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SYNTHESIS, BIOLOGICAL AND PHARMACOLOGICALSTUDIES OF SOME SUBSTITUTED PYRAZOLINES DERIVED FROM ARYLOXY ACETYL HYDRAZINES

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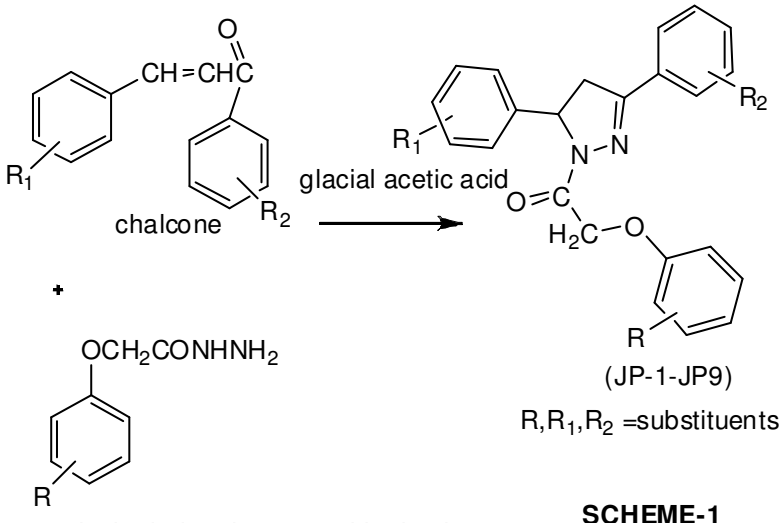
A series of some novel pyrazoline derivatives were synthesized and evaluated for biological and pharmacological activities. The structures of newly synthesized compounds were confirmed by the spectral analysis. The purity of the synthesized compounds were checked by their melting points. Further all the synthesized compounds were evaluated for antifungal, antibacterial and anti-inflammatory activities.

The development of new and clean synthetic routes toward focused libraries of nitrogen containing heterocyclic compound is of great importance to both medicinal and synthetic chemists. Consequently, the design and development of procedures for the generation of new heterocyclic compounds by means of multi steps reactions is a matter of growing interest. Pyrazole, pyrazoline, and pyrazolidine are important heterocyclic that are attracting increasing interest of many researchers, because of their antibacterial[1], antifungal[2], antiviral[3], antiparasitic[4], antitubercular[4], insecticidal[5] and anti-inflammatory[6] properties.

Antibacterial and Antifungal Activity

The microorganisms *B.subtilis, S.aureus, E.coli,P.aeruginosa* were used to study the antibacterial activity of synthesized compounds whereas antifungal activity of synthesized compounds was studied against *Candida albicans*. Ampicillin and



SCHEME-1

Table-1
Physical data of synthesized compounds

Comd	R	R_1	R_2	Physical nature	M.P. (°C)	Yield (%)
JP1	2-Cl	4-Cl	4-OH	White amorphous	239-241	65
JP2	2-Cl	3-NO_2	4- OH	Yellow crystals	198-200	73
JP3	2-Cl	4-Cl	2 -OH	Yellow amorphous	188-190	69
JP4	2-NO_2	4-Cl	2-OH	Brown crystals	138-140	55
JP5	4-NO_2	4-OCH_3	2-OH	White crystals	157-160	62
JP6	4-NH_2	4-Cl	2 -OH	Violet crystals	117-119	59
JP7	4-NO_2	4-Cl	2-OH	Brown crystals	110-111	78
JP8	4-H	4-Cl	2-OH	White crystals	170-172	71
JP9	4-H	3-NO_2	4-OH	White crystals	127-129	73

Griseofulvin were taken as standard drug for the comparison of the activity of the synthesized compounds for antibacterial and anti-fungal activity respectively.

Most of the compounds showed promising anti-bacterial activity, compounds specially JP2, JP6, JP7, & JP9 showed very good activity whereas JP4, JP8 showed moderate activity.

