MICROWAVE ASSISTED SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SOME PYRAZOLE AND PYRIMIDINE DERIVATIVES

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The synthesis of pyrazoles and pyrimidines can be achieved from different chalcones using microwave irradiation within 5-8 min. Pyrazole and pyrimidine are nitrogen containing heterocyclic rings which are versatile lead compound for designing potent bioactive agents. The structures of the products were supported by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The synthesized compounds showed a good antibacterial and antifungal activity.

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INTRODUCTION

Heterocyclic chemistry is currently experiencing a renaissance because of the interest in heterocyclic scaffolds as templates for combinatorial chemistry.[1] As heteroaromatic compounds are present in many natural products,[2] and are constituents of numerous therapeutic agents,[3] they represent ideal drug-like structures for the elaboration of an increase in molecular diversity. Nitrogen containing heterocyclic compounds has received considerable attention due to their wide range of pharmacological activity. The pyrazoles and the pyrimidines constitute interesting class of organic compounds with diverse chemical and biological application. They are known to possess variety of biological activities such as analgesic, anti-inflammatory, protein kinase C inhibitor.[4] Many pyrazole derivatives possess remarkable antiepileptic and antimicrobial,[5] antiamoebic,[6] and antiandrogenic activities.[7] The pyrazole nucleus is a ubiquitous feature of pharmacological interest and has been proven to be a fertile source of medicinal agents. Some of these compounds have also exhibited antidiabetic,[8] anaesthetic[9] properties.

The biological activities of condensed pyrimidines as sedatives and antibacterials are well documented.[10-13] Numerous reports have been patented[14] and have delineated the antiallergic,[15] antiviral,[16] antibacterial,[17] antioxidant[18] and hepatoprotective properties[19] of fused pyrimidines.

The use of microwaves in organic synthesis has increased dramatically in the last years, receiving widespread acceptance and becoming an indispensable tool.[20] Microwave technology has become a powerful tool in organic synthesis, since by employing this technique it is generally possible to prepare organic compounds very fast, with high purity and better yields compared to other more conventional methods.[21-23] So, due to increasing demand and everlasting longing for the biologically active heterocycles, it is considered worthwhile to synthesize some novel pyrimidine and pyrazole moiety, which might possess enhanced biological activity.

EXPERIMENTAL

All the reactions were carried out in a microwave oven (Kenstar, OM26.EGO). Melting points of synthesis compounds were determined in open capillaries in liquid paraffin are uncorrected. Purity of the compounds in addition to elemental analysis were verified by percolated TLC using silica gel G as a adsorbent using ethyl acetate : n-hexane (7:3) as a eluent and spot was detected by using iodine vapors.

The IR (KBr pellets) spectra were recorded on a Perkin Elmer-1800- spectrophotometer and ^{1}H NMR spectra were recorded on BRUKER DRX- 300MHz spectrophotometer, (TMS as a internal reference) and chemical shifts are expressed in δ. MASS spectra were recorded on Jeol D30 spectrophotometer. Elemental analyses for C, H and N were conducted using a Perkin -Elmer CHN analyzer.

General procedure for microwave induced synthesis of 1-(2,4-dinitrophenyl)-3-methyl-1H-pyrazole-5(4H)one (1)

2,4-dinitropheny hydrazine (0.01 mole), ethyl-3-oxobutanoate (0.01 mole) and two to three drops of glacial acetic acid were taken in an Erlenmeyer flask. Then the well-stirred mixture was irradiated in microwave oven for 7 min at 600 W (i.e, 50 % microwave power). The completion of the reaction was monitored by TLC. The solid thus obtained was dried and the product was recrystallized from ethanol to give compound **1**. The physical and spectral data are given in Table 1 and 2.

