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SYNTHESIS AND EVALUATION OF ANTI-BACTERIAL ACTIVITY OF N-PHENYLPIPERAZIN-1-AMINE DERIVATIVES

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ABSTRACT

The aim of the present work to the synthesis of different piperazine derivatives by using different aldehydes. The Structure of the synthesized compounds will be confirmed by spectral analysis like IR, NMR and Mass spetrum. The physical characterizations like molecular weight, melting point, R_f value and solubility of the synthesized compounds will be determined. The synthesized compounds will be subjected for Anti-bacterial evaluation.

KEYWORDS

Synthesis, Spectrum analysis, Physical characterizations and Anti- bacterial evaluation.

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INTRODUCTON

Antibacterial agents[1-3]

The synthetic or naturally occurring agents, which can kill or inhibit the growth of bacterial cells are called antibacterial agents.

In the year of 1935 was important in chemotherapy of systemic bacterial infections. The discovery of antibacterial activity of penicillin turned the attention of investigators to antibiotics as potentially useful chemotherapeutic compounds. In 1940's and 1950's Streptomycin, Tetracycline, Chloramphenicol, Polymyxin and Bacitracin greatly increased the range of effectiveness of antibacterial chemotherapy.

MATERIALS AND METHOD

Materials

The antibacterial screening was carried out in the Pharmaceutical Biotechnology laboratory and Pharma lab, Pondicherry. The following materials are used. Nutrient Agar, Beef Extract, Peptone and Sodium chloride.

Method[4,5]

Preparation of Compound

Synthesis of compound-1

A mixture of 12 gm of chloro aniline and 10.64 gm of aldehyde dissolved in sufficient quantity of ethanol. The preparation is boiled at 300 volts for 5-7 min in the microwave oven. After heating it is cooled in ice bath and water was added continuously till it becomes precipitate. The precipitate is filtered and dried at room temperature (Table No.1).

Synthesis of compound-2

A mixture of compound 1 is dissolved in 10 ml of DMF and Morpholine was dissolved in 5ml of DMF. The preparation is boiled at 300 volts for 3-5 min in the microwave oven. After microwave oven heating and cooled at room temperature and mixed with ice water by continuous stirring until the precipitate should be formed and the precipitate is filtered and dried (Table No.1).

Synthesis of compound-3

A mixture of compound 2 and sufficient quantity of Hydrazine hydrate dissolved in 25 ml of ethanol. It was heated at microwave oven at 100 volts for 3-5 mins. The mixture was cooled and poured in ice water by continuous stirring until precipitate should be formed it is filtered and dried. The product was recrystallized from ethanol[6] (Table No.1).

PREPARATION

Antibacterial Study

The ingredients were dissolved in water and adjust the pH value was 7.2 to 7.4 by using dilute alkali or dilute acid in autoclave at 121°C for 20 minutes. 30-35 ml of nutrient agar was transferred to a Petri dish.

Screening of Anti-bacterial activity

Bacterial strains of *Escherichia coil* (Gram –ve) and *Bacillus subtilis* (Gram +ve) were collected from Pharma lab, Pondicherry. 1000 µg/disc, 100 µg/disc and 10 µg/disc concentration of the test compounds are prepared and Dimethyl sulfoxide (DMSO) was used as vehicle. AMIKACIN (10 µg/disc) and KANAMYCIN (10 µg/ disc) was used as standards.

Nutrient agar plates were prepared aseptically to get a thickness of 5-6 mm. The plates were allowed to solidify and inverted to prevent condensate falling on the agar surface. The plates were dried at 37°C just before inoculation.

The standard inoculum medium is inoculated in the plates prepared earlier aseptically by dipping a sterile swab in the inoculum, removing the excess of inoculum by pressing and rotating the swab firmly against the sides of the culture tube above the level of the liquid and finally streaking the swab all over the surface of 60^0 angle after each application. Finally press the swab round the edge of the agar surface. The sterilized discs for the test drugs were placed in the Petri dishes aseptically. Incubate the Petri dish at 37°C for about 18-24 hrs, after placing them in the refrigerator for one hour to facilitate and uniform diffusion. The average zone of diameter of the plates were measured and recorded[7-11].

