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Synthesis And Biological Activity Of Some New Schiff Bases Of Para Chloro Aniline

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Abstract:
In the present study new Schiff base compounds derived from para chloro aniline with iso vaniline and pyridine 2 carboxaldehyde. Both the ligand/complexes were characterized by IR, and 1H NMR spectroscopy. The Schiff base ligands have also been tested in vitro for their antibacterial and anti fungal activity. The experimental results suggest that Schiff base ligands are more potent in anti bacterial and anti fungal activities.

Key words*: Schiff bases, 4 chloro aniline, isovaniline, pyridine 2 carboxaldehyde, Antibacterial activity;Antifungal activity*

1.Introduction

In the last couple of years, antibiotic resistance, especially multiple drug resistance, has appeared as one of the most significant challenges in the management of infectious diseases. The wider use of antibiotics in humans and animals and in areas other than the treatment and prophylaxis of disease have resulted in a serious problem of drug resistance. Various strategies have been worked out and tried to cope with the resistance problem and enhance the activity, or broaden the spectrum of drugs. [1-4]

Nitrogen containing compounds is very widely distributed in nature and are essential to life; they play a vital role in the metabolism of all living cells. At present, greater than 75% drugs and drug candidates incorporate amine functionality. Among the large number of synthetic and naturally occurring nitrogen donor molecules, Schiff bases are of the greatest interest. The synthesis of these nitrogen-containing compounds by the easily available imine is one of the most important and convenient routes. Schiff bases are the important compound owing to their wide range of biological activities and industrial application. [5-8]

Schiff's bases containing heterocyclic scaffolds have been known to possess a wide range of biological and pharmacological activities for a long time. [9-17]

The presence of various substituents in the phenyl rings of aromatic Schiff bases are responsible for antifungal activity, which can be changed depending upon the type of substituent present on the aromatic rings.

In view of these above the biological importance of Schiff bases, we have synthesized some new Schiff bases evaluated for their bioactivity.

2.Schiff Base Formation And Mechanism

The reaction between a carbonyl compound and an amine leading to the formation of Schiff bases due to the good electrophilic and nucleophilic characteristic properties of the carbonyl and amine groups, respectively.

Oxygen is more electronegative than carbon, and thus draws electron density away from carbon to increase the bond's polarity. Therefore, the carbonyl carbon becomes electrophilic, and thus more reactive with nucleophiles.

Figure 1

Since the nitrogen of the resulting bond has the basic character (indicated by the lone pair shown explicitly on the nitrogen atom in the figure), it can take up a proton to form the conjugate acid of the Schiff base, or the protonated Schiff base.
Note that in the reaction between a nucleophile and a carbonyl group the carbon atom changes hybridization from sp2 (trigonal planar) to sp3 (tetrahedral). That means that the attack of the nucleophile occurs at an angle of approximately 109° (tetrahedral angle) to the existing C=O bond.

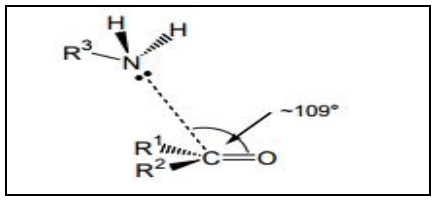

Figure 2

The reactions of the carbonyl group begin with the formation of a bond between the carbonyl carbon and an attacking nucleophile. The nucleophile provides the electrons to form the new bond and the π bond of the carbonyl group is broken as it "gets out of the way." The electrons are moved from this π bond onto what was the carbonyl oxygen.
A strong nucleophile can attack directly, without help from an acid catalyst. For a weak nucleophile, an acid catalyst is needed so that the carbonyl carbon is prepared to share a pair of electrons as a new covalent bond.
The reaction can also proceed in an E2 like fashion with the elimination of water occurring at the same time another water deprotonates the nitrogen so it can form a new N=C bond, forming the imine.

