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Research Article

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Synthesis, Characterization, and Antimicrobial Activity of Some New N- Pyrazoline derivatives from Chalcones.

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Abstract

In the present work various Chalcones were condensed with hydrazine hydrate in ethanol to get the corresponding pyrazolines (4a-j) by refluxing for 4-5hrs. The compounds were synthesized and characterized by TLC, melting points, IR, and ^{1}H-NMR spectra. All the synthesized compounds have been screened and evaluated for antibacterial activity against *Staphylococcus aureus gr +ve*, *Escherichia coli gr –ve, Bacillus subtilis gr +ve, Salmonella typhi gr –ve* , and antifungal activity against *Aspergillus oryzoe, Aspergillus niger*, using disc diffusion method. Synthesis and biological evaluation of pyrazolines have been a topic of special interest to organic and medicinal chemists

Keywords: Pyrazoline, Synthesis, Antibacterial activity, Antifungal activity.

Introduction

Pyrazoline derivatives constitute an interesting class of organic compounds. By the literature review we saw pyrazoline nucleus is quite stable and has inspired chemists to utilize these stable fragments in bioactive moieties to synthesize new compounds possessing biological activities[1,2]. The biological activity of Pyrazolines due to the presence of important nitrogen containing heterocycles possessing diverse activity[3]. So Several pyrazoline derivatives possess important pharmacological activities. like antimicrobial, anti-inflammatory, analgesic, antidepressant,antitubercular and antimalarial activities[4-8]. Many of the therapeutically useful compounds such as phaenylbutazone, oxyphenbutazone, celecoxib, belonging to pyrazoles exhibited antipyretic, anti inflammatory and analgesic properties[9]. Among various pyrazoline derivatives, 2-pyrazolines seem to be the most frequently studied pyrazoline type compounds. Earlier studies by Ratnadeep et al, demonstrated analgesic activity of 3,2-(4,5- dihydro-5-(4-morphilinophenyl)-1H-pyarazol-3-yl)phenols[10], Suresh et al, reported a novel series of 5-substituted aryl-3-(3-coumarinyl)-1-phenyl-2-pyrazolines as novel antiinflammtory and analgesic agents[11], Manna et al, reported analgesic and antipyretic activity of some new N-acetyl-Δ2-pyrazolines and dihydrothieno coumarines[12]. The reaction of an α, β-unsaturated ketone with phenylhydrazine became a generally used, simple and convenient procedure for the synthesis of pyrazolines[13]. The derivatives of pyrazoline are used in applications such as dyestuffs, analytical reagents and as agrochemicals.[14]

Materials and Methods

The purity and completion of reaction was monitored by TLC .Melting points of the compounds were determined in open capillary tubes and are uncorrected, IR Spectra were recorded on Shimadzu FT-IR, the sample was

mixed with KBr and pellet technique was adopted to record the spectra in cm -1,^{1}H NMR spectra was determined on a Bruker Avance II 400 Spectrometer against TMS as internal standard DMSO-d6 as solvent. Mass spectra were recorded on waters Micromass Q-T of Micro spectrometry.

General procedure for the Synthesis of N-Substituted 2-Pyrazolines and their Derivatives

A mixture of 2'-hydroxychalcone and hydrazine hydrate in methanol was heated under reflux for 4-5 hour. After completion of the reaction, the reaction mixture was cooled and poured into ice cold water. The separated solid was filtered, washed with ice cold water, dried and recrystallized from ethanol. The purity of synthesised pyrazolines was checked by TLC. Their structures were assigned by spectral analysis (IR, ^{1}H NMR, and MS).

Scheme-1

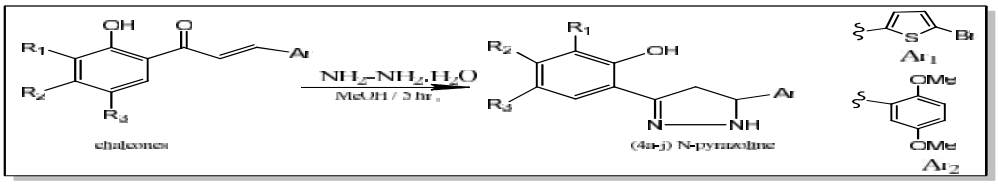


Table 1: Synthesis of N-Hydro-2-Pyrazolines

Comp.no	Entry	R_1	R_2	R_3	Ar
1	4a	I	H	I	Ar_1
2	4b	I	H	Cl	Ar_1
3	4c	I	H	CH_3	Ar_1
4	4d	I	H	Br	Ar_1
5	4e	Cl	H	I	Ar_1
6	4f	I	H	I	Ar_2
7	4g	I	H	Cl	Ar_2
8	4h	I	H	CH_3	Ar_2
9	4i	I	H	Br	Ar_2
10	4j	Cl	H	I	Ar_2

