



Synthesis, Characterization and Antimicrobial Screening of Some Novel *N*-Substituted-2-Pyrazolines, Derived from Chalcones

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Abstract : A new series of (3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)(3-(4-substituted phenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)methanone (**6a-g**) and (3-(4-fluorophenyl)-5-(6-methoxy naphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridin-4-yl)methanone (**7a-g**) were synthesized by reacting 3-(6-methoxynaphthalen-1-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (Chalcone) (**3a-g**) with hydrazine hydrate followed by 3-(2,4-dichlorophenyl)-5-methylisoxazole-4-carbonyl chloride (**5**) and isonicotinohydrazide respectively. All these compounds were characterized by means of their IR, ¹H NMR, mass and elemental analysis. All the synthesized products were evaluated for their antimicrobial activity. All the compounds exhibited significant to moderate antimicrobial activity.

Keywords : Chalcone, *N*-substituted-2-Pyrazoline, isonicotinohydrazide, Antibacterial, Antifungal activity.

Introduction

Medicinal chemistry is the science that deals with the discovery and design of new therapeutic chemicals. Many of these chemicals are used as medicine in treatment of infectious diseases. The high therapeutic properties of the related drugs have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents¹. Much attention has paid to synthesis of nitrogen containing heterocyclic compounds. Nitrogen and oxygen containing heterocycles are of special interest because they constitute an important class of natural and non-natural products, many of which exhibit broad spectrum of biological and pharmacological activities.

Much attention has paid to the synthesis of nitrogen and oxygen containing heterocyclic compounds like Pyrazoles and isoxazoles² mainly due to their broad spectrum of biological and pharmacological activities^{3,4}. Pyrazoles signifies a key motif in heterocyclic chemistry and occupies a major position in medicinal and pesticide chemistry due to its wide range of bioactivities such as antibacterial⁵, anticancer⁶, analgesic and anti-inflammatory⁷. Whereas, isoxazoles possess a broad spectrum of pharmacological activities such as antibacterial⁸, antiviral⁹, antidepressant¹⁰ and anti-TB activity¹¹ activity. As per literature review the pyridine, naphthalene derivatives also possess analgesic¹² and anti-inflammatory¹³ activities. The synthesis of heterocyclic motifs containing multi-structure in one molecule has received much interest in recent years¹⁴.

Literature survey revealed that when one biodynamic heterocyclic system was coupled with another, a molecule with enhanced biological activity¹⁵ was produced. The chemistry of these linked biheterocycles have

been the fascinating field of investigation in medicinal chemistry as they have been found to exhibit enhanced biological profile¹⁶. In view of the biological and medicinal activity of pyrazoline, isoxazoles and pyridyl/naphthyl ring, it was thought worth-while to synthesize and investigate the activity of the compounds in which pyrazoline moiety has been linked with isoxazoles, similarly pyrazoline linked with pyridyl/naphthyl ring.

Material and Methods

Experimental

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded using Perkin –Elmer spectrometer. ¹H NMR spectra were recorded on Bruker Advance II 400 spectrometer in DMSO by using TMS as internal standard. Thin layer chromatography was performed with E.Merkprecoated TLC plates, silica gel 60F₂₅₄ with thickness of 0.25mm and spots were visualized by irradiation with ultraviolet light (254 nm).

General procedure for the synthesis of 3-(6-methoxynaphthalen-1-yl)-1-(4-substituted phenyl)prop-2-en-1-one(Chalcone)¹⁷ (3a-g).

A mixture of 4-substituted acetophenone(1a-g)(0.01mole) and 6-methoxy-1-naphthaldehyde (2)(0.01mole) was stirred in methanol (50 mL) and then a solution of 15 mL potassium hydroxide (0.02mole) was added to it. The mixture was kept overnight at room temperature and then it was poured into crushed ice and acidified with dil. hydrochloric acid. The chalcones i.e. [3-(6-methoxynaphthalen-1-yl)-1-(4-substituted phenyl)prop-2-en-1-one] (3a-g)precipitate out as solid (Scheme-I). The obtained solid was filtered, washed with water, dried and purified by recrystallization from acetic acid.

General procedure for the synthesis of 5-(6-methoxynaphthalen-1-yl)-3-(4-substituted phenyl)-4,5-dihydro-1H-pyrazole¹⁸ (4a-g).