Table 1. Physical and analytical data of synthesized compound

Compd.	R	Mol. Formula	Mol. Weight	M.P., ºC	Yield, % [Time in min]	Calculated/Found % C,H, and N
1	---	$C_{10}H_8N_4O_5$	264	160-162	85 [6]	45.12/44.13 3.79/4.23 21.05/21.32
2a	4-OH-C_6H_4	$C_{17}H_{12}N_4O_6$	368	250-252	65 [5]	55.14/55.78 3.81/3.34 15.13/15.53
2b	4-Cl-C_6H_4	$C_{17}H_{11}ClN_4O_5$	386	265-267	70 [5]	52.52/52.7 3.37/3.11 14.41/14.76
2c	3-NO_2-C_6H_4	$C_{17}H_{11}N_5O_7$	397	272-274	72 [5]	51.13/51.87 3.28/3.13 17.54/17.9
2d	4-F-C_6H_4	$C_{17}H_{11}FN_4O_5$	370	160-163	75 [5]	54.84/54.46 3.52/3.05 15.05/15.8
3a	4-OH-C_6H_4	$C_{17}H_{14}N_6O_5$	382	105-107	73 [5]	53.12/52.70 4.20/4.69 21.87/20.76
3b	4-Cl-C_6H_4	$C_{17}H_{13}ClN_6O_4$	400	174-176	75 [5]	50.69/50.07 3.75/3.13 20.86/20.09
3c	3-NO_2-C_6H_4	$C_{17}H_{13}N_7O_6$	411	198-200	79 [5]	49.40/48.12 3.66/3.32 23.72/23.03
3d	4-F-C_6H_4	$C_{17}H_{13}FN_6O_4$	384	163-165	78 [5]	52.85/51.89 3.91/3.02 21.75/21.31
4a	4-OH-C_6H_4	$C_{18}H_{14}N_6O_6$	410	90-92	75 [7]	52.43/51.90 3.91/3.09 20.38/21.12
4b	4-Cl-C_6H_4	$C_{18}H_{13}ClN_6O_5$	428	80-82	76 [6]	50.18/50.90 3.51.4.97 19.51/18.87
4c	3-NO_2-C_6H_4	$C_{18}H_{13}N_7O_7$	439	115-117	72 [7]	48.98/48.05 3.43/4.13 22.22/21.87
4d	4-F-C_6H_4	$C_{18}H_{13}FN_6O_5$	412	153-155	70 [8]	52.18/52.98 3.65/4.04 20.18/20.96

Microwave induced synthesis of the chalcones (4-(substituted benzylidene)-1-(2, 4-dinitrophenyl)-3-methyl-1H-pyrazole-5(4H)-one (2a-d)

The chalcones **2a-d** were prepared as starting material to obtain the desired derivatives. Mixture of 2-(2,4-dinitrophenyl)-5-methylpyrazolidine-3-one (0.01 mol) and different aromatic aldehydes (0.01 mol) and KOH (2 to 3 drops) in 30 ml of DMF were taken in an Erlenmeyer flask and mixed thoroughly. The well-stirred mixture was irradiated in microwave oven for 5-6 min at 600 W (i.e. 50 % microwave power). The completion of the reaction was monitored by TLC. The reaction mixture was then cooled at room temperatures and poured into crushed ice. The solid obtained **2a-e** was filtered, washed with water and recrystallized from ethanol. The purity of compounds was analyzed by TLC using ethyl acetate: n-hexane (7: 3) as mobile phase

Microwave induced synthesis of 4-(substituted phenyl)-1-(2,4-dinitrophenyl)-3-methyl-1,3,4,5-tetrahydropyrazolo[3,4-c]pyrazole (3a-d)

Mixture of compound 2 (0.01 mol) and hydrazine hydrate (0.05 mol) in 30 ml of DMF were taken in an Erlenmeyer flask and mixed thoroughly. The well-stirred mixture was irradiated in microwave oven for 7-8 min at 600 W (i.e. 50 % microwave power). The completion of the reaction was monitored by TLC.

