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Synthesis Characterization and Biological Evaluation of Some Novel Schiff's Base and Amine Derivatives of Pyrazole

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ABSTRACT

A novel series of Schiff's base and amine derivatives of 5-amino-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide have been synthesized by using different aromatic aldehydes and followed by reduction of Schiff's base with sodium borohydride in very good yield. The structures of the synthesized compounds have been characterized by using IR, ^{1}H NMR and Mass spectroscopy. All the prepared new NCEs were screened for anti-microbial activity and anti-fungal activity.

Keywords: Pyrazole; Schiff's base; Amine derivatives; Imine derivatives; Carboxamide derivatives; Antimicrobial activity

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INTRODUCTION

Increasing resistance of microorganisms to currently available antimicrobial drugs is the major cause of morbidity and mortality throughout the world. Thus development of novel antimicrobial drugs is still in demand. The carboxamide derivatives of pyrazole are important biologically active heterocyclic compounds [1]. The compounds carrying Amino [–C–NH–] functional group and azomethine functional group –C=N– which are known as Amines and Schiff's bases respectively have gained importance in medicinal and pharmaceutical fields due to the most versatile organic synthetic intermediates and also showing a broad range of biological activities [2]. Pyrazole derivatives have a long history of application in agrochemicals and pharmaceutical business as herbicides and active pharmaceuticals. The recent success of pyrazole COX-2 inhibitor has further emphasized the importance of these heterocyclic rings in medicinal chemistry. A systematic investigation of this class of heterocyclic lead revealed that pyrazole containing pharmaco active agents play an important role in medicinal chemistry [3]. In the literature many pyrazole derivatives are recognized to possess antibacterial [4-7], antifungal [8-11], anti-tubercular [12-14], analgesic [15], anti-inflammatory [16,17], antipyretic [18], anticonvulsant [19,20] antidepressant [20-23], muscle relaxing [24], antiviral [25-27], anti-arrhythmic [28], Antiallergic [29] and anti-diabetic [30] activities. Motivated by all these fact, we aimed the synthesis of a series of novel afore-mentioned findings and as a continuation of our research to develop novel series of 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide and 5-(Arylamino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide and evaluated these NCE's for anti microbial activities against gram positive, gram negative bacteria and fungi.

