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"SYNTHESIS CHARACTERIZATION PHARMACOLOGICAL ACTIVITY OF SOME NOVEL SCHIFF BASE "

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ABSTRACT: - Schiff 's base are versatile ligand which are synthesized from the condensation of primary amine(benzocaine) with different- different aldehyde . These compounds are very important in medicinal and pharmaceutical field because of their wide spectrum of antimicrobial activites. Advantage of this efficient method is excellent yield of product in crystalline from, short reaction time, simplicity of work up procedure and no use of any type of hazardous solvent simply this reaction is environmentally proactive (non-polluted) and economically attractive method for this synthesis of Schiff base compound. All of these Schiff base compounds were characterizing of, Rf value, Solubility, colour, melting point and IR elemental analysis as (C, H, N, O) spectral analysis data. Above Schiff base compound show inherent new generation of series pharmaceutically important compound. They are widely used for industrial purpose and also exhibit a broad range of biological activities. All compound exhibited better activity against gram positive strains (Staphylococcus aureus, staphylococcus epidermis) than against gram negative strains (Klebsiella pneumoniae, pseudomonas aeruginosa)

KEYWORDS:- discovery, schiff base, synthesis, IR spectral, antimicrobial activity

DISCOVER OF SCHIFF BASES: -

Schiff base was first discovered by a German chemist, Nobel prize winner Hugo Schiff in 1864. Danish Chemist S.M. Jorgensen began his extensive studies on the synthesis of Schiff 's base complex compound in 1891.

INTRODUCTION:-

A Schiff base named after Hugo Schiff base is a compound with a functional group that contain a carbon- nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group. The general formula of the Schiff bases is R^1R^2 C=N-

R^3 Where, R^1 = aryl or alkyl group that makes the Schiff base a stable imine. Schiff base is usually formed by condensation reaction of a carbonyl with primary amine .

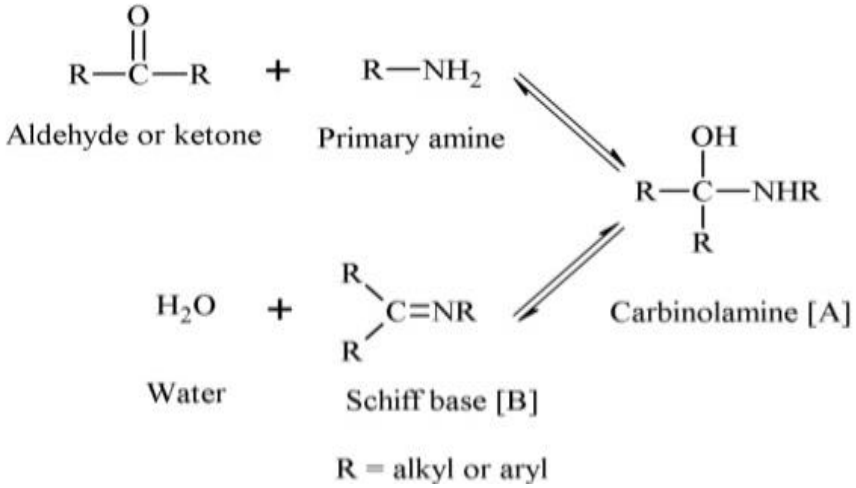


Figure 1 General Scheme

The term Schiff base is normally applied to these compounds when they are applied to these compounds when they are being used as ligand to form coordination complexes with metal ions. Such complexes with metal ion. Such Complexes occur naturally, for instance in corrin, but the majority of Schiff bases are artificial and are used to form many important catalysts, such as Jacobsen ‘s catalyst.

CHARACTERIZATION: -

The Schiff base ligands and their complexes are characterized on the basis of following: - IR Spectroscopy , Melting point, Colour , Solubility , RF value, Antimicrobial activity .

USE OF SCHIFF BASE COMPLEXES :-

Schiff base are valuable intermediate products of organic synthesis . Schiff bases are used as inhibitors. They show their efficiency in both homogenous reaction . Schiff base can be used as an important intermediates in many enzymatic reaction .

