World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 4.223

SYNTHESIS, CHARACTERIZATION, ANTI-INFLAMMATORY AND ANTIMICROBIAL ACTIVITIES OF SOME NOVEL DIHYDROPYRIMIDINONE DERIVED PYRAZOLINES

Dr. Konda Ravi Kumar*[1] and B. Lourdu Rani[2]

[1]Hindu College of Pharmacy, Amaravathi road, Guntur, India.
[2]Chalapathi Institute of Engineering and Technology, Lam, Guntur, India.

***Corresponding Author: Dr. Konda Ravi Kumar**
Hindu College of Pharmacy, Amaravathi road, Guntur, India.

Article Received on 15/06/2017 **Article Revised on 06/07/2017** **Article Accepted on 04/08/2017**

ABSTRACT
A novel series of dihydropyramidinone derived pyrazoles were synthesized from dihydropyrimidinones by acid mediated method. The newly synthesized compounds were purified by recrystallization and characterized the compounds by their spectral analysis like IR, ^{1}HNMR and Mass. Further these compounds were screened for their biological activities are anti-inflammatory and antimicrobial activities. All the compounds showed potent to moderately potent antibacterial activity. Among the compounds P 1- 22, compound 3, 4 and 21 showed potent activity and compounds 7, 8, 9, 16, 22 showed moderately potent activity antibacterial activity. Compounds 3, 9, 13 showed potent and compounds 8, 4, 15 and 18 showed moderately potent antifungal activity. Anti-inflammatory activity of synthesized compounds were evaluated against Wistar male albino rats by carrageenan induced paw edema method using indomethacin as standard drug.

KEY WORDS: Aldehydes, Dihydropyramidinone derived Pyrazoles, Anti-inflammatory, Antimicrobial activities.

INTRODUCTION

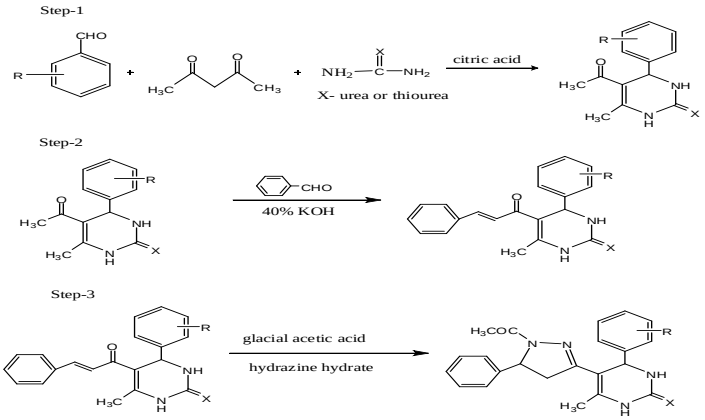
Dihydropyrimidinones are useful targets in chemical synthesis as they have been associated with a diverse range of therapeutic and medicinal properties.[1,2] The dihydropyrimidinone scaffold is also found in various marine alkaloids, which have been shown to possess antiviral,[3] antitumor,[4] antibacterial,[5] antioxidant and anti-inflammatory activities.[6,7] In particular, the batzelladine alkaloids are known to be potent HIV gp-120-CD4 inhibitors. In general dihydropyrimidinones act as anticancer, calcium channel blockers, antibacterial, α_{1a}-adrenergic receptor antagonist such as monestrol, oxo-monestrol etc. Because of their great importance as main heterocyclic moiety in broad range of natural and synthetically designed products, the development of novel synthetic methods remain challenge in research area to produce dihydropyrimidinone derivatives by the use of eco-friendly selective catalyst.[8,9] Multi-component reactions (MCR) are special types of theoretically useful organic reactions in which three or more starting materials react to give a product. Biginelli has reported the synthesis of functionalized 3,4-dihydropyrimidin-2(1*H*)-ones (DHPMs) via three-component condensation reaction of an aromatic aldehydes, urea and ethyl acetoacetate.[10]

MATERIALS AND METHODS

Purity of newly synthesized compounds was identified by thin layer chromatography was performed using precoated aluminium plates coated with silica gel GF_{254} [E.Merck]. The spots were visualized in the iodine chamber. Melting points of the synthesized compounds were determined in open capillary tubes and are uncorrected.IR spectra was recorded on ELICO FTIR spectrometer using potassium bromide pellets.^{1}H-NMR spectra of the compounds in deutiriated dimethyl sulfoxide was recorded on BRUKER Av 400 spectrometer. Mass spectra were recorded on GCMS QP 5000 shimadzu.

