

SYNTHESIS, CHARACTERISATION AND ANTIMICROBIAL STUDIES OF MIXED LIGANDS METAL (II) COMPLEXES OF SULFAMETHOXAZOLE AND N,N- DONORS HETEROCYCLES

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Abstract

Two mixed ligands of sulfamethoxazole (SMX) with N,N donor heterocycles: 1,10-phenanthroline (phen) and 2,2'-bipyridine (bipy) metal complexes having the composition [M(SMX)(phen)X].nH₂O and [M(SMX)(bipy)X].nH₂O (where M = Zn(II), Co(II), Fe(II), Mn(II), Cu(II); X = SO₄/Cl₂) have been synthesised and characterised by physicochemical methods based on their solubility, metal analysis, infrared and UV-Visible techniques. Infrared spectra data showed SMX as a bidentate ligand coordinating to the metals through the N atom of the sulfonamide group ((3195-3030cm⁻¹) and oxygen atom of the sulfonyl moiety (1158- 1103 cm⁻¹) while the heterocycles also bonded as bidentate ligands through their diimine nitrogen atoms (1606- 1423 cm⁻¹). The electronic spectra data indicated that all the metal (II) complexes were monomeric and octahedral. The *in-vitro* antimicrobial studies of these complexes and their ligands against environmental strains of microorganisms: *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Aspergillus niger* and *Candida albicans* showed that SMX-phen metal complexes [M(SMX)(phen)X].nH₂O are better heterocycle with zone of inhibition in the range 28-10mm to combine with SMX for the enhancement of its antimicrobial spectrum this may be due to their more extensive aromatic ring system which gave better lipophilicity, hence aided cell membrane penetration and promoted hostile intracellular interactions leading to death of microorganisms.

Introduction

Sulfamethoxazole (SMX) (Fig.1), a sulfonamide drug is a structural analogue of p-aminobenzoic acid that inhibits the synthesis of intermediary dihydrofolic acid from its precursors [1]

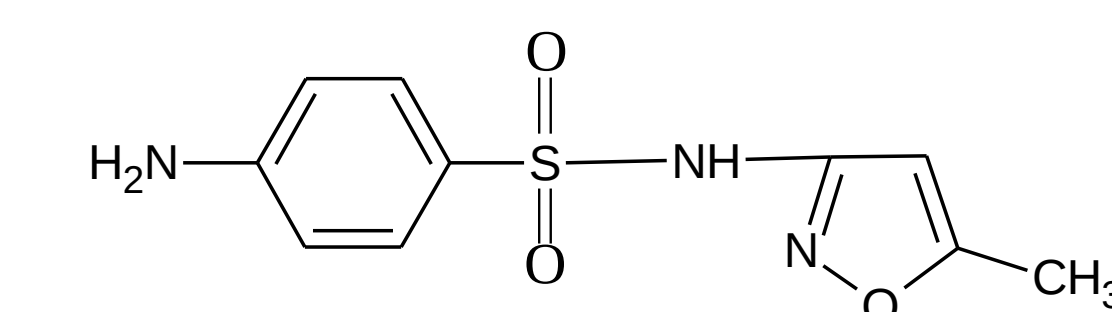


Fig 1: SMX

It is a bacteriostatic antibiotic, used in synergistic combination therapy with Trimethoprim for the treatment of urinary tract infections, respiratory tract pathogens, skin pathogens, certain enteric pathogens [2]

The clinical importance of sulfamethoxazole -trimethoprim combination has slowly declined recently due to the development and rapid spread of resistance of bacterial pathogens [3]

1,10-Phenanthroline (phen) and 2,2' bipyridine (bipy) (Fig. 2) as nitrogen heterocycles have excellent broad spectrum of biological activities [4].