The reaction mixture was cooled at room temperatures and poured into crushed ice. The obtained solid was filtered, washed with water and recrystallized from ethanol.

The purity of compounds was analyzed by TLC using ethyl acetate: n-hexane (7: 3) as mobile phase.

Table 2. Spectral data of synthesized compound

Compd.	Spectral data	
1	IR (cm^{-1})	1305(N-N), 1635(C=O), 3252(Ar-CH str.), 3300(N-H str), 1533(N-H bending), 1412(C=C str), 2864(CH_3, sp^3).
	^{1}H NMR (δ)	9.30-8.40 (m, Ar-H), 2.55(s, 2H, CH_2), 1.08(s, 3H, CH_3-methyl).
	^{13}CNMR (δ)	144.1-141.8(C-NO_2),118.4-127.9(CH-Ar),141.9(C-Ar),170.2(C=O), 32.8(CH_2),40.9(CH), 23.5(CH_3)
	Mass (m/z)	264 (M^+), , $[C_9H_6N_4O_5]^+$250, $[C_4H_7N_2O]^+$99, $[C_6H_3N_2O_4]^+$167
2a	IR (cm^{-1})	1310 (N-N), 1638(C=O), 3082(C-H str., Ar-H), 3312(N-H str), 1524(N-H bending), 3052(=C-H, SP^2), 1483 (aromatic ring str.), 2842(CH_3, SP^3), 3410 (OH).
	^{1}H NMR (δ)	9.76-8.83(m, Ar-H), 7.70(s, 1H, CH=), 1.13(s, 3H, CH_3), 6.45-6.83(m, 4H,Ar-H), 5.2(s, 1H, OH).
	^{13}CNMR (δ)	143.1-141.8(C-NO_2), 117.4-127.9(CH-Ar), 141.6(C-Ar), 170.4(C=O), 40.2(CH), 22.6(CH_3), 130.2(C=CH), 137.9(CH), 133.7-133.9(C-Ar), 125.5-129.3(CH-Ar).
	Mass (m/z)	368(M^+), $[C_{17}H_{11}N_4O_5]^+$351, $[C_{11}H_6N_4O_5]^+$274, $[C_{16}H_9N_4O_6]^+$353, $[C_{11}H_9N_2O_2]^+$201, $[C_6H_3N_2O_4]^+$167
2b	IR (cm^{-1})	1312 (N-N), 1722(C=O), 3062(C-H str., Ar-H), 3402(N-H str), 1622(N-H bending), 3154(=C-H, SP^2), 1476(aromatic ring str.), 2710CH_3, SP^3), 664(Cl).
	^{1}H NMR (δ)	9.26-8.3(m, Ar-H), 8.15(s, CH=), 1.25(s, 3H, CH_3), 6.55-7.23(m, 4H, Ar-H).
	^{13}CNMR (δ)	143.12-141.78(C-NO_2), 117.04-127.9(CH-Ar), 141.16(C-Ar), 167.3(C=O), 39.4(CH), 22.8(CH_3), 130.6(C=CH), 137.8(CH), 133.6-129.4(CH-Ar).
	Mass (m/z)	386(M^+),388(M+2), $[C_{17}H_{11}N_4O_5]^+$351, $[C_{11}H_6N_4O_5]^+$274, $[C16H_8N_4O_5]^+$371, $[C_{11}H_{10}ClN_2O]^+$221, $[C_6H_3N_2O_4]^+$167
2c	IR (cm^{-1})	1222 (N-N), 3020 (C-H str., Ar-H), 1645 (C=O str.), 1610(N-H bending), 3175(=C-H, SP^2), 1485 (aromatic ring str.), 2880(CH_3, SP^3), 1550(C-NO_2).
	^{1}H NMR (δ)	9.57-8.77(m, Ar-H), 7.16(s, CH=), 1.18(s, 3H, CH_3), 6.45-6.53(m, 4H, Ar-H).