A mixture of Chalcone (0.01mole) i.e. [3-(6-methoxynaphthalen-1-yl)-1-(4-substituted phenyl)prop-2-en-1-one](3a-g)was dissolved in 50 ml of methanol. To this reaction mixture, (0.02mole) of hydrazine hydrate was added. The reaction mass was heated under reflux for 3-4 hr. TLC checked, after completion of reaction, a reaction mixture was cooled to room temperature and kept overnight. Poured on ice cold water the obtained solid was filtered and wash with cold water for several times(Scheme-I). The final compound was crystallized from ethanol.

General procedure for the synthesis of 3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl(3-(4-substitutedphenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)methanone (6a-g).

5-(6-methoxynaphthalen-1-yl)-3-(4-substitutedphenyl)-4,5-dihydro-1H-pyrazole (0.01mole) (4a-g) was dissolved in pyridine (0.03mole) to this 3-(2,4-dichlorophenyl)-5-methylisoxazole-4-carbonyl chloride (0.01mole) (5) was added with constant stirring. The reaction mixture was refluxed for 1 hr. and then it was poured on crushed ice and acidified with dilute hydrochloric acid, a white color precipitate of (3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)(5-(6-methoxynaphthalen-1-yl)-3-(4-substitutedphenyl)-4,5-dihydro-1H-pyrazol-1-yl)methanone(6a-g) separated out. The so formed precipitate was filtered, dried and purified by crystallization from ethanol. Their percentage yield and physical constants were recorded in Table I.

General procedure for the synthesis of (3-(4-substituted phenyl)-5-(6-methoxy naphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridin-4-yl)methanone (7a-g)

A mixture of 1-(4-substituted phenyl)-3-(6-methoxynaphthalen-1-yl)prop-2-en-1-one (3a-g)(0.01mole) and isonicotinohydrazide (0.02mole) in 50 mL ethanolwas reflux for 6-8 hrs., excess ethanol was distilled and the resulting solution was keptovernight at room temperature and then it was poured on crushed ice,the precipitate of (3-(4-substituted phenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridin-4-yl)methanone(4a-g) separated out. Then it was filtered, dried and purified by crystallization from acetic acid. Their percentage yield and physical constants were recorded in Table II.