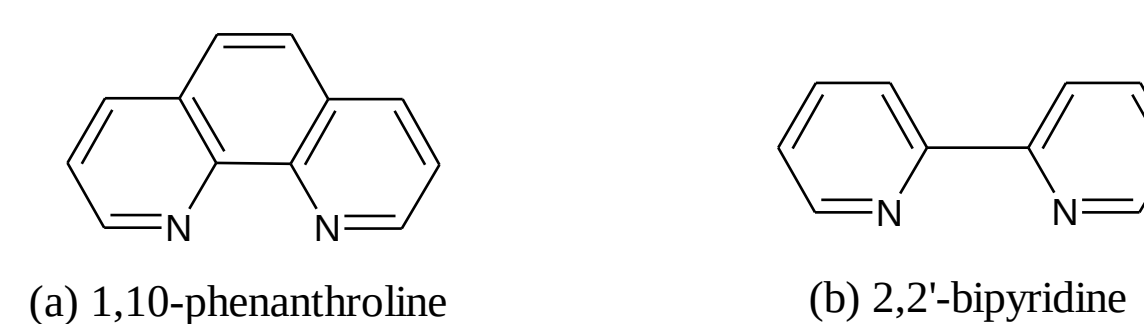


Fig. 2: (a) Phen (b) bipy

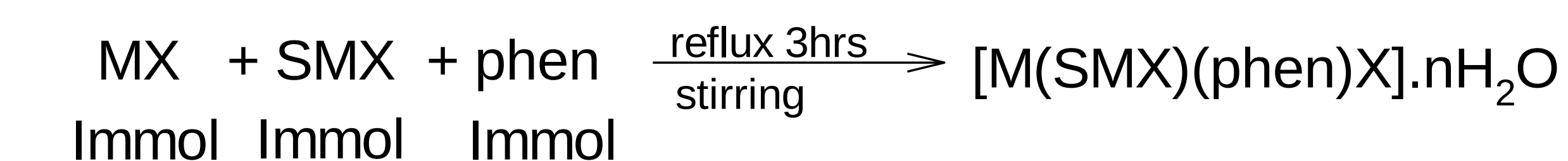
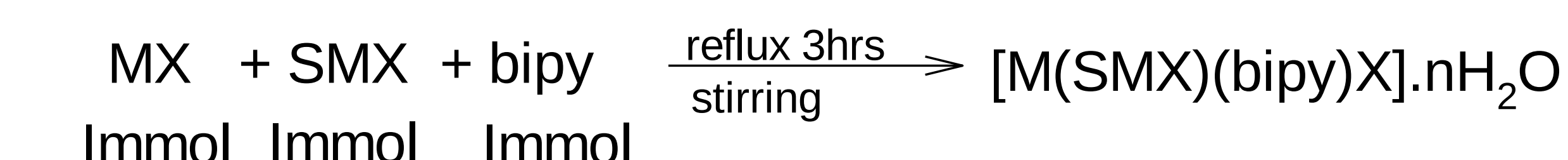
Phen and bipy with their extended planar π systems and can be used in model compounds to copy the non covalent interactions in biological processes [5]

Here, present two mixed ligands of sulfamethoxazole of 1,10-phenanthroline and 2,2'-bipyridine, their metal (II) complexes and their antimicrobial studies with the aim of comparing the extent to which each of these heterocycles can influence the antibacterial spectrum of sulfamethoxazole free drug

Materials and methods

Physical measurements: The electronic spectra of the complexes in ethanol were recorded on a Perkin-Elmer Lambda 25 Spectrophotometer and infrared spectra were recorded using KBr discs on Perkin-Elmer BX II FT-IR spectrometer. Melting points were determined with Stuart SMP10 melting point apparatus and percentage metal was obtained by complexometric titration using EDTA

Synthesis of Metal Complexes of [M(SMX)(phen)X].nH₂O and [M(SMX)(bipy)X].nH₂O, where M = Cu(II), Co(II), Mn(II), Fe(II) and Zn(II); X = SO₄ or Cl₂ [6]



Antimicrobial studies: Free ligands and the synthesized complexes were screened *in vitro* against environmental strains of bacteria and a fungus: *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Aspergillus niger* and *Candida albicans*. using Agar diffusion method [7]

Results and discussion

The mixed ligands of SMX with N, N-donor heterocycles phen and bipy with metal(II) salts of Mn, Co, Zn, Fe and Cu gave varying shades of coloured complexes in low to moderate yields (17-60 %). The ligands, SMX, phen and bipy melted at 168-172°C, 117- 118°C and 70-73°C respectively, whereas their metal complexes all decomposed on melting at > 300°C.

