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Pyrazole carbaldehydes as novel anti-inflammatory agents : Synthesis and *in vitro* membrane stabilization method

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Abstract

Pyrazole is a nitrogen containing 5-membered heterocyclic compound containing 3 carbons& 2 nitrogen atoms in the adjacent position of ring structure and is chemically known as 1, 2- diazole. Pyrazole nucleus is present in many pharmaceutically important compounds and intermediates . Majority of anti-inflammatory agents currently employed have GI irritation and enhanced acidity as side effects. As part of our efforts to develop newer and effective anti-inflammatory agents , ten newer pyrazole carbaldehydes were synthesized and evaluated for their anti-inflammatory activity using Diclofenac was the standard. Out of ten compounds synthesized, all compounds exhibited comparable activity with that of the standard.Highest percentage of haemolysis was observed for Pyrazole carbaldehydes with methoxy phenyl groups as substituents. These compounds should be considered for developing as leads for newer & safer anti-inflammatory agents.

Keywords: Pyrazole, anti inflammatory activity, membrane stabilization method,,haemolysis

INTRODUCTION

There are a number of heterocycles which have turned out to be potential chemotherapeutic and pharmacotherapeutic agents. Majority of heterocyclic compounds, which are in thetherapeutic field, contains nitrogen as the hetero atom.[1]Pyrazoleis one of the most important nitrogen containing 5-membered heterocyclic compound containing 3 carbons& 2 nitrogen atoms in the adjacent position of ring structure and is chemically known as 1, 2-diazole.[2].Pyrazole refers to the simple doubly unsaturated heterocyclic compound containing two nitrogen (in neighbouring position, among the two nitrogen atoms; one is basic and the other is neutral in nature) and three carbon atoms in the ring and the name was given by "Ludwing Knorr in 1883.[3] Numerous pyrazole derivatives have been found to possess wide spectrum of biological activities, which stimulated intense research in this field [4].Pyrazole and its derivatives represent one of the most active classes of compounds, which possess wide range of activities like anti-bacterial,[5] antioxidant,[6,]anti depressant, anti-convulsant,[7],analgesic,[8,]anticancer,[9],antifungal,[10],antiinfla mmatory[11],hypoglycaemic[12],antimalarial, [13] antiviral [14] activities to name a few.

Numerous pharmacological applications of pyrazoles have been attracting a great deal of interest in the field of medicinal chemistry. Therefore the chemistry of pyrazole is considered to be one of the most dynamic and challenging area of pharmaceutical chemistry, embracing a wide spectrum of advances in both theoretical and practical relevance. Pyrazolenuclei have been long focused for research interest in the field of medicine, due to excellent activities exhibited by its derivatives.[15].

Inflammation is part of the complex biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants, and is a protective response involving immune cells,, blood vessels and molecular mediators.[16].Inflammation usually occurs when infectious microorganisms such as bacteria, viruses or fungi invade the body, reside in particular tissues and/or circulate in the blood .Inflammation may also happen in response to processes such as tissue injury, cell death, cancer, ischemia and degeneration .[17] .Diverse classes of anti inflammatory drugs are made available by the pioneering work of drug discovery groups,[18] but all the currently marketed anti-inflammatory drugs suffer from several disadvantages , most common being GI irritation and enhanced acidity.[19].This has necessitated the need to develop newer anti-inflammatory agents.

The diverse biological properties exhibited by the pyrazole derivatives as well the necessity of developing newer anti-inflammatory agents , prompted us to take the design and synthesis of certain novel pyrazole carbaldehydes and evaluate its therapeutic potential, as anti-inflammatory agents.Thus the present communication describes the synthesis of a series of novel pyrazole carboxyladehydes and also the subsequent evaluation of their antiinflammotory activity.

EXPERIMENTAL

All the reagents were of A.R grade and wereprocured from spectrum, S.D fine chemandAlfaaesar. The melting points were determinedin open capillary tubes and are uncorrected. IR spectrum was recorded using Avatar 370and an NMR spectrum was recorded usingBrukerAvancell with TMS as internal standard.

Mass spectra were recorded using Q-Tof mass spectrometer. TLC was performed on glassplates coated with Silica gel G. Mobile phase employed was ethyl acetate: n-hexane in theratio 8:2.