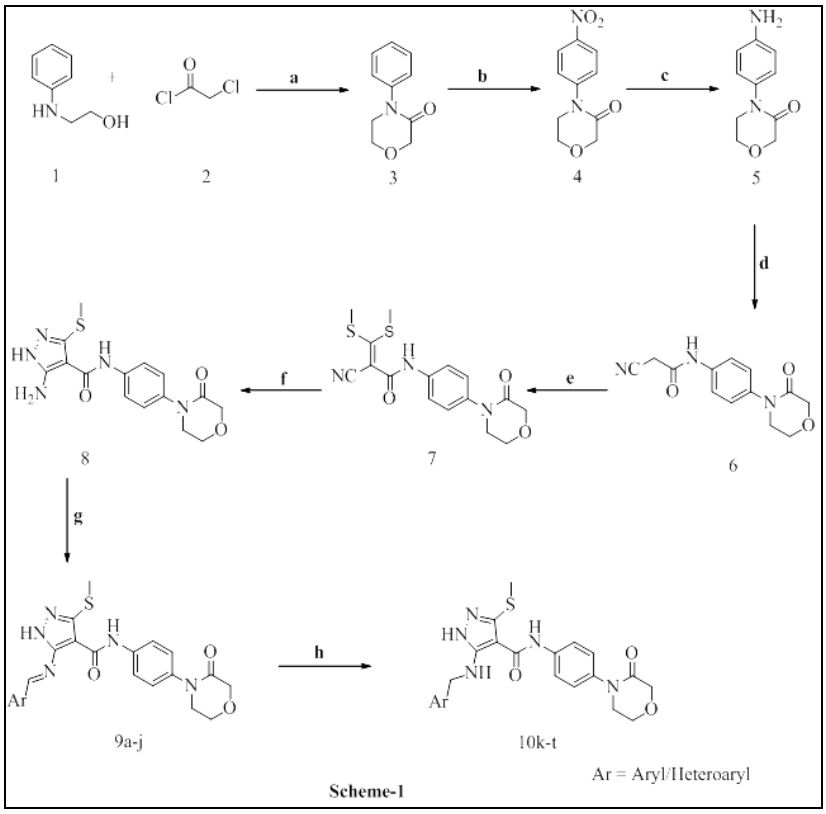
EXPERIMENTAL SECTION

All chemicals were purchased from commercial suppliers and used without further purification. The progress of the reaction was monitored by analytical TLC on precoated plates (silica gel 60, F254) and visualized with UV light. Melting points were determined using open capillary tube and are uncorrected. NMR spectra (^{1}H at 400 MHz) were

recorded using DMSO-d^6 as a solvent and chemical shifts are expressed in parts per million (ppm) related to internal TMS. Infrared spectra were determined on a Shimadzu FT-IR. The specifications of the LC/MS are as follows: electrospray (+) ionization, mass range 100-800 Da, 20-V cone voltage, and X terra MS C18 column (2.1 mm × 50 mm × 3.5 µm).

Reagents

(a) Sodium hydroxide, IPA, Water, RT 1 hr; (b) H_2SO_4, 70% HNO_3, 0-10°C and then RT 1 hr; (c) 10% Pd/C, Methanol, Ammonium formate, reflux 3 hrs; (d) Cyanoaceticacid, EDC.HCl, DCM, RT 1 hr; (e) i. CS_2, K_2CO_3, DMF, RT: ii. MeI, 0-10°C to RT; (f) NH_2NH_2, IPA, Reflux 4 hrs (g) ArCHO, cat. Acetic acid, IPA, reflux 2-3 hrs (h) Sodium borohydride, IPA, RT 1 hr.



Scheme 1: The synthesis of 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide and 5-(Arylamino)-3-(methylthio)- N- (4-(3-oxomorpholino) phenyl)-1H-pyrazole-4-carboxamide

Preparation of 4-phenylmorpholin-3-one (3)

To stirred solution of 2-(phenylamino)ethanol 1 (30 g, 218.7 mmol) in isopropyl alcohol (60 mL) and water (90 mL), chloroacetylchloride 2 (49.4 g, 437.4 mmol) and solution of sodium hydroxide (43.7 g, 1093.5 mmol) in water (70 mL) were added simultaneously at room temperature and adjust pH 13 to 14. The reaction mixture was stirred for 1 hour. The progress of the reaction was monitored by TLC. After completion of the reaction, the solid material was filtered, washed with water and dried to yield 4-phenylmorpholin-3-one 3 (32 g, 77% yield) as an off-white color solid.

Preparation of 4-(4-nitrophenyl)morpholin-3-one (4)

To a stirred solution of 4-phenylmorpholin-3-one 3 (30 g, 169.3 mmol) in sulfuric acid (133 g, 1355 mmol) at 0-10°C, 70 % nitric acid (16.8 g, 186.2 mmol) was added drop wise in the reaction mixture within 1 hour. The reaction mixture then allowed to stir at room temperature for 1 hour. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was poured in crush ice under stirring and precipitated solid material was filtered, washed with excess amount of water and dried to yield 4-(4-nitrophenyl)morpholin-3-one 4 (30 g, 80% yield) as yellow color solid.

Preparation of 4-(4-aminophenyl)morpholin-3-one (5)
To a stirred solution of 4-(4-nitrophenyl)morpholin-3-one 4 (25 g, 112.5 mmol) and 10% Pd/C (1.25 g, 5%) in methanol (250 mL) was heated at reflux temperature. Ammonium formate (35.5 g, 562.5 mmol) was added into the reaction mixture lot wise within 2 hours. The reaction mixture was then refluxed for additional 1 hour. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was allowed to cool room temperature. The reaction mixture was filtered through celite and methanol was distilled under vacuum on rotary evaporator to give 4-(4-aminophenyl) morpholin-3-one 5 (19 g, 88% yield) as a light brown color solid.