RESULTS AND DISSCUSION

Spectrum Analysis

The structures of all the compounds were confirmed by IR, ^{1}H NMR and Mass spectral studies (Table No.2-5).

Anti-bacterial activity

Bacterial strains of *Escherichia coil* (Gram –ve) and *Bacillus subtilis* (Gram +ve) were collected from Pharma lab, Pondicherry.1000 µg/disc, 100 µg/disc and 10 µg/disc concentration of the test compounds are prepared and Dimethyl sulfoxide (DMSO) was used as vehicle. AMIKACIN (10 µg/disc) and KANAMYCIN (10 µg/ disc) was used as standards. The obtained results in assessing the antibacterial activity were tabulated in the below Table No.6 and 7.

Activity against Gram Positive organisms

Compound $3a_1$, $3a_2$ and $3a_3$ at 1000 mg/ml was found to be great and good activity against *Bacilus subtilis*. Compound $3a_1$ at 100 mg/ml was found to have minimum activity against *Bacilus subtilis* (Figure No.1).

Activity against Gram negative organisms

Compound $3a_1$, $3a_2$ and $3a_3$ at 1000 mg/ml was found to be great and good activity against *Escherichia coli*.

Compound $3a_1$ and $3a_3$ at 100 mg/ml was found to have minimum activity against *Escherichia coli* (Figure No.1).

Table No.1: Synthesized different compounds

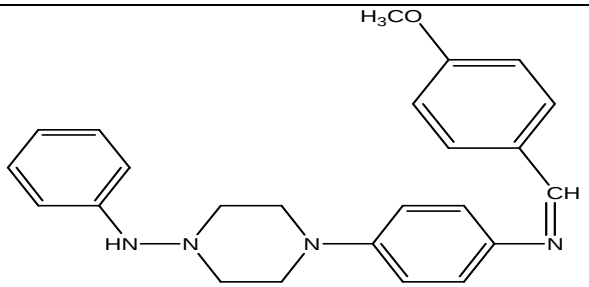
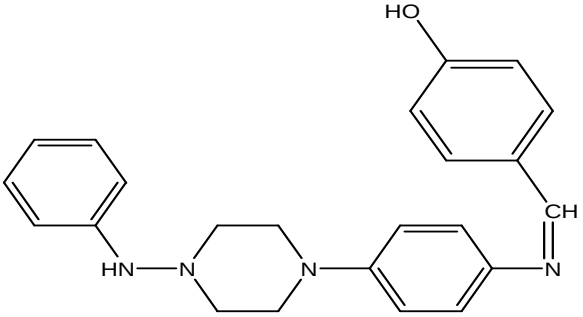
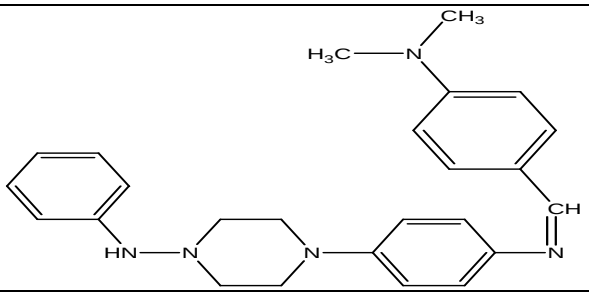
S.No	Compound code	Name	Structure
1	$3a_1$	4-(4-(4-methoxybenzylideneamino) phenyl)-N-phenylpiperazin-1-amine	
2	$3a_2$	4-((4-(4-(phenylamino) piperazin-1-yl) phenylimino) methyl)phenol	
3	$3a_3$	4-(4-(4-(dimethylamino)benzylidene amino)phenyl) -N-phenylpiperazin-1-amine	