SYNTHESIS OF ETHYL BENZOATE

3.0 gm 0.246 mol of benzoic acid was added in to 50 ml of ethanol and 2.5 ml of concentrated sulphuric acid was added and refluxed for 4 hrs and poured in to ice cold water and kept overnight, next morning the product formed (yellowish oil) was purified by washing it with diethyl ether using separating funnel and ether layer collected and evaporated.The product was a colourless liquid, B.P- Yield 84% w/w.

SYNTHESIS OF BENZOHYDRAZIDE

14.4 ml of ethyl benzoate 0.1mol was added in to 30 ml of ethanol and then 4.9 ml of hydrazine hydrate added drop wise, refluxed for 8hrs.Excess of ethanol was distilled out and the content was allowed to cool. The crystal formed was filtered, ,dried and recrystallized from ethanol.M.P, 245° C. Yield 74%. Rf Value 0.55.

IR :3432(NH bending)3079,1596

^{1}H NMR :11,7 s.8.4 d

MS:136.(M+)

SYNTHESIS OF *N*'-[(1*E*)-1-(4- SUBSTITUTED PHENYL)ETHYLIDENE] BENZOHYDRAZIDE.

0.01 mol of substituted acetophenone was added to the mixture containing 0.01 mol of benzohydrazide in 30 ml of ethanol with few drops of glacial acetic acid. The reaction mixture was refluxed for 1 hr and then cooled in an ice-bath. The product separated on cooling was filtered, purified using coloumnchromatorgraphy, dried and recrystallized from ethanol to white needle like crystals.The physical data of all the synthesized compounds are presented in table no:1.

a) SYNTHESIS OF *N*'-[(1*E*)-1-(4-METHOXYPHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3448 (NH str),3079(Ar CH bending) 1701 (CH=CH bending) 1655,(C=O str) 493, 738,(OH, out of plane bending), 625 (out of planebending).

^{1}H NMR: 11.9 (s enolic NH)6.15, (OH, s) 8.3 (s,1s CH=N,azomethine group)7.05,(Aromatic,s) 7.1, (NH, s), 3.1 0 (NCH)3, s)

MS: 268.23 (M+),

ELEMENTAL ANALYSIS: Calcd C(71.62%) H(6.01%) N(10.44%) O(11.93%)

Found C(71.72%) H(6.35%) N(10.83%) O(11.66%)

b) SYNTHESIS OF *N*'-[(1*E*)-1-(3-METHOXYPHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3464 (NH str)1745 (CH=CH bending) 1655, 493, 745,OH, (out of plane bending), 654(out of plane bending),

^{1}H NMR: 11.4 (s, enolic NH) 6.25, (OH, singlet) 7.05,(m.Aromatic) 7.1, (NH, s), 3.2 0 (NCH3)3, s

MS:268.32 (M+),

ELEMENTAL ANALYSIS: CalcdC(71.62%) H(6.01%) N(10.44%) O(11.93%).

Found C(71.72%) H(6.15%) N(10.24%) O(11.67%).

c) SYNTHESIS OF *N*'-[(1*E*)-1-(2-METHOXYPHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3397(NH str) 1720 (CH=CH bending) 1655, 493, 756, (OH, out of plane bending), 595 (out of plane bending).

^{1}H NMR: 10.9(NH,s) 6.15, (OH, singlet) 7.05,(Aromatic) 7.56, (NH, s), 3.2 0 (NCH_3)3, s

MS:268.26 (M+),

ELEMENTAL ANALYSIS CalcdC(71.62%) H(6.01%) N(10.44%) O(11.93%)

Found C(72.02%) H(6.35%) N(10.21%) O(11.23%)

d)SYNTHESIS OF *N*'-[(1*E*)-1-(4-BROMO PHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3367 (NH str) 1678 (CH=CH bending) 1675, 493, , 743, (OH out of plane bending), 665 (out of plane bending).