Preparation of 2-cyano-N-(4-(3-oxomorpholino)phenyl)acetamide (6)
To a stirred solution of cyanoaceticacid (8.3 g, 97.3 mmol) and EDC.HCl (25.4 g, 132.6 mmol) in dichloromethane (170 mL) at room temperature, 4-(4-aminophenyl)morpholin-3-one 5 (17 g, 88.4 mmol) was added into the reaction mixture lot wise within 1 hour. The reaction mixture was stirred for 1 hour. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered, washed with dichloromethane and dried to yield 2-cyano-N-(4-(3-oxomorpholino)phenyl) acetamide 6 (17.4 g, 76% yield) as a brown color solid.

Preparation of 2-cyano-3,3-bis(methylthio)-N-(4-(3-oxomorpholino) phenyl) acrylamide (7)
To a stirred solution of 2-cyano-N-(4-(3-oxomorpholino)phenyl)acetamide 6 (16 g, 61.7 mmol) in dimethylformamide (80 mL), dried potassium carbonate (9.4 g, 67.9 mmol) was added and the reaction mixture was stirred for 2 hours at room temperature. To this reaction mixture carbon disulfide (9.3 g, 123.4 mmol) was added and the reaction mixture was stirred for additional 2 hours. Then the reaction mixture was cooled to 0-5°C and methyl iodide (17.5 g, 123.4 mmol) was added within 30 minutes and stirred it for 3 hours at room temperature. The progress of the reaction was monitored by TLC. After completion of reaction, the mixture was poured into water (400 mL) and stirred it for 30 minutes. The precipitated solid material was filtered, washed with water and dried it to afford 2-cyano-3,3-bis(methylthio)-N-(4-(3-oxomorpholino) phenyl) acrylamide 7 (15.0 g, 63% yield) as a yellow color solid.

Preparation of 5-amino-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (8)
To a stirred solution of 2-cyano-3,3-bis(methylthio)-N-(4-(3-oxomorpholino) phenyl) acrylamide 7 (14.0 g, 36.4 mmol) and hydrazine hydrate (3.6 g, 72.8 mmol) in isopropyl alcohol (70 mL) was heated at reflux temperature for 4 hours. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was cooled to room temperature and water (140 mL) was added. The reaction mixture was stirred for 1 hour at room temperature. The precipitated solid material was filtered, washed with water, dried and crystallization from IPA to afford 5-amino-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide 8 (10.6 g, 83% yield) as a yellow color solid.

General procedure for the preparation of 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3- oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (9a-j)
The solution containing 5-amino-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide 8 (2.85 mmol) and different substituted aromatic aldehyde (2.85 mmol) in the presence of catalytic acetic acid in isopropyl alcohol (10 mL) was refluxed for 2-3 hours. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was allowed to cool room temperature and stirred for 1 hour. The precipitated solid was filtered, washed with isopropyl alcohol and dried to give pure 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3- oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide 9a-j as a yellow color compound in 48-90% (Table 1).

General procedure for the preparation of 5-(Arylamino)-3-(methylthio)- N- (4-(3-oxo morpholino) phenyl)-1H-pyrazole-4-carboxamide derivatives (10k-t)
To a stirred reaction mixture containing 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide 9 (5 mmol) in isopropyl alcohol (10 mL), sodium borohydride (5 mmol) was added lot wise into the reaction mixture within 30 minutes at room temperature. The reaction mixture was then stirred for additionally 1 hour. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was neutralized with acetic acid and solvent was removed on rotary evaporator under vacuum to give residue. Residue was dissolved in dichloromethane and washed with water. Solvent was evaporated on rotary evaporator under vacuum and the product was crystallized from isopropyl alcohol to give pure 5-(Arylamino)-3-

(methylthio)-N-(4-(3-oxomorpholino) phenyl)-1H-pyrazole-4-carboxamide 10k-t as a creamish to yellow color compound in 79-91%.