EXPERIMENTAL :-

DIFFERENT ALDEHYDE USED FOR THE SCHIFF BASE METHOD:-

SO NO.	ALDEHYDE	QUANTITY
I	M-hydroxy benzaldehyde	0.5 g
II	P- Chlorobenzaldehyde	0.6 g
III	P- Anisaldehyde	0.54 g
IV	Benzaldehyde	0.4 g
V	Formaldehyde	0.12 g
VI	Acetaldehyde	0.8 g
VII	Salicylaldehyde	0.5g
VIII	de	0.7g
IX		0.3g
X	Cinnamaldehyde	0.6g

Table no.1

METHOD OF SCHIFF BASE :-

a) CONVENTIONAL METHOD (REFLUX METHOD) :-

Schiff base are a 0.004 M (0.7 g) of primary amine a (Benzocaine) in a Round bottom flask .Add 10 ml of methanol and toluene as a solvent in a round bottom flask .and dissolve benzocaine completely in a solvent . and take a different - different aldehyde from a list (I, II, III,IV,V,VI, VII,VIII,VIII,IX,X) aldehyde and different quantity (mention in table) and reflux it for a 1 hour under observation and after observation it shows that solvent not completely evaporate. allow it to cool down .After completion of reaction cool the product on crushed ice . And pale yellow colour crystal will appear . and then add 14 ml of methanol and dissolve the product and re-crystalized the product .

b) MICROWAVE METHOD: -

Schiff base are a 0.004 M (0.7 g) of primary amine a (Benzocaine) in a beaker .Add 14 ml of methanol as a solvent in a beaker .and dissolve benzocaine completely in a solvent . and take a different aldehyde from a list (I, II, III,IV,V,VI, VII,VIII,VIII,IX,X) and different aldehyde and different quantity (mention in table) to it .Keep it under microwave irradiation for $4^{1/2}$ minute at medium low temperature .After completion of reaction immediately put it in cold water bath having temperature less then 17˚C . Within a short time pale yellow colour crystal will appear . and then add 10 ml of methanol and dissolve the product and re-crystalized the product .

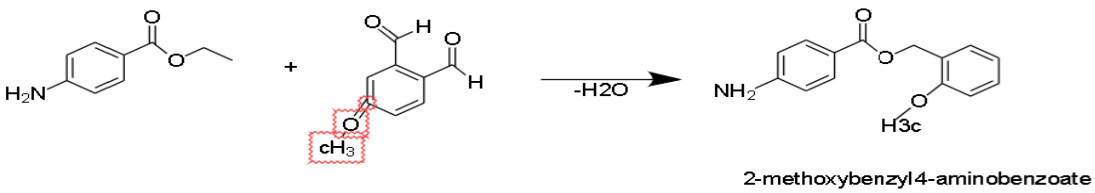
c) RT STIR METHOD :-

Schiff base are a 0.004 M (0.7 g) of primary amine a (Benzocaine) in a beaker .Add 10 ml of dichloromethane (DCM),anhydrous $Mgso_4$ as a solvent added in a beaker .and dissolve benzocaine completely in a solvent . and take a different aldehyde

from a list (I, II, III,IV,V,VI, VII,VIII,VIII,IX,X) and different aldehyde and different quantity (mention in table) . The reaction mixture was stirred 2 hour at a room temperature. The resulting mixture was filtered was concentrated under reduce pressure by rotary evaporation at room temperature to afford pale yellow oil .The resulting solution was allowed to cool to room temperature and then was cooled in an ice water bath for a 2 hour . filtration provide the crystal form .

SCHEME -1 :-

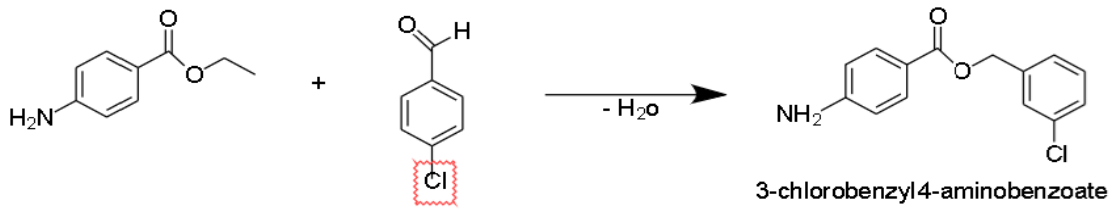
Schiff base are synthesized from benzocaine and react with meta hydroxybenzaldehyde and formation of 4- hydroxybenzyl4-aminobenzoate.