^{1}HNMR: 11.4 (NH str) 6.35, (OH, singlet) 7.05,(Aromatic) 7.4, (NH, s), 3.4 0 (NCH)3, s

MS:316.14 (M+),

ELEMENTAL ANALYSIS CalcdC(56.80%) H(4.13%) Br(25.19%) N(8.83%) O(5.04%)

Found C(56.35%) H(4.25%) Br(25.12%) N(8.56%) O(5.28%)

e)SYNTHESIS OF *N*'-[(1*E*)-1-(2-BROMO PHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3455 (NH str)1715 (CH=CH bending) 1660, 510, , 842, (OH, out of plane bending), 625 (out of plane bending).

^{1}H NMR:11.3(sAr H)6.35, (OH, singlet) 7. 15,(Aromatic) 6.29, (NH, s), 3.7 0 (NCH)3, s

MS:316.28 (M+),

ELEMENTAL ANALYSIS CalcdC(56.80%) H(4.13%) Br(25.19%) N(8.83%) O(5.04%)

Found C(57.10%) H(4.19%) Br(25.27%) N(8.75%) O(5.16%)

f)SYNTHESIS OF *N*'-[(1*E*)-1-(4-CHLORO PHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3345 (NH str) 1690 (CH=CH bending) 1655, 491, 736, (OH,out of plane bending), 715 (out of plane bending).

^{1}H NMR:10.4 (s Ar H) 6.18, (OH, singlet) 7.05,(Aromatic) 7.1, (NH, s), 3.3 0 (NCH)3, s

MS: 272.35(M+),

ELEMENTAL ANALYSIS

CalcdC(70.91%) H(5.57%) Cl(6.75%) N(10.67%) O(6.09%)

Found C(70.81%) H(5.45%) Cl(6.24%) N(10.34%) O(6.30%)

g)SYNTHESIS OF *N*'-[(1*E*)-1-(3- CHLORO PHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR: 3445(NH str) 1690 (CH=CH bending) 1655, 493, 743, (OH, out of plane bending), 625 (out of plane bending).

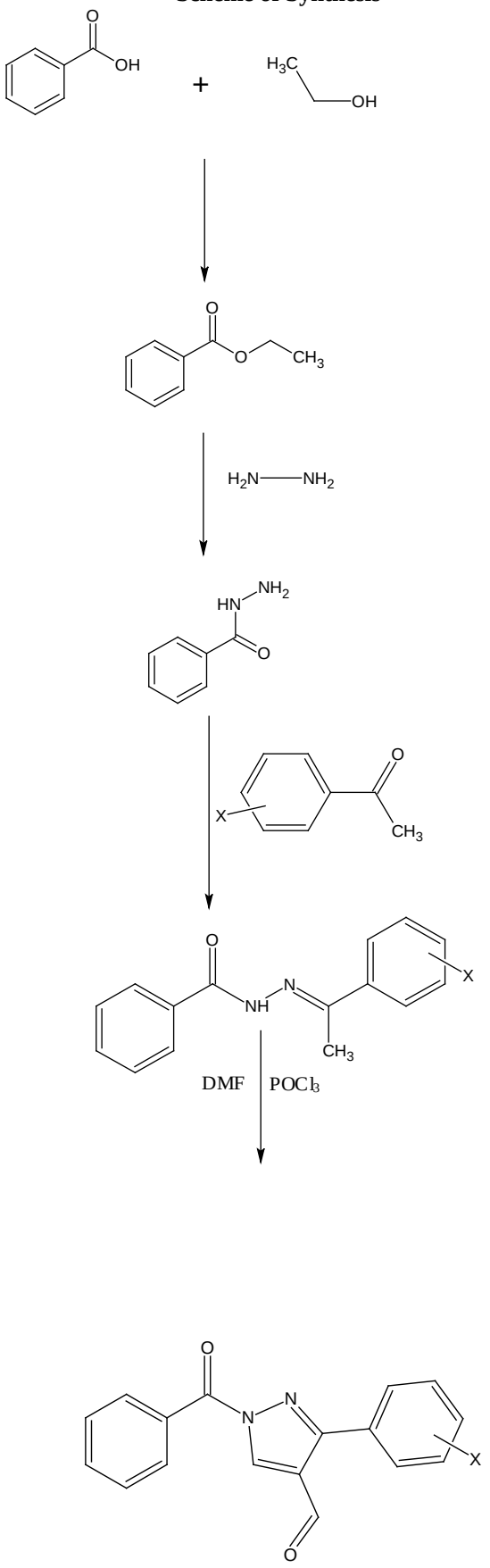
^{1}H NMR:11.4 (s Ar H), 6.25, (OH, singlet) 7.15,(Aromatic) 7.9, (NH, s), 3.1 0 (NCH)3, s

