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Evaluation of Anti-Inflammatory and Analgesic Activity of Novel Pyrazole Derivatives

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Abstract

A new series of novel derivatives of pyrazole were synthesized. These derivatives were identified on the basis of melting point range, Rf values, IR and 1H NMR spectral analysis. The derivatives were screened for anti-inflammatory and analgesic activities. The derivatives exhibited significant to moderate anti-inflammatory and analgesic activities.

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INTRODUCTION

Nitrogen containing heterocyclic compounds are synthetically the challenging models for a number of therapeutically significant products. Azoles occupy a domain of interest in natural and synthetic chemistry. Diazoles are the central building blocks for synthesizing compound libraries in pharmaceutical and agrochemical industries. One such class of compounds includes Pyrazole. Pyrazole refers to the simple doubly unsaturated compound containing two nitrogen (in neighbouring position) and three carbon atoms in the ring. The pyrazole nucleus is common in a number of biologically active molecules exhibiting antibacterial [1-2], antitubercular [3], anti depressant [4], anti-inflammatory [5-6], analgesic [7], anticancer [8-9], antioxidant [10-11] etc. activities. Research in this area is still unexplored, therefore the present study is directed towards the synthesis of novel derivatives of pyrazole with good yield and enhance anti-inflammatory and analgesic activities.

MATERIALS AND METHODS

All the chemicals procured from CHEMCO Labs, NICE chemicals. The melting points were determined in open glass capillaries and were uncorrected. Thin Layer Chromatography using silica gel G (E. Merck) plates were used to access the reaction and purity of synthesized compounds. The IR spectra were recorded on Shimadzu FTIR system in KBr pellets and noted the absorption levels (cm-1) were listed. 1H NMR spectra were run on Bruker DPX 400 FTNMR in DMSO-d6 as solvent and TMS as an internal standard. The Mass spectra were recorded on JEOL JMS600H mass spectrometer.

Step1: Synthesis of Ethyl-4-chlorobenzoate

P-chloro benzoic acid (30g) in ethanol was added with 150ml conc. sulphuric acid at 0.5 0C over a period of 30 min and refluxed for 2 hrs on a water bath. The reaction mixture was poured in to ice-cold water. The solid thus obtained was filtered, washed and dried. The dried product was recrystallised from ethanol to white needle shaped crystals.Yield:95.5% w/w.

Step2: Synthesis of 4-chloro benzohydrazide

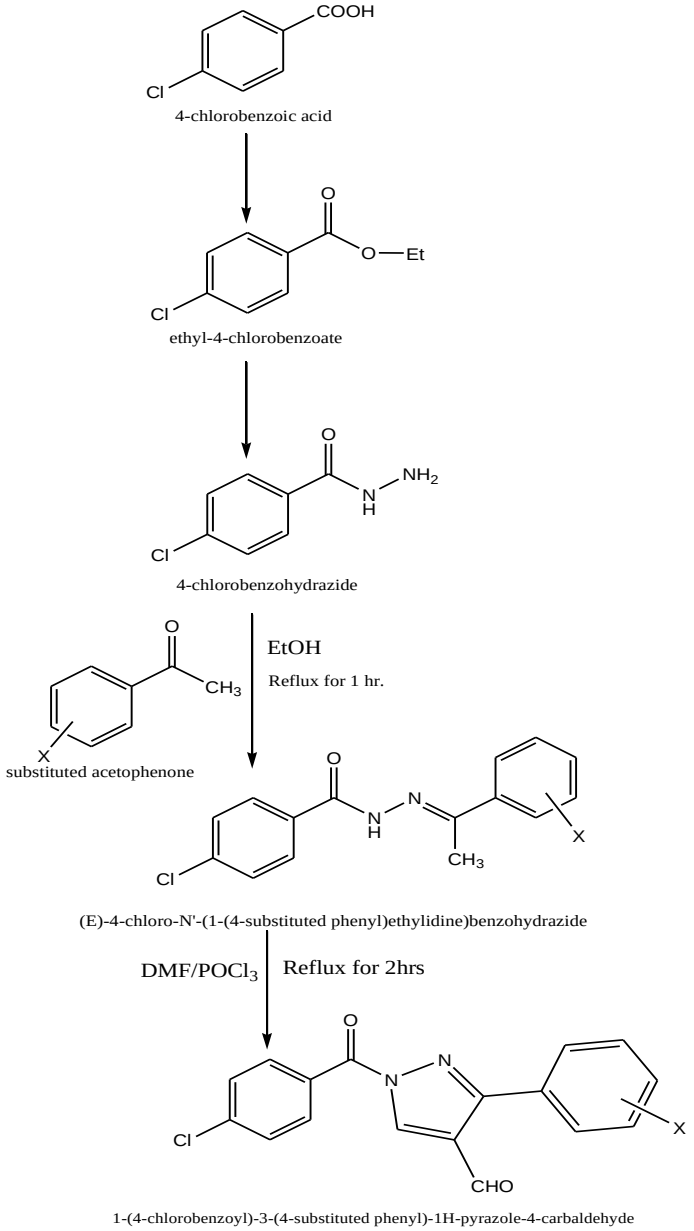
The mixture of 0.167 mol (29g) of substituted esters and 0.167 mol(5g)of hydrazine was warmed with 60ml of ethanol and few drops of glacial acetic acid. The reaction mixture was cooled and filtered. The solid thus obtained was washed with dil. HCl followed by about 12ml of cold rectified spirit. The dried product was recrystallised from ethanol to white needle shaped crystals of pure 4-chloro benzohydrazide.Yield:93% w/w.