General procedure: Dihydropyramidinone derivatives were prepared by the reaction of substituted aldehydes, acetyl acetone, urea or thiourea and citric acid. Dihydropyramidinone derivatives treated with substituted aromatic aldehydes in presence of KOH to obtained chalcone derivatives. Synthesized chalcones were dissolved in glacial acetic acid and added to hydrazine hydrate to get the targeted compounds dihydropyrimidinone derived pyrazolines.By adopting similar type of procedures, 22 compounds were synthesized. Physical and analytical data of synthesized compounds is given in Tab.1. Synthetic scheme pathway for preparation of the novel synthesized compounds is shown in Fig.1.

Scheme



R=OH, OCH_3, NO_2, Cl, furfuryl, OH, OCH_3

Fig. 1: Synthesis of Dihydropyrimidinone derived Pyrazolines.

RESULTS AND DISCUSSION

Table 1: Physical data of synthesized compounds.

Compounds(P)	Substituted benzaldehydes	X group	Melting point	Yield (%)	R_f
P1	-H	oxo	172-174	65.41	0.37
P2	3-OH	oxo	181-183	60.6	0.21
P3	2-NO_2	oxo	205-207	70.3	0.38
P4	2-Cl	oxo	210-212	74.34	0.26
P5	4-OCH_3	oxo	201-203	53.83	0.35
P6	furan	oxo	156-158	95.71	0.47
P7	3-OCH_3,4-OH	oxo	186-188	85.71	0.29
P8	4-NO_2	oxo	184-186	72.80	0.64
P9	4-Cl	oxo	210-212	77.81	0.54
P10	3,4-CH_3, 2-NH_2	oxo	243-245	33.60	0.54
P11	-H	sulphur	165-167	92.32	0.47
P12	3-OH	sulphur	178-180	87.12	0.36
P13	2-NO_2	sulphur	209-211	75.45	0.51
P14	2-Cl	sulphur	196-198	73.09	0.43
P15	4-OCH_3	sulphur	215-217	73.80	0.53
P16	furan	sulphur	154-156	98.18	0.62
P17	3-OCH_3,4-OH	sulphur	201-203	57.7	0.44
P18	4-NO_2	sulphur	206-208	73.86	0.52
P19	4-Cl	sulphur	210-212	96.10	0.37
P20	3,4-CH_3, 2-NH_2	sulphur	227-229	62.10	0.33
P21	-CH=CH_2	oxo	265-267	82.50	0.54
P22	-CH=CH_2	sulphur	232-234	94.71	0.67

Spectral data

P-1:5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-6-methyl-4-phenyl-3,4- dihydropyrimidin-2(1H)-one

IR(KBr,cm^{-1}):3479(N-H Str), 2989(C-H Str), 2269(C=N Str), 1670 (C=C Str), 1105(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.2(s, 2H, CH_2), 2.4(s, 3H, CH_3), 2.6(s, 3H, CH_3), 4.9(s, 1H, CH), 5.3(s, 1H, CH), 6.9-8.2 (m, 11H, aromatic), 8.9(s, 1H, NH); Mass *m/z*: 256, 313, 373(100%), 374(M^+)

P-2: 5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-(3-hydroxyphenyl) 6-methyl-3,4-dihydropyrimidin-2(1H)-one

IR (KBr, cm^{-1}): 3470(N-H str), 2988(C-HStr), 2276(C=N Str), 1675(C=C Str), 1230(O-H Str), 1109(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.0(s, 1H, CH), 2.3(s, 3H, CH_3), 2.6(s, 3H, CH_3), 3.2(s, 2H, CH_2), 5.2(s, 1H, CH), 6.7-9.1 (m, 12H, aromatic); Mass (*m/z):* 174, 233, 291, 391(M^{+1}).

P-3:5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-6-methyl-4-(2-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one

IR(KBr, cm^{-1}): 3484(N-H Str), 2855(C-HStr), 1682(C=C Str), 1107(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.4(s, 1H, CH), 6.8-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH); Mass(*m/z)*: 147, 249, 301(100%), 355, 419 (M^+).