	^{13}CNMR (δ)	143.12-141.78(C-NO_2), 117.04-127.9(CH-Ar), 141.16(C-Ar), 169.5(C=O), 39.4(CH), 22.6(CH_3), 130.2(C=CH), 138.7(CH), 133.9-127.4(CH-Ar).
	Mass (m/z)	397(M^+), $[C_{17}H_{11}N_4O_5]^+$351, $[C_{11}H_6N_4O_5]^+$274, $[C_{16}H_8N_5O_7]^+$382, $[C_{11}H_{10}N_3O_3]^+$232, $[C_6H_3N_2O_4]^+$167
2d	IR (cm^{-1})	1230 (N-N), 3090 (C-H str., Ar-H), 1694(C=O str.), 1578(N-H bending), 3086(=C-H, SP^2), 1470(aromatic ring str.) 2810(CH_3, SP^3), 812(C-F str.).
	^{1}H NMR (δ)	9.76- 8.85 (m, Ar-H), 7.32(s, CH=), 1.11(s, 3H, CH_3), 7.18-6.83(m, 4H, Ar-H).
	^{13}CNMR (δ)	144.12-142.78(C-NO_2), 118.9-127.9(CH-Ar), 143.16(C-Ar), 169.5(C=O), 39.7(CH), 22.5(CH_3), 130.2(C=CH), 138.5(CH), 133.9-127.4(CH-Ar).
	Mass (m/z)	370(M^+), $[C_{17}H_{11}N_4O_5]^+$351, $[C_{11}H_6N_4O_5]^+$274, $[C_{16}H_8FN_4O_5]^+$355, $[C_{11}H_{10}FN_2O]^+$205, $[C_6H_3N_2O_4]^+$167
3a	IR (cm^{-1})	1556 (C=C ring skeleton Ar. moiety), 1518 (N-H bending), 3210 (N-H str.), 3412 (OH), 2850(CH_3), 1158(C-N str.).
	^{1}H NMR (δ)	9.18-7.80(Ar-H, pyridine), 1.16(s, 3H, CH_3), 6.8 (1H, s, N-H, pyrazole), 2.80(d, 1H, CH), 4.80(d, 1H, CH), 8.08-6.93(m, 4H, Ar-H), 5.8(s, 1H, OH).
	^{13}CNMR (δ)	132.12-139.68(C-NO_2), 115.7-127.9(CH-Ar), 142.1(C-Ar), 154.3(C-pyrazolidine), 42.4-47.2(C-NH), 16.5(CH_3), 54.5(CH-pyrazole), 130.8(C-Ar), 128.6-115.2(CH-Ar), 155.2(C-Ar).
	Mass (m/z)	382(M^+), $[C_{17}H_{13}N_6O_4]^+$365, $[C_{11}H_9N_6O_4]^+$289, $[C_{16}H_{11}N_6O_5]^+$369, $[C_{11}H_{13}N_4O]^+$217, $[C_6H_3N_2O_4]^+$167
3b	IR (cm^{-1})	3410 (N-H stretching), 2788(CH_3), 1595(N-H bending), 1560(C=C), 1148(C-N str.), 747 (C-Cl).
	^{1}H NMR (δ)	9.8-7.7(m, Ar-H), 1.06(s, 3H, CH_3), 7.3 (1H, s, N-H, pyrazole), 2.70(d, 1H, CH), 4.2(d, 1H, CH), 8.8-6.3(m, 4H, Ar-H).
	^{13}CNMR (δ)	133.12-139.68(C-NO_2), 115.7-127.9(CH-Ar), 142.9(C-Ar), 154.4(C-pyrazolidine), 42.4-47.1(C-NH), 16.6(CH), 54.2(CH-pyrazole), 130.5(C-Ar), 128.4-115.1(CH-Ar), 155.2(C-Ar).
	Mass (m/z)	367(M^+),369(M+2),$[C_{17}H_{13}N_6O_4]^+$365,$[C_{11}H_9N_6O_4]^+$289, $[C_{16}H_{10}ClN_6O_4]^+$385, $[C_{11}H_{12}N_4]^+$235, $[C_6H_3N_2O_4]^+$167

Table 2. cont.