2-methoxybenzyl4-aminobenzoate

SCHEME -2 :-

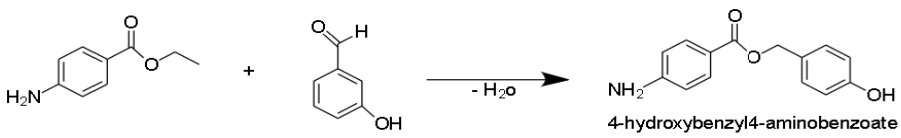
Schiff base are synthesized from benzocaine and react with p-Chloro benzaldehyde and formation of 3-Chloro benzyl 4-aminobenzoate.



3-chlorobenzyl4-aminobenzoate

SCHEME 3 :-

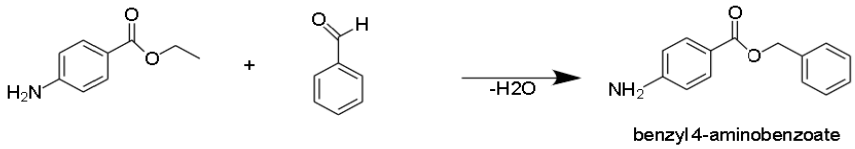
Schiff base are synthesized from benzocaine and react with p-Anisaldehyde and formed 2-Methoxy benzyl 4-aminobenzoate.



4-hydroxybenzyl4-aminobenzoate

SCHEME 4 :-

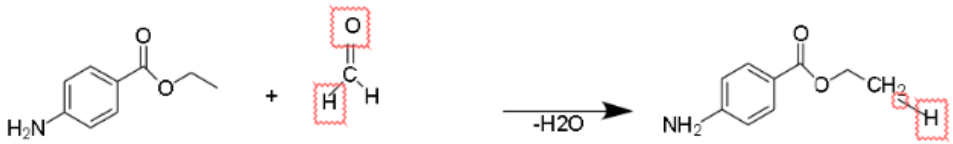
Schiff base are synthesized from benzocaine and react with benzaldehyde and formed of Benzyl 4- aminobenzoate.



benzyl 4-aminobenzoate

SCHEME 5 :-

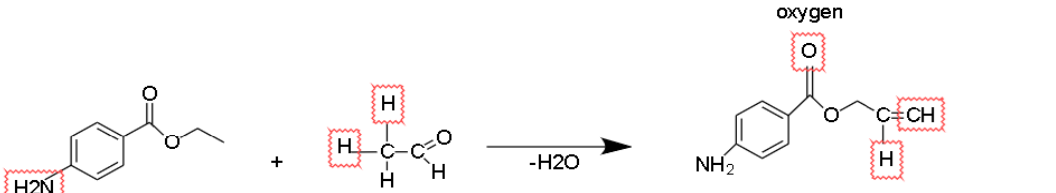
Schiff base are synthesized from benzocaine and react with Formaldehyde and formed of Butyl 4-aminobenzoatehydrogen .



butyl 4-aminobenzoatehydrogen

SCHEME 6 :-

Schiff base are synthesized from benzocaine and react with Acetaldehyde and formation of 4-(1-((2 methyl 3 γ^3-allyl) oxy)vinyl)aniline**.**



4-(1-((2-methyl-3λ^3-allyl)oxy)vinyl)aniline

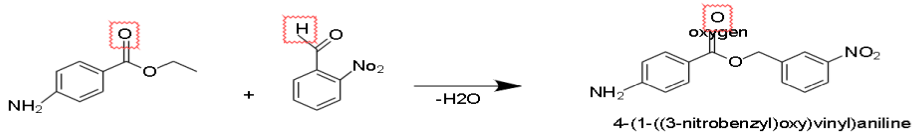
SCHEME 7 :-

Schiff base are synthesized from benzocaine and react with benzaldehyde and formation of 4-(1-((3 methylbenzyl) oxy) vinyl) aniline .