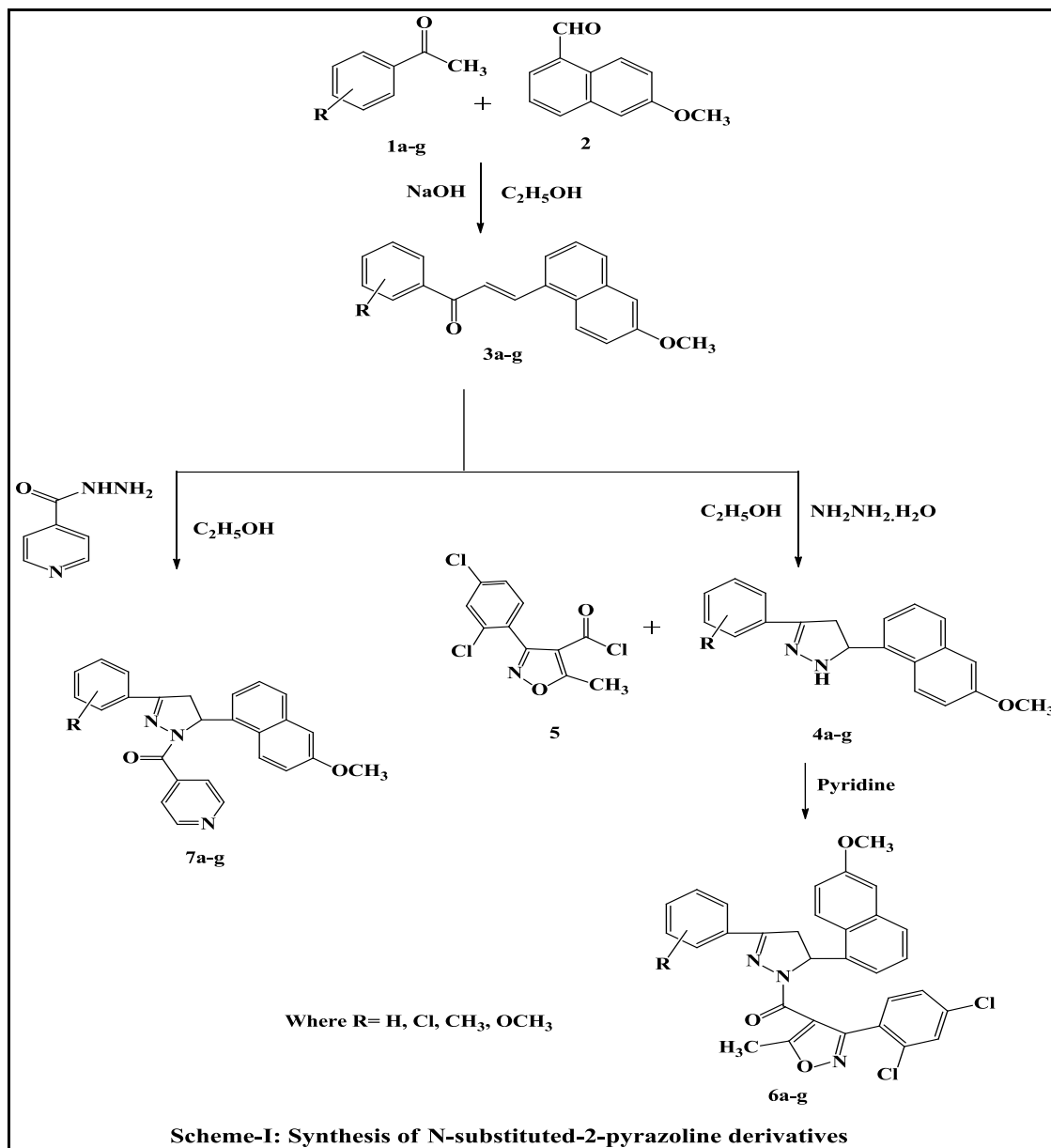


Table I. Analytical Data and Elemental Analysis of Compounds 6(a-g)

Compd.	Molecular formula	M.P. °C	Yield %	Elemental Analysis					
				%C		%H		%N	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
6a	C ₃₁ H ₂₃ Cl ₂ N ₃ O ₃	120	85	66.91	66.85	4.17	4.10	7.55	7.52
6b	C ₃₁ H ₂₂ Cl ₃ N ₃ O ₃	112	90	63.01	62.85	3.75	3.70	7.11	7.00
6c	C ₃₁ H ₂₂ BrCl ₂ N ₃ O ₃	140	87	58.60	58.55	3.49	3.40	6.61	6.55
6d	C ₃₁ H ₂₂ Cl ₂ FN ₃ O ₃	88	92	64.82	64.80	3.86	3.80	7.32	7.30
6e	C ₃₂ H ₂₅ Cl ₂ N ₃ O ₃	125	90	67.37	67.30	4.42	4.38	7.37	7.35
6f	C ₃₂ H ₂₅ Cl ₂ N ₃ O ₄	148	80	65.54	65.46	4.30	4.26	7.16	7.12
6g	C ₃₁ H ₂₁ Cl ₄ N ₃ O ₃	130	75	59.54	59.50	3.38	3.32	6.72	6.70

Table II. Analytical Data and Elemental Analysis of Compounds 7(a-g)

Compd.	Molecular formula	M.P. °C	Yield %	Elemental Analysis					
				%C		%H		%N	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
7a	C ₂₆ H ₂₁ N ₃ O ₂	188	82	76.64	76.54	5.19	5.15	10.31	10.25
7b	C ₂₆ H ₂₀ ClN ₃ O ₂	180	85	70.67	70.64	4.56	4.51	9.51	9.45
7c	C ₂₆ H ₂₀ BrN ₃ O ₂	184	78	64.21	64.14	4.14	4.10	8.64	8.58
7d	C ₂₆ H ₂₀ FN ₃ O ₂	190	80	73.40	73.30	4.74	4.72	9.88	9.85
7e	C ₂₇ H ₂₃ N ₃ O ₂	172	85	76.94	76.90	5.50	5.47	9.97	9.95
7f	C ₂₇ H ₂₃ N ₃ O ₃	158	75	76.94	76.90	5.50	5.47	9.97	9.95
7g	C ₂₆ H ₁₉ Cl ₂ N ₃ O ₂	175	70	65.56	65.50	4.02	3.97	8.82	8.75

Antimicrobial activity

All the newly synthesized compounds **6a-g** and **7a-g** was tested for their antimicrobial activity. The effects of unknown compounds were compared with the standard drug Penicillin for bacteria and Greseofulvin for fungi. Antibacterial activity was performed against *staphylococcus aureus*, *Escherichia coli*, *Salmonella Typhi* and antifungal activity against *Aspergillusniger*, *Aspergillusflavus* and *Penicilliumchrysogenum*. The antibacterial activity was assayed by cup plate method¹⁹ and antifungal activity was assayed by standard agar disc diffusion method²⁰. The results are shown in **Table III and IV** respectively.

Table III-Antibacterial screening results of the compounds 6a-g & 7a-g.

