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Synthesis of New Pyrazoline Derivative & Its Antimicrobial Activity

Pooja Jagtap[1]*, Bhushan Pawar[1], Adhikrao Yadav[1], Nilam Pawar[1]

1.Gourishankar Institute of Pharmaceutical Education & Research, Limb, Satara, Survey No.990,NH-4,A/P.-Limb,Tal.&Dist.-Satara- 415 015

ABSTRACT

Some novel series of pyrazoline derivatives were synthesized from Chalcones. Chalcones were prepared by treatment of Paracetamol with different aldehyde by Claisen-Schimidt Condensation. Various Pyrazoline derivatives were prepared by reflux reaction of Chalcone with Phenyl Hydrazine/Hydrazine Hydrate in ethanolic solution. The structures of the newly synthesized Pyrazoline derivatives have been established on the basis of their spectral data. Structures of compounds were confirmed by IR, H1 NMR. The synthesized selected compounds were screened for their antimicrobial activity.

Keywords: Pyrazoline, Chalcones, Antimicrobial activity.

*Corresponding Author Email: jagtappooja3496@gmail.com

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INTRODUCTION

Due to the rapid development of bacterial resistance antibacterial agents, it is vital to discover novels caffold for the design and synthesis of the new antibacterial agents to help in the battle against pathogenic microorganisms [1].The recent success of pyrazole COX-2 inhibitor has further highlighted the importance of these heterocycles in medicinal chemistry. A systematic investigation of this class of heterocyclic lead revealed that pyrazole containing pharmaco active agents play important role in medicinal chemistry**.** Chalcones represent an essential group of natural as well as syntheticproducts[2]. Pyrazoline derivatives have displayed wide range of biological and pharmacological activities asanalgesic, anti-inflammatory, antipyretic, antiparasitic, antimalarial, antifungal, antimicrobial[3]. The presence of reactive α, β-unsaturated keto group in chalcones is found to beresponsible for their biological activity. In the present work chalcones have been prepared according to claisen-schimidt condensation by condensing various ketones with aromatic aldehyde[4-5].

The prevalence of pyrazole cores in biologically active molecules has stimulated the need for elegant and efficient ways to make these heterocyclic lead. The treatment of pain continues to be the subject of considerable pharmaceutical and clinical research. Microbial infections often produce pain and inflammation. Chemotherapeutic, analgesic and anti-inflammatory drugs are prescribed simultaneously in normal practice [6-7].

MATERIALS AND METHOD

Procedure:

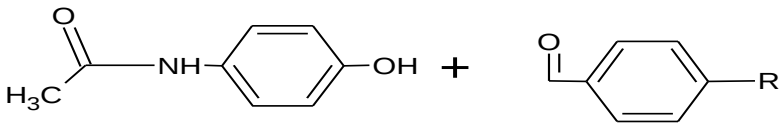
General procedure for synthesis of chalcones[8]:-

A solution of 22g of sodium hydroxide in 200ml of water and 100g(122.5ml) of rectified spirit was kept in a bath of crushed ice, (0.43mol) of freshly distilled aromatic ketone was added with stirring, and then (0.43mol) of pure aromatic aldehyde was added drop wise with stirring, temperature of the mixture was maintained at about 25°Cand stirred vigorously until the mixture is so thick that stirring is no longer effective (2-3 hrs), reaction mixture was removed and kept in the refrigerator overnight. The product was filtered, washed with cold water until the washings are neutral to litmus. The crude chalcone, after drying in the air was recrystallized from rectified spirit.

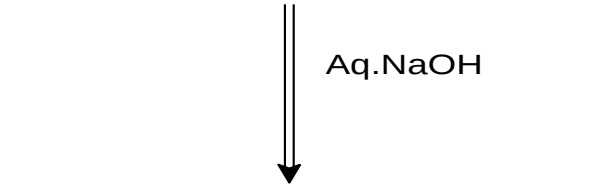
General procedure for synthesis of Pyrazoline derivatives[9]:-

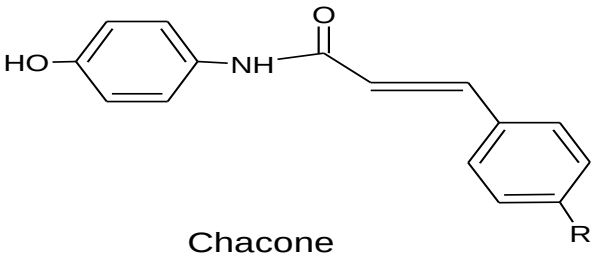
A mixture of chalcone (5mmoles) and hydrazine hydrate (5mmoles) was dissolved in absolute alcohol (25ml) and refluxed for 9-10 hrs. The reaction mixture was poured onto crushed ice and

stirred, the solid thus obtained was filtered off and washed with water and taken for the next step immediately.