4-(1-((3-methylbenzyl)oxy)vinyl)aniline

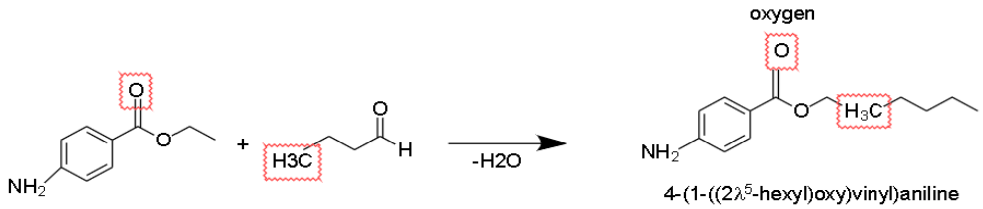
SCHEME 8 :-

Schiff base are synthesized from benzocaine and react with O-Nitro benzaldehyde and formation of 4-(1-((3-nitrobenzyl)oxy)vinyl)aniline .



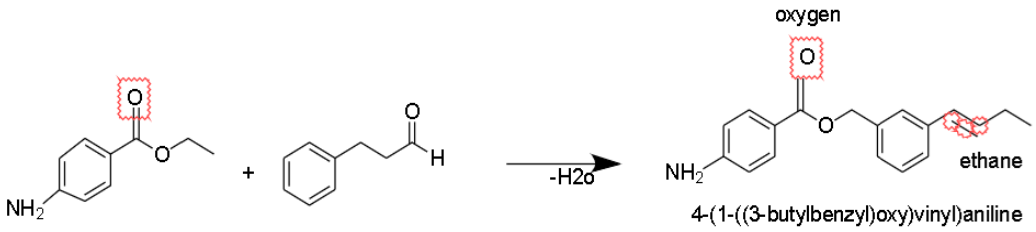
SCHEME 9 :-

Schiff base are synthesized from benzocaine and react with Butyraldehyde and formation of 4-(1-((2 γ^5-hexyl)oxy)vinyl)aniline.



SCHEME 10 :-

Schiff base are synthesized from benzocaine and react with Cinnamaldehyde and formation of 4 –(1-(3-butylbenzyl)oxy)vinyl)aniline



5.RESULT AND DISCUSSION

DETERMINATION OF MELTING POINT :-

Minimum amount of substance was taken in a small capillary tube with one end fushed . A thermometer was kept in a sulphuric acid both along with the stir .The capillary tube was made to add hence the thermometer such that substance containing portion was to bulb of thermometer and is heated slowly with continent stiring .The temp. at which substance begin to melt was recorded .

MELTING POINT OF COMPOUNDS :-

So no.	Compound Name	Melting point
1.	M-hydroxy benzaldehyde	80-85 ˚c
2.	P- Chlorobenzaldehyde	52-53˚c
3	P- Anisaldehyde	41 ˚c
4.	Benzaldehyde	19 -20 ˚c
5.	Formaldehyde	-50 ˚c
6.	Acetaldehyde	-100 ˚c
7.	Salicylaldehyde	200 ˚c
8.	o- nitro benzaldehyde	30 ˚c
9.	Butyraldehyde	70-80 ˚c
10.	Cinnamaldehyde	23 ˚c

Table no.2

OBSERVATION OF COLOUR: -

After New synthesized of schiff base compound. different -different colour show in various compound and the observation in given below.

So no.	Compound Name	Colour
1.	M-hydroxy benzaldehyde	Brown
2.	P- Chlorobenzaldehyde	Pale Yellow
3	P- Anisaldehyde	Light yellow
4.	Benzaldehyde	Yellow
5.	Formaldehyde	Light white
6.	Acetaldehyde	colourless
7.	Salicylaldehyde	Pale yellow
8.	o- nitro benzaldehyde	Orange
9.	Butyraldehyde	Light brown
10.	Cinnamaldehyde	Yellow

Table no.3

DETERMINATION OF SOLUBILITY: -

The individual components of the complex were having different solubility in a different solvent. A little amount of complex was taken in a test tube and dissolve a synthesized compound of a solvent. The experiment was carried out with solvent liker in case the solubility of molecular complex was recorded.

