Acta Chimica & Pharmaceutica Indica

Acta Chim. Pharm. Indica: 2(3), 2012, 143-150
ISSN 2277-288X

SYNTHESIS AND FUNGITOXICITY OF 1-[N-BENZOYL-3-(2^1-SUBSTITUTED-3^1-SULPHONYL-5^1-METHOXYINDOL-3^1-YL)-2-PYRAZOLINES AND 1-(N-PHENYLSULPHONYL)-3-(2^1-SUBSTITUTED-3^1-SULPHONYL)-5^1-METHOXYINDOL-3^1-YL)-2-PYRAZOLINES

RISHI PRATAP SINGH*, D. V. SINGH, CHAVI RAJ SINGH and SHAILENDRA SINGH

Department of Chemistry, Rashtirya Post Graduate College, Jamuhai, JAUNPUR – 222001 (U.P.) INDIA

(*Received : 06.04.2012; Revised : 18.04.2012; Accepted : 20.04.2012*)

ABSTRACT

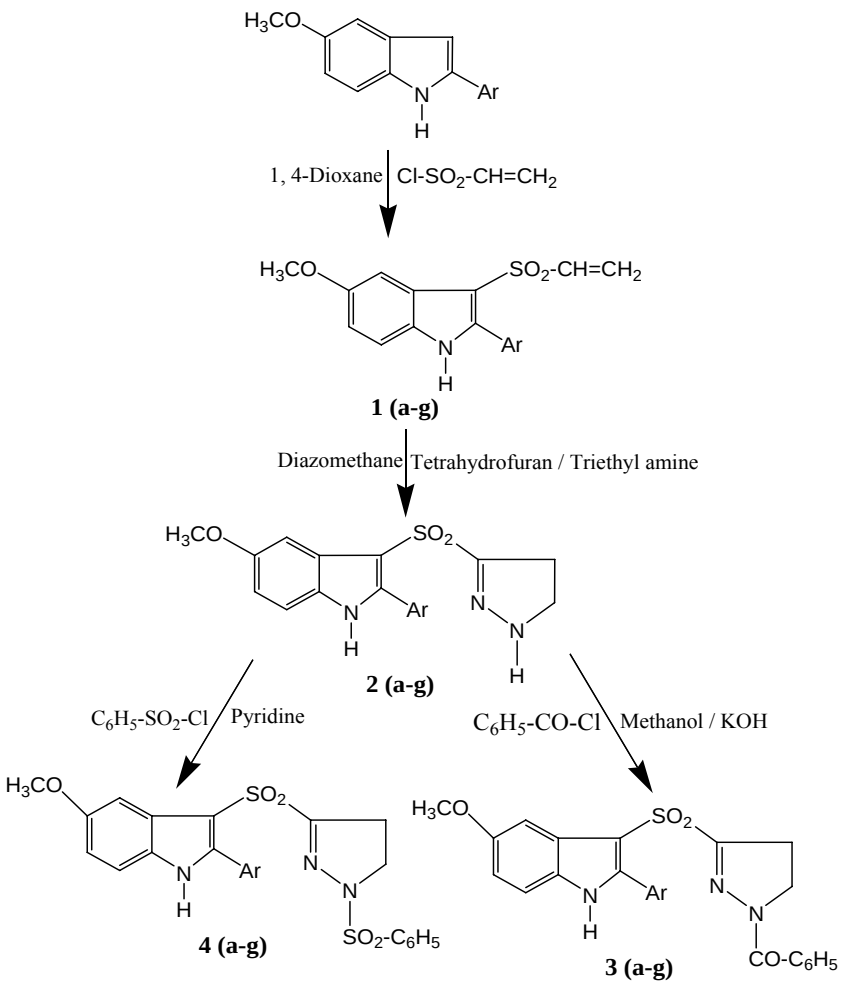
Starting material 2-substituted-3-vinylsulphonyl-5-methoxyindols **(1a-g)** have been synthesized from easily available 2-substituted-5-methoxyindols in 1, 4-dioxane and chlorosulphonyl chloride. Compound **(1a-g)** reacts with triethyl amine in dry tetrahydrofuran and treated with diazomethane to form 3-(2^1-substituted-3-sulphonyl-5^1-methoxyindol-3^1-yl)-2-pyrazolines **(2a-g)**. Compound **(2a-g)** reacts with benzoyl choride, potassium hydroxide and methanol to give 1-[N-Benzoyl-3-(2^1-substituted-3^1-sulphonyl-5^1-methoxyindol-3^1-yld-2-pyrazolines **(3a-g)** and again reacts with benzenesulphonyl chloride in pyridine and neutralize with dilute HCl to formed 1-(N-phenylsulphonyl)-3-(2^1-substituted-3^1-sulphonyl)-5^1-methoxyindl-3^1-yl)-2-pyrozalines **(4a-g)**. Antifungal activity has been compaired with dithane M-45, a commercial fungicide, for their fungitoxic action against *Phytophthora infestance* and *Collectotricum fulcatium*, and the result correlated with their structural features.

