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Microwave Induced Synthesis and Antimicrobial activities of Various substituted Pyrazolidines from Chalcones

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Abstract

Microwave-assisted organic synthesis is an enabling technology for accelerating drug discovery and development processes. Pyrazolidine are well-known and important five membered heterocyclic compounds and various methods have been worked out for their synthesis. Therefore, in this work a new series of pyrazolidine derivatives were synthesized by different Chalcones under microwave irradiation. These derivatives were screened for their antimicrobial activity against different microorganism. The structures of synthesized compounds were established on the basis of elemental analysis IR, [1]HNMR and [13]CNMR spectra.

Key words: Pyrazolidine, microwave irradiation, pyrazole, pyrimidine, antimicrobial.

Introduction

"Preventing pollution and minimizing waste generation will gradually clean up sins of the past." In this environmental conscious era, the role of chemistry and chemists[1] involved is to incorporate processes and design products, which can eliminate or minimize the generation of associated pollutants. The application of green chemistry presented a new boom of area of research in the field of organic chemistry called Microwave Assisted Organic Synthesis that particularly revolutionized the drug synthesis[2]. Drug discovery in the post genomic era is characterized by the ability to efficiently develop drugs against the vast number of potential drug targets[3]. The efficiency of MW flash heating has resulted in dramatic reductions in reaction times (reduced from days and hours to minutes and seconds[4]. The short reaction time and the expanded reaction range offered by the microwave assisted organic synthesis are well suited to the increased demand in the industry[5-8].

Microwave irradiation has been also applied to carry out synthesis in open vessel, using organic solvent such as ethanol, N,N-Dimethylformamide (DMF), 1,2-Dichloroethane (DCE), 1,2-Dichlorobenzene etc. as energy transfer media which absorb microwave energy efficiently through dipole rotation. Heterocyclic compounds have always been on the forefront of attention due to their numerous uses in pharmaceutical applications[9]. Heterocyclic moieties also serve as an integral part of a broad variety of biologically active natural products and synthetic compounds[10]. The overwhelming majority of commercially available synthetic drugs (up to 80%) have a heterocyclic structural component[11]. Due to the widespread interest in heterocycles, the synthesis of these compounds has always been among the most important research areas in synthetic chemistry, resulting in the development of several classic named reactions[12].

Pyrazolidine derivatives are well established in the literature as important biologically active heterocyclic compounds[13-14]. These derivatives are the subject of many research studies due to their widespread potential biological activities such as anti-inflammatory, antipyretic, antimicrobial, antiviral, antitumor, anticonvulsant, antihistaminic, antidepressant, insecticides[15-18]. α, β-Unsaturated ketones (Chalcones) display a wide range of pharmacological properties antibacterial, antiviral, anti-inflammatory activities. They are well known inter-mediates for synthesizing various heterocyclic derivatives. In the view of the above-mentioned facts and our continued interest in the synthesis of heterocyclic compounds derived from Chalcones precursors, it was thought of interest to synthesize some new heterocyclic compounds containing pyrazolidine rings and examination of their antimicrobial properties. This characteristic suggested that a pyrazolidine would make a good template for a lead generation library.

Methodology

Materials and equipments: All reactions were carried out in a modified microwave oven (KENSTAR- OM-20DSP, 2450 Hz). Melting points were determined in open capillaries and are uncorrected. Reaction was monitored by thin layer chromatography using silica gel-G as adsorbent using ethyl acetate: benzene (7:3) as eluent and products were detected by iodine vapour. IR spectra (KBr pellets) were recorded on Perkin-Elmer 1800 (FTIR) spectrometer. ^{1}H NMR spectra (DMSO-d_6) were taken on a Bruker DRX spectrometer (300 MHz, FT NMR) using TMS as internal standard and chemical