Table 1: Physical data for the product 9a-j and 10k-t

Sr. No.	Compound Code	Ar	M.P. (°C)	Yield (%)	M. F.	M. Wt.
1	9a	4-Methoxy phenyl	277-279	60	$C_{23}H_{23}N_5O_4S$	465.5
2	9b	2-Hydroxy phenyl	286-288	85	$C_{22}H_{21}N_5O_4S$	451.5
3	9c	4-Hydroxy phenyl	285-287	89	$C_{22}H_{21}N_5O_4S$	451.5
4	9d	4-Bromo phenyl	270-272	83	$C_{22}H_{20}BrN_5O_3S$	514.4
5	9e	4-Fluoro phenyl	144-146	68	$C_{22}H_{20}FN_5O_3S$	453.5
6	9f	4-Chloro phenyl	232-234	73	$C_{22}H_{20}ClN_5O_3S$	469.9
7	9g	Phenyl	281-283	81	$C_{22}H_{21}N_5O_3S$	435.5
8	9h	Thiophene	284-286	88	$C_{20}H_{19}N_5O_3S_2$	441.5
9	9i	4-Hydroxy-3-methoxy phenyl	281-283	48	$C_{23}H_{23}N_5O_5S$	481.5
10	9j	3,4-Difluoro phenyl	285-287	90	$C_{22}H_{19}F_2N_5O_3S$	471.5
11	10k	4-Methoxy phenyl	253-255	90	$C_{23}H_{25}N_5O_4S$	467.5
12	10l	2-Hydroxy phenyl	242-244	79	$C_{22}H_{23}N_5O_4S$	453.5
13	10m	4-Hydroxy phenyl	240-242	82	$C_{22}H_{23}N_5O_4S$	453.5
14	10n	4-Bromo phenyl	251-253	88	$C_{22}H_{22}BrN_5O_3S$	516.4
15	10o	4-Fluoro phenyl	261-263	79	$C_{22}H_{22}FN_5O_3S$	455.5
16	10p	4-Chloro phenyl	230-232	80	$C_{22}H_{22}ClN_5O_3S$	471.9
17	10q	Phenyl	248-250	85	$C_{22}H_{23}N_5O_3S$	437.5
18	10r	Thiophene	220-222	82	$C_{20}H_{21}N_5O_3S_2$	443.5
19	10s	4-Hydroxy-3-methoxy phenyl	203-205	91	$C_{23}H_{25}N_5O_5S$	483.5
20	10t	3,4-Difluoro phenyl	261-263	90	$C_{22}H_{21}F_2N_5O_3S$	473.5

5-((4-fluorobenzylidene) amino)-3-(methylthio)-N-(4-(3-oxomorpholino) phenyl) -1H-pyrazole-4-carboxamide (9e)

Yield: 68%. **^{1}H NMR (400 MHz, DMSO-d^6):** δ=2.581 (s,3H), 3.701-7.736 (t, 2H), 3.961-3.987 (t,2H), 4.200 (s,2H), 7.371-7.392 (d,2H), 7.459-7.502 (t,2H), 7.672-7.694 (d,2H), 8.133-8.209 (m,2H), 8.926-9.195 (d,1H), 9.916-10.259 (d,1H), 13.162-13.598 (d,1H) ppm; **MS:** m/z 454.2 $(M+H)^+$, m/z 452.1 $(M-H)^-$; **IR cm^{-1}:** 3236.55, 2970.38, 1735.93, 1658.78, 1508.33, 1477.47, 1352.10, 1226.73, 1153.43.

3-(Methylthio)-N-(4-(3-oxomorpholino)phenyl)-5-((thiophen-2-ylmethylene) amino)-1H-pyrazole-4-carboxamide (9h)

Yield: 88%. **^{1}H NMR (400 MHz, DMSO-d^6):** δ=2.576 (s,3H), 3.721-3.746 (t, 2H), 3.962-3.988 (t, 2H), 4.202 (s,2H), 7.184-7.202 (d, 2H), 7.374-7.396 (d, 2H), 7.667-7.688 (d,2H), 8.056-8.075 (m, 2H), 8.852-9.110 (d,1H), 9.953-10.434 (d,1H), 13.077-13.505 (d,1H) ppm; **MS:** m/z 442.0 $(M+H)^+$, m/z 440.0 $(M-H)^-$; **IR cm^{-1}:** 3169.04, 2970.38, 1739.79, 1668.43, 1558.48, 1473.62, 1350.17, 1217.08, 1122.57.