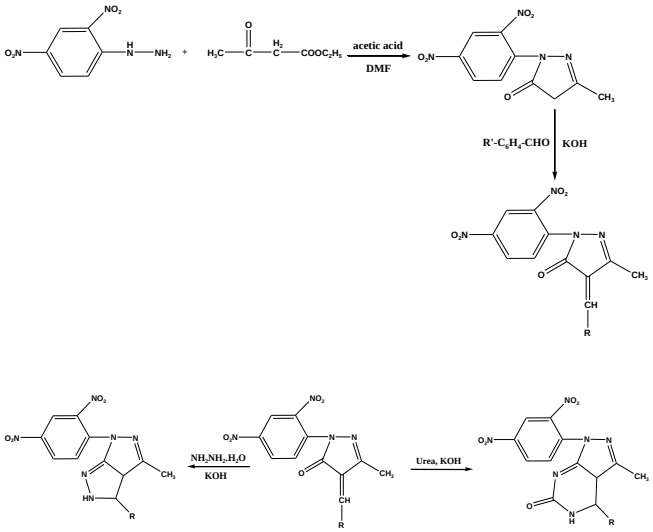
3c	IR (cm^{-1})	1565 (C=C ring skeleton Ar. moiety), 1485 (N=N), 3209 (N-H str.), 1610(N-H bending), 2795(CH_3), 1142(C-N str.), 1382 (NO_2).
	^{1}H NMR (δ)	9.50-7.8(m, Ar-H), 1.25(s, 3H, CH_3), 6.6(1H, s, N-H, pyrazole), 2.02(d, 1H, CH), 4.70(d, 1H, CH), 8.5-6.8(m, 4H, Ar-H).
	^{13}CNMR (δ)	133.12-139.68(C-NO_2), 116.7-127.9(CH-Ar), 142.5(C-Ar), 154.3(C-pyrazolidine), 42.2-47.4(C-NH), 16.7(CH_3), 54.5(CH-pyrazole), 130.8(C-Ar), 128.6-115.2(CH-Ar), 155.3(C-Ar).
	Mass (m/z)	411(M^+), $[C_{17}H_{13}N_6O_4]^+$365, $[C_{11}H_9N_6O_4]^+$289, $[C_{16}H_{10}N_7O_6]^+$396, $[C_{11}H_{12}N_5O_2]^+$246 $[C_6H_3N_2O_4]^+$167
3d	IR (cm^{-1})	1568 (C=C), 1585(N-H bending) , 3310 (N-H str.),2792(CH_3), 1142(C-N str.), 1185 (F).
	^{1}H NMR (δ)	9.8-7.8 (m, Ar-H), 1.20(s, 3H, CH_3), 7.2 (1H, s, N-H, pyrazole), 2.6(d, 1H, CH), 4.73(d, 1H, CH), 8.2-6.7(m, 4H, Ar-H).
	^{13}CNMR (δ)	133.02-139.6 (C-NO_2), 115.7-127.9(CH-Ar), 142.0(C-Ar), 154.4(C-pyrazolidine), 42.2-47.2(C-NH), 16.9(CH_3), 54.8(CH-pyrazole), 130.5(C-Ar), 128.5-115.2(CH-Ar), 155.0(C-Ar).
	Mass (m/z)	384(M^+),$[C_{17}H_{13}N_6O_4]^+$365,$[C_{11}H_9N_6O_4]^+$289, $[C_{16}H_{10}FN_6O_4]^+$369,$[C_{11}H_{12}FN_4]^+$219, $[C_6H_3N_2O_4]^+$167
4a	IR (cm^{-1})	1558 (C=C ring skeleton Ar. moiety), 1510 (N-H bending), 1698(C=O), 3210 (N-H str.), 2852(CH_3), 1155(C-N str.), 3410 (OH).
	^{1}H NMR (δ)	9.8-7.80(Ar-H), 2.15(1H, s, NH of Pyrazolidine), 3.5(CH-pyrazolidine), 1.11(CH_3), 2.85(CH), 4.84(CH), 8.08-6.93(m, 4H, Ar-H), 5.6(NH-pyrimidine), 5.7(OH).
	^{13}CNMR (δ)	133.12-139.6(C-NO_2), 115.7-127.9(CH-Ar), 142.0(C-Ar), 163.9(C-pyrazolidine), 164.2(C=O, urea), 49.2(C-CH_3, pyrazolidine), 17.3(CH_3), 51.9(CH), 36.7(CH-NH, pyrimidine), 133.9(C-Ar), 130.3-116.2(CH-Ar), 156.2(C-Ar).
	Mass (m/z)	410(M^+),$[C_{18}H_{13}N_6O_5]^+$393,$[C_{12}H_9N_6O_5]^+$317,$[C_{17}H_{13}N_6O_6]^+$397, $[C_{12}H_{13}N_4O_2]^+$245, $[C_6H_3N_2O_4]^+$167