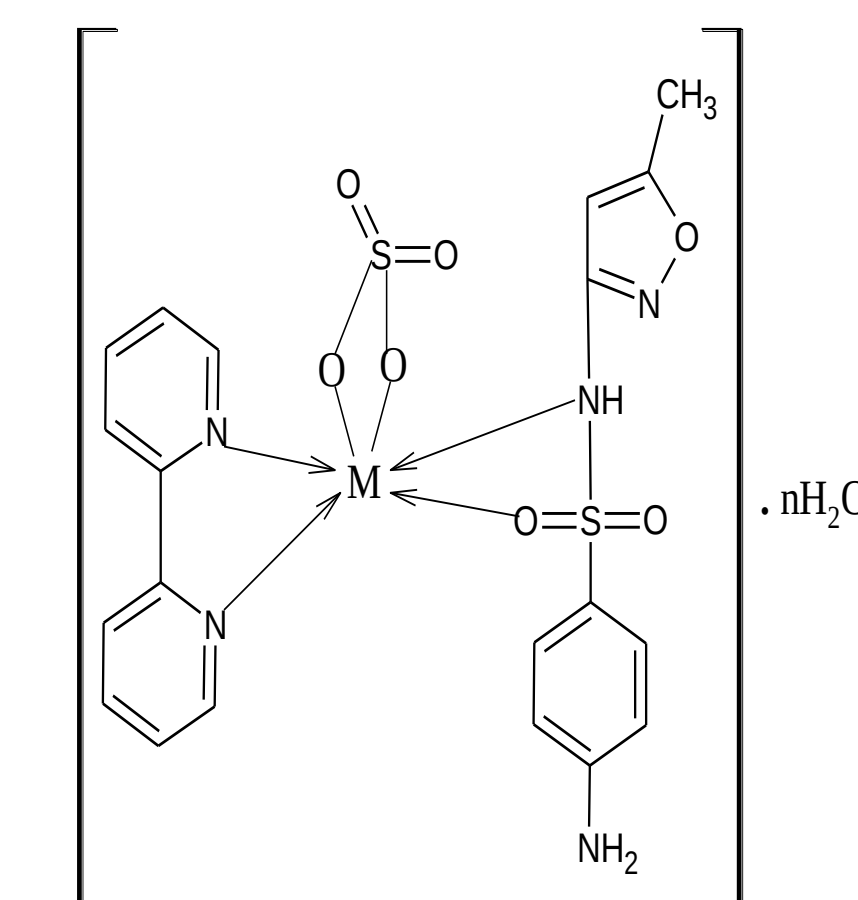
IR studies

SMX acts as a bidentate ligand coordinating to the metals through the N atom of the sulfonamide group ((3195 -3030cm⁻¹) and oxygen atom of the sulfonyl moiety (1158-1103 cm⁻¹) [7]

phen and bipy through their diimine group (C=C/C=N: 1606- 423 cm⁻¹) also bonded as bidentate ligands to the metal [8]