5-((4-hydroxy-3-methoxybenzylidene)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (9i)

Yield: 48%. **^{1}H NMR (400 MHz, DMSO-d^6):** δ=2.573 (s,3H), 3.713-3.737 (t, 2H), 3.887 (s, 3H), 3.961-3.986 (t, 2H), 4.200 (s,2H), 7.317-7.416 (m, 3H), 7.702-7.750 (t, 2H), 7.909-8.106 (m,2H), 9.075-9.338 (d,1H), 9.952-10.379 (d,1H), 13.146-13.609 (d,1H) ppm; **IR cm^{-1}:** 3209.55, 2970.38, 1739.79, 1668.43, 1581.63, 1471.69, 1352.10, 1217.08, 1116.78.

5-((3,4-difluorobenzylidene) amino) -3- methyl thio) - N-(4- (3-oxomorpholino) phenyl) -1H-pyrazole-4-carboxamide (9j)
Yield: 90%. **^{1}H NMR (400 MHz, DMSO-d^6): MS:** m/z 472.1 $(M+H)^+$, m/z 470.1 $(M-H)^-$; **IR Cm^{-1}:** 305.10, 2941.44, 1739.79, 1662.64, 1558.48, 1473.62, 1363.67, 1217.08, 1118.71.

5-((4-bromobenzyl)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (10n)
Yield: 88%. **^{1}H NMR (400 MHz, DMSO-d^6):** δ= 2.480 (s, 3H), 3.697-3.722 (t, 2H), 3.954-3.979 (t, 2H), 4.190 (s, 2H), 4.387-4.404 (d, 2H), 7.216-7.226 (m, 2H), 7.324-7.346 (d,2H), 7.378-7.441 (m, 2H), 7.628-7.650 (d, 2H), 9.203 (s, 1H), 12.506 (s, 1H) ppm; **MS:** m/z 516.0 & 518.1 $(M+H)^+$, m/z 514.1 and 516.1 $(M-H)^-$; **IR Cm^{-1}:** 3342.64, 3292.49, 2970.38, 1716.65, 1629.85, 1541.12, 1506.41, 1342.46, 1217.08, 1122.57.

5-(benzylamino)-3-(methylthio)-N-(4-(3-oxomorpholino) phenyl)-1H-pyrazole-4-carboxamide (10q)
Yield: 85%. **^{1}H NMR (400 MHz, DMSO-d^6):** δ= 2.482 (s, 3H), 3.696-3.720 (t, 2H), 3.953-3.978 (t, 2H), 4.189 (s, 2H), 4.389 (d, 2H), 7.301-7.343 (t, 4H), 7.519-7.530 (d,2H), 7.623-7.645 (d, 2H), 9.136 (s, 1H), 12.467 (s, 1H) ppm; **IR Cm^{-1}:** 3361.93, 3236.55, 2947.23, 1739.79, 1643.35, 1539.20, 1506.41, 1348.24, 1217.08, 1120.64.

5-((4-hydroxy-3-methoxybenzyl)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (10s)
Yield: 91%. **^{1}H NMR (400 MHz, DMSO-d^6):** δ=2.483 (s, 3H), 3.689-3.714 (t, 2H), 3.740 (s, 3H), 3.948-3.974 (t, 2H), 4.186 (s, 2H), 4.272-4.288 (d, 2H), 6.710-6.784 (m, 2H), 6.969 (s,1H), 7.310-7.332 (d,2H), 7.606-7.628 (d, 2H), 8.912 (s,1H), 9.187 (s, 1H), 12.504 (s, 1H) ppm; **MS:** m/z 484.1 $(M+H)^+$; **IR Cm^{-1}:** 3325.28, 2943.37, 1716.65, 1635.64, 1506.41, 1363.67, 1217.08, 1122.57.

5-((4-hydroxy-3-methoxybenzyl)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (10t)
Yield: 91%. **MS:** m/z 474.1$(M+H)^+$; **IR Cm^{-1}:** 3344.57, 3294.42, 2929.87, 1716.65, 1645.28, 1541.12, 1506.41, 1354.03, 1217.08, 1120.64.