- Experimental section

3.Materials And Method

All the chemicals used were of analytical grade (AR). Melting points of the synthesized compounds were determined by open capillary and are uncorrected. The purity of the compounds was checked by TLC using silica gel plates and spots were developed in iodine chamber, IR spectra were recorded with KBr pellets on Shimadzu FTIR model 8400 spectrophotometer, H1NMR spectra in CdCl3 on a Varian NMR mercury-300 instrument, Mass spectra were recorded on VG 7070H mass spectrometer

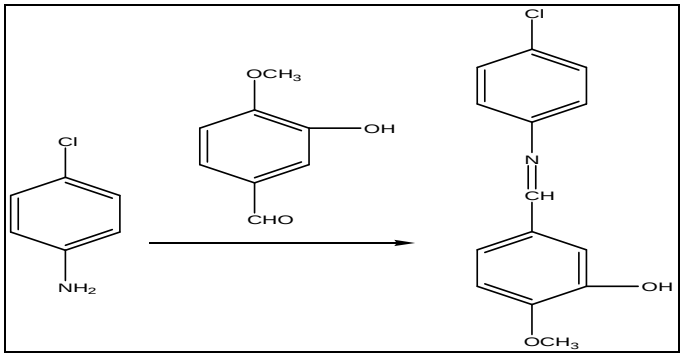

Figure 3: Schiff base 1: Synthesis of 5-((4-chlorophenylimino) methyl)-2-methoxyphenol

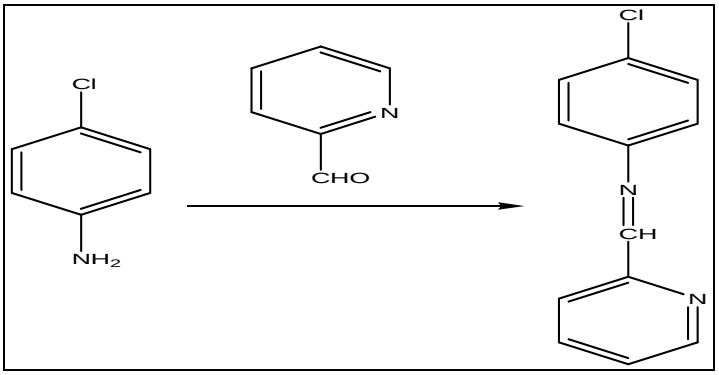

Figure 4: Schiff base 2: Synthesis of 4-chloro-N- (pyridin-2-ylmethylene) benzenamine

4.Biological Activity

4.1.Antibacterial

The in vitro biological screening effects of the investigated compounds were tested against the bacteria Bacillus subtilis. Paper discs of Whatman filter paper no. 1 were cut and sterilized in an autoclave. The paper discs were saturated with 10 µl of the compounds dissolved in DMSO solution or DMSO as negative control and was placed aseptically in the Petri dishes containing Nutrient agar media inoculated with the above mentioned two bacteria separately. The petridishes were incubated at 370C and the inhibition zones were recorded after 24 h of incubation.

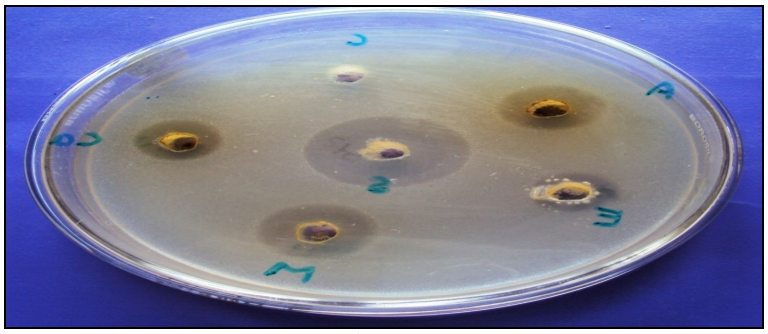

Figure 5

5-((4-chlorophenylimino) methyl)-2-methoxyphenol Observations after 24 hrs.
Description of markings on petriplate.
A - Standard (amoxycillin) C - Control Ca- 40 mg (Soluble in DMF) E - 20 mg S - 60 M - 80 mg

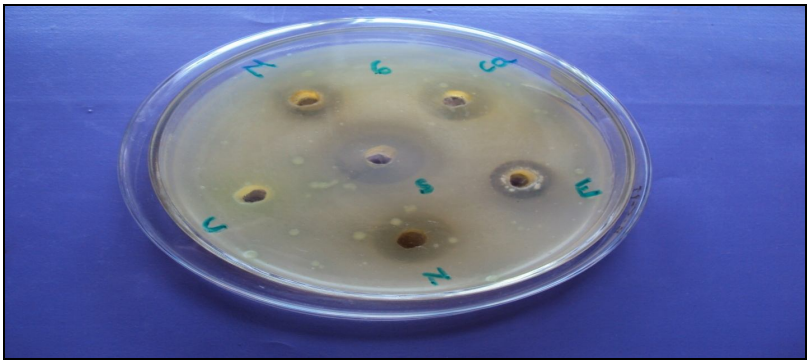

Figure 6

4.2.Antifungal

The Schiff base complexes were screened for their antifungal activity against fungi viz. candida. Filter paper discs of 5 mm in size, prepared by using Whatman filter paper no. 1 (sterilized in an autoclave) was saturated with 10 µl of the compounds dissolved in DMSO solution. The fungal culture plates were inoculated and incubated at 25± 20C for 48 h. The plates were then observed and the diameters of the inhibition zones (in mm) were measured and tabulated.