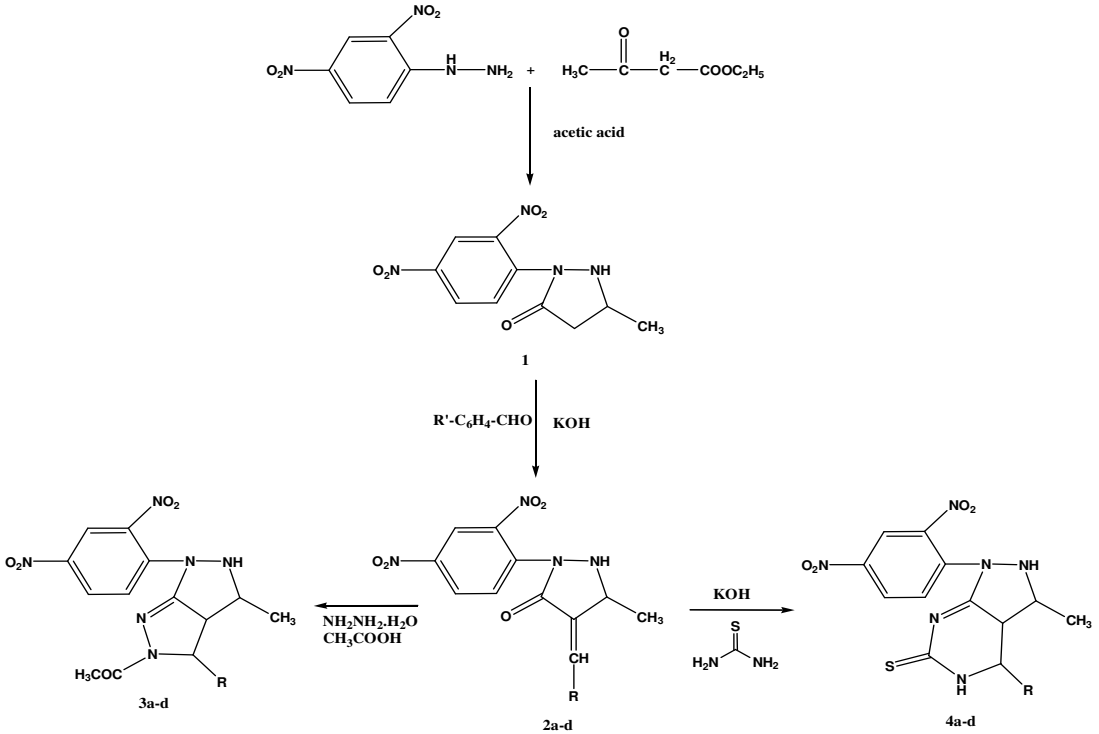
shift were expressed in δ. The starting compounds were prepared according to reported method.

General Procedure for Microwave induced Synthesis of 2-(2,4-dinitrophenyl)-5-methylpyrazolidine-3-one (1): A mixture of 2, 4-dinitrophenyl hydrazine (0.01 mol) and ethyl-3-oxobutanoate (0.05 mol), acetic acid (4-5drops) in ethanol (20 ml.) were taken in an Erlenmeyer flask and mixed thoroughly. The mixture was irradiated under microwave for 7 min at 600 W (i.e., 50 % microwave power) with constant shaking and intermittent radiation of 30 sec interval. The progress of the reaction was monitored by TLC. The solid thus obtained was dried and recrystallised from alcohol to yield compound.

Microwave induced Synthesis of the Chalcones (4-(substituted benzylidene)-2-(2,4-dinitrophenyl)-5-methylpyrazolidin-3-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-d 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 1-(6-(2, 4-dinitrophenyl)-3(substituted phenyl)-4-methyl-3a,4,5,6-tetrahydropyrazolo [3,4-c]pyrazol-2(3H)-yl)ethanone (3a-d): Mixture of compound **2**(0.01 mol) and hydrazine hydrate (0.05 mol) with acetic acid (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.

Microwave induced Synthesis of 1-(2, 4-dinitrophenyl)-4-(substitutedphenyl)3-methyl-1,2,3,3a,4,5-hexahydropyrazolo [3,4-d]pyrimidine-6-thione (4a-d): Mixture of compound **2**(0.01 mol) and thiourea (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_6H_4, 4-Cl-C_6H_4, 3-NO_2-C_6H_4, 4-F-C_6H_4.