P-4: 5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-(2-chlorophenyl)-6- methyl-3,4-dihydropyrimidin-2(1H)-one

IR(KBr,cm^{-1}):3476(N-H, Str),2854(C-HStr),2260(C=N, Str), 1680(C=C Str), 1222(C-N Str), 752(C-Cl Str), ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.0(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.5(s, 1H, CH), 6.7-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH);Mass(*m/z):* 174, 245, 311(100%), 347, 409 (M^{+1}).

P-5: 5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one

IR(KBr,cm^{-1}): 3412(N-H Str), 2858(C-H Str), 1679(C=C Str), 1240(C-N Str);^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.6(s, 3H, CH_3), 3.0(s, 1H, CH), 3.5(d, 1H, CH), 3.8(s, 3H, CH_3), 4.2(s, 2H, CH_2), 5.5(s, 1H, CH), 6.7-8.8 (m, 12H, aromatic); Mass*(m/z):* 314, 374, 396(100%), 404 (M^+).

P-6:5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-(furan-2-yl)-6-methyl-3,4- dihydropyrimidin-2(1H)-one

IR (KBr, cm^{-1}): 3407(N-H Str), 2871(C-H Str), 2262(C=N Str), 1678(C=C Str), 1143(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.2(s, 3H, CH_3), 2.8(s, 3H, CH_3), 3.2(s, 2H, CH_2), 5.2(s, 1H, CH), 6.7-8.0 (m, 9H, aromatic), 9.4(s, 1H, NH); Mass (*m/z)*: 163, 228, 276, 306(100%), 364 (M^+).

P-7: 5-(1-acetyl - 5-phenyl- 4,5-dihydro-1H-pyrazol-3-yl)-4-(4-hydroxy-3 methoxy phenyl) -6-methyl-3,4-dihydropyrimidin-2(1H)-one

IR(KBr, cm^{-1}): 3488(N-H Str), 2918(C-H Str), 2258 (C=N Str), 1661(C=C Str), 1216(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.6(s, 3H, CH_3), 3.0(s, 1H, CH), 3.5(d, 1H, CH), 3.8(s, 3H, CH_3), 4.2(s, 2H, CH_2), 5.5(s, 1H, CH), 6.7-8.8 (m, 12H, aromatic);Mass *(m/z):* 243, 351, 373(100%), 421 (M^{+1})

P-8: 5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-6-methyl-4-(4- nitro phenyl)-3,4-dihydropyrimidin-2(1H)-one

IR(KBr, cm^{-1}): 3484(N-H Str), 2855(C-H Str), 1682(C=C Str), 1107(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.4(s, 1H, CH), 6.8-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH) Mass *(m/z):* 147, 249, 301(100%), 355, 419 (M^+).

2.3.9.P-9: 5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-(4-chlorophenyl)-6- methyl-3,4-dihydropyrimidin-2(1H)-one

IR (KBr, cm^{-1}): 3476(N-H Str), 2854(C-H), 2260(C=N Str), 1680(C=C), 1222(C-N), 752(C-Cl); ^{1}HNMR(400MHz, DMSO-d_6, δ ppm):2.1(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.4(s, 1H, CH), 6.8-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH); Mass(*m/z):* 174, 245, 301(100%), 347, 409 (M^{+1}).

P-10:(E)-5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-(3-amino-4-Methyl hexa-1,3-dien-2-yl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one

IR(KBr, cm^{-1}): 3469 (N-H Str), 2918(C-H Str), 2250(C=N Str), 1661(C=C Str), 1210(C-N Str);^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 1.9(s, 2H, CH_2), 2.0(s, 3H, CH_3), 2.1(s, 3H, CH_3), 2.2(s, 3H, CH_3), 2.3(s, 3H, CH_3), 4.3-5.0(s, 2H), 5.5- 8.0 (s, 9H, aromatic),9.5(s, 1H, NH); Mass *(m/z):* 249, 301(100%), 355, 417(M^+).