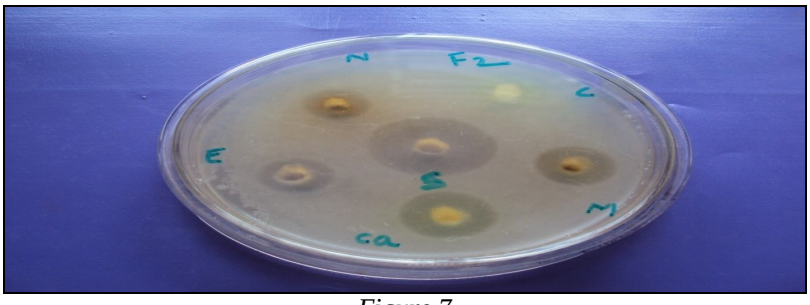

Figure 7

ANTI FUNGAL CANDIDA ALBICANS 4-chloro-N-(pyridin-2-ylmethylene)benzenamine
Ca - FLUCONAZOLE C – Control N - 20 mg (Soluble in DMF)E - 40 mg S - 60 mg M - 80 mg

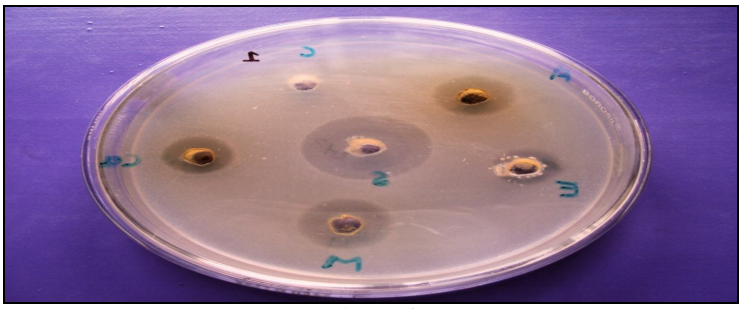

Figure 8

5-((4-chlorophenylimino) methyl)-2-methoxyphenol ANTIFUNGAL CANDIDA ALBICANS
Observations after 24 hrs.
Description of markings on petriplate.
Ca - FLUCONAZOLE C - ControlN - 20 mg (soluble in DMF) E - 40 mg . S- 60 mg M - 80 mg

5.Result And Discussion

- New Schiff bases were synthesized by refluxing the reaction mixture of 4-chloroaniline with isovaniline and pyridine 2 carboxaldehyde in methanol in the presence of glacial acetic acid. The synthesized compounds were characterized on the basis of their IR, H1NMR, mass spectral.
- Structures of compounds have been elucidated by IR, Proton NMR and Mass Spectral measurements. Schiff bases shows IR absorption peak at 1615-1530 cm-1 (C=N stretching). All the compounds show NMR signals for different kinds of protons at their respective positions.
- The synthesized Schiff base 4-chloro-N-(pyridin-2-ylmethylene)benzenamine is found to be more active than standard antibacterial drug amoxicillin against E Coli.
- The synthesized Schiff base 4-chloro-N-(pyridin-2-ylmethylene)benzenamine showed more active against E Coli compared to other Schiff base.
- The synthesized Schiff bases were found to be more active than standard antifungal drug against candida. The synthesized Schiff base 4-chloro-N-(pyridin-2-ylmethylene)benzenamine showed more active against candida compared to other Schiff base.
- In accordance with the data obtained from antimicrobial activity, all the synthesized Schiff bases of have shown good activity against the tested microbes. Among these Schiff bases has shown good activity against all the tested bacteria and fungi.

6.Conclusion

The research study report suggest that the successful synthesised Schiff bases were physically and chemically characterized through elemental analysis, IR, 1H NMR, and Mass spectral data.
Hence, further study of a synthesized Schiff base compound 4-chloro-N-(pyridin-2-ylmethylene)benzenamine in antimicrobial and anti fungal activities may become fruitful.

7.References

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