

Fe (II) AND Cu(II) COMPLEXES OF ACETYLATED AND BENZOYLATED DERIVATIVES OF CIPROFLOXACIN , SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES

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Abstract

Derivatization of ciprofloxacin shows potential alternative to the challenge of antibiotic resistance. Incorporation of substituents at the C-7 position (N-piperazine) moiety via acetylation and benzylation of ciprofloxacin have resulted in its acetylated and benzoylated derivatives (CPCOR) and (CPCOPh) with improved biological activities. Copper and iron (II) complexes of the derivatives have been synthesized and characterised by percentage metal analysis, infrared and electronic spectroscopies, room temperature magnetic moments and melting points. The derivatised ligands (CPCOR) and (CPCOPh) behave as bidentate ligands through the involvement of the carboxy group oxygen and the pyridone carbonyl oxygen. The room temperature magnetic moment and electronic spectra data indicated that the complexes have octahedral geometries which is slightly distorted in the acetylated copper(II) complex. The in-vitro antimicrobial studies were carried out on the derivatised ligands and their complexes against *Bacillus subtilis* (ATCC 39090), *Escherichia.coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538), *Pseudomonas aeruginosa* (ATCC 7306), *Klebsiella pneumonia* (ATCC 4592), and *Candida albicans* (ATCC 10231). It was observed that the ligands as well as their complexes did not exhibit antifungal activity against the tested fungus *Candida albicans*. The acetylated derivative (CPCOR) showed better activity than the standard drug ciprofloxacin against *Bacillus subtilis* and *Pseudomonas aeruginosa* and *Klebsiella pneumonia* at all the concentrations used while the benzoylated derivative (CPCOPh) exhibited reduced activity in comparison to ciprofloxacin against all the tested organisms, this might be due to the bulkiness of phenyl moiety present in its structure. However, the metal (II) complexes of both the acetylated and benzoylated derivatives showed better activities than ciprofloxacin.

Introduction

Ciprofloxacin (CP) (Fig. 1) is a synthetic, broad-spectrum fluoroquinolone antibacterial agent for oral administration¹

Active against a wide variety of aerobic gram-negative and gram-positive bacteria^{2–4}

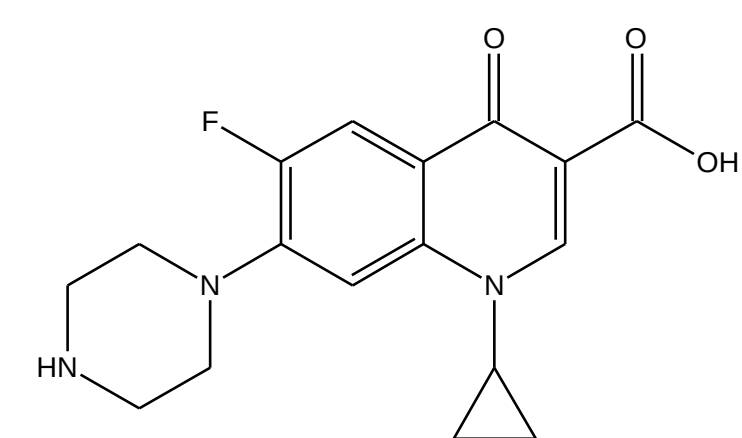


Fig. 1: CP

The derivatization of CP by acetylation and benzylation at C-7 position gave (CPCOR) and (CPCOPh) which present potential alternative to combat antibiotic resistance

Here, we present Fe(II) and Cu(II) complexes of acetylated and bezoylated derivatives (CPCOR and CPCOPh) of ciprofloxacin, their characterization and antimicrobial studies

Materials and Methods: Ciprofloxacin hydrochloride was a gift from Bond Chemical Plc Awe, Oyo State and Unique Pharmaceutical Lagos Nigeria,

Physical measurements

The electronic spectra of the complexes in distilled water were recorded on a Perkin-Elmer Lambda 25 Spectrophotometer and infrared spectra were recorded using KBr discs on a Perkin-Elmer BX II FT-IR spectrometer 4000–370 cm⁻¹. The room temperature magnetic susceptibilities at 303K were measured on Sherwood Susceptibility Balance MSB Mark 1 and diamagnetic corrections were calculated using Pascal's constant, and melting points were determined with Stuart SMP10 melting point apparatus