Sr. No.	Compounds	<i>E.coli</i>	<i>Salmonella typhi</i>	<i>Staphylococcus aureus</i>	<i>Bacillus subtilis</i>
		Diameter of growth inhibition zone (mm)			
1	6a	10	13	14	16
2	6b	17	19	26	28
3	6c	14	14	20	19
4	6d	17	15	18	20
5	6e	13	12	10	17
6	6f	14	17	22	24
7	6g	12	13	15	17
8	7a	12	10	15	18
9	7b	16	17	22	24
10	7c	16	18	20	22
11	7d	18	18	18	21
12	7e	13	14	21	13
13	7f	17	16	22	24
14	7g	13	16	18	16
15	Penicillium	22	25	35	38
16	DMSO	-ve	-ve	-ve	-ve
	-ve no antibacterial activity				

Table IV- Antifungal screening results of the compounds 6a-g & 7a-g.

Sr. No.	Compounds	<i>Aspergillus niger</i>	<i>Aspergillusflavus</i>	<i>Penicillumchrysogenum</i>	<i>Fusariummoneliforme</i>
1	6a	-ve	-ve	+ve	-ve
2	6b	-ve	-ve	-ve	-ve
3	6c	+ve	-ve	-ve	-ve
4	6d	-ve	+ve	-ve	-ve
5	6e	+ve	RG	+ve	-ve
6	6f	-ve	-ve	-ve	-ve
7	6g	-ve	-ve	-ve	-ve
8	7a	+ve	-ve	RG	+ve
9	7b	-ve	-ve	-ve	-ve
10	7c	-ve	-ve	RG	-ve
11	7d	-ve	-ve	+ve	-ve
12	7e	+ve	RG	+ve	-ve
13	7f	-ve	-ve	-ve	-ve
14	7g	-ve	-ve	-ve	-ve
15	Griseofulvin	-ve	-ve	-ve	-ve
16	DMSO	+ve	+ve	+ve	+ve
		-ve	No growth	Antifungal activity present	
		+ve	Growth	Antifungal activity absent	
		RG	Reduced growth		

Results and Discussion

(3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)(3-(4-substitutedphenyl)-5-(6-methoxy naphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)methanone(**6a-g**)& (3-(4-substituted phenyl) -5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridin-4-yl) methanone(**7a-g**) were successfully synthesized as per the scheme-I. The entire synthesized compounds are qualitatively analyzed by running T.L.C. and melting point. The structures of the compounds synthesized are confirmed by IR, ¹H NMR and mass spectral data.

Analytical and spectral data (IR, ¹H-NMR) of all synthesized compounds were in full agreement with proposed structure. The IR spectrum of **6a-g** exhibited a band due to 1693 Cm⁻¹ (C=N, pyrazoline ring), 1642 Cm⁻¹ (C=O), 1600 Cm⁻¹ (C=C), 1162 Cm⁻¹ (-OCH₃), but the absence of absorption peak at 3450 Cm⁻¹ due to (N-H), which is present in **4a-g**. Further, in their ¹H NMR (DMSO) spectrum, the appearance of a signal at 5.80-5.78 (dd, 1H, J=8.2 Hz, H_X), 4.24-4.19 (dd, 1H, J=9.45 Hz, H_B), 3.93 (s, 3H, -OCH₃), 3.16-3.10 (dd, 1H, J=9.3 Hz, H_A), 2.73 (s, 3H, -CH₃). Similarly, the structures of compounds **7a-g** were confirmed on the basis of spectral and elemental analysis. The IR spectrum of **7a-g** exhibited a band due to 3050 Cm⁻¹ (Aromatic C-H stretching), 1652 Cm⁻¹ (C=O), 1608 Cm⁻¹ (C=N, pyrazoline ring), 1508 (C=C), 1154 (-OCH₃). Further, in their ¹H NMR (DMSO) spectrum, the appearance of a signal at 5.65-5.61 (dd, 1H, H_Xpyrazoline), 3.77-3.53 (dd, 1H, H_Bpyrazoline), 3.35 (s, 3H, -OCH₃) 3.12-3.08 (dd, 1H, H_Apyrazoline).