P-11: 1-(3-(6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5- yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone

IR(KBr, cm^{-1}): 3472 (N-H Str), 3011(C-H Str), 1697(C=C Str), 1274(C-N Str),1185(C=S Str);^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.2(s, 2H, CH_2), 2.4(s, 3H, CH_3), 2.6(s, 3H, CH_3), 4.9(s, 1H, CH), 5.3(s, 1H, CH), 6.9-8.2 (m, 11H, aromatic), 8.9(s, 1H, NH);Mass(*m/z):* 91, 174, 23, 391(M^{+1}).

P-12:1-(3-(4-(3-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin- 5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone

IR(KBr, cm^{-1}): 3469 (N-H Str), 3009(C-H Str), 1625(C=C Str), 1186(C=S Str), 1133(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6)(δ ppm): 3.2(s, 2H, CH_2), 5.2(s, 1H, CH), 6.7-9.1 (m, 12H, aromatic); Mass (*m/z)*:151, 231, 309, 407 (M^{+1}), 435(100%).

P-13:1-(3-(6-methyl-4-(2-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone

IR(KBr, cm^{-1}): 3482 (N-H Str), 3010(C-H Str), 1617(C=C Str), 1519(N-H bend), 1184(C=S Str), 1130(C-N Str); ^{1}HNMR (400MHz DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.4(s, 1H, CH), 6.8-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH);Mass(*m/z):* 103, 174, 245, 346(100%), 437 (M^{+2}).

P-14: 1-(3-(4-(2-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4 tetrahydropyrimidin-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone

IR(KBr, cm^{-1}): 3479 (N-H Str), 3012(C-H Str), 1626(C=C Str), 1548(N-H bend), 1187(C=S Str), 1132(C-N Str), 712(C-Cl Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.4(s, 1H, CH), 6.8-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH); Mass(*m/z):* 117, 293, 323,(100%), 361, 426 (M^{+2}).

P-15:1-(3-(4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-5- phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone

IR(KBr, cm^{-1}): 3481 (N-H Str), 3008(C-H Str), 1625(C=C Str), 1551(N-H bend),1184(C=S Str), 1272(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.7(s, 3H, CH_3), 3.0(s, 3H, CH_3), 3.5(d,1H, CH), 3.7(s, 3H, CH_3), 5.5 (s, 1H, CH), 6.7-8.0 (m, 12H, aromatic); Mass(*m/z)*: 113, 191, 249, 386(100%), 422 (M^{+2}).

P-16:1-(3-(4-(furan-2-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-5-phenyl- 4,5-dihydro-1H-pyrazol-1-yl)ethanone
IR(KBr, cm^{-1}): 3477 (N-H Str), 3007(C-H Str), 1625(C=C Str), 1539(N-H bend), 1189(C=S Str), 1132(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6)(δ ppm): 2.2(s, 3H, CH_3), 2.8(s, 3H, CH_3), 3.2(s, 2H, CH_2), 5.2 (s, 1H, CH), 6.7-8.0 (m, 9H, aromatic), 9.4(s, 1H, NH); Mass(*m/z):* 119, 163, 228, 306(100%), 380 (M^+).

P-17:1-(3-(4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydro pyrimidin-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1yl)ethanone
IR(KBr, cm^{-1}):3467 (N-H Str), 3010(C-H Str), 1624(C=C Str), 1571(N-H bend), 1188(C=S Str), 1130(C-N Str), 1272(O-H Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.6(s, 3H, CH_3), 3.0(s, 1H, CH), 3.5(d, 1H, CH), 3.8(s, 3H, CH_3), 4.2(s, 2H, CH_2), 5.5(s, 1H, CH), 6.7-8.8 (m, 12H, aromatic); Mass*(m/z*): 106, 174(100%), 214, 387, 437(M^{+1}).

P-18: 1-(3-(6-methyl-4-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone
IR(KBr,cm^{-1}): 3475 (N-H Str), 3010(C-H Str), 1617(C=C Str), 1519(N-H bend), 1184(C=S Str), 1130(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.4(s, 1H, CH), 6.8-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH); Mass(*m/z):*174, 245, 345(100%), 387, 437(M^{+2})

P-19: 1-(3-(4-(4-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone
IR(KBr, cm^{-1}): 3472 (N-H Str), 3012(C-H Str), 1626(C=C Str), 1548(N-H bend), 1187(C=S Str), 1132(C-N Str), 712(C-Cl Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 2.1(s, 1H, CH), 2.2(s, 3H, CH_3), 3.6(s, 3H, CH_3), 5.4(s, 1H, CH), 6.8-8.0 (m, 11H, aromatic), 9.4(s, 2H, NH); Mass (*m/z):*117, 293, 323(100%), 426(M^{+2}).