4b	IR (cm^{-1})	3410 (N-H stretching), 1658 (C=O stretching), 2782(CH_3), 1593(N-H bending), 1562(C=C), 1150(C-N str.), 746 (C-Cl).
	^{1}H NMR (δ)	9.8-7.7(Ar-H), 2.15 (1H, s, NH of Pyrazolidine), 3.8(CH-pyrazolidine), 1.18(CH_3), 2.62(CH), 4.9(CH), 8.9-6.3(m, 4H, Ar-H), 6.5(NH-pyrimidine).
	^{13}CNMR (δ)	134.9-139.6(C-NO_2), 116.7-127.9(CH-Ar), 142.6(C-Ar), 163.4(C-pyrazolidine), 164.5(C=O, urea), 49.5(C-CH_3, pyrazolidine), 17.9(CH_3), 51.5(CH), 36.4(CH-NH, pyrimidine), 133.3(C-Ar), 130.5-116.2(CH-Ar), 156.7(C-Ar).
	Mass (m/z)	428(M^+), 430(M+2), $[C_{18}H_{13}N_6O_5]^+$393, $[C_{12}H_9N_6O_5]^+$317, $[C_{17}H_{12}ClN_6O_5]^+$416, $[C_{12}H_{12}ClN_4O]^+$263, $[C_6H_3N_2O_4]^+$167
4c	IR (cm^{-1})	1565 (C=C ring skeleton Ar. moiety), 1693 (C=O), 3219 (N-H str.), 1612(N-H bending), 2793(CH_3), 1144(C-N str.), 1382 (NO_2).
	^{1}H NMR (δ)	9.50-7.8(Ar-H), 2.37(1H, s, NH of Pyrazolidine), 3.95(CH-pyrazolidine), 1.23(CH_3), 2.71(CH), 4.75(CH), 8.4-6.9(m, 4H, Ar-H), 6.5(NH-pyrimidine).
	^{13}CNMR (δ)	134.02-139.4(C-NO_2), 116.3-127.3(CH-Ar), 142.5(C-Ar), 163.6(C-pyrazolidine), 164.2(C=O, urea), 49.2(C-CH_3, pyrazolidine), 17.2(CH_3), 51.6(CH), 36.6(CH-NH, pyrimidine), 133.5(C-Ar), 130.3-116.6(CH-Ar), 155.2(C-Ar).
	Mass (m/z)	439(M^+), $[C_{18}H_{13}N_6O_5]^+$393, $[C_{12}H_9N_6O_5]^+$317, $[C_{17}H_{12}N_7O_7]^+$427, $[C_{11}H_{10}N_5O_3]^+$260, $[C_6H_3N_2O_4]^+$167
4d	IR (cm^{-1})	1565 (C=C), 1584(N-H bending), 1680 (C=O, 3310 (N-H str.), 2790(CH_3), 1142(C-N str.), 1185 (F).
	^{1}H NMR (δ)	9.8-7.8(Ar-H), 2.51(1H, s, NH of Pyrazolidine), 3.74(CH-pyrazolidine), 1.20(CH_3), 2.83(CH), 4.76(CH), 8.2-6.6(m, 4H, Ar-H), 6.4(NH-pyrimidine).
	^{13}CNMR (δ)	134.12-139.3(C-NO_2), 116.8-127.9(CH-Ar), 142.7(C-Ar), 163.7(C-pyrazolidine), 164.9(C=O, urea), 49.5(C-CH_3, pyrazolidine), 17.9(CH_3), 51.9(CH), 36.5(CH-NH, pyrimidine), 133.9(C-Ar), 130.3-116.0(CH-Ar), 156.3(C-Ar).
	Mass (m/z)	412(M^+), $[C_{18}H_{13}N_6O_5]^+$393, $[C_{12}H_9N_6O_5]^+$317, $[C_{17}H_{12}FN_6O_5]^+$399 $[C_{12}H_{12}FN_4O]^+$247, $[C_6H_3N_2O_4]^+$167