Key words: Chemo-selectivity, Sulphonyl pyrazoline derivatives, Fungicidal activity, Pharmacological properties, Infrared spectra, ^{1}H NMR spectra.

INTRODUCTION

Pyrazolines have served as a starting point for the synthesis of 2-substituted-5-methoxyindoles, which show useful anti-inflammatory drugs and pharmacodynamic heterocyclic, indole nucleus which are used clinically for the treatments of different inflammatory disorders. Further, indole derivatives possessed a wide range of pharmacological and biological or biochemical activities such as anti-inflammatory[1-3], analgesic[4], antipyretic[5], anticonvulsant[6] and antibacterial[7]. Moreover, pyrazoline derivatives have also been reported to possess potent antifungal activity. With a view to develop better antifungal agents, we have, therefore, synthesized some indole derivatives possessing pyrazoline moiety at 3-position of indole to get enhanced potency to get compounds with their antifungal activity, the reaction sequences leading to the formation of title compounds are given in Scheme 1.

Available online at www.sadgurupublications.com
*Author for correspondence; E-mail: pratap.rishi@rediffmail.com



Ar: a = C_6H_5; b = o-ClC_6H_4; c = p-ClC_6H_4; d = o-$OCH_3C_6H_4$; e = p-$OCH_3C_6H_4$; f = o -$CH_3C_6H_4$; g = p-$CH_3C_6H_4$

Scheme 1

EXPERIMENTAL

All melting point determined in open glass capillaries. All the solvents and reagents used were of Analytical grade. All the reactions were monitored by TLC using Benzene: Methanol (9 : 2), Methylene dichloride : Ethyl acetate: Methanol (60 : 35 : 05) and Toluene: Ethyl acetate (7 : 3) as a solvent system TLC plates were prepared by spreading method. These were dried in the air and then activated by heating in hot air oven at 110°C for 30 minutes Iodine vapors were used for visualization of TLC plates. IR spectra in KBr were recorded on Perkin-Elmer infrared spectrophotometer (λ_{max} in cm^{-1}) and ^1H NMR spectra in $CDCl_3$ on EM-360L (60 MHz) NMR Spectrometer using TMS as internal references (Chemical shifts in δ ppm). All the compounds have given satisfactory elemental analysis (C, H, N and S), IR and ^1H NMR spectra.

2-Substituted-3-vinylsulphonyl-5-methoxyindoles (1)

In vigorously stirred solution of 2-substitued-methoxyindoles (0.05 M) in dry 1, 4-dioxane, chlorosulphonyl chloride (0.10 M) was added at 0°C drop by drop. The reaction mixtures were stirred for 4.0 hrs and left for overnight and excess of solvents were distilled off and the products were re-crystallized from appropriate solvents; Yield, m. p., molecular formula and elemental analysis with IR and ^1H NMR spectra of the representative compounds are recorded in Table 1.

3-(2^1-Substituted-3^1-sulphonyl-5^1-methoxyindol-3^1-yl)-2-pyrazolines (2)

A mixture of compound (1) (0.01 M) were dissolved in dry tetrahydrofuran separately having 5-6 drops of triethyl amine and the solution treated with excess of dry and cool ethereal diazomethane (0.01 M) in each case. The reaction mixture was maintained below 0^oC for 48.0 hrs in deep freezer during which fresh amount of diazomethane was added. The excess of solvent was distilled off in vacuum and the resulting solids were washed with petroleum ether ($60-80^o$) and then recrystallized from appropriate solvents; yield, m.p., molecular formula and elemental analysis with IR and ^1H NMR spectra of the representative compounds are recorded in Table 1.