Scheme-1

Synthesis of substituted pyrazolidine compounds

Table-1
Physical data of synthesized compounds

Compounds	R	Mol formula	Mol Wt.	M.P.	CHN Calculated / Found	Yield% [Time in min]
1	_	$C_{10}H_{10}N_4O_5$	266	160-162	**C:**45.12/44.13 **H:**3.79/4.23 **N:**21.05/21.32	85 [7]
2a	4-OH-C_6H_4	$C_{17}H_{14}N_4O_6$	370	250-252	**C:**55.14/55.78 **H:**3.81/3.34 **N:**15.13/15.53	65 [5]
2b	4-Cl-C_6H_4	$C_{17}H_{13}ClN_4O_5$	388	265-267	**C:**52.52/52.7 **H:**3.37/3.11 **N:**14.41/14.76	70 [5]
2c	3-NO_2-C_6H_4	$C_{17}H_{13}N_5O_7$	399	272-274	**C:**51.13/51.87 **H:**3.28/3.13 **N:**17.54/17.9	72 [5]
2d	4-F-C_6H_4	$C_{17}H_{13}FN_4O_5$	372	160-163	**C:**54.84/54.46 **H:**3.52/3.05 **N:**15.05/15.8	75 [5]
3a	4-OH-C_6H_4	$C_{19}H_{18}N_6O_6$	426	205-207	**C:**53.52/53.64 **N:**4.26/4.75 **C:**19.71/19.3	72 [8]
3b	4-Cl-C_6H_4	$C_{19}H_{17}ClN_6O_5$	444	162-164	**C:**51.30/ 51.7 **H:**3.85/3.70 **N:**18.89/18.29	74 [8]
3c	3-NO_2-C_6H_4	$C_{19}H_{17}N_7O_7$	455	195-197	**C:**50.11/50.83 **H:**3.76/3.30 **N:**21.53/21.76	69 [8]
3d	4-F-C_6H_4	$C_{19}H_{17}FN_6O_5$	428	180-182	**C:**53.27/53.8 **H:**4.00/4.12 **N:**19.62/19.09	71 [8]
4a	4-OH-C_6H_4	$C_{18}H_{16}N_6O_5S$	428	252-254	**C:**40.46/40.30 **H:**3.76/3.56 **N:**19.62/19.50	70 [5]
4b	4-Cl-C_6H_4	$C_{18}H_{15}ClN_4O_4S$	446	170-172	**C:**48.38/48.9 **H:**3.38/3.14 **N:**18.81/18.20	64 [5]
4c	3-NO_2-C_6H_4	$C_{18}H_{15}N_7O_6S$	457	160-162	**C:**47.26/47.60 **H:**3.31/3.91 **N:**21.43/21.11	77 [5]
4d	4-F-C_6H_4	$C_{18}H_{15}FN_6O_4S$	430	175-178	**C:**50.23/50.58 **H:**3.51/3.10 **N:**19.53/19.78	79 [5]