MS:242(M+),

ELEMENTAL ANALYSIS;Calcd C(70.91%) H(5.57%) Cl(6.75%) N(10.67%) O(6.09%)

Found C(71.11%) H(5.37%) Cl(6.85%) N(10.57%) O(6.23%)

Scheme of Synthesis



h)SYNTHESIS OF *N*'-[(1*E*)-1-(2-CHLORO PHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3235(NH str) 1715 (CH=CH bending) 1655, 493, 3125, 733,OH, (out of plane bending), 631 (out of plane bending).

^{1}H NMR:11.4 (s Ar H)6.15, (OH, singlet) 7.05,(Aromatic) 7.1, (NH, s), 3.6 0 (NCH)3, s

MS:272.12 (M+),

ELEMENTAL ANALYSIS CalcdC(70.91%) H(5.57%) Cl(6.75%) N(10.67%) O(6.09%)

Found C(70.61%) H(5.37%) Cl(6.79%) N(10.74%) O(6.29%)

i)SYNTHESIS OF *N*'-[(1*E*)-1-(4- IODO PHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3455 (NHstr) 1695 (CH=CH bending) 1655, 493, 3125, 733, (OH, out of plane bending), 595 (out of plane bending).

^{1}H NMR:10.8(s Ar) 6.15, (OH, singlet) 7.05,(Aromatic) 6.9, (NH, s), 3.4 0 (NCH)3, s

MS:364.17 (M+),

ELEMENTAL ANALYSIS CalcdC(49.47%) H(3.60%) I(34.85%) N(7.69%) O(4.39%).

Found C(49.37%) H(3.68%) I(34.81%) N(7.64%) O(4.56%).

j)SYNTHESIS OF *N*'-[(1*E*)-1-(2- IODO PHENYL) ETHYLIDENE] BENZOHYDRAZIDE.

IR:3355 (NHstr) 1690 (CH=CH bending) 1655, 493, 3125, 753, (OH, out of plane bending), 618 (out of plane bending).

^{1}HNMR:10.5(s Ar)6.15, (OH, singlet) 7.05,(Aromatic) 7.1, (NH, s), 3.3 0 (NCH)3, s

MS:364.09 (M+),

ELEMENTAL ANALYSIS Calcd C(49.47%) H(3.60%) I(34.85%) N(7.69%) O(4.39%)

Found C(49.42%) H(3.50%) I(34.78%) N(7.59%) O(4.32%).

SYNTHESIS OF 1-BENZOYL-3-(4-METHOXYPHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).

The substituted hydrazone (0.05mol) was added into the mixture of Vilsmeier-Haack (DMF& POCl3) reagent, prepared by drop wise addition of phosphorous oxy chloride (0.015mol) to an ice-cold solution of N,N-dimethyl formamide, 20 ml. The reaction mixture was refluxed for 2 hrs, then poured into ice-cold water and neutralized using an excess of sodium bicarbonate solution. The product was washed with water, purified using coloumn chromatography and recrystallized from ethanol. The physical data of all the synthesized compounds are presented in table no:2.

a)SYNTHESIS OF 1-BENZOYL-3-(4-METHOXYPHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).

IR:3072 (Ar CH str,)2930,(aliphatic CH str),1667(C=Ostr),1591,1498,1443,(phenyl &pyrazole rings (C=C,C=N,)
^{1}H NMR: 3.18 (dd,1H),3.58(3H,d)2,65 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS:306.31 (M+)
ELEMENTAL ANALYSIS:Calcd C(70.58%) H(4.61%) I(34.85%) N(9.15%) O(15.67%)

Found C(70.61%) H(4.57%) I(34.78%) N(9.32%) O(15.75%).