IR and ^1H NMR spectra of compound 2a: IR (KBr): 3360-3420 (N-H), 1320-1300 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.40 (s, 3H, $-CH_3$), 3.42 (s, 3H, $-OCH_3$), 5.62-5.98 (m, 4H, $-CH_2-CH_2$), 6.46 (br, 1H, NH), 7.8-8.07 (m, 7H, Ar-H), 8.26 (br, 1H, N-H).

IR and ^1H NMR spectra of compound 2b: IR (KBr): 3318-3410 (N-H), 1315-1295 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.46 (s, 3H, $-OCH_3$), 5.60-5.99 (m, 4H, $-CH_2-CH_2$), 6.40 (br, 1H, N-H), 7.30-8.01 (m, 8H, Ar-H), 8.29 (br, 1H, N-H).

IR and ^1H NMR spectra of compound 2c: IR (KBr): 3320-3400 (N-H), 1325-1300 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.46 (s, 6H, $-2OCH_3$), 5.53-5.90 (m, 4H, $-CH_2-CH_2$), 6.40 (br, 1H, NH), 7.62-8.00 (m, 7H, Ar-H), 8.16 (br, 1H, N-H).

IR and ^1H NMR spectra of compound 2f: IR (KBr): 3335-3395 (N-H), 1336-1305 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.42 (s, 3H, $-CH_3$), 5.51-5.95 (m, 4H, $-CH_2-CH_2$), 6.41 (br, 1H, N-H) 7.60-7.92 (m, 7H, Ar-H), 8.26 (br, 1H, N-H).

IR and ^1H NMR spectra of compound 2g: IR (KBr): 3312-3418 (N-H), 1305-1290 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 2.40 (s, 3H, $-CH_3$), 5.46-5.98 (m, 4H, $-CH_2-CH_2$), 6.43 (br, 1H, N-H), 7.08-7.99 (m, 7H, Ar-H), 8.24 (br, 1H, N-H).

1-[N-Benzolyl-3-(2^1-substituted-3^1-sulphonyl-5^1-methoxyindol-3^1-yl)-2-pyrazolines (3)

To a cool potassium hydroxide, methanol solution of compounds (2) (0.075 M), benzoyl chloride (0.075 M) was added with stirring. The reaction mixture was stirred for 1.0 hrs and then refluxed for 2.0 hrs. The product thus obtained was recrystallized from a mixture of dimethyl formamide and water (1 : 2) to yield, m. p., molecular formula and elemental analysis with IR and ^1H NMR spectra of the representative compounds are recorded in Table 1.

IR and ^1H NMR spectra of compound 3a: IR (KBr): 3360-3410 (N-H), 3040 (C-C of aromatic ring), 2460-2510 (aliphatic C-H), 1650 (C=O), 1320-1300 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.46 (s, 3H, $-OCH_3$), 5.72-6.61 (m, 4H, $-CH_2-CH_2$), 7.60-8.16 (m, 13H, Ar-H), 8.71 (br, 1H, NH).

IR and ^1H NMR spectra of compound 3c: IR (KBr): 3355-3415 (N-H), 3045 (C-C of aromatic ring), 2465-2515 (aliphatic C-H), 1655 (C=O), 1325-1305 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.41 (s, 3H, $-OCH_3$), 5.70-6.62 (m, 4H, $-CH_2-CH_2$), 7.55-8.05 (m, 13H, Ar-H), 8.72 (br, 1H, NH).

IR and ^1H NMR spectra of compound 3d: IR (KBr): 3350-3420 (NH), 3050 (C-C of aromatic ring), 3455-2530 (aliphatic C-H), 1665 (C=O), 1328-1310 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.40 (s, 6H, $-2OCH_3$), 5.72-6.65 (m, 4H, $-CH_2-CH_2$), 7.50-8.03 (m, 12H, Ar-H), 8.71 (br, 1H, NH).

