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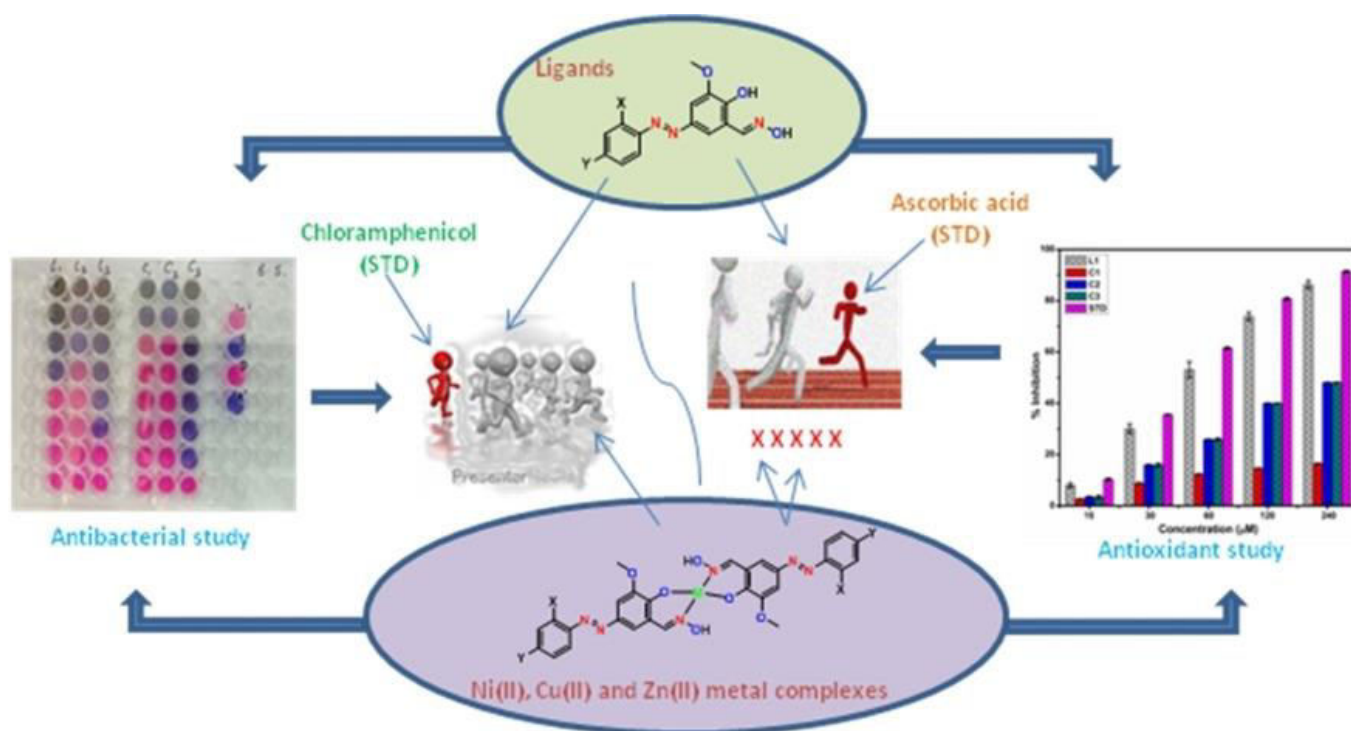
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Microbiological Activity of Schiff Bases and their Cu (II) and Zn (II) Complexes