b)**SYNTHESIS OF 1-BENZOYL-3-(3-METHOXYPHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR:3122 Ar CH str,2989,(aliphatic CH str,)1672(C=Ostr),1591,1498,1353,(phenyl & pyrazole rings (C=C,C=N,)
^{1}HNMR:3.21 (dd,1H),3.68(3H,d)2,45 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS:306.31(M+)
ELEMENTAL ANALYSIS:Calcd C(70.58%) H(4.61%) I(34.85%) N(9.15%) O(15.67%)

Found C(70.35 %) H(4.34%) I(34.90%) N(9. 27%) O(15.25 %).

c)**SYNTHESIS OF 1-BENZOYL-3-(2-METHOXYPHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR: 3066(Ar CH str,)2945,(aliphatic CH str),1712 (C=O str),1610,1508,1422,(phenyl &pyrazole rings (C=C,C=N,)
^{1}HNMR:3.19 (dd,1H),3.38(3H,d)2,55 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS: 306.31(M+)
ELEMENTAL ANALYSIS:Calcd C(70.58%) H(4.61%) I(34.85%) N(9.15%) O(15.67%)

Found C(70.92 %) H(4.45%) I(34.73 %) N(9. 15%) O(15.36 %).

d)**SYNTHESIS OF 1-BENZOYL-3-(4-BROMO PHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR: . 3122(Ar CH str),2945(,aliphatic CH str,)1597(C=Ostr),1591,1518,1443,(phenyl &pyrazole rings C=C,C=N,)
^{1}HNMR:3.18 (dd,1H),3.58(3H,d)2,65 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS: 355.18 (M+) 356.05(M+1)
ELEMENTAL ANALYSIS: Calcd C(57.49%) H(3.12%) Br(22.50%) N(7.89%) O(9.01%)

Found C(57.29%) H(3.43%) Br(22.36%) N(7.5 7 %) O (8.96 %)

e)**SYNTHESIS OF 1-BENZOYL-3-(2-BROMO PHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR:3134(Ar CH str,)2938,(aliphatic CH str,)1678 (C=Ostr),1601,1508,1453,(phenyl &pyrazole rings C=C,C=N,)
^{1}HNMR:3.15 (dd,1H),3.40(3H,d)2.72 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS: 355.18(M+)
ELEMENTAL ANALYSIS;CalcdC(57.49%) H(3.12%) Br(22.50%) N(7.89%) O(9.01%)

Found C(57.58%) H(3.32 %) Br(22.57 %) N(7.53%) O (9.13%)

f)**SYNTHESIS OF 1-BENZOYL-3-(4-CHLORO PHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR:3176(Ar CH str,)2885(,aliphatic CH str,)1517(C=Ostr),1522,1498,1423,(phenyl &pyrazole rings C=C,C=N,)
^{1}HNMR:3.27 (dd,1H),3.45(3H,d)2.75 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS:310.73 (M+), 312.45 (M+2)
ELEMENTAL ANALYSIS: CalcdC(65.71%) H(3.57%) Cl(11.41%) N(9.02%) O(10.30%)

Found C(65.77%) H(3.63 %) Cl(11.33 %) N(9.18 %) O(10.45 %)

g)**SYNTHESIS OF 1-BENZOYL-3-(2-CHLORO PHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR: 3145(Ar CH str,) 2953(,aliphatic CH str,)1637(C=Ostr),1611,1428,1433,(phenyl &pyrazole rings C=C,C=N,)
^{1}HNMR:3.16 (dd,1H),3.48(3H,d)2,56 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS: 310.73 (M+),312.55 (M+2)

ELEMENTAL ANALYSIS:CalcdC(65.71%) H(3.57%) Cl(11.41%) N(9.02%) O(10.30%)

Found C(65.67%) H(3.43%) Cl(11.53%) N(9.25 %) O(10.48%)

h)**SYNTHESIS OF 1-BENZOYL-3-(3-CHLOROPHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR: 3122(Ar CH str,) 2930,(aliphatic CH str,)1654 (C=Ostr),1584,1505,1456,(phenyl &pyrazole rings C=C,C=N,)
^{1}HNMR:3.22 (dd,1H),3.57(3H,d)2,75 (s 1H)
C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)
MS: 310.73 (M+)
ELEMENTAL ANALYSIS:CalcdC(65.71%) H(3.57%) Cl(11.41%) N(9.02%) O(10.30%)