Results and Discussion

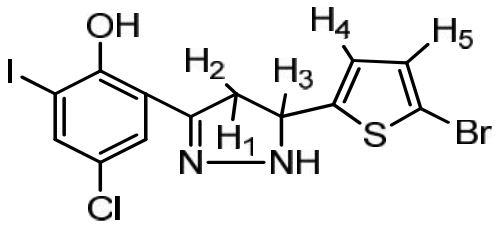
A variety of novel N-pyrazoline were synthesized of substituted chalcones with hydrazine hydrate in methanol. The reaction proceeded at room temperature. Work up procedure is simple and yield of the product is excellent.

All the newly synthesized N-pyrazolines were characterized by their chemical, physical and spectral analysis data and are further subjected to antimicrobial studies which exhibit moderate to good activity (Table. 2).

Table -2 Physical Data for Synthesised compounds (4a-j)

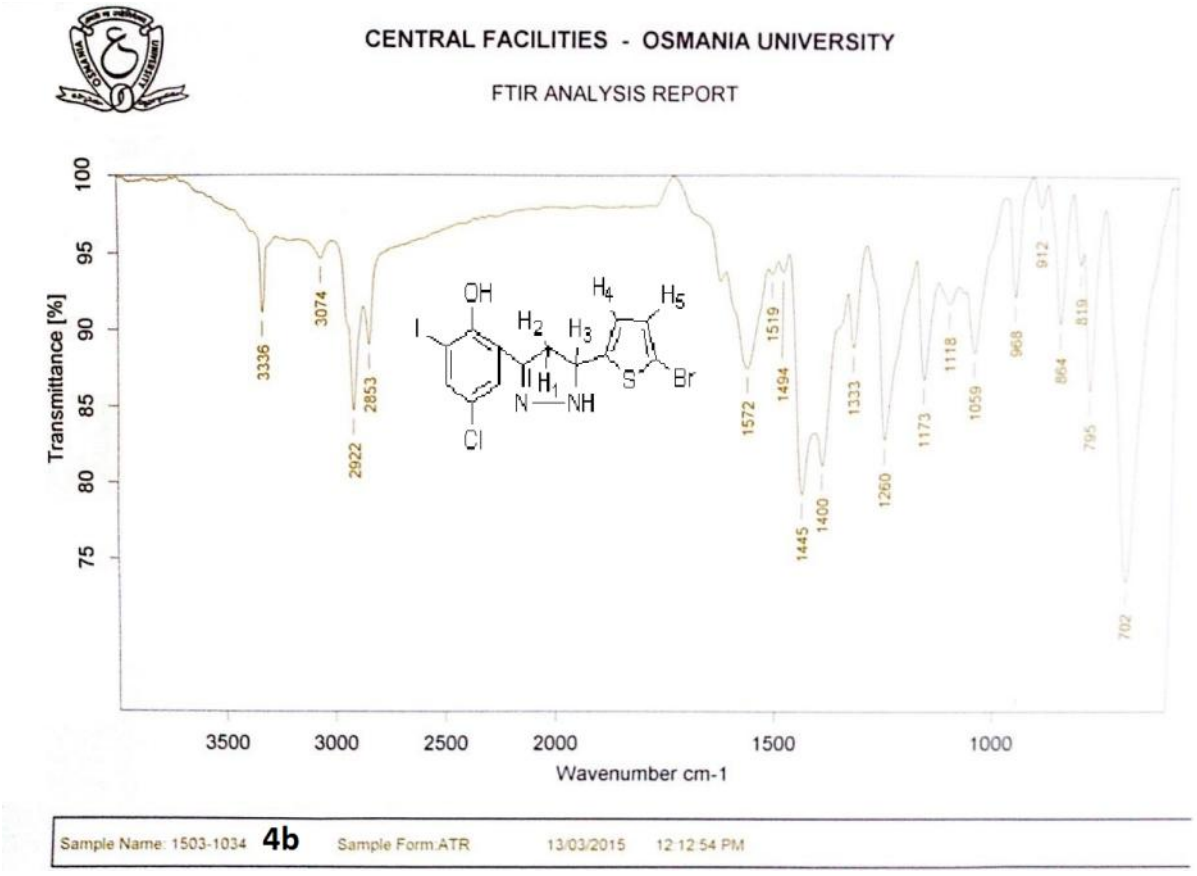
Comp.no	Product	Mol. Formula	Yield %	M.P.(°C)	Solubility
1	4a	$C_{13}H_9BrI_2N_2OS$	85	175-177	Methanol
2	4b	$C_{13}H_9BrClIN_2OS$	90	126-130	Methanol
3	4c	$C_{14}H_{12}BrIN_2OS$	75	140-142	Methanol
4	4d	$C_{13}H_9Br_2IN_2OS$	80	174	Methanol
5	4e	$C_{13}H_9BrClIN_2OS$	85	220	Methanol
6	4f	$C_{17}H_{16}I_2N_2O_3$	75	148-150	Methanol
7	4g	$C_{17}H_{16}ClIN_2O_3$	80	184-186	Methanol
8	4h	$C_{18}H_{19}IN_2O_3$	85	145	Methanol
9	4i	$C_{17}H_{16}BrIN_2O_3$	80	168-170	Methanol
10	4j	$C_{17}H_{16}ClIN_2O_3$	85	160-162	Methanol