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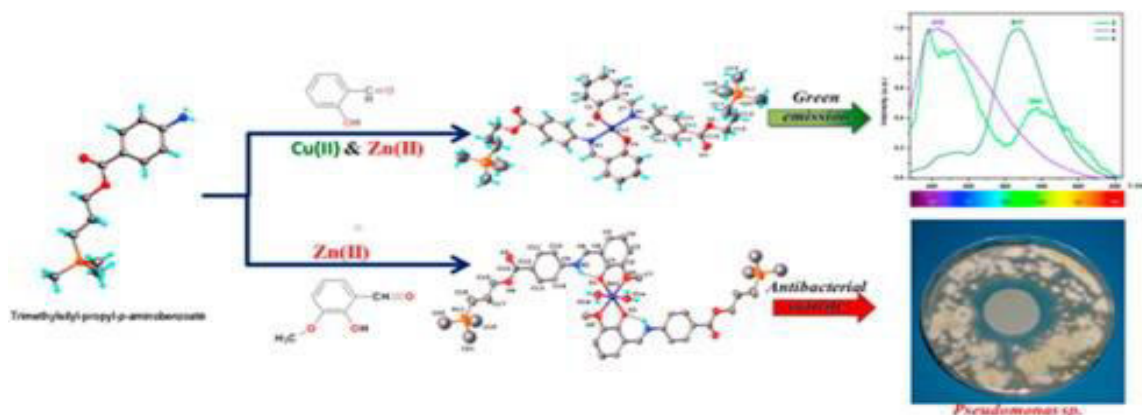
ABSTRACT: The ever-increasing spread of bacterial infection with rising antibacterial drug resistance has become a matter of global concern in the modern times. Therefore, such serious infections leading to high mortality rate has necessitated the search for new classes of effective antibacterial agents with minimum toxicity. Herein, we report the synthesis and identification of a new class of benzofuran based Schiff ligands (6a-6e) and their Cu/Zn complexes (7a-7j) via sequential reactions starting with Salicylaldehyde. Compounds 6a, 7c and 7e exhibit activity in the low microgram range against *M. tuberculosis*, showing the minimum inhibitory concentrations (MICs) of 1.6 µg/mL. The compounds 6e and 7b also show interesting antibacterial activity against *S. Aureus*, *E. coli* and *B. Subtilis* with comparable area of inhibition of standard drugs under study. This research suggests that benzofuran based compounds can serve as a promising lead scaffold in developing new drugs to combat microbial infections.



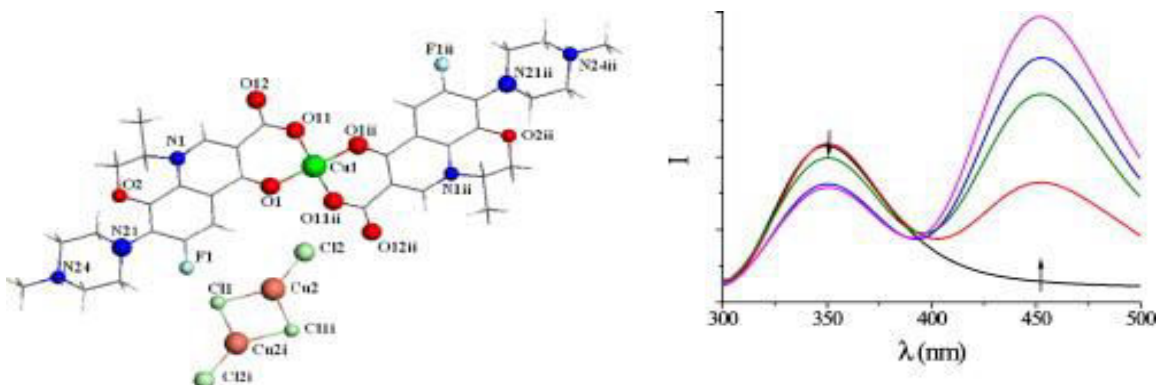
KEYWORDS: microbiological, Cu/Zn complexes, compounds, Schiff bases, inhibitory, drugs