Step3: Synthesis of (E)-4-chloro-N'-(1-(4-substituted phenyl)ethylidene) benzohydrazide

0.01mol of substituted acetophenone was added to the mixture containing 0.01mol of 4-chlorobenzohydrazide in 30ml of ethanol and few drops of glacial acetic acid. The reaction mixture was refluxed for 1 hr and then cooled in ice-bath. The product separated on cooling was filtered, dried and recrystallised from ethanol to white needle like crystals. (PZ1-PZ5)

Step 4 : Synthesis of 1-(4-chlorobenzoyl)-3-(4 substituted phenyl)-1H-pyrazole-4-carbaldehyde

Cyclisation: The substituted hydrazone (0.005mol) was added in to the mixture of Vilsmeier-Haack (DMF&POCl3) reagent, prepared by drop wise addition of phosphorous oxy chloride 140ml (0.015mol) to an ice-cold solution of N,N-dimethyl formamide 20ml.The reaction mixture was refluxed for 2 hrs, then poured in to ice-cold water and neutralized using an excess of sodium bicarbonate solution. The product was washed with water and recrystallised from ethanol. (PZ1-PZ5).



X=p-methoxy,p-methyl,p-chloro,p-fluoro,p-bromo

Anti- inflammatory activity [12]

Carrageenan induced rat paw oedema method

The anti-inflammatory activity of the standard drug Acetaminophen and synthesized derivatives was determined against carrageenan induced paw oedema in albino rats (weighing 150-175g). The albino rats were divided into 4 groups containing 1 animal each. The animals were fasted for 12 hrs prior to the experiment. The 1% w/v solution of carrageenan for injection is prepared in normal saline and 0.1 ml is injected under subplanter region. The standard drug (200mg/Kg) and synthesized derivative (PZ3) (100mg/Kg, 200mg/Kg) was administered in animals by oral route. Volume of the injected paw after 3hr was measured with a plethysmometer. The differences in the paw volumes (i.e. oedema volumes) of each animal were calculated and compared with the changes in the oedema volumes of control and the drug treated animals. The results were expressed as percentage reduction in oedema volume, which can be calculated by using the formula:

Percent Reduction = (Cvt – Tvt)/ Cvt × 100

Where,

Cvt = oedema volume of control animals at time,'t'

Tvt = oedema volume of drug treated animals at time,'t'

Analgesic activity [13]

Eddy's hot plate method

Male albino mice were selected and divided into four groups, containing one animal in each group. These animals were fasted for twenty four hours, prior to the experiment. Animal of Group – I considered as Control, was administered with 1% Acacia suspension. Animal of Group – II was treated with standard drug, i.e., Aspirin (100 mg/kg), which is considered as standard group. Animals of Group – III and IV were treated with different concentration of test derivative (PZ3) (150, 75 mg/kg) respectively. The reaction time for each mouse was recorded at time interval of 30, 60 and 90 min after the administration of test substances by using Eddy's hot plate method.

The % analgesic activity (PAA) was calculated by the following formula

PAA = (T-C)/C × 100

C is the reaction time of the control and T is the reaction time of the test compound.