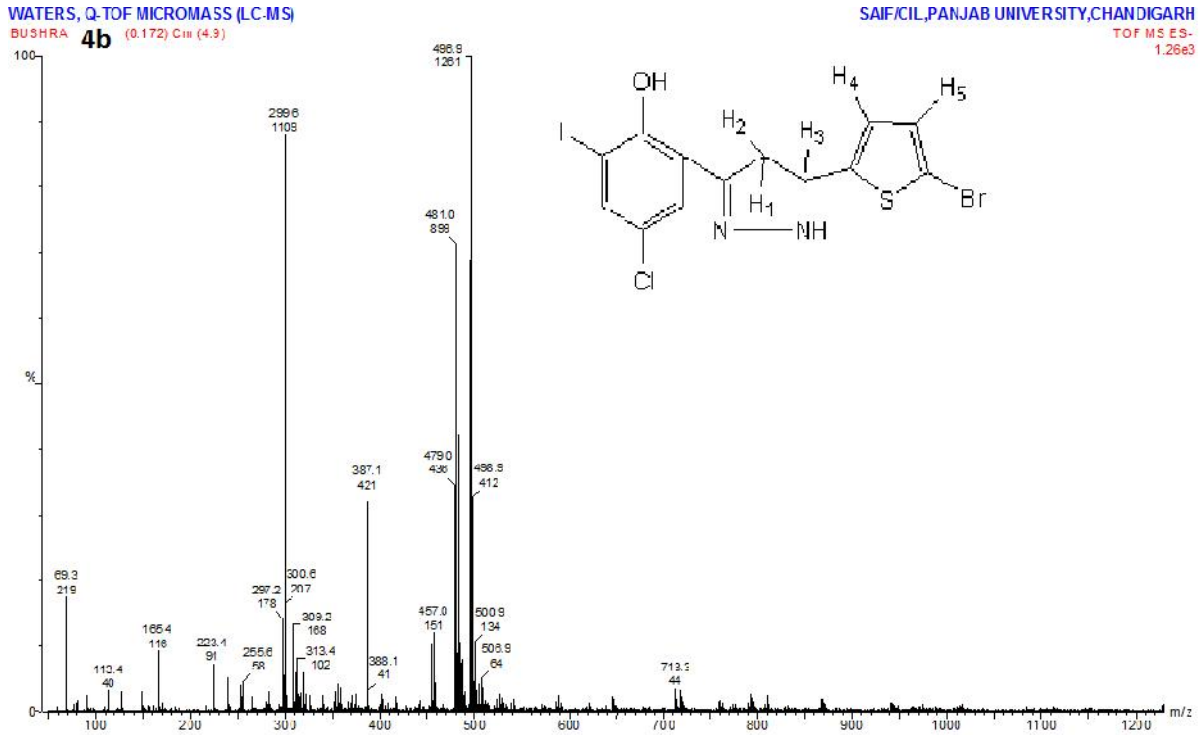
Spectral analysis of the selected compound