Table 3. Minimum inhibition concentration of synthesized compounds on bacterial and fungal strains (4,5a-d)

Compounds	R	MIC, µg mL^{-1}					
		Bacteria				Fungi	
		E. coli	*P. euroginosa*	*S. aureus*	*S. pyogenus*	*A. nigar*	*C. albicans*
4a	4-HOC$_6$H$_4$	125	250	250	125	250	125
4b	4-ClC$_6$H$_4$	250	125	125	125	250	125
4c	3-NO$_2$C$_6$H$_4$	62.5	125	62.5	125	500	250
4d	4-FC$_6$H$_4$	125	125	100	62.5	500	500
5a	4-HOC$_6$H$_4$	250	125	250	250	250	125
5b	4-ClC$_6$H$_4$	200	100	100	125	250	500
5c	3-NO$_2$C$_6$H$_4$	100	62.5	200	200	125	100
5d	4-FC$_6$H$_4$	62.5	100	125	100	500	100
Amphicilin		100	----	250	100	----	----
Greseofulvin		----	----	----	----	500	100

Microwave induced synthesis of 1-(2,4-dinitrophenyl)-4-(substituted phenyl)-3-methyl-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-(3aH)-one (4a-d)

Mixture of compound **2** (0.01 mol) and urea (0.01 mol) with KOH (2-3 drops) in 30 ml of DMF were taken in an Erlenmeyer flask and mixed thoroughly. The well-stirred mixture was irradiated in microwave oven for 7-8 min at 600 W (i.e. 50 % microwave power). The completion of the reaction was monitored by TLC. The reaction mixture was then cooled at room temperatures and poured into crushed ice. The obtained solid was filtered, washed with water and recrystallized from ethanol. The purity of compounds was analyzed by TLC using ethyl acetate: n-hexane (7: 3) as mobile phase.



R'= 4-OH, 4-Cl, 3-NO$_2$, 4-F.

R= 4-OH-C$_6$H$_4$, 4-Cl-C$_6$H$_4$, 3-NO$_2$-C$_6$H$_4$, 4-F-C$_6$H$_4$.

Reaction Scheme: Synthesis of pyrazole and pyrimidine derivatives

Antimicrobial Activity

The compounds (**4,5a-d**) were tested for their antimicrobial activities against gram-positive and gram-negative bacterial and fungal strain. The resulting MIC (µg mL^{-1}) values are indicated in Table 3. It was observed that more than half compounds exhibited excellent activity in comparison to standards used, while the remaining were good and one or two of them poor in comparison to the standards. The standard used for antifungal activity was Greseofulvin and Amphicilin were used as a standard for antibacterial assay.