The compounds **6a-g** and **7a-g** were screened for their antibacterial and antifungal activity. The investigation of antibacterial screening results indicate that compounds **6b,d, 7d,f** shows high activity against *E.coli*, similarly compounds **6b,f, 7c,d** also shows good activity against *Salmonella typhi*, compounds **6b,c,f, 7b,c,f** shows better activity against *Staphylococcus aureus* and compounds **6b,d,f, 7b,c,f** shows best activity against *Bacillus subtilis*. The investigation of antifungal activity data revealed that compounds **6a,b,d,f,g, 7b,c,d,f,g** show inhibitory effect against *Aspergillusniger* and compounds **6a,b,c,f,g, 7a,b,c,f,g** show inhibitory effect against *Aspergillusflavus*. Compounds **6b,c,d,f,g, 7b,f,g** show inhibitory effect against *Penicillumchrysogenum*. similarly most of the compounds are active against *Fusariummoneliforme*. Remaining compounds are inactive against all the fungus.

Spectral data of synthesized compounds (6a-g) &(7a-g)**Compound (6a): (3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)(4,5-dihydro-5-(6-****Methoxynaphthalen-1-yl)-3-phenylpyrazol-1-yl)methanone**

IR (KBr pellets Cm^{-1}): 1693 (C=N, pyrazoline ring), 1642 ($>\text{C}=\text{O}$), 1600 (C=C), 1162(-OCH₃); ¹H NMR (DMSO, 400 MHz) δ 8.65-7.20 (m, 14H, Ar-H), 5.80-5.78 (dd, 1H, J=8.2 Hz, H_x), 4.24-4.19 (dd, 1H, J=9.45 Hz, H_B), 3.93 (s, 3H, -OCH₃), 3.16-3.10 (dd, 1H, J=9.3 Hz, H_A), 2.73 (s, 3H, -CH₃); Mass (m/z): 556.12, 557.19(M+1).

Compound (6b):(3-(4-chlorophenyl)-4,5-dihydro-5-(6-methoxynaphthalen-1-yl)pyrazol-**1-yl)(3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)methanone**

IR (KBr pellets Cm^{-1}): 1692 (C=N, pyrazoline ring), 1640 ($>\text{C}=\text{O}$), 1600 (C=C), 1160 (-OCH₃); ¹H NMR (DMSO, 400 MHz) δ 8.60-7.18 (m, 13H, Ar-H), 5.80-5.78 (dd, 1H, J=8.0 Hz, H_x), 4.22-4.18 (dd, 1H, J=9.43 Hz, H_B), 3.92 (s, 3H, -OCH₃), 3.15-3.11 (dd, 1H, J=9.3 Hz, H_A), 2.70 (s, 3H, -CH₃); Mass (m/z): 590.12 (M+1).

Compound (6c):(3-(4-bromophenyl)-4,5-dihydro-5-(6-methoxynaphthalen-1-yl)pyrazol-**1-yl)(3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)methanone**

IR (KBr pellets Cm^{-1}): 1695 (C=N, pyrazoline ring), 1638 ($>\text{C}=\text{O}$), 1620 (C=C), 1168 (-OCH₃); ¹H NMR (DMSO, 400 MHz) δ 8.62-7.18 (m, 13H, Ar-H), 5.78-5.75 (dd, 1H, J=8.3 Hz, H_x), 4.21-4.17 (dd, 1H, J=9.48 Hz, H_B), 3.90 (s, 3H, -OCH₃), 3.15-3.11 (dd, 1H, J=9.3 Hz, H_A), 2.75 (s, 3H, -CH₃); Mass (m/z): 635.12, 637.16 (M+1).

Compound (6d):(3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)(3-(4-fluorophenyl)-4,5-**dihydro-5-(6-methoxynaphthalen-1-yl)pyrazol-1-yl)methanone**

IR (KBr pellets Cm^{-1}): 1695 (C=N, pyrazoline ring), 1642 ($>\text{C}=\text{O}$), 1623 (C=C), 1170 (-OCH₃); ¹H NMR (DMSO, 400 MHz) δ 8.60-7.16 (m, 13H, Ar-H), 5.77-5.76 (dd, 1H, J=8.2 Hz, H_x), 4.20-4.17 (dd, 1H, J=9.5 Hz, H_B), 3.95 (s, 3H, -OCH₃), 3.16-3.12 (dd, 1H, J=9.2 Hz, H_A), 2.70 (s, 3H, -CH₃); Mass (m/z): 575.10 (M+1).

Compound (6e):(3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)(4,5-dihydro-5-(6-**methoxynaphthalen-1-yl)-3-(4-methylphenyl)pyrazol-1-yl)methanone**

IR (KBr pellets Cm^{-1}): 1695 (C=N, pyrazoline ring), 1645 ($>\text{C}=\text{O}$), 1623 (C=C), 1170 (-OCH₃); ¹H NMR (DMSO, 400 MHz) δ 8.63-7.15 (m, 13H, Ar-H), 5.75-5.72 (dd, 1H, J=8.3 Hz, H_x), 4.20-4.17 (dd, 1H, J=9.5 Hz, H_B), 3.90 (s, 3H, -OCH₃), 3.15-3.13 (dd, 1H, J=9.3 Hz, H_A), 2.70 (s, 3H, -CH₃), 2.65 (s, 3H, -CH₃); Mass (m/z): 570.13 (M+1).