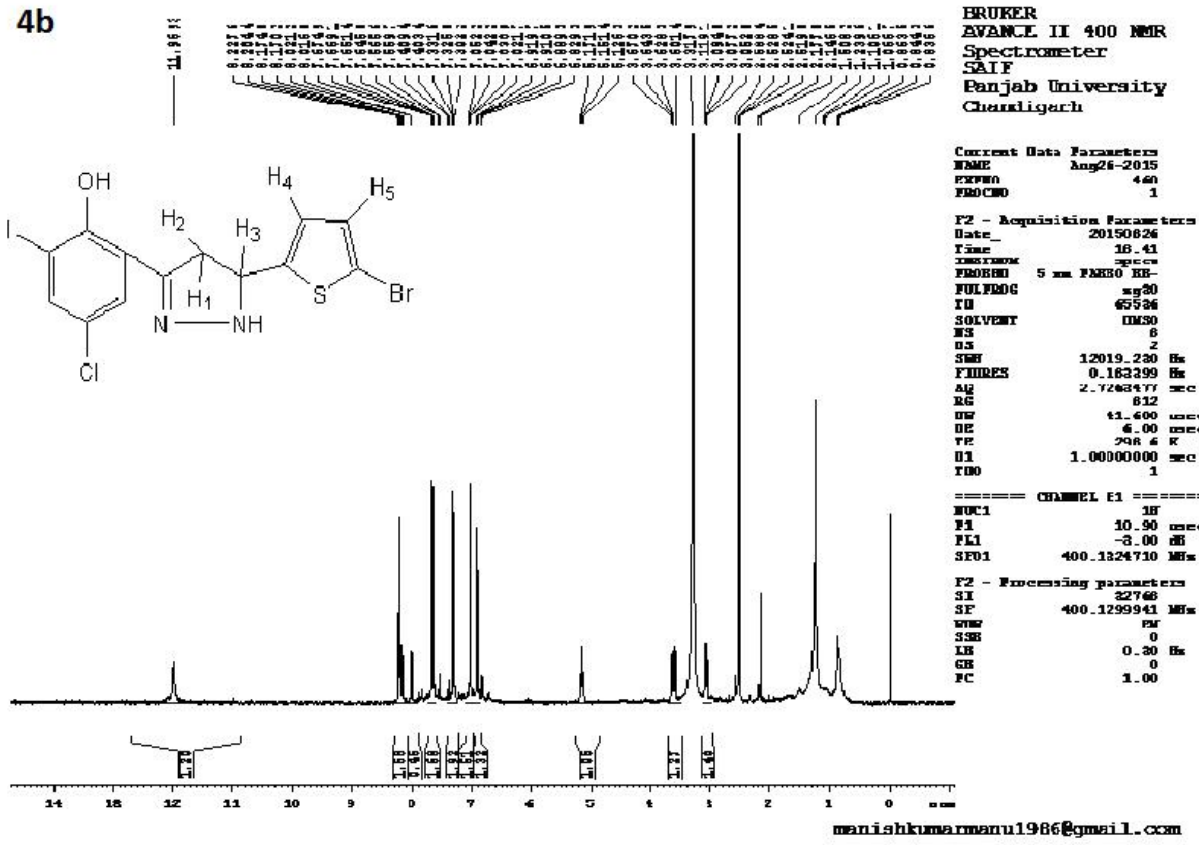


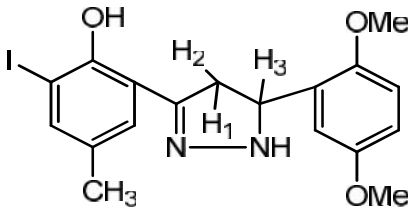
4b-2-(5-(5-bromothiophen-2-yl)-4,5-dihydro-1H-pyrazol-3-yl)-4-chloro-6-iodophenol

M.P=126-130^{0}C,Yield=90%
FTIR (KBr, cm-1): 3336(NH), 1572(C=N), 1445(C-C Aromatic str), 702(C-Br).
1HNMR:-3.09(dd, 1H_1, J=12Hz), 3.64(dd, 1H_2, J=12Hz), 5.12 (t,1H ,H_3 J=12Hz), 6.91(d,1H, H_5 ,J=3.6Hz),7.02(d, 1H,H_4,J=3.6Hz), 7.30 (s, 1H, H_7), 7.67(s, 1H, H_6), 8.20(s, 1H, NH), 11.96(s, 1H, OH).-
M.S. (m/z): (M) = 481 (M-2) .