Table-2
Spectral data of synthesized compounds

Compds.	R	IR(cm^{-1})	^{1}HNMR (400MHz,DMSO) δ ppm	^{13}CNMR	MS
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).	9.30-8.40(Ar-H), 8.24(1H,s,NHof Pyrazolidine), 2.55(CH_2),3.17(CH), 1.08(CH_3-methyl)	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)	266$[M]^{\cdot+}$
2a	4-OH-C_6H_4	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).	9.76-8.83,(Ar-H), 8.74(1H,s,NHof Pyrazolidine), 7.70(CH=),3.55(CH-pyrazolidine), 1.13(CH_3), 6.45-6.83(m, 4H,Ar-H), 5.2(OH)	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).	370$[M]^{\cdot+}$
2b	4-Cl-C_6H_4	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)	9.26-8.3(Ar-H), 8.04(1H, s, NH of Pyrazolidine), 8.15(CH=),3.43(CH-pyrazolidine), 1.25(CH_3), 6.55-7.23(m, 4H, Ar-H).	143.12-141.78(C-NO_2),117.04-127.9(CH-Ar),141.16(CAr),167.3(C=O),39.4(CH),22.8(CH_3),130.6(C=CH),137.8(CH), 133.6-129.4(CH-Ar).	390[M+2]$^{+}$, 388 $[M]^{\cdot+}$
2c	3-NO_2-C_6H_4	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)	9.57-8.77(Ar-H), 8.05(1H,s,NHof Pyrazolidine), 7.16(CH=),3.29(CH-pyrazolidine), 1.18(CH_3), 6.45-6.53(m, 4H,Ar-H).	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).	399$[M]^{\cdot+}$
2d	4-F-C_6H_4	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.)	9.76-8.85(Ar-H), 8.11(1H,s,NHof Pyrazolidine), 7.32(CH=),3.55(CH-pyrazolidine), 1.11(CH_3), 7.18-6.83(m, 4H, Ar-H).	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).	372$[M]^{\cdot+}$
3a	4-OH-C_6H_4	1182(N-N), 3076 (C-H str., Ar-H), 1567(N-H bending), 1485 (aromatic ring str.), 2812(CH_3, SP^3), 1140 (C=N str.), 1615 (C=N)3290(OH), 1145(C-N str.)	9.26-8.55(Ar-H), 8.9(1H, s, NH of Pyrazolidine), 4.48(CH-pyrazolidine), 1.11(CH_3),2.12(CH), 4.34(CH), 7.18-6.93(m, 4H,Ar-H), 2.9($COCH_3$), 4.93(OH).	133.12-139.78(C-NO_2), 115.9-127.9(CH-Ar), 142.6(C-Ar),154.5(C-pyrazolidine),47.8(C-pyrazolidine),16.2(CH_3), 62.5-54.3(CH-pyrazole), 167.4($COCH_3$-pyrazole), 22.8($COCH_3$-pyrazole), 130.7(C-Ar),128.3-115.2(CH-Ar), 155.2(C-Ar).	426$[M]^{\cdot+}$
3b	4-Cl-C_6H_4	1175(N-N), 3054 (C-H str., Ar-H), 1452(aromatic ring str.), 2815(CH_3, SP^3), 1612 (C=N), 1130 (C=N str.), 1660(C=C), 766 (C-Cl), 1150(C-N str.)	9.56-8.87(Ar-H), 8.8(1H, s, NH of Pyrazolidine), 3.11(CH-pyrazolidine), 1.29(CH_3),2.32(CH), 4.24(CH),7.08-6.9(m, 4H, Ar-H), 2.8($COCH_3$),	133.11-139.78(C-NO_2), 115.8-127.3(CH-Ar), 142.3(C-Ar),154.5(C-pyrazolidine),47.5(C-pyrazolidine),16.7(CH_3), 62.5-54.8(CH-pyrazole), 167.5($COCH_3$-pyrazole), 22.7($COCH_3$-pyrazole), 130.8(C-Ar),128.3-115.2(CH-Ar), 155.0(C-Ar).	446[M+2]$^{+}$, 444$[M]^{\cdot+}$
3c	3-NO_2-C_6H_4	3380 (N-H str.), 3090 (C-H str., Ar-H), 2920 (C-H str.), 2819(CH_3, SP^3), 1618 (C=N)1138 (C=N str.), 1548 (NO_2), 1145(C-N str.)	9.76-8.5(Ar-H), 8.8(1H, s, NH of Pyrazolidine), 3.8(CH-pyrazolidine), 1.04(CH_3),2.52(CH), 4.40(CH), 7.18-6.23(m,	133.02-139.18(C-NO_2), 115.9-127.9(CH-Ar), 142.9(C-Ar),154.9(C-pyrazolidine),47.9(C-pyrazolidine),16.3(CH_3), 62.6-54.8(CH-pyrazole), 167.6($COCH_3$-	455$[M]^{\cdot+}$