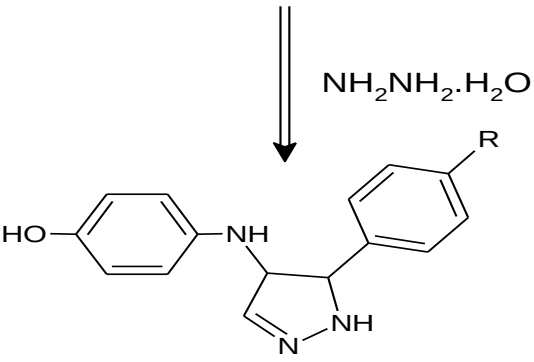
Paracetamol Aldehyde





Chacone

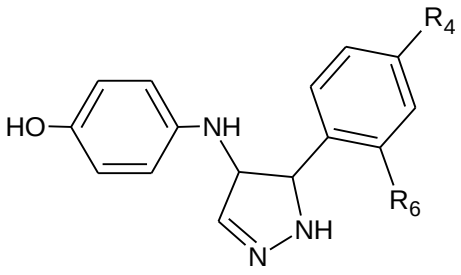
3-n-phenylphenyl-2-propenamide



5-(4-R_1phenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine

Pyrazoline

REACTION:-



5-(4-R phenyl)-N-phenyl-4, 5-dihydro-1H-pyrazol-3-amine

Table 1: Observation table

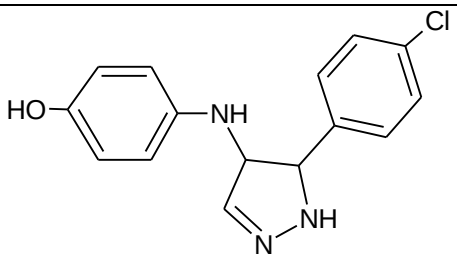
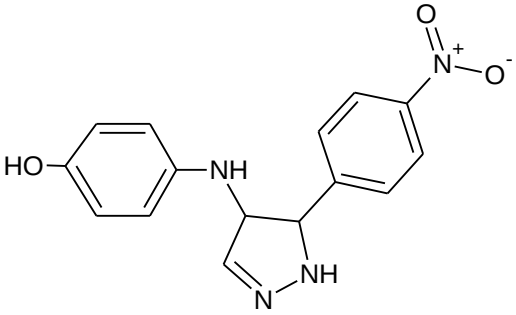
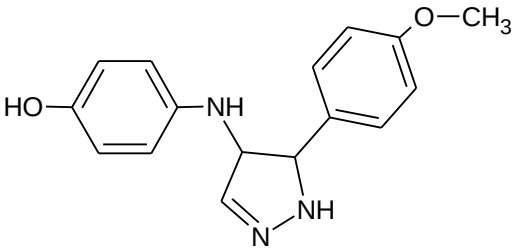
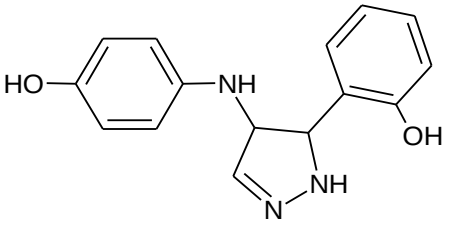
R_4	R_6	Structure	% yield	Molecular formula	Molecular weight	Melting point(^{o}c)
Cl	H	 5-(4-chlorophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	78%	$C_{15}H_{13}N_3OCl$	287	190-192
NO_2	H	 5-(4-nitrophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	80%	$C_{15}H_{13}O_3N_4$	297	182-184
OCH_3	H	 5-(4-methoxyphenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	75%	$C_{16}H_{16}N_3O_2$	282	143-145
H	OH		66%	$C_{15}H_{14}O_2N_3$	268	164-166

