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SCHIFF BASE LIGAND SYNTHESIZED FROM ANTIBIOTIC CEFUROXIME AND SALICYLDEHYDE; CHARACTERIZATION AND DISCUSSION THE ANTIMICROBIAL POTENTIALS OF IT.

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Farhana Hoque* Department of Pharmacy, University of Science and Technology Chittagong (USTC), Bangladesh *Corresponding Author farhanahoquebd@yahoo.com

Tanjina Akter Anni Department of Pharmacy, University of Science and Technology Chittagong (USTC), Bangladesh

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Abstract:

Schiff base ligand N-salicylcefuroxime was synthesized from cefuroxime and salicyldehyde to develop a more effective antibiotic. Bacterial infections have been a major health problem and the emergence of multi drug resistant complicates the situation. In the purpose of discovering more effective procurement, several antibiotics have been procured or synthesized. Advanced research of synthetic chemistry has pointed out several organic compounds with antimicrobial potentials, Schiff bases are one of such compounds. Cefuroxime is a bactericidal antibiotic. This research aimed to discuss the synthesis of a new schiff base from common antibiotic cefuroxime and salicyldehyde. This ligand synthesized and characterized by elemental analysis and some other physicochemical techniques. This synthesized compound was also characterized by different spectroscopic techniques. It was subjected to melting point determination, TLC (thin layer chromatography) determination, chemical tests, solubility test, etc. The synthesizedschiff base was found more anti-bacterial potential than cefuroxime; in future it may be used as an antibiotic.

INTRODUCTION:

There are several areas of research within the general area of organic synthesis, total synthesis, semi-synthesis and methodology.Organic synthesis involves the conversion of a substrate to the desired molecule. Most organic syntheses require the use of a series of one step reactions. Determining which reactions to use follows a technique called retro synthetic analysis.[1] Organic chemists use synthesis for variety purposes. The synthesis of natural products increase the available supply of the compounds for further study or use.[2]Many Schiff bases can be hydrolyzed back to their aldehydes or ketones and amines by aqueous acid or base. In the first part of the mechanism, the amine reacts with the aldehyde or ketone to give an unstable addition compound called carbinolamine. The carbinolamine loses water by either acid or base catalyzed pathways.[3]Schiff bases have been investigated in relation to a wide range of contexts, including antimicrobial, antiviral and anticancer activity. They have also been considered for the inhibition of amyloid-β aggregation.[4]

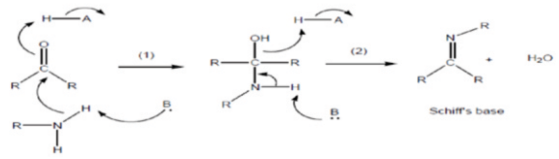

Fig: Mechanism of action of Schiff base

Antibiotics are used to treat or prevent bacterial infections,[5] and sometimes protozoan infections. (Metronidazole is effective against a number of parasitic diseases). When an infection is suspected of being responsible for an illness but the responsible pathogen has not been identified, an empiric therapy is adopted[6] This involves the administration of a broad-spectrum antibiotic based on the signs and symptoms presented and is initiated pending laboratory results that can take several days.[6,7]Cefuroxime is a cephalosporin (SEF a low spor in) antibiotic. It works by fighting bacteria in your body. Cefuroxime is used to treat many kinds of bacterial infections, including severe or life-threatening forms.It is on the World Health Organization's List of Essential Medicines, which lists the safest and most effective medicines needed in a health system. It is available as a generic medication.Salicylic aldehyde (2-hydroxybenzaldehyde) is the organic compound. Salicylaldehyde is a key precursor to a variety chelating agents, some of which are commercially important.

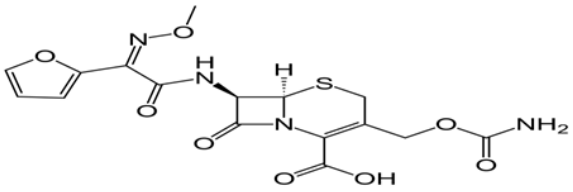

Fig: Cefuroxime

MATERIALS AND METHODS

Chemicals and reagents:

All chemicals and reagents were of analytical grade and used as received. API (cefuroxime) was collected in pure state.

Physical properties measurement and spectral analysis:

IR spectra were registered on a Shimadzu Infrared Spectrophotometer using potassium bromide disc, within the range of 4000-400 cm^{-1} at the University of Chittagong. UV-visible spectrum was recorded on a UV-visible spectrophotometer at the University of Science and Technology Chittagong (USTC). ^{1}HNMR spectra were registered on a Bruker NMR spectrophotometer using deuterated chloroform as solvent, at BCSIR laboratories, Dhaka. Melting points were determined on an electro-thermal melting point apparatus and TLC was performed using conventional TLC plates at the University of Science and Technology Chittagong. All chemical tests were performed in the University of Science and Technology Chittagong, Bangladesh.

Antimicrobial screening:

Two pathogenic bacteria *Staphylococcus aureus* (gram positive) and *Escherichia coli* (Gram negative) were collected from the Department of Microbiology, University of Chittagong, Bangladesh. Nutrient agar was used as a culture media for bacteria while potato dextrose agar was employed in antifungal studies. The Schiff base was dissolved in methanol. The in-vitro antimicrobial activity of the Schiff base was assessed by disc diffusion method. The diameter of the zone of inhibition produced by the compound was compared

with the parent drug, cefuroxime.