			4H, Ar-H), 2.6($COCH_3$),	pyrazole), 22.7($COCH_3$-pyrazole), 130.8(C-Ar),128.4-115.2(CH-Ar), 155.7(C-Ar).	
3d	4-F-C_6H_4	3360 (N-H str), 2932 (C-H str.), 3073(C-H str., Ar-H), 3176(Ar-CH), 2820(CH_3, SP^3), 1620 (C=N), 1120(C=N), 1180(C-F), 1145(C-N str.)	9.96-8.80(Ar-H), 8.4(1H, s, NH of Pyrazolidine), 3.8(CH-pyrazolidine), 1.6(CH_3),2.70(CH), 4.48(CH), 8.18-6.93(m, 4H,Ar-H), 2.8($COCH_3$),	133.12-139.68(C-NO_2), 115.7-127.9(CH-Ar), 142.9(C-Ar),154.4(C-pyrazolidine),47.2(C-pyrazolidine),16.6(CH_3), 62.5-54.4(CH-pyrazole), 167.6($COCH_3$-pyrazole), 22.8($COCH_3$-pyrazole), 130.8(C-Ar),128.6-115.2(CH-Ar), 155.2(C-Ar).	428$[M]^{\cdot+}$
4a	4-OH-C_6H_4	3212 (N-H str.), 1510 (N-H bending), 2850(CH_3), 1560 (C=C ring skeleton Ar. moiety), 1657(C=N str.), 3415 (OH), 1250 (C=S str.).	9.4-7.80(Ar-H), 8.14(1H, s, NH of Pyrazolidine), 3.6(CH-pyrazolidine), 1.15(CH_3), 2.93(s, 1H, CH), 4.87(s, 1H, CH), 8.08-6.83(m, 4H,Ar-H), 5.5(NH-pyrimidine), 5.9(OH).	131.12-138.3(C-NO_2), 114.8-126.9(CH-Ar), 144.7(C-Ar), 162.7(C-pyrazolidine), 188.7(C=S),49.7(C-CH_3,pyrazolidine), 15.9(CH_3),51.9(CH), 36.7(CH-NH, pyrimidine),135.9(C-Ar),130.3-116.0(CH-Ar), 148.4(C-Ar).	428$[M]^{\cdot+}$
4b	4-Cl-C_6H_4	3412 (N-H str.), 2782(CH_3), 1593(N-H bending), 1562(C=C), 1650(C=N str.), 748(C-Cl), 1255 (C=S str.).	9.2-7.7(Ar-H), 8.11 (1H, s, NH of Pyrazolidine), 3.4(CH-pyrazolidine), 1.18(CH_3), 2.64(s, 1H, CH), 4.9(CH),8.9-6.3(m, 4H,Ar-H),6.2(NH-pyrimidine).	131.22-138.3(C-NO_2), 114.2-126.4(CH-Ar), 144.6(C-Ar),162.6(C-pyrazolidine), 188.2(C=S),49.6(C-CH_3,pyrazolidine), 15.9(CH_3),51.9(CH), 36.2(CH-NH, pyrimidine),135.2(C-Ar),130.3-116.0(CH-Ar), 148.9(C-Ar).	448$[M+2]^{+}$, 446$[M]^{\cdot+}$
4c	3-NO_2-C_6H_4	3219 (N-H str.), 1612(N-H bending), 1565 (C=C ring skeleton Ar. moiety), 2795(CH_3), 1644(C=N str.), 1382 (NO_2), 1242 (C=S str.).	9.50-7.8(Ar-H), 8.37(1H, s, NH of Pyrazolidine), 3.95(CH-pyrazolidine), 1.22(CH_3),2.5(s,1H, CH),4.72(CH),8.2-6.9(m,4H,Ar-H), 6.1(NH-pyrimidine).	131.33-138.30(C-NO_2), 114.80-126.8(CH-Ar), 144.1(C-Ar),162.9(C-pyrazolidine),188.5(C=S),49.4(C-CH_3, pyrazolidine),15.4(CH_3), 51.9(CH),36.4(CH-NH, pyrimidine),135.8(C-Ar),130.8-116.0(CH-Ar), 148.8(C-Ar).	457$[M]^{\cdot+}$
4d	4-F-C_6H_4	1585(N-H bending), 3312 (N-H str.), 2792(CH_3), 1568 (C=C), 1644(C=N str.), 1184 (F), 1245 (C=S str.).	9.8-7.8(Ar-H), 8.5(1H, s, NH of Pyrazolidine), 3.54(CH-pyrazolidine), 1.10(CH_3), 2.43(s, 1H, CH),4.66(CH),8.2-6.6(m,4H,Ar-H), 6.4(NH-pyrimidine).	131.54-138.37(C-NO_2), 114.8-126.9(CH-Ar), 144.2(C-Ar),162.9(C-pyrazolidine),188.6(C=S,urea),49.6(C-CH_3, pyrazolidine),15.7(CH_3), 51.9(CH),36.6(CH-NH, pyrimidine),135.3(C-Ar),130.2-116.8(CH-Ar), 148.7(C-Ar).	430$[M]^{\cdot+}$

In Vitro Anti–Microbial Screening: The synthesized compounds were subjected to antimicrobial screening by Broth Dilution Method for Minimum inhibition concentrations (MIC). The Antibacterial activity was tested against various gram positive and Gram negative bacteria and anti fungal activity against various fungal strains compared with standard drug (Ampicillin and Griseofulvin).

Antimicrobial Activity: Each synthesized drug was diluted obtaining 2000 microgram /ml concentration, as a stock solution.

Primary screen: In primary screening 1000 micro/ml, 500 micro/ml, and 250 micro/ml concentrations of the synthesized drugs were taken. The active synthesized drugs found in this primary screening were further tested in a second set of dilution against all microorganisms.