SOLUBILITY OF COMPOUNDS: -

So. No.	Compound Name	I	II	III	IV	V	VI	VII	VIII	IX
1.	M-hydroxy benzaldehyde	SS	S	S	S	SS	S	S	S	SS

2.	P- Chlorobenzaldehyde	IS	S	S	SS	S	SS	S	S	S
3.	P- Anisaldehyde	IS	SS	Ss	S	SS	S	S	S	S
4.	Benzaldehyde	IS	S	S	S	S	S	S	S	S
5.	Formaldehyde	IS	S	S	IS	SS	Ss	S	S	SS
6.	Acetaldehyde	SS	Ss	S	SS	S	S	Ss	S	IS
7.	Salicylaldehyde	IS	S	S	S	SS	S	S	S	SS
8.	o- nitro benzaldehyde	IS	S	S	S	S	S	S	S	IS
9.	Butyraldehyde	S	S	S	SS	S	IS	S	S	IS
10.	Cinnamaldehyde	S	S	SS	IS	S	SS	IS	S	SS

(I-water ,II-Ethanol, III- Methanol ,IV -DMSO , V-Acetone , VI -Diethyl ether ,VII-Chloroform ,VIII-hexane, IX- CCl4)

(SS- slightly soluble, IS – Insoluble, S-Soluble, Ss -Sparingly soluble)

Table no.4

DETERMINATION OF RF VALUE IN TLC :-

In thin-layer chromatography, the retention factor (Rf) is used to compare and help identify compounds. The Rf value of a compound is equal to the distance travelled by the compound divided by the distance travelled by the solvent front (both measured from the origin).

Formula: -

Rf = DSU / DSV

DSU = Distance travel by solute

DSV= Distance travel by solvent

RF VALUE OF COMPOUNDS: -

So. No.	Compound Name	RF Value
1.	M-hydroxy benzaldehyde	0.85
2.	P- Chlorobenzaldehyde	0.86
3.	P- Anisaldehyde	0.7
4.	Benzaldehyde	0.8
5.	Formaldehyde	0.9
6.	Acetaldehyde	0.7
7.	Salicylaldehyde	0.9
8.	o- nitro benzaldehyde	0.7
9.	Butyraldehyde	0.7
10.	Cinnamaldehyde	0.8

Table no.5

FT- IR SPECTROSCOPY: -

FT- IR spectral data in (KBR pellets) of the compound are given in also information of hydrogen bonding existence in Schiff bases is presented. The IR spectra of the Schiff bases shows medium or strong intensity absorption bands at 1615 – 1650 cm-1 assigned to C=N stretching mode. The presence of aromatic ring has been identified by their characteristic ring vibrations at 1500-1400,1100-1050 and 900-700 cm-1 regions. The absence of bands characteristic of v (C=O),primary amine (NH) confirms the formation of the proposed Schiff base framework. The broad band between 2800 and 2400 cm-1 in the spectra of the compound 1,2,3,4beaucase of the keto-enol tautomerism. The characteristic(C-H) modes of ring residues are observed at near 3050 cm-1.methoxy and CH=N group stretching vibrations appear between 3000 and 2800 cm-1 . The strong or medium bands between 3428 and 3325 cm-1 at the schiff bases that not including hydrogen bonding can be assignment at v (OH) .