I. INTRODUCTION

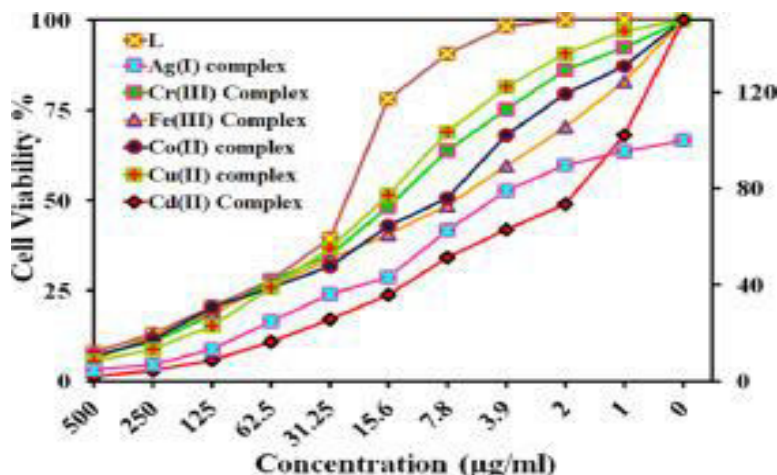
Schiff bases have been widely studied in recent years due to its easy preparation procedures and potential applications [1, 2]. Schiff bases containing nitrogen and oxygen donor atoms generally acts as a tetradentate chelating ligands to different metal ions [3, 4] and have shown potential as antibacterial, antiviral, antifungal and anticancer agents [5, 6].



Metal complexes containing Schiff base are of interest because of their electronic properties that can be modified by suitable functionalization with amine and cyclic substituents [7-10]. Also, tetradentate Schiff base complexes have shown high stability when coordinated to metal ion using the N₂O₂ donor atoms [11-14]. Hence, they are used as structural probes in chemistry of nucleic acid [15], as antimicrobial and anticancer agents [16-18]. Reactive oxygen species (ROS) or free radicals are products of the in vivo physiological and bio-chemical processes in the living cells [19] that could cause lipid peroxidation [19] and may lead to diseases such as cancer, cardiovascular diseases, immunodeficiency, liver injury and other infections [20]. In order to safeguard the human body against cell damage by oxidative species, antioxidant is of paramount importance [21, 22]. They protect different cells in human body, such as hepatocytes, myocytes, erythrocytes, endothelial cells, against oxidative damages [23]. The present study report the synthesis of copper(II), zinc(II), complexes containing symmetrical tetradentate Schiff-base ligand (N₂O₂) obtained from the condensation reaction of 4- acetylresorcinol and ethylene-1,2-diamine. Characterized by elemental analysis, molar conductivity measurements, UV-visible spectrophotometry, Fourier transform infrared (FT-IR) spectroscopy, proton NMR spectroscopy. The ligand and its metal complexes were screened for their antimicrobial properties against some bacteria isolates and their DPPH and ABTS radical scavenging assays were potentials were also evaluated.