Compound (6f): (3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)(4,5-dihydro-5-(6-**methoxynaphthalen-1-yl)-3-(4-methoxyphenyl)pyrazol-1-yl)methanone**

IR (KBr pellets Cm^{-1}): 1690 (C=N, pyrazoline ring), 1635 ($>\text{C}=\text{O}$), 1610 (C=C), 1165 (-OCH₃); ¹H NMR (DMSO, 400 MHz) δ 8.55-7.10 (m, 13H, Ar-H), 5.82-5.80 (dd, 1H, J=8.2 Hz, H_x), 4.25-4.19 (dd, 1H, J=9.45 Hz, H_B), 3.90 (s, 6H, 2 X -OCH₃), 3.15-3.10 (dd, 1H, J=9.3 Hz, H_A), 2.70 (s, 3H, -CH₃); Mass (m/z): 587.12 (M+1).

Compound (6g):(3-(2,4-dichlorophenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-**pyrazol-1-yl)(3-(2,4-dichlorophenyl)-5-methylisoxazol-4-yl)methanone**

IR (KBr pellets Cm^{-1}): 1695 (C=N, pyrazoline ring), 1642 ($>\text{C}=\text{O}$), 1623 (C=C), 1170 (-OCH₃); ¹H NMR (DMSO, 400 MHz) δ 8.57-7.15 (m, 12H, Ar-H), 5.80-5.84 (dd, 1H, J=8.2 Hz, H_x), 4.26-4.20 (dd, 1H, J=9.40

Hz, H_B), 3.92 (s, 3H, -OCH₃), 3.15-3.10 (dd, 1H, J=9.3 Hz, H_A), 2.73 (s, 3H, -CH₃); Mass (m/z): 625.12, 627.22 (M+1).

Compound (7a):(5-(6-methoxynaphthalen-1-yl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)

(pyridin-4-yl)methanone

IR (KBr pellets Cm⁻¹): 3050 (Aromatic C-H stretching), 1652 (>C=O), 1608 (C=N, pyrazoline ring), 1508 (C=C), 1154 (-OCH₃); ¹H NMR (DMSO, 400 MHz) 8.75-6.45 (m, 15H, Ar-H), 5.65-5.61 (dd, 1H, H_xpyrazoline), 3.77-3.53 (dd, 1H, H_B pyrazoline), 3.35 (s, 3H, -OCH₃) 3.12-3.08 (dd, 1H, H_Apyrazoline); Mass (m/z): 408.17 (M+1).

Compound (7b):(3-(4-chlorophenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-

pyrazol-1-yl)(pyridin-4-yl)methanone

IR (KBr pellets Cm⁻¹): 3020 (Aromatic C-H stretching), 1650 (>C=O), 1615 (C=N, pyrazoline ring), 1520 (C=C), 1160 (-OCH₃); ¹H NMR (DMSO, 400 MHz) 8.79-6.50 (m, 14H, Ar-H), 5.64-5.60 (dd, 1H, H_xpyrazoline), 3.77-3.53 (dd, 1H, H_B pyrazoline), 3.33 (s, 3H, -OCH₃) 3.14-3.09 (dd, 1H, H_Apyrazoline); Mass (m/z): 423.12 (M+1).

Compound (7c):(3-(4-bromophenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-

pyrazol-1-yl)(pyridin-4-yl)methanone

IR (KBr pellets Cm⁻¹): 3022 (Aromatic C-H stretching), 1645 (>C=O), 1620 (C=N, pyrazoline ring), 1520 (C=C), 1162 (-OCH₃); ¹H NMR (DMSO, 400 MHz) 8.78-6.50 (m, 14H, Ar-H), 5.64-5.60 (dd, 1H, H_xpyrazoline), 3.75-3.50 (dd, 1H, H_B pyrazoline), 3.35 (s, 3H, -OCH₃) 3.15-3.09 (dd, 1H, H_Apyrazoline); Mass (m/z): 486.08, 488.13 (M+1).