IR and ^{1}H NMR spectra of compound 3e: IR (KBr): 3335-3425 (N-H), 3055 (C-C of aromatic ring), 3455-2545 (aliphatic C-H), 1665 (C=O), 1320-1305 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.46 (s, 6H, -2OCH_3), 5.70-6.60 (m, 4H, -CH_2-CH_2), 7.50-8.01 (m, 12H, Ar-H), 8.70 (br, 1H, NH).

IR and ^{1}H NMR spectra of compound 3f: IR (KBr): 3355-3425 (N-H), 3045 (C-C of aromatic ring), 2455-2525 (aliphatic C-H), 1655 (C=O), 1300-1280 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 2.42 (s, 3H, -CH_3), 3.43 (s, 3H, -OCH_3), 5.65-6.70 (m, 4H, -CH_2-CH_2), 7.40-8.06 (m, 12H, Ar-H), 8.75 (br, 1H, NH).

IR and ^{1}H NMR spectra of compound 3g: IR (KBr): 3362-3415 (N-H), 3048 (C-C of aromatic ring), 2462-2510 (aliphatic C-H), 1655 (C=O), 1310-1295 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 2.46 (s, 3H, -CH_3), 3.42 (s, 3H, -OCH_3), 5.70-6.65 (m, 4H, -CH_2-CH_2), 7.45-8.05 (m, 12H, Ar-H), 8.73 (br, 1H, N-H).

1-(N-Phenylsulphonyl)-3-(2^1-substituted-3^1-sulphonyl)-5^1-methoxyindol-3^1-yl)-2-pyrazolines (4)

To a cooled solution of compounds (2) (0.075 M) in pyridine (dry, 50.0 mL), benzenesulphonyl chloride (0.075 M) was added drop wise with stirring. The reaction mixture was refluxed for 2.0 hrs. The reaction mixtures were neutralized with dilute HCl. The product was filtered, washed with water and dried and recrystallized from ethanol; yield, m. p., molecular formula and elemental analysis with IR and ^{1}H NMR spectra of the representative compounds are recorded in Table 2.

IR and ^{1}H NMR spectra of compound 4a: IR (KBr): 3350-3420 (N-H), 3060 (C-C of aromatic ring), 2490-2540 (aliphatic C-H), 1700 (C=0), 1680 (C=O), 1300-1325 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.48 (s, 3H, -OCH_3), 5.82-6.26 (m, 4H, -CH_2-CH_2), 7.01 – 8.00 (m, 12H, Ar-H), 8.63 (br, 1H, NH).

IR and ^{1}H NMR spectra of compound 4c: IR (KBr): 3345-3425 (N-H), 3065 (C-C of aromatic ring), 2495-2535 (aliphatic C-H), 1710 (C=O), 1682 (C=O), 1305-1340 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.42 (s, 6H, -2OCH_3), 5.85-6.29 (m, 4H, -CH_2-CH_2), 7.01-8.00 (m, 12H, Ar-H), 8.63 (br, 1H, NH).

IR and ^{1}H NMR spectra of compound 4e: IR (KBr): 3350-3410 (N-H), 3055 (C-C of aromatic ring), 2485-2530 (aliphatic C-H), 1725 (C=O), 1675 (C=O), 1305-1335 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 2.46 (s, 3H, -CH_3), 3.41 (s, 3H, -OCH_3), 5.82-6.25 (m, 4H, -CH_2-CH_2), 7.02-7.90 (m, 12H, Ar-H), 8.61 (br, 1H, NH).

IR and ^{1}H NMR spectra of compound 4f: IR (KBr): 3342-3417 (N-H), 3065 (C-C of aromatic ring), 2482-2535 (aliphatic C-H), 1730 (C=O), 1678 (C=O), 1303-1338 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 2.41 (s, 3H, -CH_3), 3.45 (s, 3H, -OCH_3), 5.82-6.25 (m, 4H, -CH_2-CH_2), 7.06-8.01 (m, 12H, Ar-H), 8.63 (br, 1H, NH).

IR and ^{1}H NMR spectra of compound 4g: IR (KBr): 3355-3430 (N-H), 3065 (C-C of aromatic ring), 2485-2535 (aliphatic C-H), 1705 (C=O), 1685 (C=O), 1305-1335 (SO_2) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.41 (s, 3H, -OCH_3), 5.80-6.20 (m, 4H, -CH_2-CH_2), 7.01-7.89 (m, 13H, Ar-H), 8.60 (br, 1H, NH).