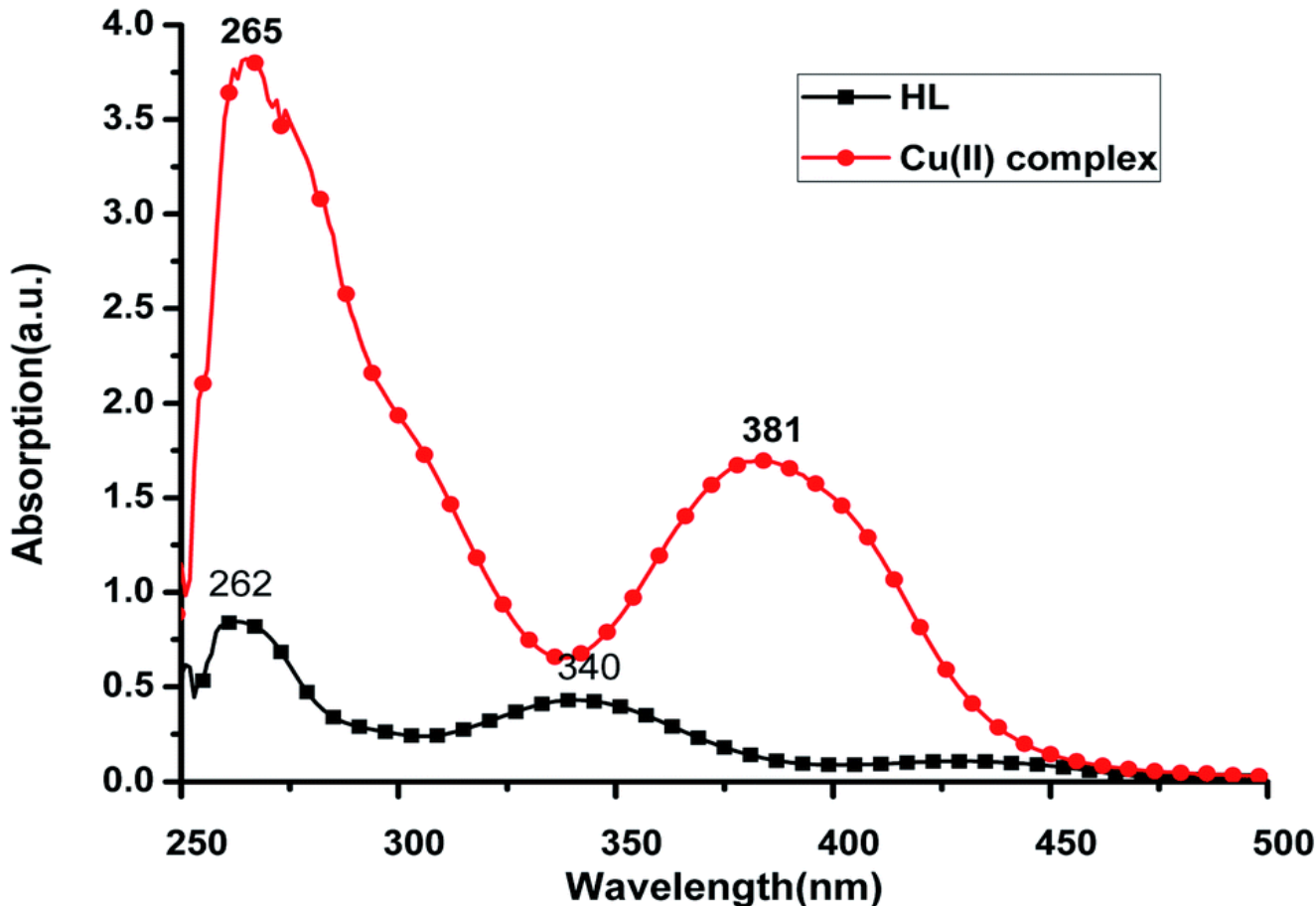


The synthesized compounds were tested to assess their growth inhibitory activities against six bacteria strains by agar diffusion method [24]. *Staphylococcus aureus* (ATCC 25923), *Streptococcus faecalis* (ATCC 29212), *Bacillus cereus* (ATCC 10702)-Gram-positive bacteria and *Pseudomonas aeruginosa* (ATCC 19582), *Escherichia coli* (ATCC 25922) and *Shigella flexneri* (KZN)- Gram negative bacteria, while ciprofloxacin and amoxicillin were used as standards. Sub-culturing of the bacteria isolates on nutrient agar (SAARCHM, Gauteng SA) plates was done by incubating at 37 °C for 24 h. 50 ml of nutrient broth in a 250 ml flask was stirred vigorously to incubate the bacteria cells from the nutrient agar plates at 37 °C for 16 h. The culture was diluted with fresh media, after incubation to obtain D_{600nm} of 0.1. After which, 100 µL of the culture cells were drop onto the plate and spread into a bacterial lawn with a sterile glass spreader. Agar dilution method as contained in NCCLS [25] was used for minimum inhibitory concentration (MIC) of the OpdH2 and Cu(II), Co(II), Zn(II) and Ni(II) complexes as previously described [26].