Derivatization reaction to synthesise CPCOR and CPCOPh

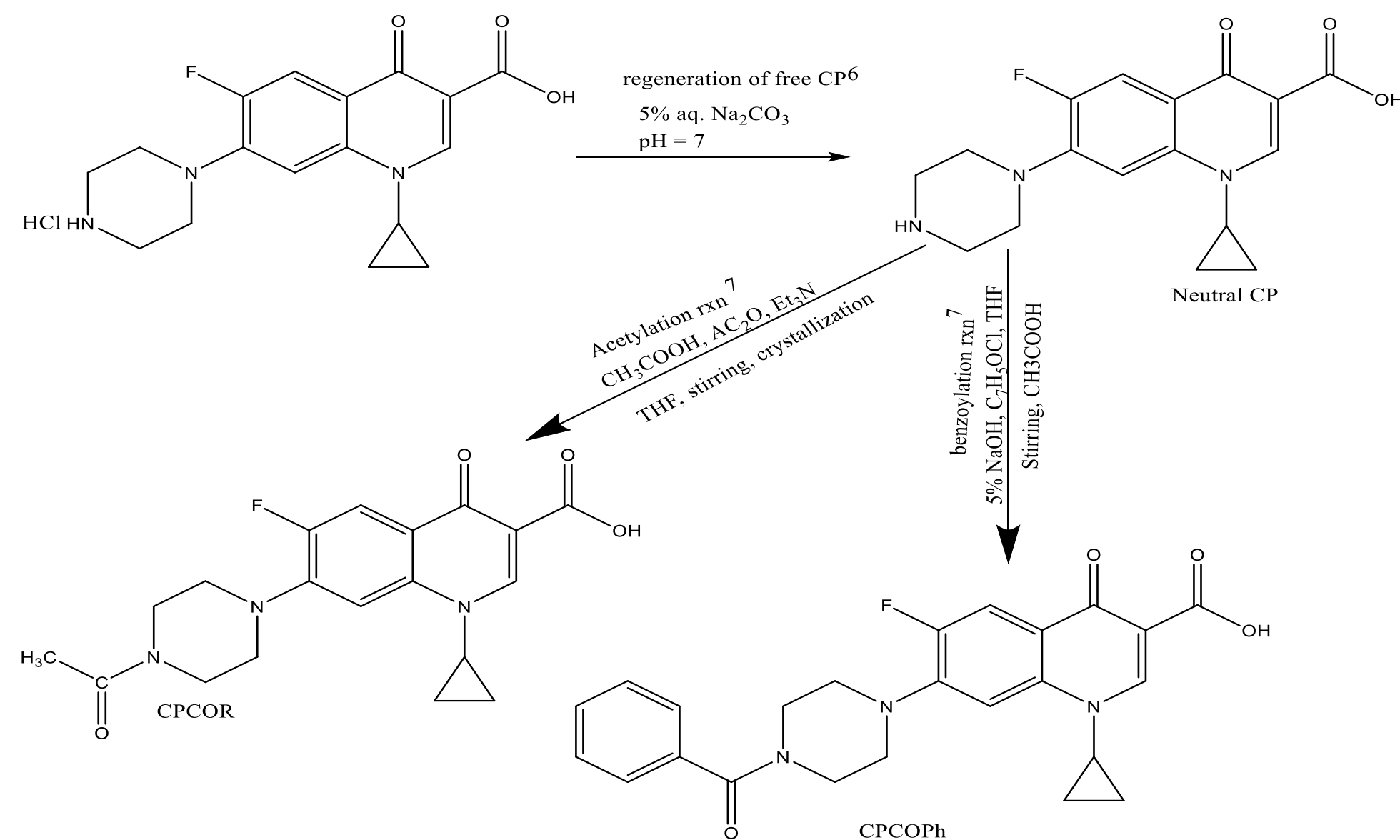
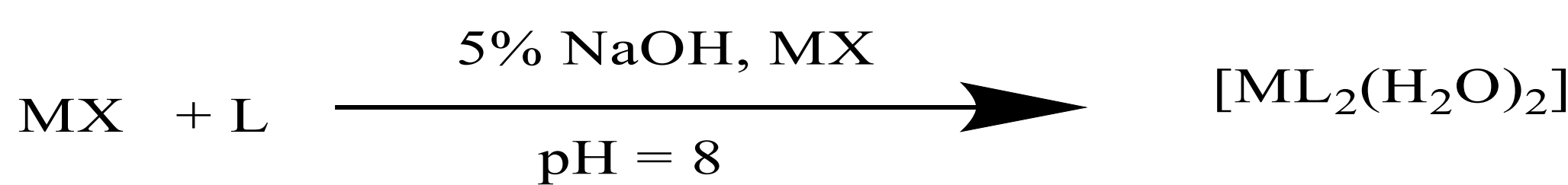


Fig.3: Synthesis of Fe and Cu (II) complexes CPCOR and CP



where L = CPCOR/CPCOPh, Fe, Cu

Antimicrobial studies: Derivatized CP and their complexes were tested against standards strains of bacteria and a fungus: *Bacillus subtilis* (ATCC 39090), *Escherichia.coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538), *Pseudomonas aeruginosa* (ATCC 7306), *Klebsiella pneumonia* (ATCC 4592), and *Candida albicans* (ATCC 10231) using agar diffusion method.⁸

Results and discussion

The Fe and Cu (II) complexes of CPCOR and CPCOPh are stable at room temperature exhibiting variety of colours with good yields in the range 50-91%

The CP derivatives decomposed at 256 °C and 273°C respectively while the complexes melted in the range 257-293°C

IR studies: The absence of band at 1580cm⁻¹ showed the destruction of the zwitterion ion character of CP due to acetylation and benzylation. The ligands acts as bidentate ligands coordinating via the carboxy group oxygen and pyridone carbonyl oxygen.