Antifungal activities

The antifungal activity of the compounds **(3a-g)** and **(4a-g)** were evaluated against *phytophthora infestans* and *collectotricum fulcatum* by usual agar plate technique[8] at 1000, 100 and 10 ppm concentrations[9-13]. Dithane M-45 a standard commercial fungicide was also tested under similar conditions for comparison. The antifungal activity results of the compounds **(3a-g)** and **(4a-g)** are summarized in Table 3. It is appeared from the screening result that most of the compounds **(3a-g)** and **(4a-g)**. Significantly inhibited the mycelia growth of both test fungi at 1000 ppm but their activity decreased considerably at lower

concentration (100 and 10 ppm). The compounds **3b**, **3**c, **4b** and **4e** had similar activity to mancozed at 1000 ppm and showed growth 54-48% inhibition of both the test fungi at 10 ppm concentration. It was significant alteration in the antifungal activity with the change in the relative position of the substituent on sulphonyl pyrazoline rings, for example compounds 3b and 4b bearing 2-chloro groups were more active than 3d and 4d 2-methoxy groups. Likewise, introduction of chloro group was for more effective than that at methoxy group.

Table 1: Characterization data of 2-substituted-3-vinylsulphonyl-5-methoxyindoles (1 a-g) and 3-(2^1-substituted-3^1-sulphonyl-5^1-methoxyindol-3^1-y^l)-2-pyrazolines (2 a-g) and 1-[N-benzoyl-3-(2^1-substituted-3^1-sulphonyl-5^1-m-ethoxyindol-3^1-yl)–2-pyrazolines (3 a-g)

Compound No.	Ar	Molecular formula	M.P. (^{o}C)	Yield (%)	Found (Calcd.) %		
					C	N	S
1a	o-ClC_6H_4	$C_{17}H_{14}O_3NSCl$	112-114	80	58.73 (58.70)	04.05 (04.03)	09.23 (09.20)
b	C_6H_5	$C_{17}H_{15}O_3NS$	106-108	78	65.15 (65.17)	04.46 (04.47)	10.24 (10.22)
c	p-ClC_6H_4	$C_{17}H_{14}O_3NSCl$	110-111	79	58.68 (58.70)	04.05 (04-03)	09.21 (09.20)
d	o-$OCH_3C_6H_4$	$C_{18}H_{17}O_4NS$	102-103	76	62.95 (62.97)	04.06 (04.08)	09.31 (09.32)
e	o-$CH_3C_6H_4$	$C_{18}H_{17}O_3NS$	100-101	75	66.06 (66.05)	04.26 (04.28)	09.79 (09.79)
f	p-$OCH_3C_6H_4$	$C_{18}H_{17}O_4NS$	103-105	77	62.96 (62.97)	04.09 (04.08)	09.33 (09.32)
g	p-$CH_3C_6H_4$	$C_{18}H_{17}O_3NS$	102-103	78	66.04 (66.05)	04.26 (04.28)	09.77 (09.79)
2a*	o-$CH_3C_6H_4$	$C_{19}H_{19}N_3O_3S$	168-169	60	61.76 (61.78)	11.40 (11.38)	08.65 (08.67)
b*	C_6H_5	$C_{18}H_{17}N_3O_3S$	151-153	56	60.85 (60.84)	11.85 (11.83)	09.16 (09.14).
c*	o-$OCH_3C_6H_4$	$C_{19}H_{19}N_3O_4S$	154-156	58	59.20 (59.22)	10.89 (10.90)	08.30 (08.31)
d	p-$OCH_3C_6H_4$	$C_{19}H_{19}N_3O_3S$	152-154	56	59.23 (59.22)	10.92 (10.90)	08.32 (08.31)
e	p-$CH_3C_6H_4$	$C_{19}H_{19}N_3O_3S$	156-157	58	61.75 (61-78)	11.39 (11.38)	08.69 (08.67)
f*	o-ClC_6H_4	$C_{18}H_{16}N_3O_3SCl$	157-159	59	55.46 (55.45)	10.75 (10.78)	08.22 (08.21)