Compound (7d):(3-(4-fluorophenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-

pyrazol-1-yl)(pyridin-4-yl)methanone

IR (KBr pellets Cm⁻¹): 3056 (Aromatic C-H stretching), 1655 (>C=O), 1606 (C=N, pyrazoline ring), 1508 (C=C), 1157 (-OCH₃); ¹H NMR (DMSO, 400 MHz) 8.14-6.32 (m, 14H, Ar-H), 5.69-5.66 (dd, 1H, H_xpyrazoline), 3.68-3.55 (dd, 1H, H_B pyrazoline), 3.82 (s, 3H, -OCH₃) 3.15-3.10 (dd, 1H, H_Apyrazoline); Mass (m/z): 426.16 (M+1).

Compound (7e):(5-(6-methoxynaphthalen-1-yl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-

yl)(pyridin-4-yl)methanone

IR (KBr pellets Cm⁻¹): 3036 (Aromatic C-H stretching), 1652 (>C=O), 1610 (C=N, pyrazoline ring), 1508 (C=C), 1160 (-OCH₃); ¹H NMR (DMSO, 400 MHz) 8.20-6.30 (m, 14H, Ar-H), 5.60-5.66 (dd, 1H, H_xpyrazoline), 3.68-3.55 (dd, 1H, H_B pyrazoline), 3.75 (s, 3H, -OCH₃) 3.15-3.10 (dd, 1H, H_Apyrazoline), 2.73 (s, 3H, -CH₃); Mass (m/z): 422.16 (M+1).

Compound (7f):(5-(6-methoxynaphthalen-1-yl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-

pyrazol-1-yl)(pyridin-4-yl)methanone

IR (KBr pellets Cm⁻¹): 3040 (Aromatic C-H stretching), 1651 (>C=O), 1610 (C=N, pyrazoline ring), 1525 (C=C), 1155 (-OCH₃); ¹H NMR (DMSO, 400 MHz) 8.20-6.30 (m, 14H, Ar-H), 5.62-5.68 (dd, 1H, H_xpyrazoline), 3.68-3.53 (dd, 1H, H_B pyrazoline), 3.83 (s, 6H, 2 x -OCH₃) 3.16-3.12 (dd, 1H, H_Apyrazoline); Mass (m/z): 438.22 (M+1).

Compound (7g):(3-(2,4-dichlorophenyl)-5-(6-methoxynaphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridin-4-yl)methanone

IR (KBr pellets Cm^{-1}): 3040 (Aromatic C-H stretching), 1657 ($>\text{C}=\text{O}$), 1615 (C=N, pyrazoline ring), 1520 (C=C), 1156 (-OCH₃); ¹H NMR (DMSO, 400 MHz) 8.25-6.28 (m, 13H, Ar-H), 5.60-5.68 (dd, 1H, H_xpyrazoline), 3.68-3.53 (dd, 1H, H_B pyrazoline), 3.73 (s, 3H, -OCH₃) 3.15-3.11 (dd, 1H, H_Apyrazoline); Mass (m/z): 477.12 (M+1).

Conclusion

In conclusion, we have reported some novel *N*-substituted-2-pyrazolines, in which pyrazoline moiety is linked with isoxazoles, similarly pyrazoline linked with pyridyl/naphthyl ring, which possess good to moderate antimicrobial activity. In this study the pharmacophore which possess pyrazoline moiety which is coupled with isoxazoles ring, pyridyl ring and groups substituted like bromo, chloro, fluoro, and methoxy may provide us the fruitful results in biological and medicinal purposes.

