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Abstract

The uses of conventional antibiotics as both preventive and curative measures for antimicrobial infections have increased multidrug resistance infections which have negatively impacted humans. Thus, better antimicrobial agents are needed. We investigated for the first time the antimicrobial and antioxidant activities of 4,4'-{ethane-1,2-diylbis[nitrilo(Z)methylidene]}bis(2-methoxyphenol) ligand (SV) and its metal complexes represented as CoSV, CuSV, NiSV, ZrOSV, VOSV, and UO₂SV. The complexes were characterized using different spectroscopic techniques; such as Fourier Transform Infrared (FT-IR), UV absorption spectra, and elemental analysis. The antibacterial properties of the complexes were evaluated using standard methods. The results showed that all the complexes exhibited strong to moderate activities against *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa* bacterial compared to the parent ligand alone. Increased antibacterial properties of the complexes were attributed to the increased lipophilic nature of the ligand upon coordination with metal. The IC₅₀ (µg/mL) value of the 2,2-Diphenyl-1-picrylhydrazyl radical scavenging activities of the Schiff base metal complexes ranged from 3.24 to 6.44 which was higher than that of standard ascorbic acid (IC₅₀ (µg/mL) = 1.22) or Gallic acid (IC₅₀ (µg/mL) = 2.02) used. The strong antibacterial properties and pronounced radical scavenging activities show that the complexes could be a promising alternative as antibacterial and antioxidant agents.

Keywords

Antimicrobial activities, Schiff base metal-ligand, antioxidant agent, spectra studies

Materials and Methods

The metal complexes of the Schiff base ligand were prepared by the addition of 0.75 mmol of each metal ion (such as VO(acetate)₂, UO₂(NO₃)₂·6H₂O, CoCl₂·6H₂O, CuCl₂·2H₂O, ZrClO₂·8H₂O, and NiCl₂·6H₂O) dissolved in 20 mL of ethanol to the hot ethanolic solution (20 mL) of the bidentate ligand (1.5 mmol, 0.7895 g) in a ratio of 1:2 while stirring [3].

Introduction

Microbial infections are life-threatening diseases; they weaken the immune system and deteriorate most disease conditions. The burden of infections due to antimicrobial resistance especially in Africa and Asia is alarming. According to the European center for disease prevention and control about 33,000 people die annually from infections [1-3]. Antibiotic-resistant bacteria are one of the underlining conditions that are increasing the coronavirus disease (COVID-19) virus mortality rate to date, in which over 5 million people had been affected according to the World Health Organization (WHO) as of September 2021 [3,4]. Most approved antibiotics are inefficient in treating bacterial infections due to their ability to form biofilms, regularly change strains, and develop complex structures with other pathogens [1,5]. Oxidative stress may deteriorate the health of patients already infected by bacteria or fungi, resulting in more severe conditions, these challenges call for potential novel drugs that will combat the challenges of infections and oxidative stress [2,3]. Schiff base ligands have received attention recently due to structural flexibility, and a wide range of biological applications. Transition metal complexes containing Schiff base ligands have been used in the treatment of several pathogenic infections and have been shown to have great antioxidant properties; these complexes scavenge free radicals that are causative factors in cardiovascular diseases and cancer [4-6]. In this study, we report the antibacterial and antioxidant activities of the 4,4'-{ethane-1,2-diylbis[nitrilo(Z)methylidene]}bis(2-methoxyphenol) ligand (SV) Schiff base complexes of Cu(II), Co(II), Ni(II), Zr(IV), VO(IV), and UO₂(II) against strains.

Electronic spectra

The electronic spectral of the SV ligands and metal Schiff base complexes were recorded in 10⁻³M DMF solutions are shown in Fig. 2. The synthesized complexes (CoSV, CuSV, NiSV, ZrOSV, VOSV, UO₂SV) showed characteristic λ_{max} when compared to the ligand alone, and this also confirm successful coordination. Three bands were observed in the spectrum of the ligand (SV) at about 295, 315, and 405 nm. The peaks at about 295 and 315 nm are due to aromatic π-π* and imino π-π* transitions, the band at 405 nm is attributed to the n→π* [1-3].

Results and Discussion

Chemistry of the complexes

The proposed structures of the synthesized ligands (SV) and their corresponding metal Schiff base complexes represented as CoSV, CuSV, NiSV, ZrOSV, VOSV, UO₂SV are shown in Fig. 1. The compounds were characterized using spectroscopic methods UV-visible, FT-IR, and elemental analysis.