IR FREQUENCY OF COMPOUNDS: -

Compound	Frequency cm-1 ,KBR pellets	H- bonding in the IR spectra
Z1	3050 m, 2955 m, 2829 m, 1644 s, 1595 m, 1510 s, 1428 m, 1286 m, 1252 m, 1066 m, 901 m, 811 m, 750 m, 573 m	Considerable H-bonding
Z2	3071 m,br, 2970 m,br, 2909 m,br, 1649 s, 1621 s, 1592 m, 1525 m, 1504 s,1479 s,1429 s,1278 m,903m 1479 s, 1429 s, 1278 m, 1226 s, 903 m, 831 m, 800 m, 772 m, 656 m	Considerable H- bonding
Z3	3054 m,br, 3002 m,br, 2930 m,br, 1623 s, 1594 m, 1504 s, 1443 m, 1251 m, 1140 m, 906 m, 827 m, 799 m, 646 m	Weak H-bonding
Z4	3099 m,br, 3054 m,br, 2939 m,br, 1623 s, 1596 m, 1531 m, 1508 m, 1434 m, 1251 s, 978 m, 854 m, 822 m, 748 m, 569 m, 513 w	Considerable H-bonding
Z5	3428 m,br, 3317 m,br, 3065 m, 2965 m, 1616 m, 1583 m, 1511 s, 1487 m, 1441 m, 1273 s, 1253 s, 910 m, 863 m, 793 m, 766 m, 541 m	No hydrogen bonding
Z6	3361 s, 3242 m, 3081 m, 2980 m, 2930 m, 1623 m, 1589 m, 1549 s, 1483 m, 1416 m, 1332 s, 1278 s, 1249 m, 928 m, 876 m, 813 m, 698 m	No hydrogen bonding
Z7	3350 s, 3082 m, 2962 m, 2838 m, 1623 m, 1583 s, 1513 s, 1491 s, 1420 s, 1273 s, 1246 s, 906 m, 872 m, 799 m, 578 m	No hydrogen bonding
Z8	3391 m, 3359 s, 3063 w, 3005 m, 2935 m, 2838 m, 1627 m, 1592 s, 1486 s, 1282 m, 1070 s, 915 m, 822 m, 685 m	No hydrogen bonding
Z9	3420 s, 3072 w, 3007 m, 2966 m, 2941 m, 1621 m, 1585 m, 1501 m,	No hydrogen bonding

	1434 m, 1285 s, 1045 m, 908 m, 815 m, 725 m, 646 m	
Z10	3368 m, 3081 w, 3002 m, 2935 m, 2833 m, 1623 m, 1577 m, 1486 s, 1367 m, 1268 s, 1079 m, 915 m, 863 m, 790 m, 751 m, 649 m	No hydrogen bonding

Table no.6

SCREENING FOR ANTIMICROBIAL ACTIVITY:-

The in vitro antimicrobial activity of Schiff base compound Z1 ,Z2, Z3, Z4, Z5, Z6,Z7,Z8,Z9,Z10 towards gram positive bacteria (Staphylococcus aureus (S.A), Staphylococcus epidermidis (S.E) and gram negative bacteria Klebsiella pneumoniae (K.P) and disc diffusion method pseudomonas aeruginosa (P.A) in muller Hinton agar medium were investigated by. The solution of the intended compounds was prepared in methanol at a concentration of ,400 μg/ml, 300 μg/ml,200 μg/ml, 250 μg/ml, and 100 μg/ml. At general procedure100 μl of test bacteria was growth in 10ml of fresh media till they reach a growth of 1x 10^9 cells/ ml . The microbial suspension was spread on to agar in Petri dish, which has been maintained in the same condition kept for bacterial growth. Then methanolic solution of test solution are spotted in the Petri dish with bacterial growth .it was then incubated for 23 h at 35˚C and then the diameter of the inhibition zone were measured in millimetres.

Standard antibiotic chloramphenicol and ciprofloxacin were used as positive control to evaluated the potency of the tested compound under the same condition .Activity was determined by measuring the diameter of the zone showing complete inhibition (mm).The same concentration and amount of solvent (methanol) was a negative control .Finally the activity result were calculated as a mean +-standard deviation . ciprofloxacin and chloramphenicol compared with the commercially available ,the new synthesized compound show antibacterial activity .

