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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME PYROZOLIDINE DERIVATIVES

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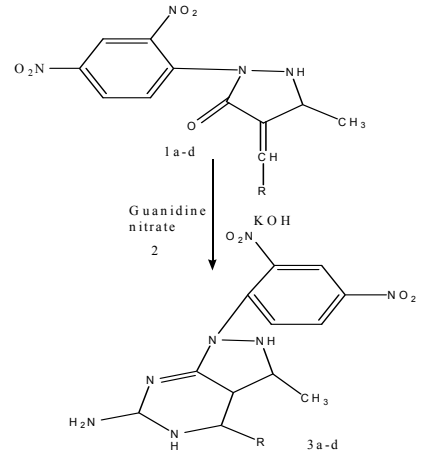
ABSTRACT
Pyrazolidine derivatives (3a-d) were synthesized by reacting the chalcones (1a-d) with Guanidine nitrate (2) in presence of potassium hydroxide in ethanol. These derivatives were screened for their antimicrobial activity against different microorganism.The structures of synthesized compounds were established on the basis of elemental analysis IR, ^{1}HNMR, Mass and ^{13}CNMR spectra.

KEY WORDS : Pyrazolidine,Chalcones, pyrazole, pyrimidine, antimicrobial.

INTRODUCTION
Pyrazolidine derivatives are well established in the literature as important biologically active heterocyclic compounds[i-ii].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[iii-vi].α ,ß-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: 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. 1H NMR spectra (DMSO-d_6) were taken on a Bruker DRX spectrometer (300MHz, FT NMR) using TMS as internal standard and chemical shift were expressed in δ. The starting compounds were prepared according to reported method.



3a R= 4-OH-C_6H_4,3b R= 4-Cl-C_6H_4, 3c R=3-NO_2-C_6H_4, 3d R=4-F-C_6H_4.

Scheme-1

Synthesis of pyrazolidine derivatives

Synthesis of 1-(2, 4-dinitrophenyl)-4-(substitutedphenyl)3-methyl-1,2,3,3a,4,5-hexahydropyrazolo[3,4-d]pyrimidine-6-amine (3a-d): Mixture of compound **1a-d** (0.01 mol) and guanidine nitrate (0.01 mol) with KOH (2-3 drops) in ethanol(20ml) the well-stirred mixture was refluxed on oil bath at 70-80^{0}C for 6 hours. 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.

Synthesis of 1-(2, 4-dinitrophenyl)-4-(4-hydroxyphenyl)3-methyl-1,2,3,3a,4,5-hexahydropyrazolo[3,4-d]pyrimidine-6-amine (3a); MP 252-254^{0}C **yield**,70 % ,**IR(cm^{-1})** 3212 (N-H str.), 1510 (N-H bending), 2850(CH_3), 1560(C=C ring skeleton Ar. moiety), 1657(C=N str.),3415 (OH), 1340-1200 (C-NH_2 str.). **^{1}HNMR (400MHz,DMSO$_6$)** δ **ppm** 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),6.38(s,2H,NH_2), 5.9(OH).**^{13}CNMR** 131.12-138.3(C-NO_2),114.8-126.9(CH Ar),144.7(C)162.7(Cpyrazolidine), 188.7(CHNH_2),49.7(CCH_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).413$[M]^{\cdot+}$ $C_{18}H_{19}N_7O_5$ Anal. Calcd/Found **C:**52.29/52.30 , **H:**4.62/4.60 , **N:**23.72/23.70

Synthesis of 1-(2, 4-dinitrophenyl)-4-(4-chlorophenyl)3-methyl-1,2,3,3a,4,5-hexahydropyrazolo[3,4-d]pyrimidine-6-amine (3b) ;Yield 64% **, MP** 170-172^{0}C, **IR(cm-1)** 3412 (N-H str.), 2782(CH_3),1593(N-H bending),1562(C=C), 1650(C=N str.),748(C-Cl), 1342-1220(C-NH_2 str.). **^{1}HNMR(400MHz,DMSO)** δ **ppm** 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(NHpyrimidine),6,35(s,2H,NH_2). **^{13}CNMR** 131.22-138.3(C-NO_2), 114.2-126.4(CH-Ar),144.6(C Ar),162.6(C pyrazolidine),188.2(CH-NH_2), 49.6(CCH_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). **MS** 431$[M]^{\cdot+}$ MF $C_{18}H_{18}ClN_7O_4$ Anal. Calcd/Found **C:** 50.06/50.05 , **H:**4.19/4.19 ,**N:**22. 70/22.71