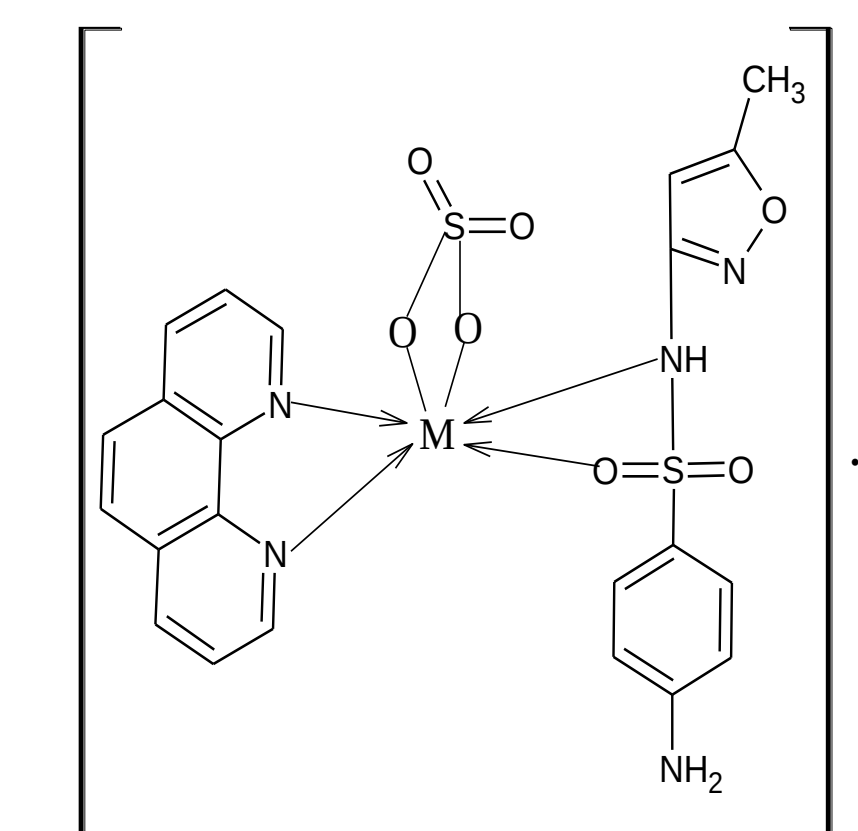
Electronic spectra studies

electronic spectra data indicated that all the metal (II) complexes were monomeric and octahedral.