The newly synthesized compounds **(4,5a-d)** were screened for their antibacterial activity against gram-negative bacteria *Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 441) and gram-positive bacteria *Staphylococcus aureus* (MTCC 96) and *Streptococcus pyogenes* (MTCC 442) and antifungal activity against *A. nigar* and *C. albicans.* The samples were tested by broth dilution method. The screening for antimicrobial activity was carried out by diluting the solution and preparing the sets consecutively from 1000, 500, 250, 200, 100, 50, 25, 12.5, 6.25 micro/ml. The highest dilution showing at least 99 % inhibition zone is taken as MIC. The result of this is much affected by the size of the inoculum. The test mixture should contain 10^8 organism/ml. Among all the synthesized derivatives **4c, 5c** and **5d** were exhibited the best MIC values. **4a, 5a** and **5c** showed equivalent activity to standard and rest of compounds were showed moderate to poor activity.

In fungal activity only **5c** was showed excellent activity against *A. nigar* and **4c, 4d** and **5d** showed equivalent activity to standard and rest of compounds showed moderate to poor activity against fungal standard.

RESULT AND DISCUSSION

Ethyl-3-oxobutanoate on condensation with 2, 4-dinitrophenyl hydrazine in presence of glacial acetic acid in DMF as solvent afforded compound **1.** The compound **1** was characterised by the appearance of IR bands at 3300 cm^{-1} for N-H str., 1635 cm^{-1} for C=O and 1305 cm^{-1} for (N-N).

The compound **1** was treated with various aromatic aldehydes in the presence of KOH to give (4-(substituted benzylidene)-1-(2,4-dinitrophenyl)-3-methyl-1H-pyrazole-5(4H)-one **2a-d.** Compounds **2a-d** were confirmed by disappearance of signal at 2.55 ppm due to CH_2 and appearance of multiplet for five aromatic protons at 7.16-8.15 ppm and =C-H stretching frequency at 3052-3175 cm^{-1}.

Chalcones **2a-d** are convenient starting material for the synthesis of pyrazoles, and pyrimidines due to their α,β-unsaturated moiety.

In first pathway **3a-d** were synthesized by treating compounds **2a-d** with hydrazine hydrate. The formation of pyrazole **3a-d** were explained by the appearance of bands at 1142-1158 cm^{-1} due to (C=N str.) and disappearance of band at 3052-3186 cm^{-1} due to (=C-H) in IR spectrum and singlet at 6.6-7.3 δ due to –NH (pyrazole) in ^1H NMR spectra.

In second pathway formation of pyrimidine derivative were synthesized by compound **2a-d** with urea in basic medium.

Formation of **4a-d** were explained by the appearance of bands at 1142-1155 cm^{-1} due to (C-N str.) and disappearance of band at 3052-3186 cm^{-1} due to (=C-H) in IR spectrum. The compounds were confirmed by the appearance of IR band at 1658-1698 cm^{-1} for C=O stretching. The NMR signal of =C-H at 7.16-8.15 ppm is disappeared and one signal –NH is appeared at 5.6-6.5 ppm. The ^1H NMR and ^{13}C NMR spectroscopic data, as well as IR spectra are in good agreement with the proposed structure of the synthesized compounds.

CONCLUSION

The purpose of the research is the development of new potent bioactive molecules with less toxic, safer and easily available methods. From the literature survey it is evident that Microwave Induced Organic Reaction Enhancement (MORE) chemistry offers a simple, nonconventional technique for the synthesis of wide variety of compounds including biologically important heterocyclic compounds, co-ordination compounds etc. By thorough study of physical, spectral and biological data, it can be concluded that meaningful results were obtained. So pyrimidine and pyrazole moiety were found to possess considerable biological activity, there is a great scope for potent derivatives which can be obtained by structural modifications. As a result, the synthesized derivatives appear to be potential candidates for further exploration.

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