Preparation of Schiff base ligand of Cefuroxime:

Cefuroxime and salicyldehycde were taken (1:1 ratio) in a round bottom flask using methanol as a solvent. The magnet was introduced as stirrer into the reaction medium. The reaction was carried out at 80°C for 8 hours. Reaction was monitored by TLC. After the product was condensed,it was filtered and collected. The ligand was brown crystalline solid.

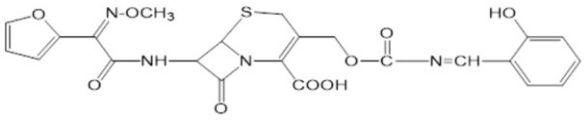

Fig: The structure of synthesized schiff base ligand derived from salicyldehyde and cefuroxime

RESULTS AND DISCUSSIONS:

Determination of R_f value:

A mixture of the solvents N-hexane and methanol was used at ratio of 5:2. R_f value of cefuroxime = 0.03 and prepared schiff base lignd = 0.62.

UV spectral analysis:

The electronic absorption spectra are often very helpful in the evaluation of results furnished by other methods of structural invesstigation. Methanol was used as solvent. Wavelength maxima of Cefuroxime = 405, 335, 305 (nm); and prepared schiff base lignd = 510, 420, 400, 295 (nm). The maximum wavelength was observed at 510 nm which was different from cefuroxime.

^{1}HNMR spectral analysis:

From the 1HNMR spectrum of the SB ligand N-salicylcefuroxime we found a sharp singlet signal at 7.5 ppm for 1 azomithine (-CH=N-) proton. A singlet for phenolic proton (Ar-OH) was observed at 6.9 ppm. The carboxylic proton (-COOH)was observed as singlet signal at 11.0 ppm, methyl (-CH_3) proton observed at 1.7 ppm and amide(CO-NH) proton observed at 3.5 ppm. It has been confirmed through research that azomethines show chemical shift in the vinicity of 7.0-8.0.[8,9]

IR spectral analysis:

IR spectra of Schiff base ligand of cefuroxime and active cefuroxime were recorded using KBr-discs in the range of 4000-500 cm^{-1}. The spectrum of cefuroxime displayed the characteristics bands for Phenolic group at 3450 cm^{-1},Carboxylic acid group for O-H at 1200 cm^{-1},couple bonds for C=C at 1500 cm^{-1}, and for O-CH_3 group show band at 1150 cm-1 and for C=H group shows band at 1300 cm^{-1}. The spectrum of N-salicylcefuroxime displayed the characteristics bands for Phenolic group at 3050 cm^{-1},Carboxylic acid group for O-H at 1250 cm^{-1}, bond for C=C at 1400 cm^{-1} , and for O-CH_3 group show band at 1600 cm^{-1} and for C=H group shows band at 1400 cm^{-1} and most importantly for azomethine group C=N bands shows at 1600 cm^{-1}.

Antimicrobial assay:

Antibacterial assay was performed by disk diffusion method. The diameters of zone of inhibition (in mm) of the standard drug Cefuroxime (30mg/disc) and new schiff base ligand N-salicylcefuroxime (30mg/disc) were found 13 and 18 for *Escherichia coli* and 14 and 16 mm for *Staphylococcus aureus*. The ligand found to be active against the bacteria Staphylococcus aureus and activity are more than standard. It also found more activity against the bacteria *Escherichia coli*.

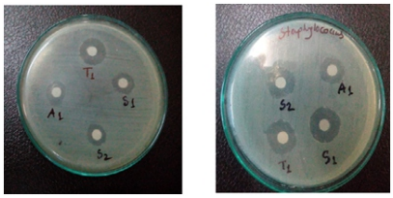

Fig: Left disk is for *E. coli* and right disk for S. aureus. A1 is for cefuroxime and T1 is for the prepared Schiff base ligand.

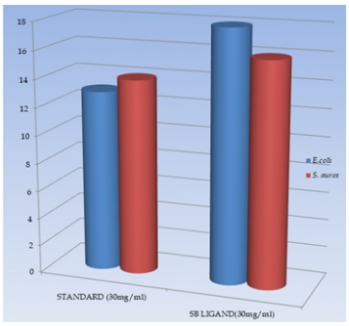

Fig: Graphical representation of anti-bacterial activity

CONCLUSION:

Schiff base ligand N-Salicylcefuroxime was synthesized by using condensation reaction method. Cefuroxime which is an antibiotic, reacts with salicylaldehyde to form the schiff base ligand. This ligand was characterized on the basis of IR, ^{1}HNMR and UV spectral data. This product was confirmed by checking melting point, TLC, R_f value, colour test, chemical tests, several spectral data etc. Antimicrobial activities against *E. coli* and *S. aureus* were determined. New Schiff base ligand was found more active than the sample compound cefuroxime against those bacteria. So, the synthesized compound may be further used as a antibiotic. The synthesized compound also can be used as a starting material of any organic reaction or Schiff base synthesis reaction. The prepared Schiff base can be used to prepare complex compounds by using the transition elements such as Fe (II), Fe(III), Cu(II), Co(II), Ni(II), etc.

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