Cont…

Compound No.	Ar	Molecular formula	M.P. (^oC)	Yield (%)	Found (Calcd.) %		
					C	N	S
g*	p-ClC_6H_4	$C_{18}H_{16}N_3O_3SCl$	154-156	57	55.43 (55.45)	10.77 (10.78)	08.20 (08.21)
3a*	C_6H_5	$C_{25}H_{21}N_3O_4S$	216-218	73	65.36 (65.35)	09.18 (09.15)	06.95 (06.97)
b	o-ClC_6H_4	$C_{25}H_{20}N_3O_4SCl$	218-220	75	60.78 (60.79)	08.52 (0.8.51)	06.50 (06.48)
c*	p-ClC_6H_4	$C_{25}H_{20}N_3O_4SCl$	216-218	72	60.80 (60.79)	08.50 (08.51)	06.53 (06.48).
d*	o-$OCH_3C_6H_4$	$C_{26}H_{23}N_3O_5S$	210-212	70	63.81 (63.80)	08.56 (08.58)	06.56 (06.54)
e*	p-$OCH_3C_6H_4$	$C_{26}H_{23}N_3O_5S$	211-213	71	63.79 (63.80)	08.57 (08.58)	06.55 (06.54)
f*	o-$CH_3C_6H_4$	$C_{26}H_{23}N_3O_4S$	216-217	71	65.98 (65.96)	08.8 (08.87)	06.78 (06.76)
g*	p-$CH_3C_6H_4$	$C_{26}H_{23}N_3O_4S$	213-214	73	65.95 (65.96)	08.85 (08.87)	06.75 (06.76)

Table 2: Characterization data of 1-(N-Phenylsulphonyl)-3-(2^1-substituted-3^1-sulphonyl)-5^1-methoxy-indol-3^1-yl)-2-pyrazolines (4 a-g)

Compound No.	Ar	Molecular formula	M.P. (^0C)	Yield (%)	Found (Calcd.) %		
					C	N	S
4a*	p-ClC_6H_4	$C_{24}H_{20}N_3O_5S_2Cl$	196-198	60	54.40 (54.39)	54.40 (54.39)	12.10 (12.08)
b	o-ClC_6H_4	$C_{24}H_{20}N_3O_5S_2Cl$	205-207	61	54.42 (54.39)	07.94 (07.93)	12.09 (12.08)
c*	o-$OCH_3C_6H_4$	$C_{25}H_{23}N_3O_6S_2$	194-196	58	57.12 (57.14)	08.02 (08.00)	12.20 (12.19)
d	p-$OCH_3C_6H_4$	$C_{25}H_{23}N_3O_6S_2$	197-199	57	57.13 (57.14)	08.01 (08.00)	12.19 (12.18)
e*	o-$CH_3C_6H_4$	$C_{25}H_{23}N_3O_5S_2$	203-205	59	58.91 (58.93)	08.26 (08.25)	12.55 (12.57)
f	p-$CH_3C_6H_4$	$C_{25}H_{23}N_3O_5S_2$	200-201	60	58.90 (58.93)	08.24 (08.25)	12.58 (12.57)
g*	C_6H_5	$C_{24}H_{21}N_3O_5S_2$	190-192	58	58.20 (58.18)	08.49 (08.48)	12.90 (12.92)

Table 3: Antifungal activity 1-[N-benzoyl-3-(2^1-substituted-3^1-sulphonyl-5^1-methoxy-indol-3^1-yl)-2-pyrazolines (3a-g) and 1-(N-phenylsulphonyl)-3-(2^1-substituted-3^1-sulphonyl)-5^1-methoxy-indol-3^1-yl)-2-pyazolines (4 a-g)

Compound No.	Average % inhibition against					
	Phytophthora infestans at			*Collectotricum fulcatum* at		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
3a	94	78	38	93	56	36
b	99	73	53	99	70	51
c	98	69	49	98	67	48
d	96	62	42	95	60	40
e	95	61	43	94	60	38
f	93	59	39	92	58	37
g	92	56	32	90	55	31
4a	96	60	40	95	58	39
b	99	72	54	99	70	51
c	98	68	49	98	67	48
d	95	60	40	95	58	37
E	92	56	38	92	54	37
f	91	52	32	90	50	31
g	90	50	30	90	49	30
Dithane M-45	100	82	67	100	80	65