RESULTS AND DISCUSSION

The synthesis of 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide and 5-(Arylamino)-3-(methylthio)- N- (4-(3-oxomorpholino) phenyl)-1H-pyrazole-4-carboxamide is outlined in scheme 1. 2-(phenylamino)ethanol is reacted with chloro acetyl chloride in the presence of sodium hydroxide to give 4-phenylmorpholin-3-one (3), which is reacted with 70% nitric acid in the presence of con. Sulfuric acid to affords 4-(4-nitrophenyl)morpholin-3-one (4). This nitro compound is reduced to amino compound with 10% Pd/C and ammonium formate in methanol to give 4-(4-aminophenyl) morpholin-3-one (5). This amino compound is reacted with cyano acetic acid in the presences of EDC.HCl in dichloromethane to afford 2-cyano-N-(4-(3-oxomorpholino)phenyl) acetamide (6), which on reaction with carbon disulfide in the presence of potassium carbonate, followed by methyl iodide to yield of afford 2-cyano-3,3-bis(methylthio)-N-(4-(3-oxomorpholino) phenyl) acrylamide (7) (ketene dithio derivative). Ketene dithio derivatives cyclized with hydrazine hydrate to give amino pyrazole derivative as 5-amino-3-(methylthio)-N-(4-(3-oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (8), which on reaction with different aromatic aldehyde in the presence of catalytic acetic acid to afford 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3- oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (9a-j). These Schiff bases reduced with sodium borohydride in isopropyl alcohol to yield 5-(Arylamino)-3-(methylthio)- N- (4-(3-oxomorpholino) phenyl)-1H-pyrazole-4-carboxamide (10k-t) (Figures 1 and 2).

Antimicrobial Activity
The *in vitro* antimicrobial activity of all the synthesized compounds was carried out by broth micro dilution method. Mueller Hinton broth was used as nutrient medium to grow and dilute the compound suspension for the test bacteria and Sabouraud Dextrose broth used for fungal nutrition. The appropriate inoculum size for standard MIC is 104 to 105 CFU/ml. The Minimal bactericidal concentration showed that, some of the newly synthesized compound showed little improved bactericidal activity. All compounds displayed moderate to poor activity against all bacterial strains compared to standard drug. 9c, 9d, 9f, 9g and 10q is broad spectrum drug which can inhibit the growth of gram positive, gram negative bacteria and fungi (Tables 2 and 3).

Table 2: Antibacterial and antifungal activity of 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3- oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (9a-j)

Compounds	Antibacterial MIC (µg/mL)				Antifungal MIC (µg/mL)	
	B. megaterium MTCC2444	*S. aureus* MTCC737	*E. coli* MTCC1687	*P. aeruginosa* MTCC3541	*A. niger* MTCC282	*A. flavus* MTCC418
Streptomycin			50	50		
Ampicillin	100	100				
Nystatin					100	100
9a	1000	1000	1000	1000	1000	1000
9b	1000	1000	1000	1000	1000	1000
9c	500	500	500	500	500	500
9d	500	500	500	500	500	500
9e	1000	1000	1000	1000	1000	1000
9f	500	500	500	500	500	500
9g	250	250	250	500	250	250
9h	1000	1000	1000	1000	1000	1000
9i	1000	500	1000	500	1000	1000
9j	1000	500	1000	1000	1000	1000

Table 3: Antibacterial and antifungal activity of 5-(Arylamino)-3-(methylthio)- N- (4-(3-oxomorpholino) phenyl)-1H-pyrazole-4-carboxamide (10k-t)

Compounds	Antibacterial MIC (µg/mL)				Antifungal MIC (µg/mL)	
	B. megaterium MTCC2444	*S. aureus* MTCC737	*E. coli* MTCC1687	*P. aeruginosa* MTCC3541	*A. niger* MTCC282	*A. flavus* MTCC418
Streptomycin			50	50		
Ampicillin	100	100				
Nystatin					100	100
10k	500	1000	1000	1000	1000	500
10l	1000	1000	1000	1000	1000	500
10m	1000	1000	1000	500	1000	1000
10n	500	500	500	500	500	1000
10o	500	1000	1000	1000	1000	500
10p	1000	1000	1000	1000	500	500
10q	500	500	500	500	500	500
10r	1000	1000	1000	1000	1000	1000
10s	1000	1000	1000	1000	1000	1000
10t	500	500	500	500	1000	1000