Anti-fungal activity data revealed that the most of the compounds were active towards *Candida albicans*. Compounds JP3, JP4 & JP5 showed very good activity

Anti-Inflammatory Activity

All the synthesized compounds were screened by Carrageenin induced rat paw edema model (acute-inflammatory model) for the screening of anti-inflammatory activity. Diclofenac was taken as standard drug.Compounds JP1, JP4 and JP6 showed very good anti-inflammatory activity whereas JP2and JP9 showed moderate anti-inflammatory activity

Experimental

Melting points of newly synthesized compounds were determined by open capillary method and are uncorrected. All the synthesized compounds were purified by TLC method and characterised by IR, ^{1}H NMR and mass spectral method.IR spectra were recorded in Shimadzu spectrophotometer in KBr pallets ^{1}H NMR spectra were recorded in (DMSO) on a Avance 300MHz spectrophotometer using TMS as an internal standard .The mass spectra were recorded using LC-MS (SHIMADZU 2010-AT) under electro spray ionisation (ESI)technique.

Synthesis of Pyrazolines

A solution of chalcone (0.01mol) and the appropriate aryloxy acetyl hydrazine (0.02mol) in 20ml of glacial acetic acid was refluxed for 10 hours and cooled. Excess of solvent was removed under reduced pressure and the reaction mixture was poured into 250ml ice cold water. The product was filtered, washed with cold water and recrystallized from ethanol.

Table-2
Antimicrobial activity effect of substituted Pyrazolines

Compd	Diameter of zone of inhibition (mm)					
	S.aureus	*B.subtitis*	*E.coli*	*P.aeruginosa*	*C.albicans*	*A.niger*
JP1	12	20	15	16	9	10
JP2	9	7	18	10	-	-
JP3	16	20	24	15	10	12
JP4	24	21	18	20	25	16
JP5	13	10	15	10	-	-
JP6	18	16	-	-	13	14
JP7	15	22	14	10	9	9
JP8	14	10	17	12	5	4
JP9	20	19	15	13	10	11
Ampicillin	15	14	22	10	-	-
Griseofulvin	-	-	-	-	16	17

4-[1-(2-chlorophenoxy) acetyl]-3-(4-chlorophenyl) 4,5-dihydro-1*H*-pyrazol-5yl) phenol (JP-1)

IR : 3356 (OH str)1632(C=O str),3092 (N–N str), 1598 (C=N str) ,730 (C –Cl str), ^{1}H NMR :9.15 (s, 1H of OH), 7.66 to 6.67(m,12H of phenyl),5.48 (dd, 1H$_c$ of pyrazoline),4.72 (s, 2H of CH_2) ,3.66 (dd, 1H$_a$ of pyrazoline) ,3.09 (dd, 1H$_b$ of pyrazoline), Mass; M+1 peak at *m/z* 442.

2-[1-[(2-chlorophenoxy) acetyl]-3-(4-chlorophenyl) 4,5-dihydro-1*H*-pyrazol-5 yl) phenol (JP-3)

IR : 3352 (OH str) ,1630 (C=O str) ,3092 (N–N str), 1598 (C=N str) ,776 (C –Cl str). ^{1}H NMR :6.57 (s, 1H of OH),7.66 to 6.81(m,12H of phenyl), 5.74 (dd, 1H$_c$ of pyrazoline) ,4.77 (s, 2H of CH_2) ,3.65 (dd, 1H$_a$ of pyrazoline) ,3.09 (dd, 1H$_b$ of pyrazoline), Mass; M+1 peak at *m/z*442.