RESULTS AND DISCUSSION

The melting points of all synthesized derivatives were found in open capillary tubes and readings were uncorrected. The structures of the synthesized derivatives were supported by physical data (Table 1) and following spectral analysis

Compound Code	R	MW (D)	M.P (^{0}C)	Rf	Solvent system
PZ1	4-OCH3	342.783	201-203^{0}C	0.67	Chloroform:Methanol (9:1)
PZ2	4-CH3	326.784	210-212^{0}C	0.72	Chloroform:Methanol (9:1)
PZ3	4-Cl	347.202	192-194^{0}C	0.60	Chloroform:Methanol (9:1)
PZ4	4-F	330.747	205-208^{0}C	0.79	Chloroform:Methanol (9:1)
PZ5	4-Br	391.653	189-192^{0}C	0.64	Chloroform:Methanol (9:1)

Table1: Physical data of the derivatives

Only three derivatives i.e. PZ1, PZ2 and PZ3 were taken for spectral studies. The results showed the presence of derivatives which were predicted in the synthetic scheme.

1-(4-chlorobenzoyl)-3-(4-methoxy phenyl)-1H-pyrazole-4-carbaldehyde (PZ1)

IR (υ cm-1): 3093(C-H, Ar-H),1087(C-Cl),1415(C=C),1712(C=O),1288(C-N)1174 (NN=C), 2665(C-H,aliphatic),808(C-C)1236(C-O-C),1HNMR(DMSO-d6)δ:9.879(1H,S,-CHO),6.87(1H, S, -CH),3.34(3H,S,-OCH3),7.5-7.9(8H,M,-Ar), LC-MS: m/z 342.727(M+).

1-(4-chlorobenzoyl)-3-(4-methylphenyl)-1H-pyrazole-4-carbaldehyde (PZ2)

IR (υ cm-1): 3068(C-H, Ar-H), 1091(C-Cl),1425(C=C),1699(C=O),1282(C-N)1176(NN= C), 2954(C-H,aliphatic),819(C-C),1HNMR(DMSO-d6)δ:8.975(1H,S,-CHO),6.79(1H,S,-CH),2.50 (3H,S,-CH3),7.5-7.9(8H,M,-Ar), LC-MS: m/z 326.516 (M+).

1-(4-chlorobenzoyl)-3-(4-chlorophenyl)-1H-pyrazole-4-carbaldehyde (PZ3)

IR (υ cm-1): 3051(C-H, Ar-H)1091(C-Cl),1490(C=C),1668(C=O),1294(C-N)1128(NN= C), 2980(C-H,aliphatic),852(C-C),1HNMR(DMSO-d6)δ:9.824(1H,S,-CHO),7.3-7.7(8H,M,-Ar), 6.176(1H,S,-CH), LC-MS: m/z 347.202(M+).

Carrageenan induced rat paw edema method in Swiss albino rats was used for screening anti-inflammatory activity of derivatives. The derivative PZ3 was selected for anti-inflammatory activity at 100 and 200 mg/kg body weight. Acetaminophen was used as the standard drug at a dose 200 mg/kg. The control group was given 0.1% CMC. The results obtained were shown in Table 2 and Figure 1. The test derivative PZ3 showed significant anti-inflammatory activity

Group	Dose	Difference In Paw Volume After 3hr.	% Inhibition
Control	_	0.078	_
Test1(PZ3)	100mg/kg	0.038	51.28%
Test 2(PZ3)	200mg/kg	0.024	69.23%
Standard(acetaminophen)	200mg/kg	0.018	76.92%

Table 2: Anti-inflammatory activity screening of derivative PZ3

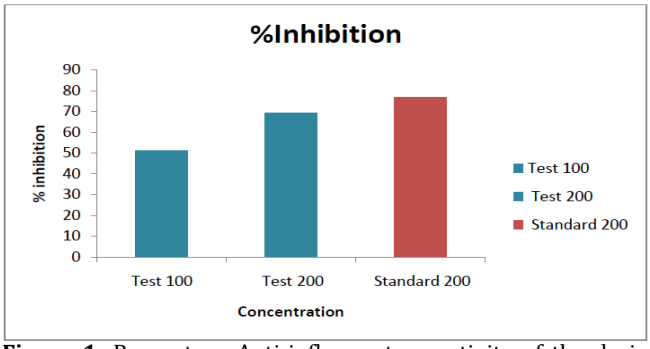


Figure 1: Percentage Anti-inflammatory activity of the derivative PZ3

Analgesic activity of the derivative PZ3 was determined using Eddy's hot plate at a dose of 150, 75mg/kg. The standard drug aspirin was used at a dose of about 100mg/kg. The results observed for analgesic activity is given in Table 3 and Figure 2.