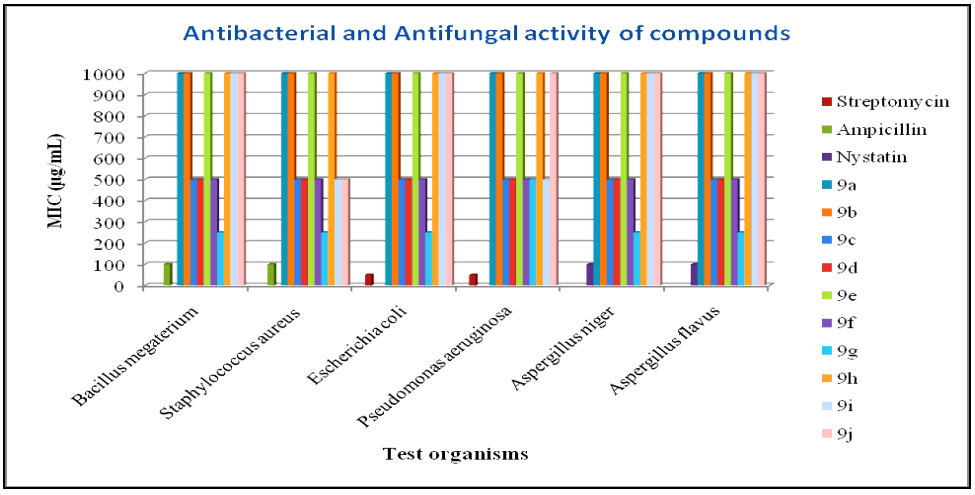


Figure 1: Antibacterial and antifungal activity chart of 5-((Arylidene)amino)-3-(methylthio)-N-(4-(3- oxomorpholino)phenyl)-1H-pyrazole-4-carboxamide (9a-j)

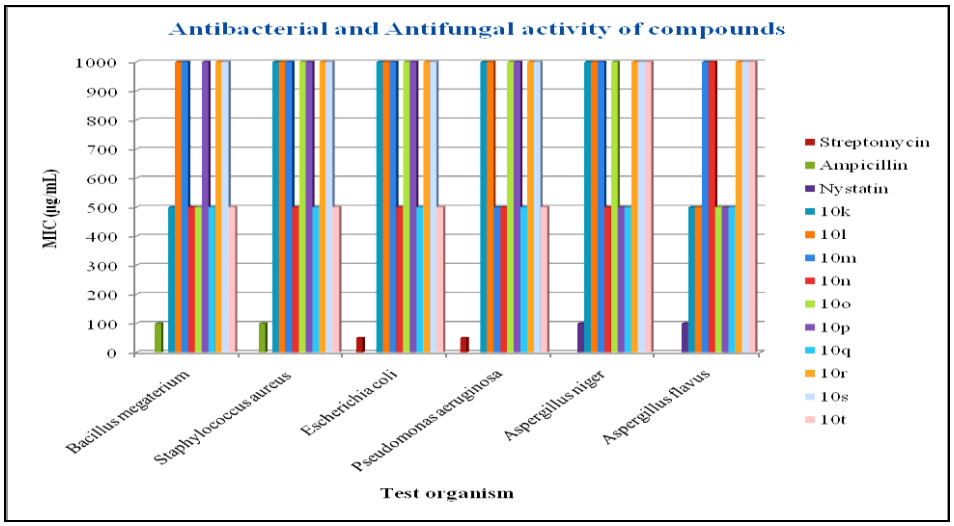


Figure 2: Antibacterial and antifungal activity chart of 5-(Arylamino)-3-(methylthio)-N- (4-(3-oxomorpholino) phenyl)-1H-pyrazole-4-carboxamide (10k-t)

CONCLUSION

An efficient method for preparing Schiff's base and amine derivatives of pyrazole was described and the structure of synthesized compounds was determine by IR, ^{1}H NMR and Mass spectroscopic analysis and evaluated for their in vitro antimicrobial activity by broth dilution method.

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