4h

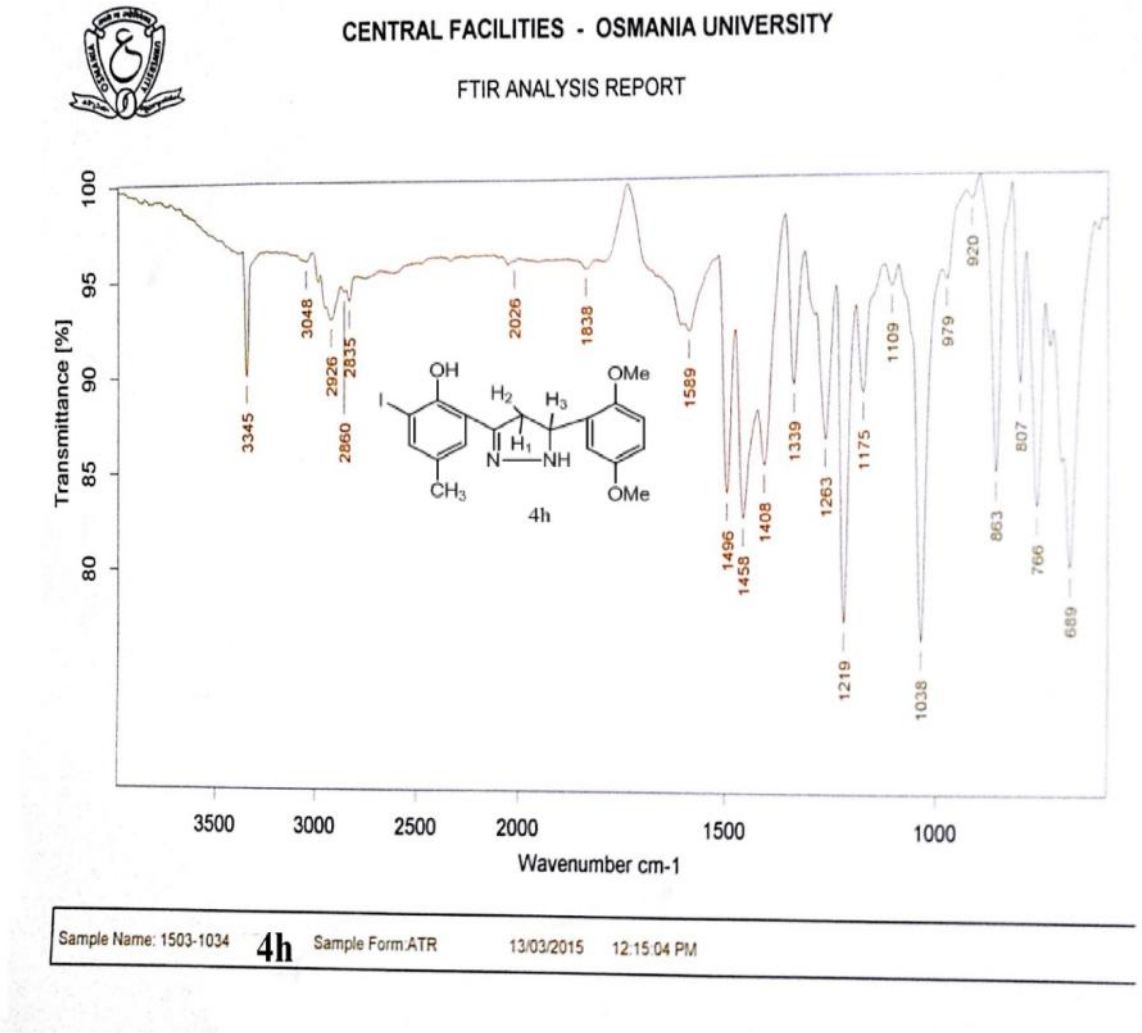
4h-2-(5-(2,5-dimethoxybenzyl)-4,5-dihydro-1H-pyrazol-3-yl)-6-iodo-4-methylphenol