P-20:1-(3-(4-(2-amino-3,4-dimethylphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydro pyrimidin-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1yl)ethanone
IR(KBr, cm^{-1}): 3457 (N-H Str), 3010(C-H Str), 1625(C=C Str), 1567(N-H bend), 1191(C=S Str), 1347(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 1.9(s, 2H, CH_2), 2.0(s, 3H, CH_3), 2.1(s, 3H, CH_3), 2.2(s, 3H, CH_3), 2.3(s, 3H, CH_3), 4.3-5.0(s, 2H), 5.5- 8.0(s, 9H, aromatic), 9.5(s, 1H, NH); Mass*(m/z)*: 144, 174(100%), 214, 387, 435(M^{+2}).

P-21:(E)-5-(1-acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-6-methyl-4-styryl-3,4-dihydropyrimidin-2(1H)-one
IR(KBr, cm^{-1}): 3473(N-H Str), 3038(C-H Str), 2258(C=N Str), 1679(C=C Str), 1284(C-N Str);^{1}HNMR (400MHz, DMSO-d_6, δ ppm): 1.8(s,2H, CH_2), 2.2(s,3H, CH_3),2.3(s,3H, CH_3), 2.4(s,3H, CH_3), 4.5-5.4 (d, 2H, CH_2), 5.8-8.2(s, 9H,aromatic), 9.7(s,2H, NH); Mass (*m/z)*: 154, 251, 305(100%), 327, 399(M^{-H}).

P-22:(E)-1-(3-(6-methyl-4-styryl-2-thioxo-1,2,3,4-trahydropyrimidin-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone
IR(KBr, cm^{-1}): 3473(N-H Str), 3018(C-H Str), 1626(C=C Str),1187(C=S Str), 1274(C-N Str); ^{1}HNMR (400MHz, DMSO-d_6)(δ ppm): 1.7(s,2H, CH_2), 1.9 (s,3H, CH_3),2.1(s,3H, CH_3), 2.4(s,3H, CH_3), 4.3-5.2 (d,2 H, CH_2), 5.5-8.0 (s, 9H, aromatic), 9.5(s,2H, NH); Mass (m/z): 166, 207, 350(100%), 392, 417(M^{+1}).

Anti-inflammatory Activity
Anti-inflammatory activity of synthesized compounds were evaluated against Wistar male albino rats by carrageenan induced paw edema method[11,12] using indomethacin as standard drug. Among the 10 compounds evaluated, some compounds have shown significant reduction in paw oedema. Anti-inflammatory activity of synthesized compounds has given in Tab. 2.

Table 2: Anti-inflammatory activity of the synthesized compounds Carrageenan induced Paw oedema method.

Group	1 hr	2 hr	3 hr	4 hr	5 hr
Control 1% Water (1 ml/kg)	0.32±0.01	0.58±0.04	0.64±0.02	0.72±0.01	0.84±0.02
P-1(100 mg/kg)	0.30±0.02(7.28%)	0.46±0.01(20.26%)	0.57±0.03(38.06%)	0.26±0.04(52.24%)	0.22±0.02(64.38%)
P-2 (100mg/kg)	0.29±0.03(8.26%)	0.48±0.02(20.86%)	0.57±0.03(38.42%)	0.21±0.01Z(66.46%)	0.16±0.04**(72.64%)
P-3 (100mg/kg)	0.26±0.02(8.42%)	0.52±0.04(09.10%)	0.56±0.02(40.48%)	0.28±0.03(65.29%)	0.19±0.02* (79.42%)
P-4 (100mg/kg)	0.31±0.01(06.52%)	0.50±0.03(28.46%)	0.52±0.04(34.28%)	0.26±0.02(58.14%)	0.21±0.01**(75.28%)
P-6 (100 mg/kg)	0.28±0.02(10.24%)	0.52±0.03(28.21%)	0.34±0.02(47.60%)	0.28±0.01(64.64%)	0.18±0.02**(73.84%)
P-13 (100mg/kg)	0.28±0.03(10.86%)	0.53±0.04(29.64%)	0.35±0.02(40.52%)	0.29±0.02(63.86%)	0.17±0.03**(76.52%)
P-14 (100mg/kg)	0.30±0.01(10.64%)	0.50±0.03(32.10%)	0.42±0.04(41.48%)	0.27±0.03(64.29%)	0.16±0.01*(78.22%)
P-20 (100mg/kg)	0.24±0.02(7.62%)	0.50±0.01(22.92%)	0.44±0.02(32.68%)	0.28±0.04(62.82%)	0.20±0.03**(74.04%)
Standard (10 mg/kg) **Indomethacin**	0.26±0.01(15.55%)	0.52±0.02(36.92%)	0.32±0.01**(62.40%)	0.24±0.03***(76.66%)	0.15±0.02***(82%)