Secondary screen: The drugs found active in primary screening were similarly diluted to obtain 200 micro/ml 100 micro/ml, 50 micro/ml, 25 micro/ml, 12.5 micro/ml, 6.250 micro/ml, and concentrations.

Reading Result: 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.

Commercial antibacterial Amphicilin and antifungal Griseofulvin were also screened under similar condition for comparison. In our study, new series of compounds namely substituted Pyrazolidines (3,4a-d) showed moderate to significant antibacterial and antifungal activity when compared

with standard drugs. However it is less than standard drugs like Ampicillin and Griseofulvin but compounds 3c, 3d, 4a, 4b, 4c Showed significant antibacterial activity and 3d, 4c and 4d Showed significant antifungal activity when compared to standard drug. The effect of synthesized pyrazoles and pyrimidines on bacterial and fungal strains are summarized in table 3.

Results 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). It is also supported by ^1H NMR signal for 8.24 δ (1H, s, NH). The compound (1) was treated with various aromatic aldehydes in the presence of KOH to give (4-(substituted benzylidene)-2-(2,4-dinitrophenyl)-5-methylpyrazolidin-3-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 6.45-7.18 ppm and =C-H stretching frequency at 3052-3175 cm^{-1}.

Compounds (2a-d) were used as intermediate for the synthesis of compounds (3a-d) and (4a-d). In first pathway, pyrazole derivatives (3a-d) were synthesized by treating compounds (2a-d), with hydrazine hydrate in acidic medium. The products were confirmed by the appearance of IR bands at 1621-1620 cm^{-1} for C=N stretching, whereas NMR signal was disappeared at 7.16-8.15 ppm due to =C-H.

In second pathway formation of pyrimidine derivatives were synthesized by compound 2a-d with thiourea in basic medium. Formation of 4a-d were explained by the appearance of bands at 1144-1157 cm^{-1} due to (C=N str.) and disappearance of band at 3052-3175 cm^{-1} due to (=C-H) in IR spectrum. The compounds were confirmed by the appearance of IR band at 1644-1657 cm^{-1} for C=N stretching and C=O band is replaced by C=S bond which, confirmed by an IR band at 1242-1255 cm^{-1}. The NMR signal of =C-H at 7.16-8.15 ppm is disappeared.

Conclusion

5-Membered *N*-heterocycles such as pyrazolidine and pyrazole are important structural motifs in an extensive number of biologically active compounds. They are of exceptional interest in the pharmaceutical industry, as they appear in the core structure of several drugs. 6-Membered aromatic rings containing two nitrogen atoms, such as pyrimidines and pyridines possess a broad spectrum of biological activities and are therefore of interest as target compounds in pharmaceutical and medicinal chemistry. In conclusion, the preparation procedure follows in this work for synthesis of new pyrazolidine derivatives via substituted Chalcones offers reduction in the reaction time, operation simplicity, cleaner reaction, easy work-up and improved yields. In this work, we have reported different substituted pyrazolidine derivatives, which were characterized by IR and ^1H NMR spectral analysis. Synthesized compounds were screened for their antifungal and antibacterial activity.

Table-3
Minimum inhibition concentration of synthesized compounds

Compd.	R	Bacteria				Fungi		
		E. coli **(MTCC 443)**	***S. aureus*** **(MTCC 441)**	***P. euroginosa*** **(MTCC 96)**	***S.pyogenus*** **(MTCC 442)**	***A. nigar*** **(MTCC 282)**	***C. albicans*** **(MTCC 227)**	***A. clavatus*** **(MTCC 1323)**
3a	4-OH-C_6H_4	250	200	250	200	500	1000	1000
3b	4-Cl-C_6H_4	200	125	250	250	1000	1000	500
3c	3-NO_2-C_6H_4	125	**100**	**62.5**	250	500	250	250
3d	4-F-C_6H_4	250	**62.5**	125	**100**	**250**	250	500
4a	4-OH-C_6H_4	250	**62.5**	250	500	1000	1000	250
4b	4-Cl-C_6H_4	**62.5**	200	100	125	500	1000	1000
4c	3-NO_2-C_6H_4	**100**	**62.5**	125	200	**250**	500	**250**
4d	4-F-C_6H_4	200	250	**100**	125	500	**250**	1000
				Standards				
1	Amphicilin	100	250	----	100	-	-	-
2	Griseofulvin	-	-	-	-	500	100	100

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