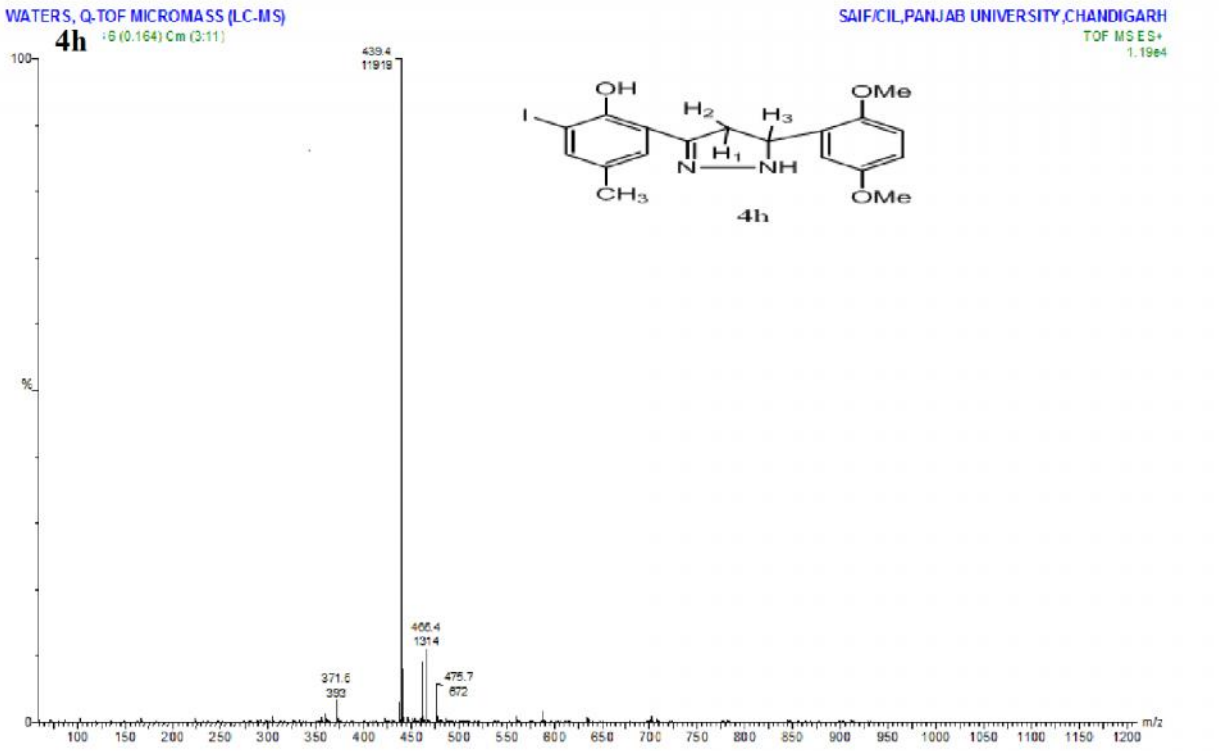
M.P=145^{0}C,Yield=85%

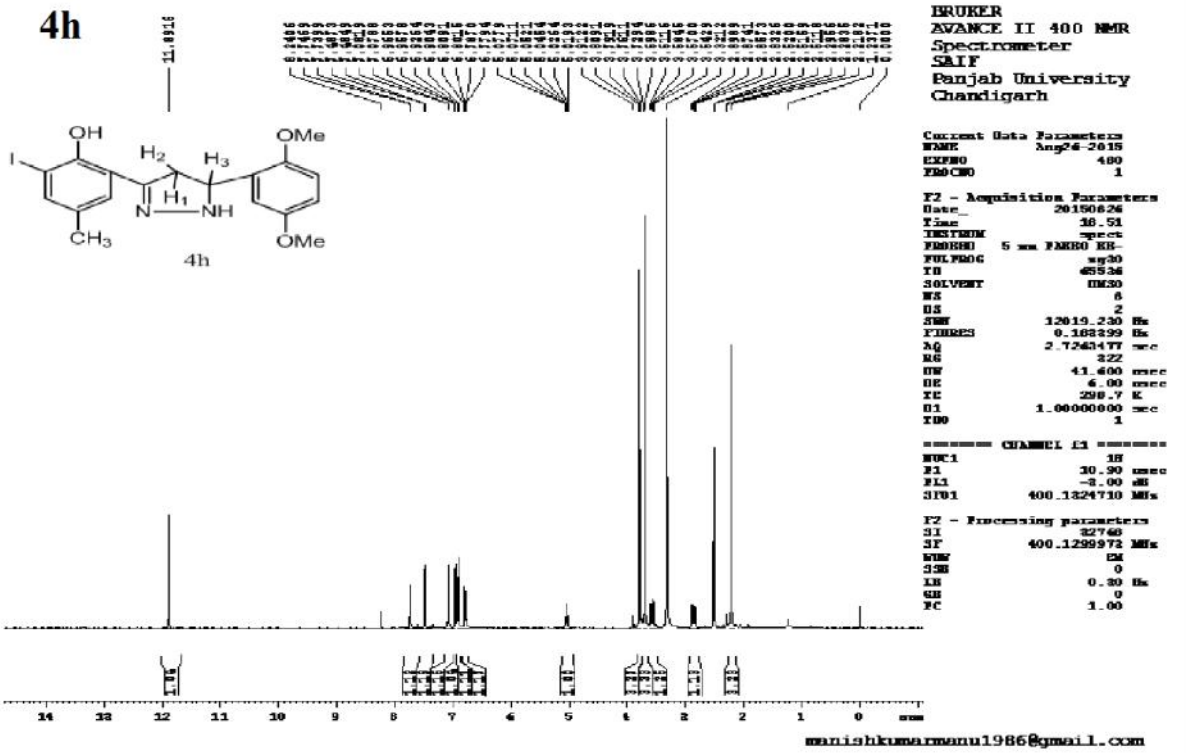
FTIR (KBr, cm-1): 3345(NH), 2926(OCH_3), 1589(C=N), 1458(C-C Aromatic str) .

1HNMR:- 2.21(s 3H, CH_3), 2.54(dd, $1H_1$, J=12Hz), 3.58(dd, $1H_2$, J=12Hz) 3.79(s, 6H, OCH_3), 5.07 (t,1H ,H_3 J=12Hz), 6.77-7.37(m, 5H, Ar-H), 7.48 (s, 1H, NH), 11.89(s, 1H, OH).

M.S. (m/z): (M) = 439 (M+1) .







Antimicrobial activity.

Antimicrobial screening was done using disc diffusion method [15] at a concentration of 100µg/ml. Procedure:- The test was performed according to the disk diffusion method [15] adopted with some modification for the prepared compound using Penicillin and streptomycin as references. The prepared compounds were tested against one strain of Gram +ve bacteria, Gram –ve bacteria, fungi. Whatman filter paper disk of 5mm diameter were sterilized by autoclaving for 15 min at 121^0C. The sterile disk were impregnated with different compounds (600gm/disk). Agar plates were surface inoculated uniformly from the both culture of the tested microorganism. The disk were placed on the medium suitably spaced apart on the plate