Antimicrobial activity of ligand (Z1,Z2,Z3,Z4,Z5,Z6,Z7,Z8,Z9,Z10) Observation of growth gram positive bacteria :-

GRAM POISTIVE BACTRIA OBSERVATION OF GROWTH A COMPOUNDS: -

Name of gram-positive bacterial pathogen	Observation of growth μg/ml									
	Z1	Z2	Z3	Z4	Z5	Z6	Z7	Z8	Z9	Z10
S.E.	200	100	300	100	200	400	200	100	200	100
S.A.	100	300	500	200	100	300	100	200	200	100

Table no.7

Bacteria name :- (Staphylococcus aureus (S.A), Staphylococcus epidermidis (S.E)

Antimicrobial activity of ligand (Z1,Z2,Z3,Z4,Z5,Z6,Z7,Z8,Z9,Z10) Observation of growth gram Negative bacteria :-

TABLE 5.7 GRAM NEGATIVE BACTRIA OBSERVATION OF GROWTH A COMPOUNDS: -

Name of gram-Negative bacterial pathogen	Observation of growth μg/ml									
	Z1	Z2	Z3	Z4	Z5	Z6	Z7	Z8	Z9	Z10
K.P.	200	100	200	200	100	300	200	100	200	100
P.A.	300	200	100	100	100	200	400	200	200	100

Table no.8

Bacteria name :- Klebsiella pneumoniae (K.P.), Pseudomonas aeruginosa (P.A.)

The solvent methanol exhibited activity against all bacterial species used with IZ s ranging from 7 ±0.25 to 20 ±0.29 while the standard antibiotic ciprofloxacin and

chloramphenicol exhibited high activities with IZS ranging from 24.0 ± 0.25 to 28.2 ± 0.32 and 22.7± 0.35 mm to 28.3 ± 0.21 mm, respectively. However the newly synthesized schiff base organic compound Z1,Z2,Z3,Z4,Z5,Z6,Z7,Z8,Z9,Z10 showed IZS ranging from

ANTIMICROBIAL ACTIVITY OF A COMPOUNDS: -

Compound	Antimicrobial activity (mean IZ diameter (mm) ± SD)			
	Gram Positive		Gram Negative	
	S.E.	S.A.	K.P.	P.A.
Z1	10.5±0.24	14.5±0.33	7.4±0.32	17±0.29
Z2	12.3±0.21	11.5±0.22	10±0.23	23±0.30
Z3	13.3±0.28	10.3±0.12	11±0.13	8±0.29
Z4	35±0.19	32±0.10	10±0.20	9+0.20
Z5	11.1±0.29	10.4±0.19	9±0.10	8.5±0.10
Z6	15.1±0.30	7.5±0.13	10±0.10	10±0.15
Z7	9.2±0.41	19.2±0.14	13±0.15	12±0.12
Z8	12.1±0.25	16.1±0.20	14±0.29	10±0.19
Z9	10.5±0.31	5.9±0.13	15±0.29	12±0.33
Z10	11.9±0.15	10.2±0.10	19±0.27	18±0.29
Methanol	7±0.25	11±0.55	13±0.29	20±0.29
Chloramphenicol	22.7±0.35	22.8±0.25	25.3±0.35	28.3±0.21
Ciprofloxacin	25.0±0.23	24±0.25	26.3±0.31	28.2±0.32

Table no. 9

Respectively . Furthermore ,the mode of action of the compounds may involve formation of a hydrogen bond through the new formation synthesized group with the active centres of cell constitute ,resulting in interference with the normal cell process. The variation in the effectiveness of the different compounds against different organism depends on the permeability of the cell of the microbes or difference in ribosome of microbial cells .

All the schiff bases were synthesized by ethanol condensation reaction and subsequently characterized by element analysis, IR, and NMR spectra. .Compound are in soluble in almost non polar solvents and soluble in most polar solvents like methanol etc. The formation of schiff base compound has been confirmed which is based on the analytical and spectroscopic results . on comparing the antibacterial activities of the synthesized compounds higher than the activity of standard antibiotic. The major limitation of these synthesized compounds are that in some of the bacterial strains they showed less activity than the standard antibiotic ciprofloxacin and chloramphenicol . however, their antibacterial activity can be improved by tunning their functionality during schiff base synthesis.

CONCLUSION: -

The structure of synthesized compound were confirmed by IR spectroscopy and TLC, Solubility, melting point, colour. All compound exhibited significant antimicrobial activity further bioassay, optimization and structure activity relationship of the title compounds are underway .

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