Synthesis of 1-(2, 4-dinitrophenyl)-4-(3-nitrophenyl)3-methyl-1,2,3,3a,4,5-hexahydropyrazolo[3,4-d]pyrimidine-6-amine (3c); Yield 77% **MP** 170-172, **IR(cm^{-1})** 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), 1345-1215 (C-NH_2)str.).**^{1}HNMR(400MHz,DMSO)** δ **ppm** 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) ,6.30(s,2H,NH_2), **^{13}CNMR** 131.33-138.30(C-NO_2), 114.80-126.8(CH-Ar),144.1(C-Ar),162.9(Cpyrazolidine),188.5(CH-NH_2),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). **MS** 442$[M]^{\cdot+}$ MF $C_{18}H_{18}N_8O_6$. Anal Calcd/Found **C:**48.87/48.85, **H:**4.09/4.08, **N:**25.35/25.33

Synthesis of 1-(2, 4-dinitrophenyl)-4-(4-fluorophenyl)3-methyl-1,2,3,3a,4,5-hexahydropyrazolo[3,4-d]pyrimidine-6-amine (3d) ; Yield 80% **MP** 175-178^{0}C, **IR(cm^{-1})** 1585(N-H bending), 3312(N-H str.), 2792(CH_3), 1568(C=C), 1644(C=N str.),1184 (F), 1345-1215 (C-NH_2 str.). **^{1}HNMR(400MHz,DMSO)** δ **ppm** 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) ,6.40(s,2H,NH_2),**^{13}CNMR** 131.54-138.37(C-NO_2), 114.8-126.9(CH-Ar),144.2(CAr),162.9(Cpyrazolidine),188.6(CH-NH_2), 49.6 (CCH_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). **MS** 415$[M]^{\cdot+}$ MF $C_{18}H_{18}FN_7O_4$ Anal.Calcd/Found **C:**52.04/52.05 ,**H :**4.36/4.35, **N:**23.62/23.60

BIOLOGICAL EVALUTION

Evaluation of Antimicrobial Activity:

The in–vitro antimicrobial activity of compounds (3a-d) were determined by agar cup plate method , The results of which are summarized in Table -1

.

Table-1 Antibacterial and Antifungal data of compound (3a-d)

	Zone of inhibition in mm							
Compound	S.aures		E.coli		C.albicans		A.niger	
	50 ug	100 ug	50 ug	100ug	50 ug	100 ug	50 ug	100 ug
3a	14	16	13	14	14	16	13	15
3b	18	17	17	19	19	22	16	18
3c	14	17	13	17	22	20	12	14
3d	15	20	12	12	22	23	19	22
Ciprofloxacin	20	24	20	24	-	-	-	-
Griseofulvin	-	-	-	-	20	24	20	24

RESULTS AND DISCUSSION

Antimicrobial Activity :

The in-vitro antimicrobial activity of compounds(3a-d) were determined by agar plate method .The results of which are summarized in table- 1. The antimicrobial data in table -1 clearly showed that the halogen nitrophenyl, hydroxyphenyl groups is by for the most active substituted phenyl group .The chlorophenyl group generally confers weak antimicrobial activity. Phenyl

substitution are weakly active to inactive among the synthesized compounds . Compounds 3b, 3c & 3d showed good activity against S.aureous and E.coli. The compounds 3a & 3b exhibit promising activity against C. albicans and A. niger. However, the compounds were less active in comparison to Ciprofloxacin and Griseofulvin (standard Durgs).

CONCLUSION

In conclusion, the results of this investigation revealed that the observed increase in antimicrobial activities are attributed to the presence of , 4-OH, 4-Cl ,3-NO_2 , 4-F in phenyl ring at 4- position of pyrimidine ring of synthesized compounds containing pyrozolidine. it is clear that the comparative evaluation of active compounds will required further studies ; the data reported in this article may be helpful guide for the medicinal chemist who are working in this area.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 workup 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.

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REFERENCES

i. Al-Abdullah E. S., *Molecules,* **16,** 3410**(2011)**

ii. Shah S. H. and Patel P. S., *J. Chem. Pharma. Res.,* **4,**2096**(2012)**

iii. Bouabdallah I., Mbarek L. A., Zyad A., Ramadan A.,Zidane I. and Melhaoui A., *Nat. Prod. Res.,* **20,**1024**(2006)**

iv. Michon V., Du Penhoat C. H., Tombret F., Gillardin J. M.,Lepagez F. and Berthon L., *Eur. J. Med. Chem.*147**(1995)**

v. Yildirim I., Ozdemir N., Akcamur Y., Dincer M. and Andac O., *Acta Cryst.,* **61,** 256**(2005)**

vi. Bailey D. M., Hansen P. E., Hlavac A. G., Baizman E. R.,Pearl J., Defelice A. F. and Feigenson M. E., *J. Med. Chem.,* **28,** 256**(1985)**

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