were incubated at 50^0C for 1 hr to permit good diffusion and then transferred to an incubator at 37^0C. for 24hr for bacteria and 28^0C for 72hrs for fungi. The compounds were evaluated for antibacterial activity against *Staphylococcus aureus* gr +ve, *Escherichia coli* gr –ve *Bacillus subtilis* gr +ve, *Salmonella typhi* gr –ve, and antifungal activity against *Aspergillus oryae*, *Aspergillus niger.* DMSO was used as solvent control. The results of antimicrobial data are summarized in table 3, Figure 1.

Table 3. Antimicrobial activity of synthesized compounds

compounds	Gram positive bacteria		Gram negative bacteria		Fungus	
	Bacillus subtilis	***Staph aureus***	***S. typhi***	***Escherichia coli***	***Aspergillus oryzae***	***Aspergillus niger***
4a	+	+	-	-	-	-
4b	+	+	-	-	-	-
4c	+	+	-	-	-	-
4d	+	+	-	-	-	-
4e	+	+	+	-	-	-
4f	-	+	-	-	-	-
4g	+	+	-	-	-	-
4h	+	+	-	-	-	-
4i	+	+	-	-	-	-
4j	+	+	+	-	-	-
Penicillin 1	+	+	+	+	x	x
Streptomycin 2	++	++	++	++	x	x
Greseofulvin	x	x	x	x	-	-

+ = Minimum Zone of Inhibition , - = No Effect , X = Not applicable Standard 1 Penicillin + Standard 2 Streptomycin ++ (bacteria). Greseofulvin (fungus)