Antimicrobial activity

The synthesized compounds (P1-22) were screened for in vitro antibacterial activity against two Gram-positive bacterias like Staphylococcus aureus, Bacillus subtilis and Gram-negative bacterias are klebsiella pneumonia, Escherichia coli by well diffusion method.[13,14] All the synthesized compounds were evaluated for antibacterial activity of which compounds possessed potent activity when compared with that of the standard ciprofloxacin (30µg/ml). Anti fungal activity was conducted against Aspergillus niger and Aspergillus flavus by well diffusion method and compared with that of the standard fluconzole (50µg/ml).[15,16] Anti-bacterial and antifungal activities of synthesized compounds has given in Tab.3&4.

Table 3: Invitro antibacterial activity of synthesized compounds (P1-22) Zone of inhibition (mm).

S NO.	Compounds	Minimum inhibitory concentration microorganisms			
		S. aureus	*B. subtilis*	*E. coli*	*K. pneumonia*
1	P1	20	24	25	20
2	P2	22	20	20	22
3	P3	23	25	22	24
4	P4	25	23	24	23
5	P5	21	22	21	20
6	P6	20	21	20	21
7	P7	24	20	25	22
8	P8	23	21	21	20
9	P9	24	23	24	21
10	P10	22	25	23	23
11	P11	21	24	22	23
12	P12	23	23	20	24
13	P13	20	21	21	22
14	P14	21	20	25	21
15	P15	23	22	24	20
16	P16	24	23	24	22
17	P17	22	24	20	24
18	P18	25	22	21	25
19	P19	21	21	24	23
20	P20	24	23	25	20
21	P21	23	24	20	21
22	P 22	22	20	22	23

Table 4: Antifungal activity of synthesized compounds against Aspergillus niger and Aspergillus flavus.

S.No.	Compound	Zone of inhibition					
		A.niger			*A.flavus*		
	Concentrations µg/ml	50	100	150	50	100	150
1.	P 1	R	R	7	R	R	8
2.	P 2	R	R	6	R	R	7
3.	P 3	6	10	12	7	9	11
4.	P 4	6	9	11	R	7	9
5.	P 5	7	9	12	5	7	9
6.	P 6	R	R	8	R	R	7
7.	P 7	R	R	R	R	R	R
8.	P 8	6	8	10	7	9	11
9.	P 9	7	9	12	8	10	13
10.	P 10	R	R	8	R	R	9
11.	P 11	R	R	8	R	R	6
12.	P 12	R	7	10	R	R	9
13.	P 13	6	9	13	8	10	13
14	P 14	7	10	12	R	8	11
15.	P 15	R	R	9	R	8	11
16.	P 16	R	7	9	R	8	11
17.	P 17	R	R	R	R	R	R
18.	P 18	7	9	12	8	10	11

19.	P 19	8	11	14	7	9	11
20.	P 20	R	R	8	R	R	7
21.	P 21	R	R	6	R	R	7
22.	P 22	R	R	8	R	R	9
23.	Standard Fluconazole (50µg/ml)	5			16		
24.	DMSO	-	-	-	-	-	-