Table No.2: IR Spectral Data of Compound $3a_1$

S.No	Frequency	Mode of vibration
1	3313	s C-H stretching
2	1601	N-H in plane bending
3	1361 - 1295	O-H in plane bending
4	1130- 992	C-H in plane bending
5	1314	m (C-N stretching)
6	808	s C-H out of plane bending

Table No.3: IR Spectral Data of Compound $3a_2$

S.No	Frequency	Mode of vibration
1	3301	m N-H stretching
2	1599	N-H in plane bending
3	1357	C-N stretching
4	1315	C-N stretching
5	1128-943	N-N stretching
6	829	s C-H out of plane bending

Table No.4: H^1 NMR Spectral Data of Compound $3a_1$ - $3a_2$

S.No	Compound Code	H^1 NMR (ppm) (300 MHz, $CDCl_3$)
1	$3a_1$	H^1 NMR (ppm):δ 7.0-8.0 (m,15H, Ar-H), δ 7.89-7.86 (d,1H,olefinic) J=9Hz, δ 7.69-7.66 (d,1H,olefinic) J=9Hz
2	$3a_2$	δ 7.0-8.0 (m,14H, Ar-H), δ 7.86-7.89 (d,1H,olefinic) J=9Hz, δ 7.47-7.50 (d,1H,olefinic) J=9Hz, δ 2.4 (s,3H, CH_3)

Table No.5: Mass Spectral Data of Compound $3a_1$ - $3a_2$

S.No	Compound Code	Mass fragmentation pattern
1	$3a_1$	386.49 (100.0%), 383.20 (25.2%), 379.20 (3.6%), 381.19 (1.5%)
2	$3a_2$	372.20 (100.0%), 373.20 (25.2%), 374.20 (3.6%), 373.19 (1.5%)

Table No.6: Antibacterial activity against of *Escherichia coli*

Organism used - *Escherichia coli* (Gram –ve)
Reference Standard - Amikacin

S.No	Compound code	Zone of inhibition in diameter (mm)			
		1000 µg /ml (A)	100 µg /ml (B)	10 µg /ml (C)	Standard (S)
1	Compound $3a_1$	16 mm	5 mm	-	23 mm
2	Compound $3a_2$	14mm	-	-	27mm
3	Compound $3a_3$	19mm	6 mm	-	30mm

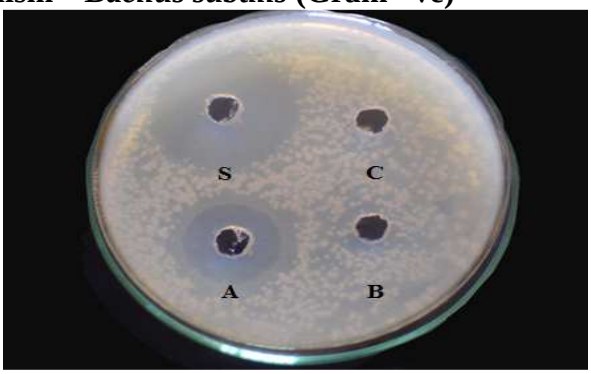
Table No.7: Antibacterial Activity against *Bacillus subtilis*

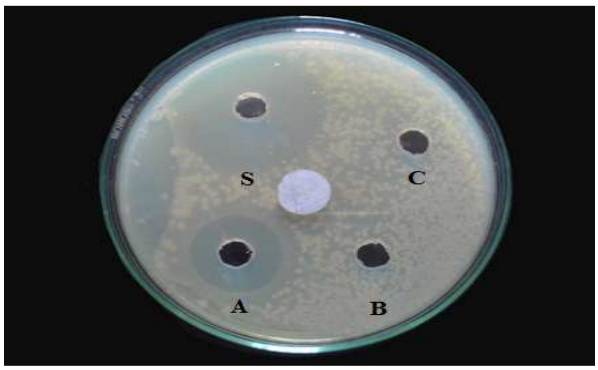
Organism used - *Bacillus subtilis* (Gram +ve)
Reference standard- Kanamycin