Table 2: Spectroscopic Evaluation

Name of compound	Functional Group	Value
3-(4-chorophenyl)-n-phenyl acrylamide Chalcone	Ar. C-H (str.)	3053.32
	C=O	1685.79
	C=C	1583.56
	C-Cl	704.02
	C-N	1286.52
5-(4-chlorophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	Ar. C-H (str.)	3045.6
	C=C	1581.63
	C-Cl	709.04
	N-H	3350.35
	C-N	1284.59
3-(4-nitrophenyl)-N-phenylacrylamide (Chalcone)	Ar. C-H (str.)	3051.39
	C=O	1602.85
	C=C	1602.85
	Ar.-NO_2	1529.55
	C-N	1340.53
5-(4-Nitrophenyl)-N-phenyl-4, 5-dihydro-1H-pyrazol-3-amine	Ar. C-H (str.)	3105.39
	C=C	1595.13
	Ar-NO_2	1517.98
	N-H	3388.93
	C-N	1334.74
5-(2-hydroxyphenyl)-N-phenyl-4, 5-dihydro-1H-pyrazol-3-amine	Ar. C-H (str.)	3045.6
	C=C	1570.06
	-OH	2945.3
	N-H	3352.28
	C-N	1327.03

NMR spectroscopy:

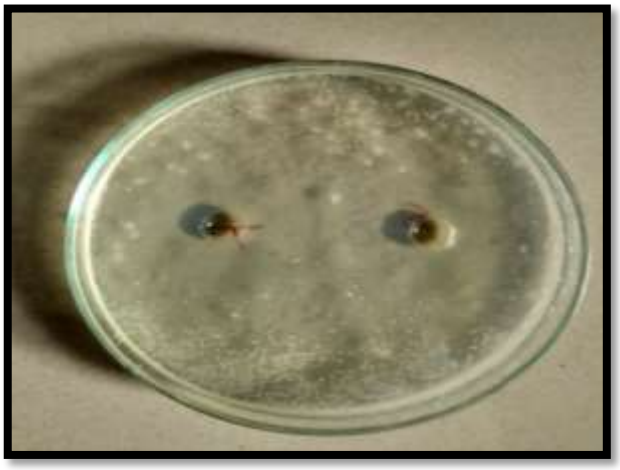
Table 3: 5-(4-Nitrophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine

Sr.No	Spectral Data	δ ppm
1	-CH_2	2.93
2	-Ar -CH	4.00
3	-NH	5.615
4	-Ar - Benzene	8.179

Antimicrobial activity:-

5-(4-chlorophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine

5-(4-Nitrophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine



5-(2-hydroxyphenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine

Figure 1: Photographs of antimicrobial activity

Table 4: Antimicrobial activity data of pyrazoline derivatives is represented in table

Plate no.	Compounds	Zone of inhibition (mm)	
		Test	Standard(Ciprofloxacin)
1	5-(4-chlorophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	21.5	19.2
2	5-(4-Nitrophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	25	24.3
3	5-(4-hydroxyphenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	24.5	19.8

Table 5: Mobile phase used for TLC is Toluene: Acetone: Ammonia (7:3:0.1)

Sr. No.	Name of compounds	Rf Value
1	5-(4-chlorophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	0.62
2	5-(4-Nitrophenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	0.74

3	5-(4-methoxyphenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	0.59
4	5-(4-hydroxyphenyl)-N-phenyl-4,5-dihydro-1H-pyrazol-3-amine	0.60

RESULT AND DISCUSSION

The compounds were synthesized according to the procedures as given in the experimental section. The purpose of the present study was to examine whether molecular modification might result in detection of new potential antimicrobial drugs. A series of compounds were prepared and assayed in a biological test for antimicrobial activity. The compounds were further characterized by IR and H^1 NMR. All synthesized pyrazoline derivatives shows antimicrobial activity. These compounds are found to be active against staphylococcus aureus (Gram-positive).

CONCLUSION

In conclusion, the results of this investigation revealed that the observed increase in antimicrobial activities are attributed to the presence of 4-NO_2, 4-Cl, 4-OCH_3, and 2-OH in phenyl ring at 5-position of pyrazoline ring of synthesized compounds. .Obviously, 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.

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