 40 and 80 µG/mL concentration using sulforhodamine B assay method. The activity was carried out by Advanced Centre for Treatment, Research and Education in Cancer (ACTREC) Mumbai. Adriamycin (Doxorubicin) was used as positive control drug for comparing anticancer efficiency and DMSO as vehicle. Two compounds have been found to show dose dependent activity against breast cancer. The parameters GI50, TGI and LC50 have been reported. The results have been incorporated in Table **1** and diagram. Compounds **3a** and **3c** were found to show dose dependent activity.

Table 2: Anticancer activity against Human Brest Cancer Cell Line MDA-MD-435

	Drug Concentration (µg/ml)															
	Experiment 1				Experiment 2				Experiment 3				[a]Average Values			
Comp	10	20	40	80	10	20	40	80	10	20	40	80	10	20	40	80
3a	45.3	5.4	-4.4	-90.8	60.7	9.1	-35.6	-63.7	60.5	13.9	-45.7	-81.8	55.5	9.5	-28.6	-78.8
3b	92.7	65.6	46.7	25.8	108.3	81.6	60.7	30.1	87.2	94.6	59.3	11.4	96.1	80.6	55.6	22.4
3c	15.8	-28.1	-69.8	-91.6	60.9	39.6	7.5	-69.8	59.2	27.9	-14.3	-87.6	43.2	13.1	-25.5	-83.0
3d	79.1	99.2	71.9	38.2	82.1	95.0	86.4	35.8	90.9	99.9	84.1	23.0	84.0	98.0	80.8	32.4
3e	86.8	83.4	55.0	4.6	90.8	84.6	61.8	11.4	86.2	84.7	42.2	-18.7	87.9	84.2	53.0	-0.9
ADR	-34.2	-50.3	-55.1	-25.2	7.8	10.5	5.4	0.3	-36.9	-64.9	-43.0	-42.3	-21.1	-34.7	-30.9	-22.4

[a] Average values of tested compounds

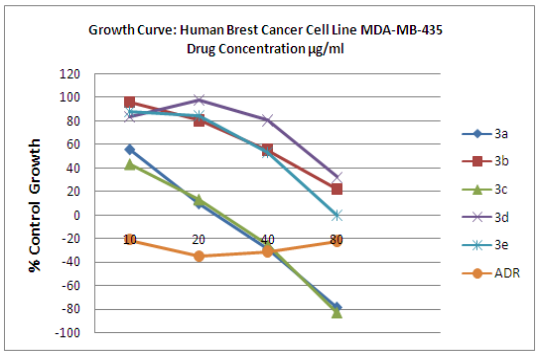


Fig. 1: Graphical representation of anticancer activity

Table 3: Parameter study table (LC50, TGI, and GI50)

Compound	LC50	TGI	GI50
3a	60.2	36.5	12.7
3b	>80	>80	51.7
3c	59.4	35.5	11.7
3d	>80	>80	66.9
3e	>80	>80	42.6
ADR	>80	29	<10

Anti tuberculosis activity

Procedure for Anti Tb

The procedure we have followed for anti-Tb activity mainly involves the use of Middlebrook 7H-9 broth and standard strain of M. tb h37Rv. The basal medium was prepared according to manufacture's instructions (Hi-Media) and sterilized by autoclaving. 4.5 ml of broth was poured into each one of the sterile bottles. To this, 0.5ml of ADC supplement was added. This supplement contains catalase, dextrose and bovine serum albumin fraction v. Then a stock solution of the compound was prepared (10mg / ml). From this appropriate amount of solution was transferred to media bottles to achieve final concentrations of 25, 50, 100µg/ml. Finally, 10 ul suspension of M. tb strain (100000 organisms / ml, adjusted by McFarland's turbidity standard) was transferred to each of the tubes and incubated at 37^{0}c. Along with this, one growth control without compound and drug controls was also set up. The bottles were inspected for growth twice a week for a period of three weeks. The appearance of turbidity was considered as growth and indicates resistance to the compound. The growth was confirmed by making a smear from each bottle and performing a ZN stain. Antibiotic standards used include streptomycin 7.5µg/ml and Pyrazinamide 7.5µg/ml.

Table 4: Anti tuberculosis studies of synthesised compounds

S. No.	Compound	5 µg/ml	10 µg/ml	25 µg/ml
1	3a	S	S	S
2	3b	S	S	S
3	3c	S	S	S
4	3d	R	R	R
5	3e	R	R	R

RESULTS AND DISCUSSION

All the synthesized compounds have been purified by column chromatography and recrystalized with ethyl acetate. The structures have been confirmed by elemental analysis and spectroscopic techniques like IR, ^{1}H-NMR, LC-MS. Some of the selected compounds have been tested for *invitro* anticancer and antituberculosis activity. Two compounds have been found to show dose dependent activity against cervical cancer. The parameters GI50, TGI and LC50 have been reported. The results have been incorporated in Table **1** and diagram. Compounds **3a** and **3c** were found to show dose dependent activity Out of these tested compounds **3a**, **3b** and **3c** have been found active against tuberculosis. In the above table **3**, R indicates resistivity and S indicates sensitivity of the tested compounds against the standard.

CONCLUSION

The research work is focused on the efficient synthesis of cyclopropyl piperazine derivatives. The reactions performed are eco-friendly. In addition, some of the tested compounds have exhibited significant antituberculosis and anticancer activity. The publication of these facts would be of significant use for the scientific community. Some selected cyclopropyl piperazine derivatives have been tested for antituberculosis and *invitro* anticancer activity. Three compounds **3a, 3b** and **3c** have shown significant antituberculosis and two compounds **3a** and **3c** have shown *in vitro* anticancer activity. Recommended compounds have been under

screen for *invivo* anticancer activity. Compound **3c** showed both antituberculosis and anticancer activity.

CONFLICT OF INTERESTS

Declared None

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