Found C(65.83 %) H(3.72%) Cl(11.52%) N(9.11 %) O(10.23%)

i)**SYNTHESIS OF 1-BENZOYL-3-(4-IODO PHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR:3088(Ar CH str,)2911(aliphatic CH str,)1617(C=Ostr),1571,1488,1393,(phenyl &pyrazole rings C=C,C=N,)

^{1}HNMR:3.19 (dd,1H),3.63(3H,d)2.73 (s 1H)

C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)

MS:401.98(M+) 402.65(M+1)

ELEMENTAL ANALYSIS: CalcdC(50.77%) H(2.76%) I(31.55%) N(6.97%) O(7.96%)

Found C(50.72%) H (2.45%) I (31.25%) N (6.87%) O(7.64 %)

j)**SYNTHESIS OF 1-BENZOYL-3-(2-IODO-PHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE (PQ1).**

IR: 3112 (Ar CH str,)2947,(aliphatic CH str),1677(C=Ostr),1521,1478,1443,(phenyl &pyrazole rings C=C,C=N,)

^{1}HNMR:3.21 (dd,1H),3.62(3H,d)2,62 (s 1H)

C13 NMR :132.41(C in Ar) 21.55(C-C) 29.11(C=N)

MS: 401.98(M+)

ELEMENTAL ANALYSIS: Calcd C(50.77%) H(2.76%) I(31.55%) N(6.97%) O(7.96%)

Found C(50.52%) H (2.61 %) I (31.63%) N (6.35%) O(7.88%)

Table NO:1 PHYSICAL DATA OF *N*'-[(1*E*)-1-(4- SUBSTITUTED PHENYL) ETHYLIDENE] BENZOHYDRAZIDES.

COMPD. CODE	X	MOLECULAR FORMULA	M.P (ºC)	Rf VALUE	% YIELD
PQ1	4-OCH3	$C_{18}H_{14}N_2O_3$	168	0.58	60
PQ2	3-OCH3	$C_{18}H_{14}N_2O_3$	178	0.68	62
PQ3	2-OCH3	$C_{18}H_{14}N_2O_3$	170	0.65	58
PQ4	4-Br	$C_{17}H_{11}BrN_2O_2$	185	0.55	59
PQ5	2-Br	$C_{17}H_{11}BrN_2O_2$	180	0.58	66
PQ6	4-Cl	$C_{17}H_{11}BrN_2O_2$	176	0.60	65
PQ7	2-Cl	$C_{17}H_{11}ClN_2O_2$	192	0.56	58
PQ8	3-Cl	$C_{17}H_{11}ClN_2O_2$	190	0.63	62
PQ9	4-I	$C_{17}H_{11}IN_2O_2$	200	0.68	53
PQ10	2-I	$C_{17}H_{11}IN_2O_2$	205	0.67	48

Table NO:2 PHYSICAL DATA OF1-BENZOYL-3-(SUBSTITUTED PHENYL)-1*H*-PYRAZOLE-4-CARBALDEHYDES.

COMPD. CODE	X	MOLECULAR FORMULA	M.P (ºC)	Rf VALUE	% YIELD
PQ1	4-OCH3	$C_{18}H_{14}N_2O_3$	168	0.71	60
PQ2	3-OCH3	$C_{18}H_{14}N_2O_3$	178	0.75	62
PQ3	2-OCH3	$C_{18}H_{14}N_2O_3$	170	0.68	58
PQ4	4-Br	$C_{17}H_{11}BrN_2O_2$	185	0.72	59
PQ5	2-Br	$C_{17}H_{11}BrN_2O_2$	180	0.65	66
PQ6	4-Cl	$C_{17}H_{11}ClN_2O_2$	192	0.59	58
PQ7	2-Cl	$C_{17}H_{11}BrN_2O_2$	176	0.58	65
PQ8	3-Cl	$C_{17}H_{11}ClN_2O_2$	190	0.65	62
PQ9	4-I	$C_{17}H_{11}IN_2O_2$	200	0.71	53
PQ10	2-I	$C_{17}H_{11}IN_2O_2$	205	0.71	48