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References

1. Zienab M. nofal, Elsyed. A. soliman, Aladdin. M. srour, Shalinisethyamadavan Timothy. J .maher, Novel benzimidazole derivatives as expected anticancer agents, *ActaPoloniae, Pharmaceutical and DrugResearch*, 2011, 8(4), 519-534.
2. Singh G., Ila H., Junjappa H., Polarised ketene dithioacetals. Part 50. Reactions of α -aroyl- α -bromoketenedithioacetals with hydrazine hydrate: formation of rearranged Pyrazoles, *J.ChemSoc Perkin Trans.*, 1987, 1, 1945-1949; DOI:10.1039/P19870001945.
3. Mirzaei Y. R., Balasubramaniam T. N., Lefler B. J., Natale N. R., Selective lateral metalation and electrophilic quenching of c-4 functionalized isoxazoles. IX. Direct formation of the C-N bond utilizing an electrophilic nitrogen source, *J. Heterocyclic Chem.*, 1990, 27(7), 2001-2004; DOI:10.1002/jhet.5570270729
4. R. Kalirajan, S.U.Sivakumar, S. Jubie, B. Gowramma, B. Suresh, Synthesis and Biological evaluation of some heterocyclic derivatives of Chalcones, *Int. J. Chem Tech Res.* 2009,1(1).
5. Sarveswari S., Vijayakumar V., Synthesis and Antibacterial Screening of 3-(4,5-Dihydro-5-Aryl-1H-Pyrazol-3-YL)-4-Hydroxyquinolin-2(1H)-Ones, *Int. J. Chem Tech Res.* 2015, 8(6), 782-788.
6. Manna F., Chimenti F., Fioravanti R., Bolasco A., Secci D., Chimenti P., Synthesis of some pyrazole derivatives and preliminary investigation of their affinity binding to P-glycoprotein, *Bioorg. Med. Chem. Lett.*, 2005, 15(20), 4632-4635.
7. Yadav Ajay Kumar, Baheti K. G., RawatPreeti, Synthesis, Pharmacological Screening of Ethyl (5-Substitutedacetamido)-3-Methylthio-1-Phenyl-1h-Pyrazole-4-Carboxylate As Anti-Inflammatory And Analgesic Agents, *International Journal of PharmTech Research*, 2015,8(5), 828-835.
8. Desai, J.T., Desai, C.K., and Desai, K.R., A Convenient, Rapid and Eco-Friendly Synthesis of Isoxazoline Heterocyclic Moiety Containing Bridge at 2°- Amine as potential pharmacological agent. *J.Iran. Chem. Soc.* 2008, 5, 67-73.
9. Lee, Y.S., Park, S.M., Kim, B.H., Synthesis of 5-isoxazol-5-yl-2'-deoxyuridines exhibiting antiviral activity against HSV and several RNA viruses, *Bioorg. Med. Chem. Lett*, 2009, 19, 1126-1128.
10. Bailey D. M., Hansen P. E., Hlavac A. G., Baizman E. R., Pearl J., DeFelice A. F., Feigenson M. E., 3,4-Diphenyl-1H-pyrazole-1-propanamine antidepressants *J. Med. Chem.*, 1985, 28, 256.
11. NareshvarmaSeelam, Synthesis, characterization and in-vitro anti TB studies of Isoxazole analogues, *International Journal of PharmTech Research*, . 2015, 8(9), 127-134.

12. Diouf O., Depreux P., Chavatte P., Poupaert J. H., Synthesis and preliminary pharmacological results on new naphthalene derivatives as 5-HT(4) receptor ligands *Eur. J. Med. Chem.*, 2000, 35, 699–706.
13. Meotti F. C., Silva D. O., Santos A. R. S., Zeni G., Rocha J. B. T., Nogueira C. W., Thiophenes and furans derivatives: a new class of potential pharmacological agents, *Environ. Toxic. Pharmacol.*, 2003, 37, 37-44.
14. Piyush N. Kalaria,* Shailesh P. Satasia and Dipak K. Raval, Synthesis, identification and in vitro biological evaluation of some novel 5-imidazopyrazole incorporated pyrazoline and isoxazoline derivatives, *New J. Chem.*, 2014, 38, 2902--2910
15. Donatella Boschi, Clara Cena, Antonella Di Stilo, Roberta Fruttero, Alberto Gasco, Nicorandil analogues containing NO-donor furoxans and related furazans, 2000, 8(7), 1727.
16. Robin D. Clark, Joan M. Caroon, Arthur F. Kluge, David B. Repke, Adolph P. Roszkowski, Arthur M. Strosberg, Stephen Baker, Susan M. Bitter, Marlys D. Okada, Synthesis and antihypertensive activity of 4'-substituted spiro[4H-3,1-benzoxazine-4,4'-piperidin]-2(1H)-ones, *J. Med. Chem.*, 1983, 26 (5), 657–661; DOI: 10.1021/jm00359a007
17. Jadhav Satish B., Synthesis and Antimicrobial study of some novel 2,4-disubstituted- 1,5-benzodiazepine derivatives, *Int. J. Pharm. Pharm. Sci.*, 2011, 3(2), 181-184.
18. Jadhav S. B., Shastri R. A., Gaikwad K. V., Gaikwad S. V., Synthesis and Antimicrobial Studies of Some Novel Pyrazoline and Isoxazoline Derivatives, *e- Journal of Chemistry*, 2009, 6(S1), S183-S188
19. Smith Q. E., *Int. pharmacological Screening tests progress in medicinal chemistry*, Butterworths London, 1960, 1, 1-33.
20. Pai S. T., Platt M. W., Antifungal of *Allium sativum* (garlic) extract against the *Aspergillus* species involved in otomycosis, *Letters Applied Microbiology*, 1995, 20(1), 14-18; DOI:10.1111/j.1472-765X.1995.tb00397.x