Electronic spectra and magnetic moment: The room temperature magnetic moment and electronic spectra data indicated that the complexes have octahedral geometries which is slightly distorted in the acetylated copper(II) complex.

Antimicrobial studies

The acetylated derivative (CPCOR) showed better activity than the standard drug ciprofloxacin (CP) against *Bacillus subtilis* and *Pseudomonas aeruginosa* and *Klebsiella pneumonia* at all the concentrations, while the benzoylated derivative (CPCOPh) exhibited reduced activity compare to CP against all the tested organisms, this might be due to the bulkiness of phenyl group in it. However, complexes of Fe(II) and Cu(II) of both CPCOR and CPCOPh showed better activities than CP.

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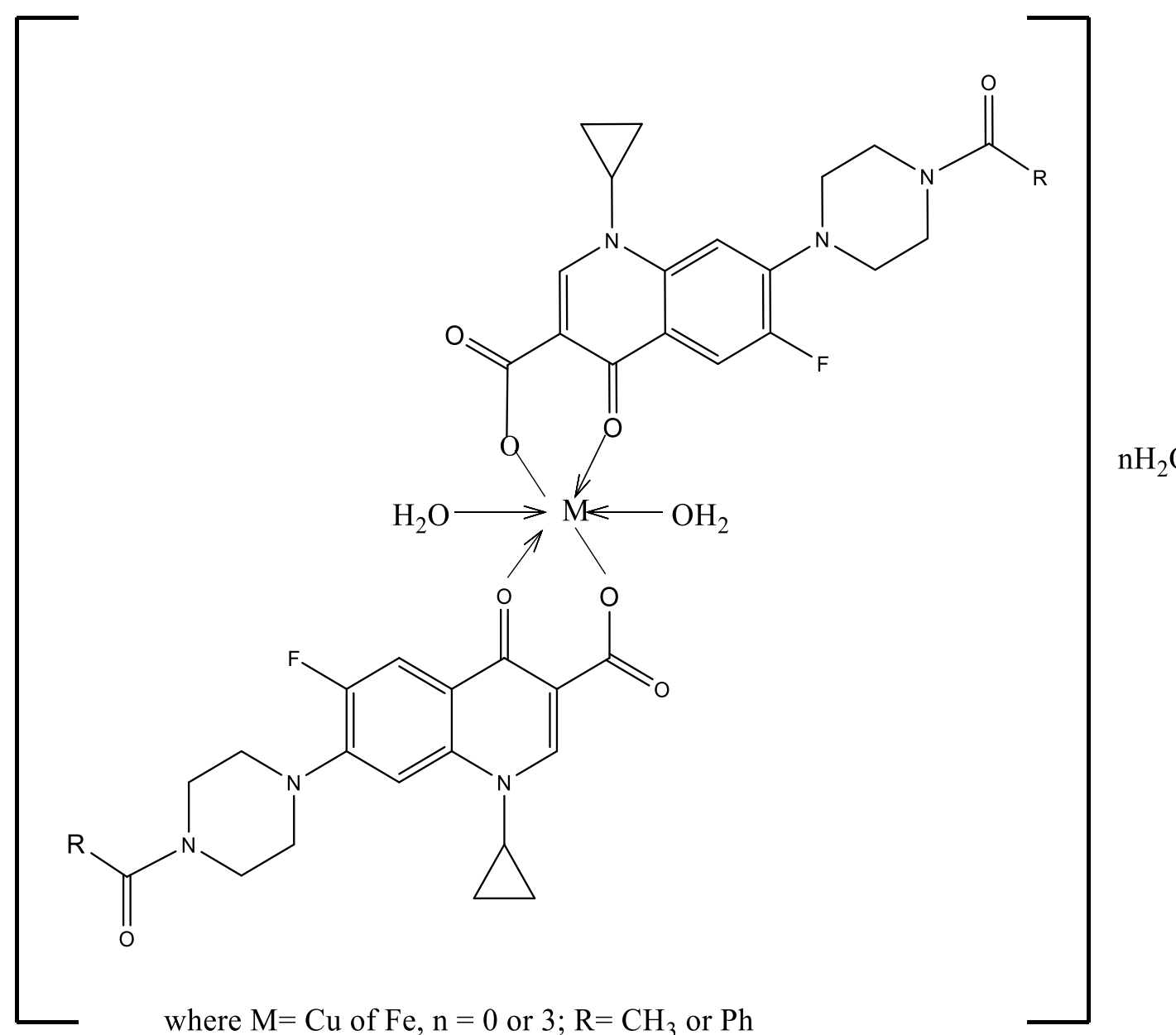


Fig 4: Proposed structures of Fe(II) and Cu(II) complexes

Conclusion:

Ciprofloxacin has been derivatised through acetylation and benzylation at the C-7 position (N-piperazine) moiety to give (CPCOR) and (CPCOPh). The complexes and the derivatives have been characterised and subjected to antimicrobial studies. All the complexes exhibited better activities compare to CP also CPCOR exhibited better activities than CPCOPh.

Aknowledgement

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