TABLE NO.3 HRBC MEMBRANE STABILIZATION METHOD PERCENTAGE HAEMOLYSIS RESULTS

COMPOUND CODE	ABSORBANCE AT 560 nm			PERCENTAGE HAEMOLYSIS		
	100 µg/ml	250 µg /ml	500 µg/ml	100 µg/ml	250 µg/ml	500 µg/ml
PQ1	0.28	0.25	0.22	61.11	65.27	69.44
PQ2	0.22	0.20	0.16	69.44	72.22	77.77
PQ3	0.23	0.22	0.20	68.05	69.44	72.22
PQ4	0.28	0.26	0.25	61.11	63.88	65.27
PQ5	0.27	0.25	0.24	62.5	65.27	66.66
PQ6	0.25	0.24	0.23	65.27	66.66	68.05
PQ7	0.25	0.22	0.21	65.27	69.44	68.34
PQ8	0.26	0.25	0.23	66.75	65.27	68.05
PQ9	0.25	0.24	0.23	65.27	66.66	68.5
PQ10	0.26	0.23	0.22	66.75	68.05	69.44
Diclofenac	0.07	0.04	0.02	90.27	94.44	97.22
Solvent	0.00	0.00	0.00	0.00	0.00	0.00

ANTI INFLAMMATORY ACTIVITY

The anti-inflammatory activity studies of the synthesized compounds were studied at department of pharmacology, SJCP, Cherthala. The test compounds were studied for *in-vitro* anti-inflammatory activity studies by means of Human Red Blood Corpuscles (HRBC) membrane stabilizing method.[20]**.**The test compounds (PQ1, PQ2, PQ3, PQ4, PQ5, and PQ6,PQ7,PQ8,PQ9,PQ10) at the concentration (500µg/ml, 250µg/ml, 100µg/ml) exhibited varying degree of anti-inflammatory activities when compared to that of the standard drug.The anti-inflammatory activities of the synthesized compounds were presented in table number no. 3.

RESULTS AND DISCUSSION

All the synthesized derivatives were screened for their *in-vitro* anti-inflammatory activityby using **Human Red Blood Corpuscles (HRBC) membrane stabilizing method.** Diclofenac sodium (500µg/ml) was used as the standard drug. Compounds PQ1, PQ2& PQ3 e**.**showed 75%, 77% and 74% haemolysis compared to the standard drug Diclofenac sodium (97%). The other compounds showed more than 65% haemolysis.PQ1 is 1-benzoyl-3-(4-methoxyphenyl)-1*H*-pyrazole-4-carbaldehyde where as PQ2 is 1-benzoyl-3-(3-methoxyphenyl)-1H-pyrazole-4-carbaldehyde and PQ3 is 1-benzoyl-3-(2-methoxyphenyl)-1H-pyrazole-4-carbaldehyde. Among the series of 1-benzoyl-3-(substituted phenyl)-1-H-pyrazole-4-carbaldehyde compounds synthesized, compounds with methoxy substituted phenyl groups attached to pyrazole moiety exhibited comparable anti-inflammatory activity with that of the standard drug, diclofenac.

CONCLUSION

In the present study,ten novel 1-benzoyl-3-(substituted phenyl)-1-H-pyrazole-4-carbaldehydes were synthesized,by means of novel synthetic scheme and screened for their anti-inflammatory activities. Out of ten compounds, synthesized and screened for anti-inflammatory activity three compounds exhibited comparable anti-inflammatory activity with that of the standard.It was observed that the compounds that exhibited comparable anti-inflammatory activity with the standard were 1-benzoyl-3 (merthoxysubstituted phenyl)-1-H-pyrazole-4-carbaldehydes Among the compounds of the series, the compound with comparatively more anti-inflammatory activity is 1-benzoyl-3 (3-merthoxy phenyl)-1-H-pyrazole-4-carbaldehyde. From these results, it can be concluded that of 1-benzoyl-3-(methoxyphenyl)-1-H-pyrazole-4-carbaldehydes can be developed as potential antiinflamatory agents. Further it can be concluded that these structures can be developed as a promising lead for the development of new anti-inflammatory agents.

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