2-[1-[(3-Aminophenoxy)acetyl]-3-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-5 yl] phenol (JP-6)

IR : 3676 (OH str) ,1650 (C=O str), 3131 (N–N str), 1492 (C=N str), 764 (C–Cl str), 3058 (N–H stretching), ^{1}H NMR :6.57 (s, 1H of OH), 7.66to6.30(m,12H of phenyl),5.75 (dd, , 1H$_c$ of pyrazoline) ,5.12 (s, 2H of NH_2) ,4.62 (s, 2H of CH_2), 3.65 (dd, 1H$_a$ of pyrozoline) ,3.09 (dd, 1H$_b$ of pyrazoline), Mass; M+1 peak at *m/z*422.

4-[3-(3-nitrophenyl)-1-(phenoxyacetyl)-4,5-dihydro-1*H*-pyrazol-5-yl]phenol (JP-9)

IR : 3463 (OH str)1702 (C=O str) 3086 (N–N str) 1572 (C=N str in ring) 1501 and 1346 (ArN=O str), ^{1}H NMR:9.15 (s, 1H of OH) ,8.61 to 6.67 (m,12H of phenyl) ,5.52 (dd, 1H$_c$ of pyrazoline) ,4.66(s, 2H of CH_2), 3.76 (dd, 1H$_a$ of pyrazoline) ,3.19 (dd, 1H$_b$of pyrazoline), Mass; M+1 peak at *m/z*418.

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References

1. F.Bharmal, F, D.Kaneriya and H Parekh, *Indian J. Heterocyclic Chem.,* **12** (2002), 21.
2. M.Singhal and B.Verma, *Indian J. Heterocyclic Chem.,* **14** (2005), 343.

Table-3
Anti-inflammatory effect of substituted Pyrazolines

Treatment	Dose mg/kg	Increase in paw volume (in ml) 1h	2h	3h	4h
Control	_	0.36±0.06	0.68±0.05	0.77±0.03	0.81±0.03
Diclofenac Sodium.	10	0.18±0.03*(50)	0.35±0.05*(48.52)	0.41±0.04*(46.75)	0.45±0.05*(43.20)
JP1	50	0.20±0.04*(44.44)	00.37±0.03*(45.58)	0.42±0.03*(45.45)	0.46±0.03*(43.20)
JP2	50	0.23±0.04(36.11)	0.41±0.04*(39.70)	0.47±0.04*(38.96)	0.52±0.04*(35.80)
JP3	50	0.24±0.03*(33.33)	0.42±0.02*(38.23)	0.46±0.03*(40.25)	0.52±0.03*(35.80)
JP4	50	0.19±0.04*(47.22)	0.37±0.03*(45.58)	0.42±0.03*(45.45)	0.46±0.04*(43.20)
JP5	50	0.19±0.04*(47.22)	0.36±0.03*(47.11)	0.41±0.03*(46.75)	0.48±0.02*(40.74)
JP6	50	0.20±0.03*(44.44)	0.37±0.03*(45.58)	0.42±0.03*(45.45)	0.46±0.03*(43.20)
JP7	50	0.19±0.04*(47.22)	0.36±0.03*(47.05)	0.41±0.03*(46.75)	0.48±0.03*(40.74)
JP8	50	0.16±0.04*(17.77)	0.43±0.03*(36.76)	0.50±0.04*(35.06)	0.56±0.03*(30.86)
JP9	50	0.23±0.03*(36.11)	0.40±0.03*(41.17)	0.47±0.03*(38.96)	0.51±0.04*(37.03)

All values are expressed as

Mean ± SEM (n= 6).*P<0.05 significant compared to control.

3. J.Desai K and V.Nair , *Indian J. Heterocyclic Chem.,* **10** (2001), 261.

4. D.Azarifar and S Maseud, *Molecules,* **7** (2001), 885.

5. O.Bruno, C.Brullo, S Schenone, F.Bondavalli, *Bioorg. Med. Chem.,* **14(1)** (2006), 121.

6. S.Kolhe, A.Doshi and A.Raut, *Indian J. Heterocyclic Chem.,* **12** (2002), 281.

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