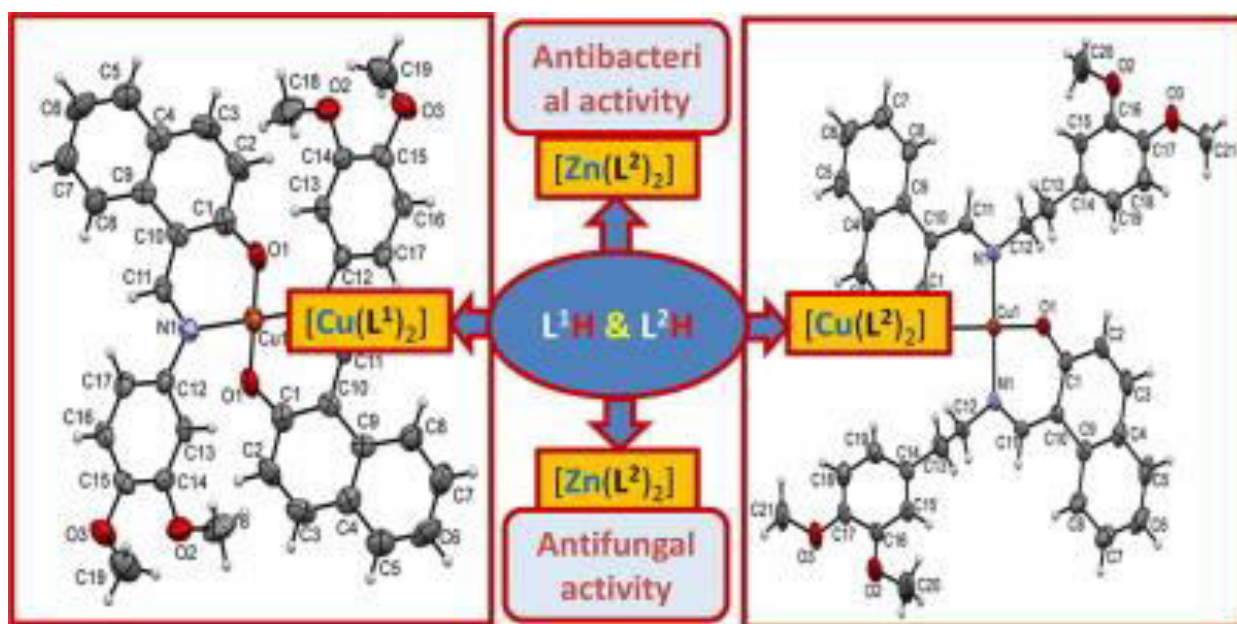


II. DISCUSSION

The UV-visible spectra of the free ligand (OpdH₂) and the metal complexes [metal = Zn(II), Cu(II)], are important. The free ligand spectra exhibits bands at 284 and 309 nm due to aromatic $\pi-\pi^*$ and imino $\pi-\pi^*$ transitions respectively [40, 41], while the band at 383 nm is attributed to the $n-\pi^*$ transitions. In the metal complexes, these absorption bands shifted to higher wavenumbers with increased intensity and this could be ascribed to ligand to metal charge transfer transitions (LMCT) [3, 38]. Copper complex in the visible region displayed two absorption bands at 559 and 447 nm ascribed to $2 B_{1g} \rightarrow 2 A_{1g}$ and $2 B_{1g} \rightarrow 2 E_g$ transitions of a squareplanar copper(II) complex [42].