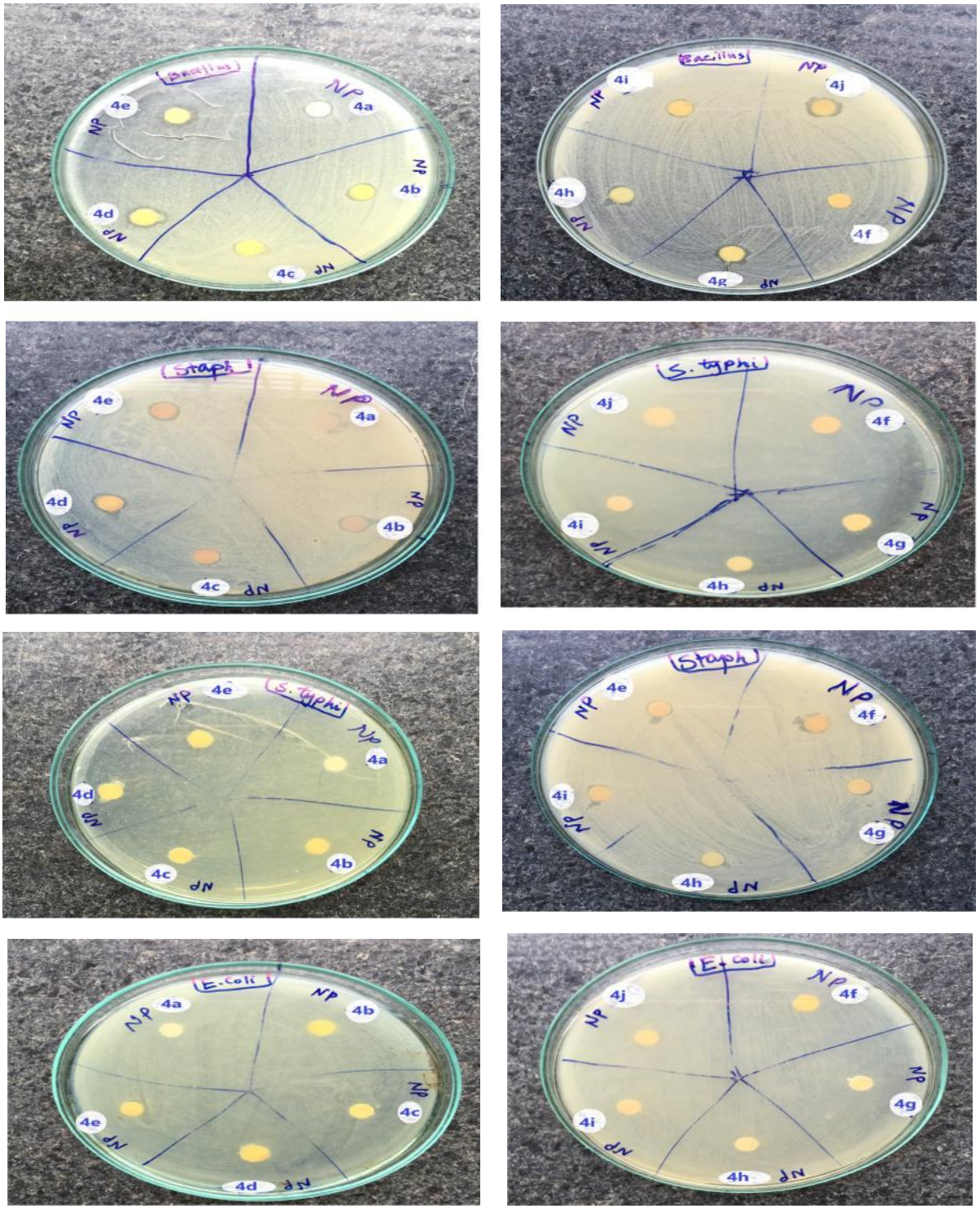


Figure 1. Antibacterial activity for synthesized compounds.

Conclusion

In conclusion, here we have reported some novel N-pyrazolines using orthohydroxy Chalcones with high yield. The newly synthesized N-pyrazolines were confirmed by spectral analysis and further evaluated for their antimicrobial activity. The antibacterial activity revealed that of the compounds showed moderate to good activity against the pathogens used, the result was negative on fungus.

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