RESULTS AND DISCUSSION

The new pyrazoline derivatives **(3a-g)** and **(4a-g)** were prepared from methoxyindole (1). Compound **(1a-g)** reacts with triethyl amine in dry tetrahydrofuran and treated with diazomethane to form 3-(2^1-substituted-3-sulphonyl-5^1-methoxyindol-3^1-yl)-2-pyrazolines **(2a-g)**. Compound **(2a-g)** reacts with benzoyl chloride, potassium hydroxide and methanol to give 1-[N-benzoyl-3-(2^1-substituted-3^1-sulphonyl-5^1-methoxyindol-3^1-yld-2-pyrazolines **(3a-g)** and again reacts with benzenesulphonyl chloride in pyridine and neutralize with dilute HCl to formed 1-(N-phenylsulphonyl)-3-(2^1-substituted-3^1-sulphonyl)-5^1-methoxy-indl-3^1-yl)-2-pyrozalines **(4a-g)**. The structures of the compounds were conformed by their melting points, elemental analysis, IR spectra and position in ^{1}H NMR spectra.

CONCLUSION

It is appeared from screening results the most of the compounds **(3a-g)** and **(4a-g)** significantly inhibited the mycelia growth of both test fungi at 1000 ppm but their activity decreased considerably at lower concentration (100 and 10 ppm). The compounds **3b**, **3c**, **4b**, **4e** had similar activity at 1000 ppm and showed 54-48% growth inhibition of both test fungi at 10 ppm concentration. Significant alteration of the fungicidal activity was observed with the change in the relative position of the substituent on sulphonyl pyrazolines with methoxyindole ring e.g. compounds **3b** and **4b** bearing 2-chloro groups were more active than **3d** and **4d** 2-methoxy groups. Likewise, introduction of chloro group was for more effective than that at methoxy group.

ACKNOWLEDGEMENT

The authors are thankful to the Head, Department of Chemistry, Rashtriya Post Graduate College, Jamuhai, Jaunpur (U.P.) and Head, Department of Chemistry, T. D. Post Graduate College, Jaunpur (U.P.), for providing necessary laboratory facilities. Also thanks to the Director, CDRI, Lucknow for providing elemental, spectral and biological activity data and to the Director, IARI, New Delhi for the testing of antifungal activity.

REFERENCES

1. M. Amir, N. Dhar and S. K. Tiwari, Indian J. Chem., **36B**, 96 (1997).
2. M. Verma, M. Tripathi, A. K. Saxena and K. Shanker, Eur. J. Med. Chem., **29**, 941 (1994).
3. O. H. Hismat, M. Y. Ebeid, S. S. Nakkady, M. M. Fathy and S. S. Mahmoud, Boll. Chim. Farm., **138**, 258 (1999).
4. M. M. F. Ismail, N. A. M. M. Shmeisis, H. I. El-Diwani and M. S. Arbid, Indian J. Chem., **36B**, 288 (1997).
5. M. Ebeid, Y. Mohamed, S. M. Lashine, S. M. El-Adl and M. E. Abou Kull, Zagazig J. Pharm. Sci., **3**, 40 (1994).
6. A. C. Bajji, K. P. Channabasavaraj and K. M. K. Swamy, Indian Drugs, **31**, 269-272 (1994).
7. B. Trivedi and V. H. Shah, J. Indian Chem. Soc., **70**, 645 (1993).
8. J. G. Horsfall, Bot. Rev., **11**, 357 (1945).
9. V. J. Ram and H. N. Pandey, Agric Biol. Chem., **37**, 2191 (1993).
10. Y. Yasuda and U. Uchiyama, Japan Kokai, **7**, 020, 355 (1974); Chem. Abstr., **81**, 73399 (1974).
11. J. C. Debaurage, D. Pillon and S. Trinh, Ger. Offen., **3**, 361, 613(1974); Chem. Abstr., **81**, 91537 (1974).
12. Y. Okada, Japanese Pat., **7**, 024, 982 (1970); Chem. Abstr., **73**, 98953 (1970).
13. F. Suzuki, K. I. Kawa, F. Matahasi and S. Hayashi, Japanese Pat., **007**, 7602 (1976); Chem. Abstr., **86**, 55451 (1977).