Compound	Dose	Reaction Time(in sec.) after 90 minutes	%Analgesic activity
Control		7.34	-
Test(PZ3)	75	10.86	47.95%
	150	12.32	67.84%
Standard(Aspirin)	200	13.53	84.33%

Table 3: Analgesic activity screening of derivative PZ3

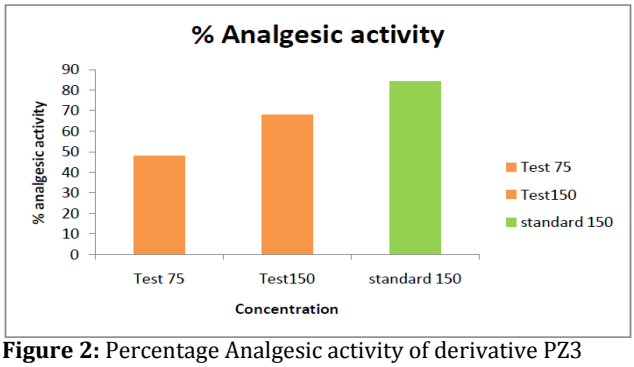


Figure 2: Percentage Analgesic activity of derivative PZ3

CONCLUSION

The research work was oriented towards the finding of novel derivatives of pyrazole with enhance anti-inflammatory and analgesic activities. The different derivatives were synthesized. The synthesized derivatives showed very good anti-inflammatory and analgesic activities against previously reported derivatives of pyrazole.

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REFERENCES

1.Sachchar SP, Singh AK, Synthesis and antibacterial activity of some novel pyrazole derivatives, Int. J. Comp. Socio., 1985; 12(3): 142-146.
2.Nada MA, Hamdi MH, Ahmed SM, Omar AM, Synthesis and antimicrobial evaluation of some new pyrazole, pyrazoline and chromeno [3,4-c] pyrazole derivatives, J. Bio.Chem., 2009; 20: 975-987.
3.Pattan SR, Synthesis and evaluation of some novel substituted 1,3,4-oxadiazole and pyrazole derivatives for antitubercular activity, Ind. J. Chem, 2009; 48(3): 1453-1456.
4.Mathew B, Suresh J, Anbazhagan S. Development of novel (1-H) benzimidazole bearing pyrimidine-torsine based MAO-A inhibitors: Synthesis, docking studies and anti depressant activity, J. Amer. Chem. Soc., 2012; 2(3): 1-8.
5.Kumar AS, Ilango K, Manikandan RS, Ramalakshmi N, Synthesis and anti-inflammatory activity of some novel pyrazole derivatives of gallic acid, Eur. J. Chem., 2009; 6(3): 123-128.
6.Sahu SK, Banerjee M, Samantray A, Behera C, Azam MA, Synthesis, analgesic, anti-inflammatory and antimicrobial activities of some novel pyrazoline derivatives, Trop. J. Pharm. Res., 2008; 7(4): 961-968.
7.Panneer ST, Saravanan G, Prakash CP, Kumar PD, Microwave assisted synthesis, characterisation and biological activity of novel pyrazole derivatives, Afri. J. Chem., 2011; 1(2): 126-129.
8.Mohareb RM, El-Sayed NN, Adbelaziz MA, Uses of cyanoacetyl hydrazine heterocyclic synthesis: Novel synthesis of pyrazole derivatives with antitumour activity, Molecules, 2012; 17(2): 8449-8463.
9.El-Sayed WA, Flefel EM, Morsy MH, Anticancer and antimicrobial activities of some synthesized pyrazole and triazole derivatives, Der. Pharm. Chem,2012; 4(3): 23-32.
10.Bole SB, Nargund LV, Nargund R, Devaraju KS, Vedamurthy AB, Synthesis of substituted fluoro pyrazoles for antibacterial and anti-oxidant activity, Int. J. Pharm. Pharma. Sci., 2011; 3(3): 161-166.
11.Tarun S, Mithilesh, Raju S, Pooja C, Saraf, SK, Syntheses and antioxidant screening of pyrazole-4-carboxaldehyde derivatives, Int. J. Res. Pharm. Sci., 2012; 2(3): 81-96.
12.Ghosh MN, Fundamentals of experimental pharmacology, New Delhi: Hilton & Company; 2003.
13.Kulkarni, S. K., Hand book of experimental pharmacology. New Delhi: Vallabh Prakashan; 1999.