where M = Zn, Co, Fe, Mn and n = 1,2,3

Fig. 3: Proposed structure of [M(SMX)(bipy)SO₄].nH₂O



where M = Zn, Co, Fe, Mn and n = 2

Fig. 5: Proposed structure of [M(SMX)(phen)SO₄].nH₂O

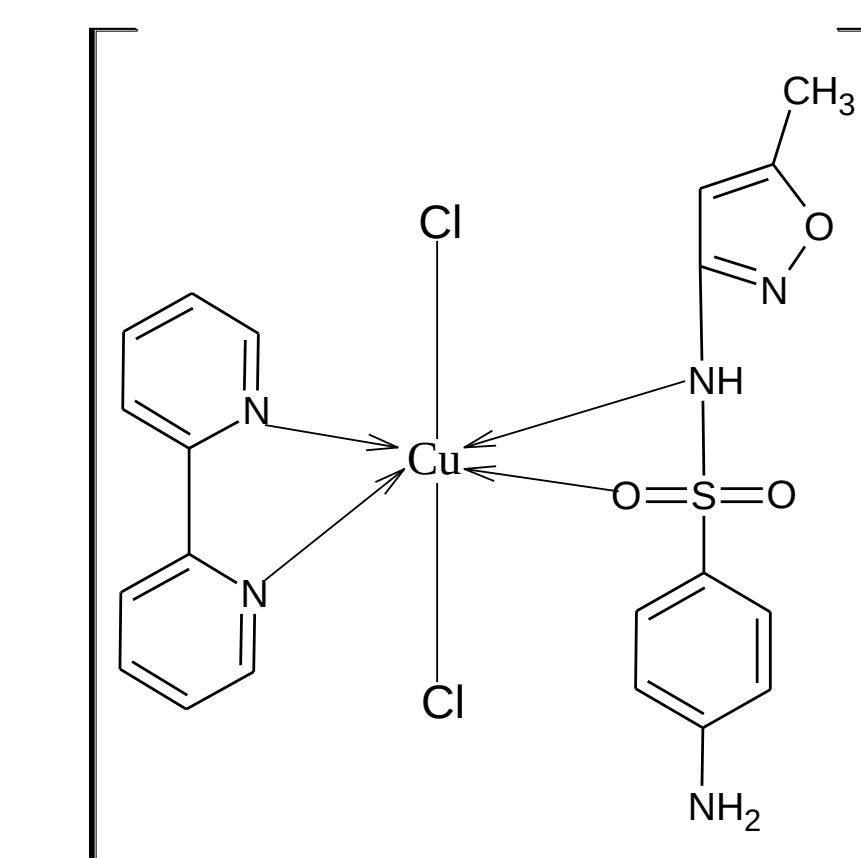


Fig. 4: Proposed structure of [Cu(SMX)(bipy)Cl₂]

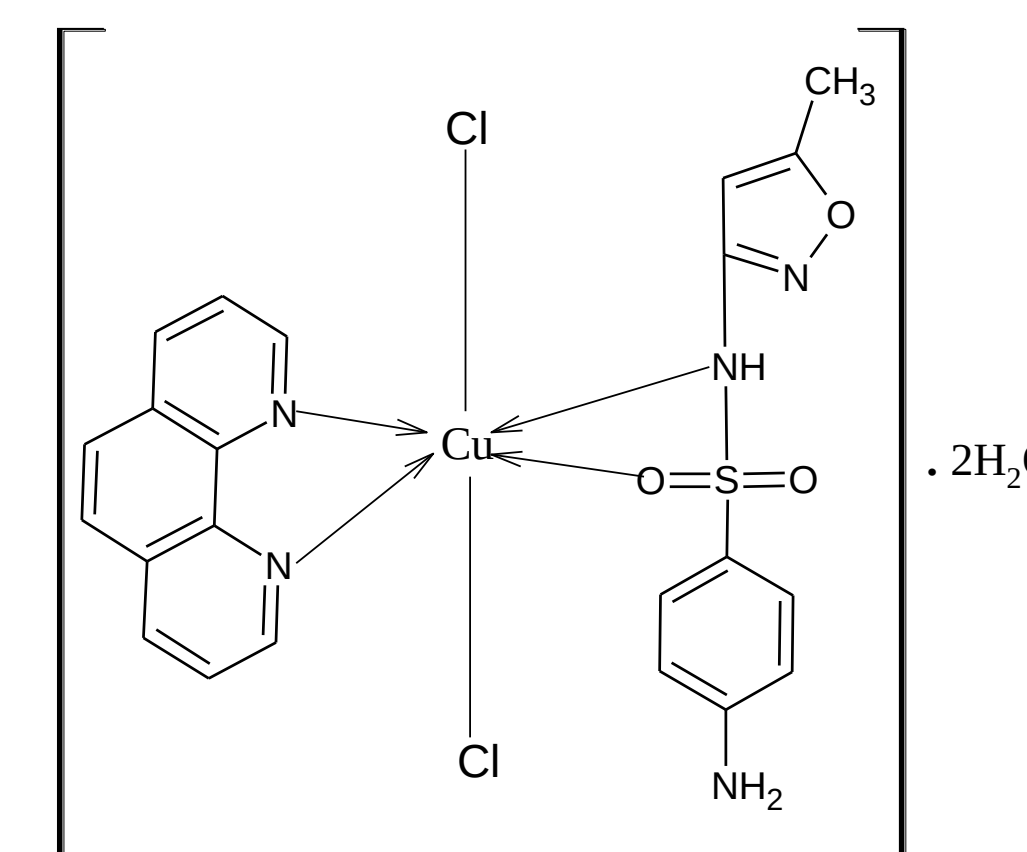
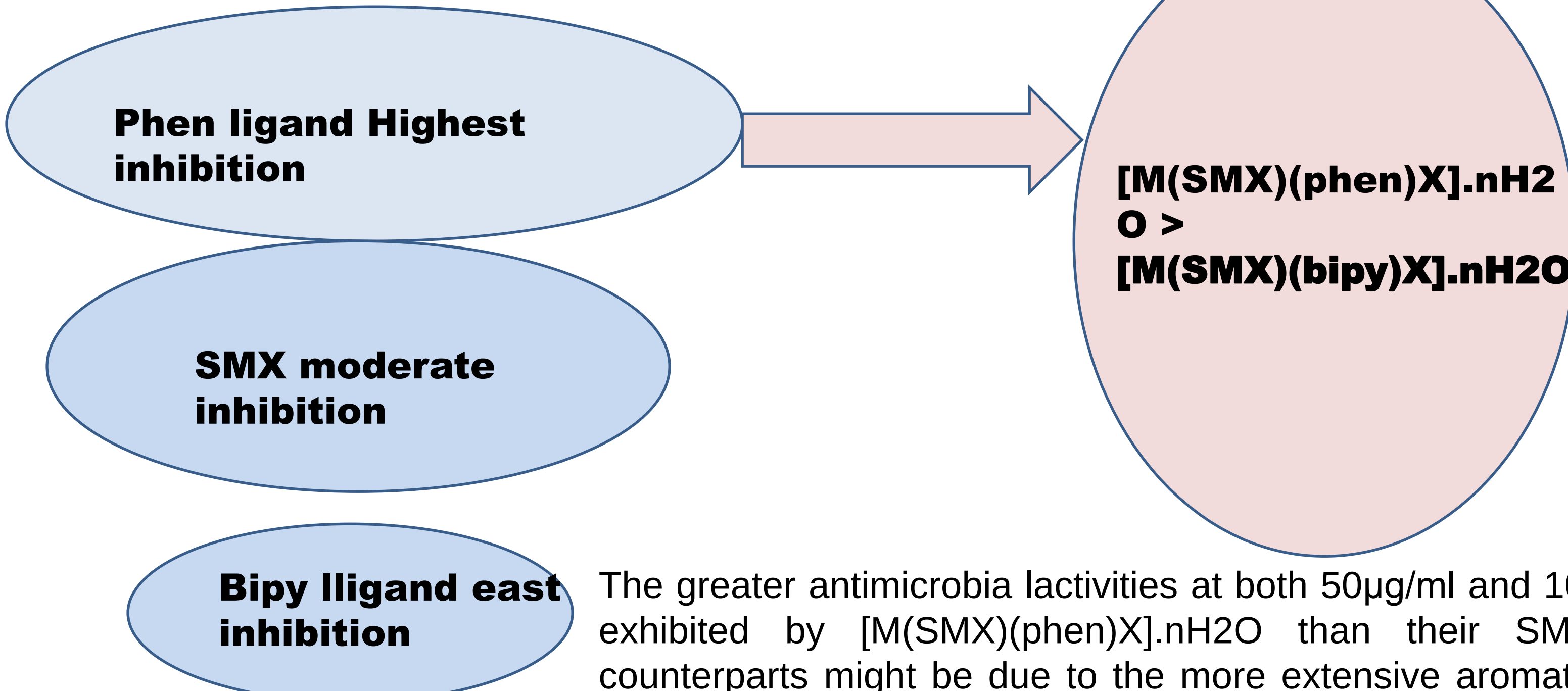


Fig. 6: Proposed structure of [Cu(SMX)(phen)Cl₂].nH₂O

Antimicrobial studies



The greater antimicrobial activities at both 50µg/ml and 10µg/ml exhibited by [M(SMX)(phen)X].nH₂O than their SMX-bipy counterparts might be due to the more extensive aromatic ring system of the phen molecule which gave the complexes better lipophilicity and aided their cell membrane penetration and promoted adverse intracellular interactions

Conclusion

Two mixed ligands of SMX with N,N donor heterocycles: phen and bipy metal(II) complexes have been synthesized and characterised. From the antimicrobial studies, phen is a better heterocycle to combine with SMX for the enhancement of its antimicrobial spectrum due to their more extensive aromatic ring system which gave better lipophilicity as evidenced by enhanced activities of their complexes.

References

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