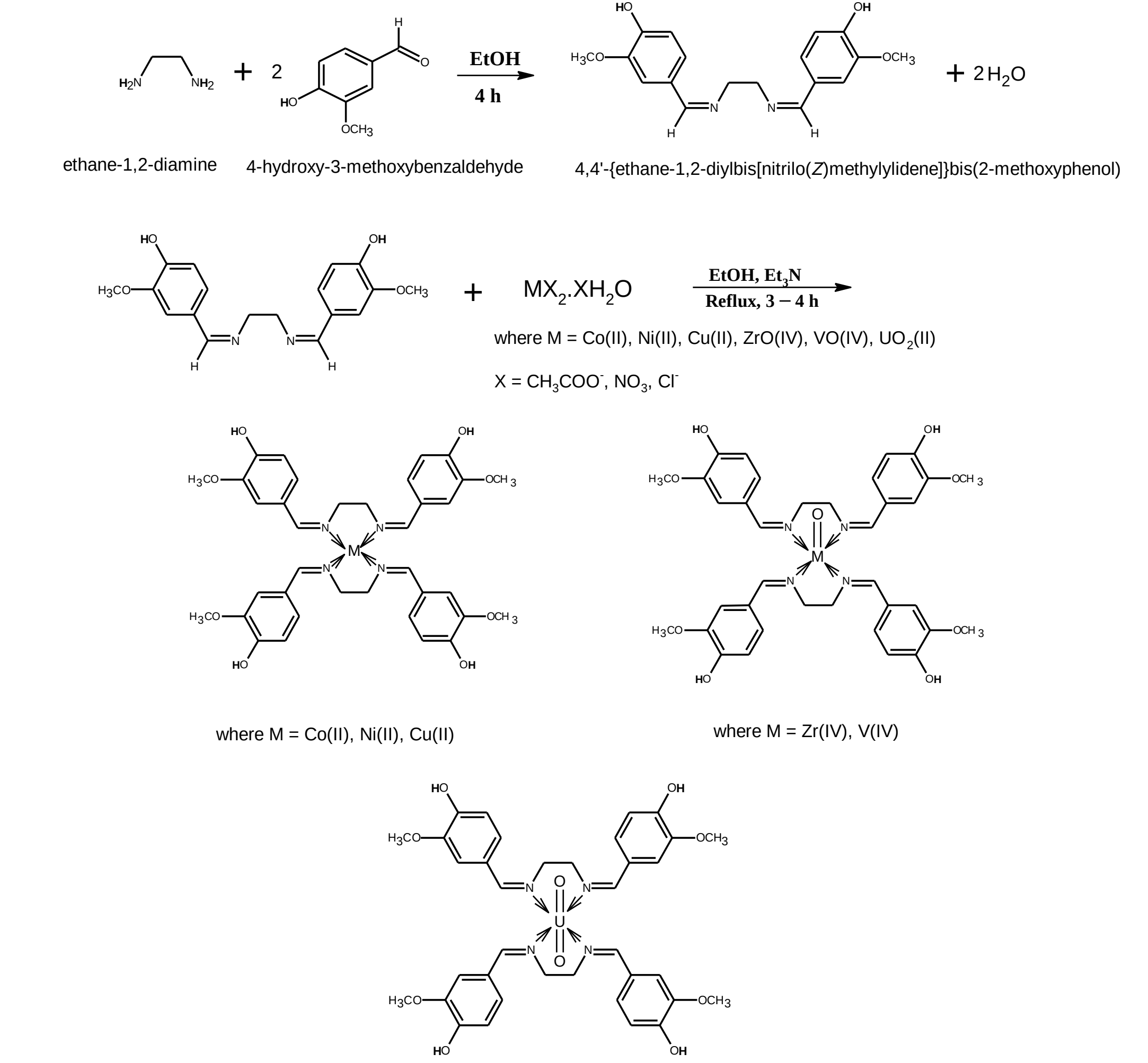


Figure 1. Schematic pathways for the synthesis of N,N' donor ligand (SV) and its metal complexes