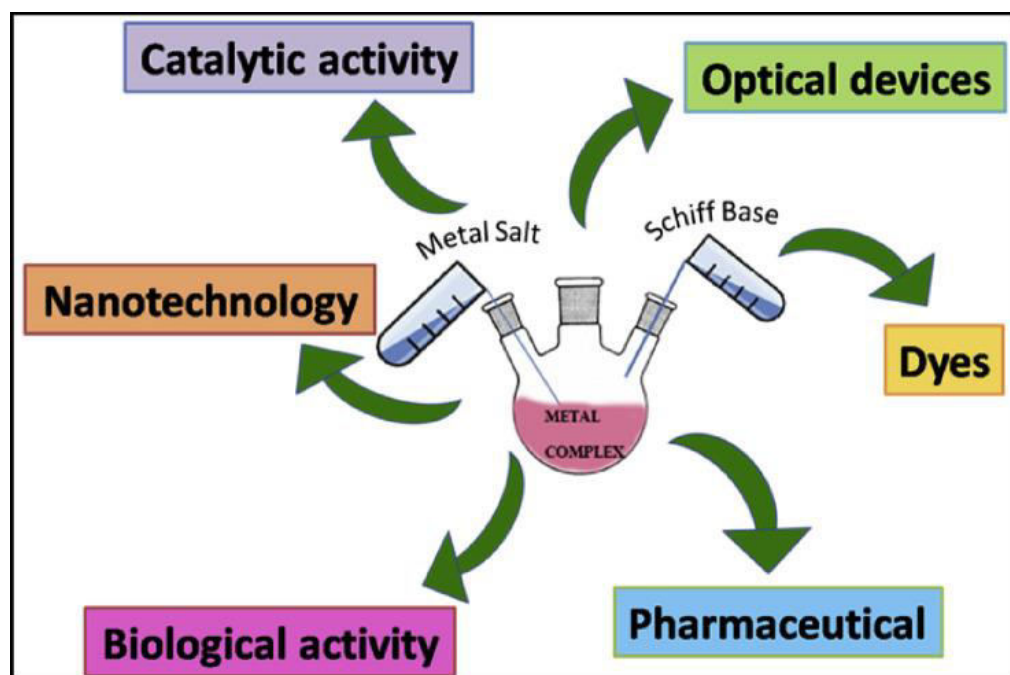


In generally, Zn(II) complexes possess completely filled d10 electronic configuration. Hence, no d-d electronic transition is expected but always shows prominent charge transfer transitions. The Zn(II) complex, showed an absorption band at 376 nm is due to the LMCT transitions of zinc complex in a tetrahedral geometry [44, 45]. The antimicrobial study of the Schiff base (OpdH2), zinc(II), and copper(II) complexes were compared with standards antibiotics, amoxicillin and ciprofloxacin against six bacterial strains: *Streptococcus faecalis* (ATCC 29212), *Staphylococcus aureus* (ATCC 25923), *Bacillus cereus* (ATCC 10702)- Gram-positive bacteria and *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 19582) and *Shigella flexneri* (KZN)- Gram-negative bacteria using agar diffusion method and DMSO as solvent. The metal complex activities were lower than that of the standard drugs: amoxicillin and ciprofloxacin. The complexes showed appreciable antibacterial potentials against *S. aureus*, *B. cereus*, *S. faecalis*, *E. coli*. The biological activity of the synthesized compounds are in the order: Cu(II) > Zn(II). Toxicity activity of the metal complexes mechanism is increased and this could be elucidated on the basis of Overtone's theory of cell penetrability in which lipid materials that are soluble are allow to pass through cell lipid membrane as a significant feature of antimicrobial activity [49] and Tweedy chelation theory [50] that supports the reduction of metal ion polarity to an extent in connection to the ligand orbital and metal ion positive charge partial sharing which enhances the complex lipophilicity [51, 52] as a result of π -electrons delocalization within the chelate ring, disturbing the respiratory activity of the cell and restricts further organism growth [53].



III. RESULTS AND CONCLUSION

Metal ions to ligand binding were confirmed by spectral analyses. Square planar geometry assigned for Opd-Cu complexes. Mycological studies showed that the metal complexes displayed higher antimicrobial activities when compared to the free ligand.



The compounds were also evaluated for their free radical scavenging property and observed varying antioxidant activities as compared to the standards; Opd-Zn, Opd-Cu, showed higher DPPH and ABTS scavenging potentials than the free ligand. The multipotential activities of the synthesised compounds support its usage for the development of chemotherapeutic agents useful for pathological radicals' related diseases treatment.

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