S.No	Compound code	Zone of inhibition in diameter (mm)			
		1000 µg /ml (A)	100 µg /ml (B)	10 µg /ml (C)	Standard (S)
1	Compound $3a_1$	15 mm	5 mm	-	22 mm
2	Compound $3a_2$	11 mm	-	-	23 mm
3	Compound $3a_3$	9 mm	-	-	11 mm

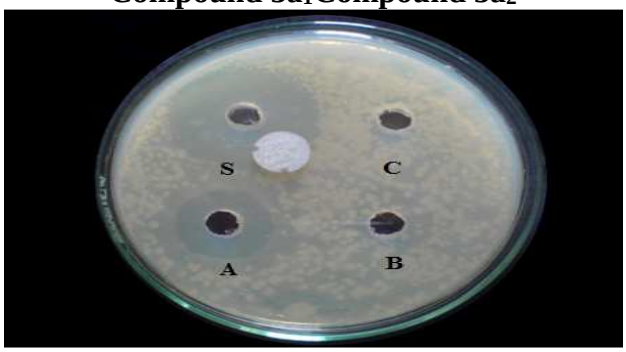
(-) indicate no zone of inhibition.

Microorganism – *Bacilus subtilis* (Gram +ve)



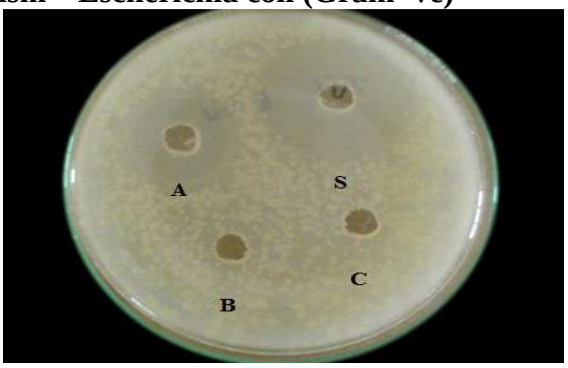


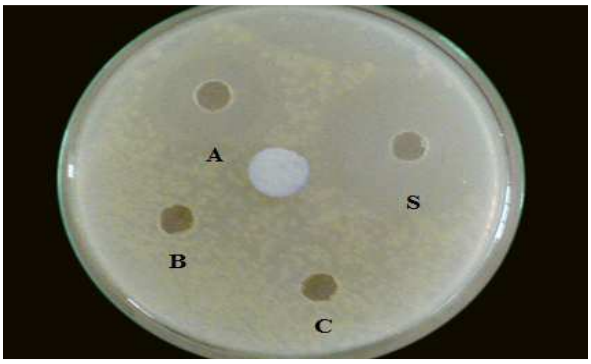
Compound 3a$_1$Compound 3a$_2$



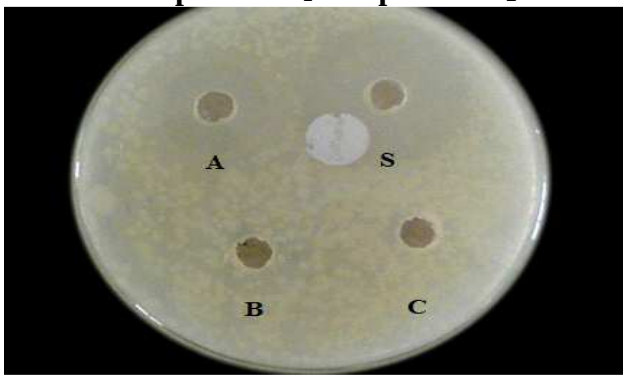
Compound 3a$_3$

Micro organism – Escherichia coli (Gram -ve)





Compound 3a$_1$Compound 3a$_2$



Compound3a$_3$

Figure No.1: Evaluation of Anti-bacterial activity

CONCLUSION

Synthesized compound was shown to exhibit good antibacterial activity against *Escherichia coil* and *Bacillus subtilis.* Finally, it could be concluded from the above results that the piperazine derivative has good Anti-bacterial activity.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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