The synthesis of dihydropyrimidinone derived pyrazolines (P 1- P 22) was accomplished in Fig.1. It involves cyclization of acetyl acetone with urea or thiourea in presence of citric acid to obtained dihydropyrimidinone derivatives, these derivatives reacts with substituted aromatic aldehydes in alkali solutions to obtained chalone derivatives. Chalcone in glacial acetic acid was treated with hydrazine hydrate resulted compounds were dihydropyrimidinone derived pyrazolines. The synthesized compounds were characterized by FT-IR, ^{1}H NMR and Mass spectrum. The FT-IR spectrum exhibited characteristic bands at 3407-3488, 2854-3035, 1105-1347 and 1184-1191cm^{-1}for NH, CH, C=N and C=S. The ^{1}H NMR spectrum showed δ ppm at 8.9-9.5 for N-H protons and 5.5-9.1 for Ar-H protons. The synthesized compounds were screened for their anti-inflammatory and antimicrobial activities. Anti-inflammatory studies were performed for some of the synthesized compounds by carrageenan induced paw oedema method and compared to standard indomethacin drug. The compounds tested have showed potent to moderately potent anti-inflammatory activity. Among the compounds evaluated, compounds P 3, 13 and 14 at 100mg/kg showed significant reduction in paw oedema when compared to compounds P 2, 4 and 20. The compound P 3, 13 and 14 showed 76-79% protection. Compounds P 2, 4, 6 and 20 showed 71-75% protection. Antimicrobial studies were performed for all the synthesized compounds by well diffusion method and compared to standard ciprofloxacin (30µg/ml) and fluconazole (50µg/ml) for antibacterial and antifungal studies respectively. The zone of inhibition of various concentrations of the synthesized compounds against *gram* positive and *gram* negative bacterias were measured and tabulated. All the compounds showed potent to moderately potent antibacterial activity. Among the compounds P 1- 22, compound 3, 4 and 21 showed potent activity and compounds 7, 8, 9, 16, 22 showed moderately potent activity antibacterial activity. Compounds 3, 9, 13 showed potent and compounds 8, 4, 15 and 18 showed moderately potent antifungal activity.

REFERENCES

1. Rafiee, E. Rafiee, F. Shahbazi, J. of Mol. Cat. A: Chem., 2006; 2(5): 57–61.
2. Bigi., F.Bigi, S. Carloni, B. Frullanti, R. Maggi, G. Sartori, Tetrahedron Lett., 1999; (4): 3465-3468.
3. Mishra., B. G. Mishra, D. Kumar, V. S. Rao, Cataly. Communi, 2006; (7): 457–459.
4. Salehi., H. Salehi, Q.X. Guo, Synth. Commun, 2004; 3(4): 171–179.
5. Jiang., Z. Jiang, R. Chen, Synth. Commun, 2005; 3(5): 503–509.
6. Ranu.,B. C. Ranu, A.S.Hajra, S. Dey, Process Research &Development, 2002; 6: 817-818.
7. Salehi., P. Salehi, M. Dabiri, M. A. Zolfigolc, M. A. Bodaghifard, Tetrahedron Lett., 2003; 4(4): 2889–2891.
8. Stadler., A.Stadler, C. O. Kappe. J. Comb. Chem, 2001; 3: 624-630.
9. Ma., Y.Ma, C. Qian, L. Wang, M. Yang, J. Org. Chem, 2000; 65: 3864-3868.
10. Jin., T. S. Jin H. X. Wang, C.Y. Xing, X. L. Li, T. S. Li, Synth. Commun, 2004; 34: 3009-3016.
11. Nasr., M. N. Nasr, S. A. Said, Arch Pharm (Weinheim), 2003; 3(3): 551-559.
12. Berghot., M. A. Berghot, E. B.Moawad, Eur. J. Pharm Sci, 2003; 20: 173-179.
13. Gokhan., N. Gokhan, A.Yesilada, G.Acar, K. Erol, A. A. Bilgin. Arch Pharm (Weinheim), 2003; 3(6): 362-371.
14. Matysiak., J.Matysiak, A. Niewiadomy, Bioorg Med Chem, 2003; 1(1): 2285-2291.
15. Tabarelli., Z. Tabarelli, M. A. Rubin, D. B. Berlese, P. D. Sauzem, T. P.Missio, M. V. Teixeira, Braz J Med Biol Res, 2004; 3(7): 1531-40.
16. Wageeh., S.Wageeh, El-Hamouly, Abdel Momen, A El-Khamry, Eman M. H. Abbas, Indian Journal of Chemistry, 2006; 45B: 2091-2098.