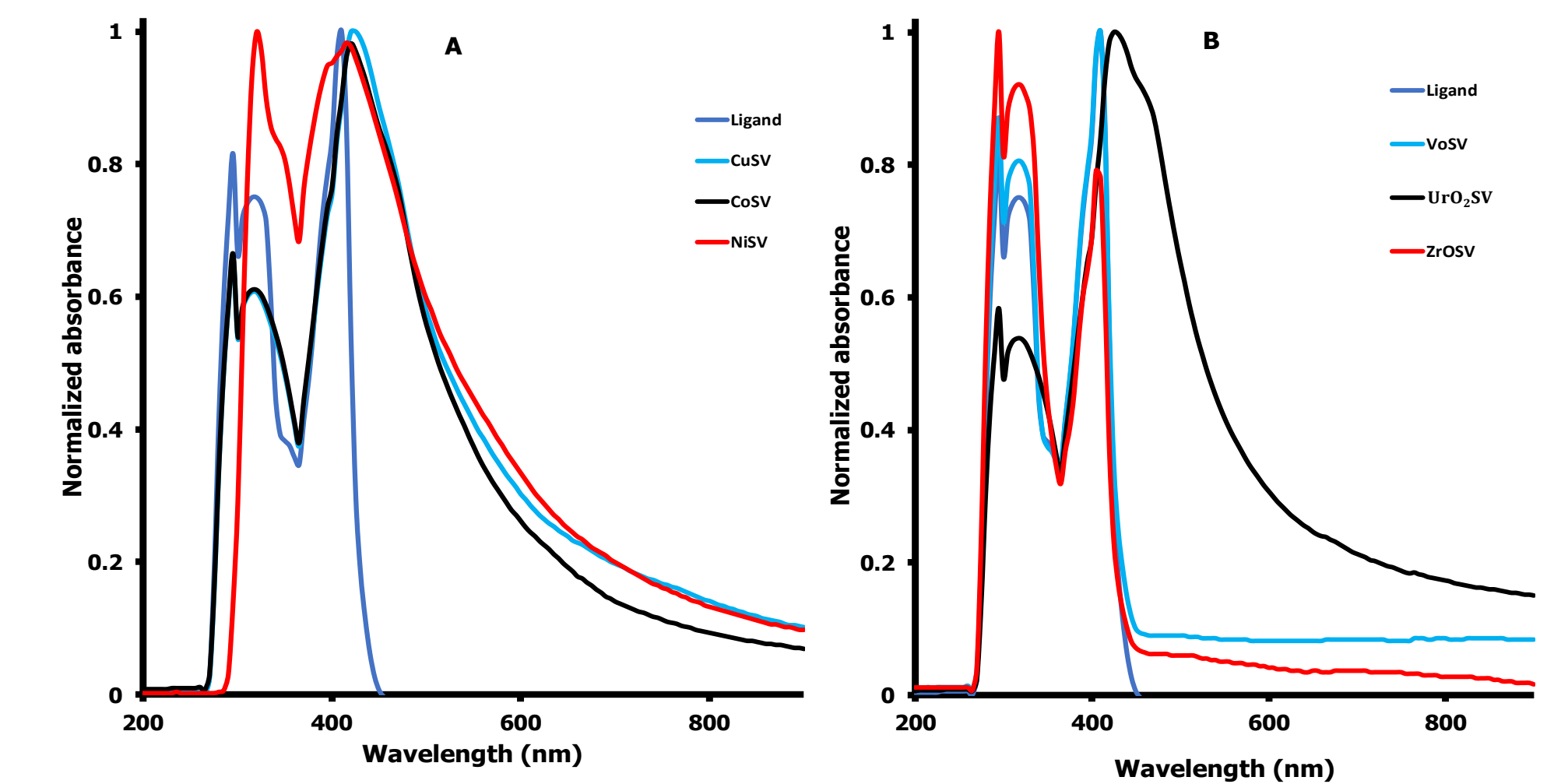


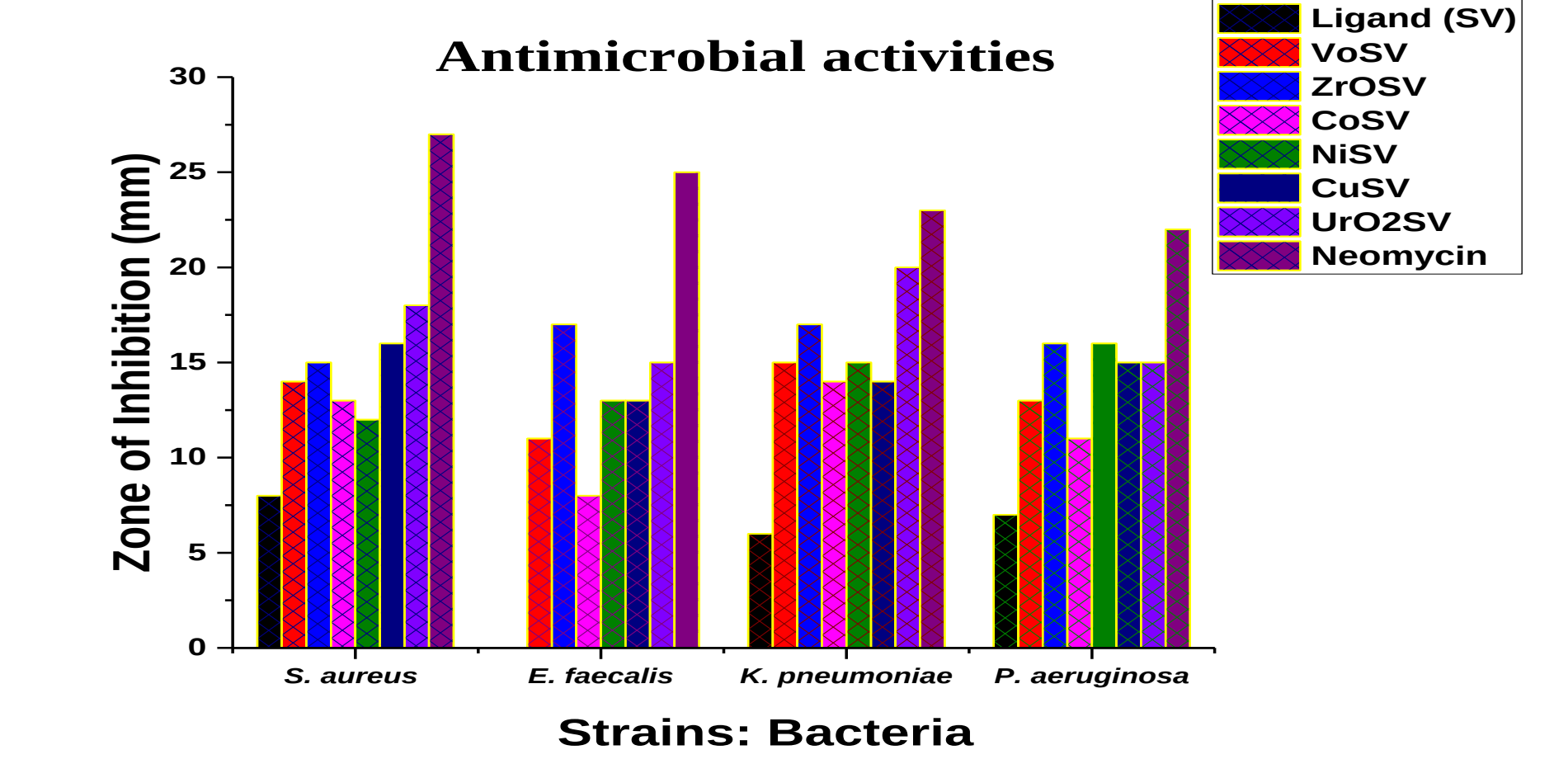
Figure 2. UV-visible spectra of the ligands and their complexes

Antioxidant properties

DPPH free radical scavenging method was adopted to test the antioxidant activities of Schiff base ligand (SV) and metal complexes represented as CoSV, CuSV, NiSV, ZrOSV, VOSV, UO₂SV. The represented metal complexes showed lower antioxidant potential when compared to standard ascorbic or Gallic acid. The synthesized complexes showed IC₅₀ (µg/mL) DPPH radical scavenging activities ranging from 3.24 ± 1.37 to 6.44 ± 0.44 with lower inhibition as compared to those of the standard agents: ascorbic and Gallic acid with IC50 (µg/mL) values of 1.22 ± 0.84 and 2.02 ± 0.42 respectively (P<0.05) [3,4].

Antimicrobial studies

Microbial infections are life-threatening diseases that affect both the health and the economy of various nations. The ingestion of food and water contaminated with both Gram-positive and Gram-negative can result in so many illnesses, such as sepsis, typhoid, fever, and diarrhea. The antimicrobial activities of the parent ligand represented as (SV) and its synthesized metal Schiff base complexes represented as CoSV, CuSV, NiSV, ZrOSV, VOSV, UO₂SV were tested against *S. aureus* (ATCC-25923), *E. faecalis* (ATCC-29212), *K. pneumonia* (ATCC-13883) and *P. aeruginosa* (ATCC-15442) and their activities. The Schiff base complexes containing metals exhibited strong to moderate inhibitory effects compared to their parent-free ligands, both in Gram-positive and negative bacteria (Fig. 3). The antimicrobial activities confirmed that the complexes possess better medicinal therapeutic potential with a wide spectrum against the activities of organisms than their free ligands. Hence, their resourcefulness in the preparation of antibiotics or chemotherapeutic agents [4-6].



Conclusion

The synthesis of 4,4'-{ethane-1,2-diylbis[nitrilo(Z)methylidene]}bis(2-methoxyphenol) (SV) ligand and their metal complexes represented as CoSV, CuSV, NiSV, ZrOSV, VOSV, and UO₂SV were successful. The complexes were physicochemically characterized by elemental analysis, melting point, UV-spectra, conductivity measurement, and FTIR. Antimicrobial analysis of the SV ligand and its metal complexes were evaluated. The antimicrobial results indicate the complexes could be used alone or in combination as alternative antibiotics. Similarly, the pronounced antioxidant properties of the complexes also indicate that they could be used as free radical scavengers.

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