Synthesis, characterization, and antimicrobial activity of 4-imidazolecarboxaldehyde thiosemicarbazone and its Pt(II) and Pd(II) complexes

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ABSTRACT

Schiff bases are versatile ligands, synthesized via condensation of primary amines with carbonyl compounds. In this study, equimolar amounts of 4-imidazolecarboxaldehyde and thiosemicarbazide were combined and the Schiff base 4-imidazolecarboxaldehyde thiosemicarbazone was prepared as a new bidentate complexing agent. The synthesized ligand was reacted with palladium (II) and platinum (II) ions yielding air-stable complexes. For characterization purpose, infrared spectra, mass spectra, electronic spectra, thermal analysis, proton nuclear magnetic resonance and 13 carbon nuclear magnetic resonance spectra studies were carried out on the obtained complexes and ligand. The characterization data showed that the ligand acts as a bidentate coordinate to the metal ions through azomethine nitrogen and sulfur atoms. An in vitro antimicrobial investigation was also carried out for the free ligand and its metal complexes against four bacteria; Bacillus cereus, Staphylococcus aureus, Salmonella typhimurium (Gram-positive), Escherichia coli and Salmonella typhimurium (Gram-negative) and one Fungi; Candida albicans, to assess their antimicrobial properties by disc diffusion technique. Antimicrobial activity of the prepared complexes showed higher activity than the free ligand.

1. Introduction

Thiosemicarbazones, an important class of synthetic compounds, have a variety of applications due to their wide spectrum of biological activities which include antifungal, antibacterial, anti-inflammatory, antimalarial antiviral, anti-tumoral, anticancer and among others as well parasitidal activity [1-12]. Thiosemicarbazones are very active ligands, in particular, that contain an imidazole moiety which is known to play an important role in biological systems as a part of the histidine residue in peptides and proteins and it has been shown that their biological activities are related to their ability to coordinate to metal centers in enzymes [13-15]. There are some research groups work about imidazole thiosemicarbazone derivatives and their metal complexes such as West et al., Casas et al. and Rodriguez-Arregués et al. [16-18]. West et al. have reported the synthesis of the substituted imidazole-2-carboxaldehydethiosemicarbazone derivatives and some of their copper(II) complexes [16]. Casas et al. synthesized an imidazole-2-carboxaldehydethiosemicarbazone ligand and some of its diorganotin (IV) complexes [17]. Rodriguez-Arregués et al. also prepared cobalt (II) and nickel (II) complexes from 2-carboxaldehydethiosemicarbazone ligands and compared their coordinative behavior besides their antimicrobial activities [18]. In this paper, the preparation and characterization of 4-imidazolecarboxaldehyde thiosemicarbazone ligand and its metal complexes were described. In addition, in vitro antimicrobial investigation was also carried out for the ligand and its metal complexes against four bacteria; Bacillus cereus, Staphylococcus aureus, Escherichia coli and Salmonella typhimurium and one Fungi; Candida albicans.

2. Experimental

2.1. Materials and measurements
All chemicals and solvents of the highest analytical grade were used as received from Sigma-Aldrich and Alfa-Aesar. The melting points of the synthesized compounds were determined by a capillary method in a Thomas Hoover apparatus. Mass spectrum of the ligand was carried out on Esquire LC-0084 electronic spray ionization (ESI) Mass spectrometer. Infrared spectra of the ligand and its metal complexes were recorded on Vertex-183387000 FT-IR spectrometer by using KBr disk in the range 4000-400 cm⁻¹. 1H and 13C NMR spectra of the ligand and its metal complexes were recorded on a Bruker AV-III 600 operating at 600 MHz for 1H and 150 MHz for 13C by using DMSO-d₆ as a solvent. UV-Vis spectra in solid state were recorded on a Cary-EL05123055 4000 UV-Vis spectrophotometer in the range 200-800 nm. Thermal analysis was carried out using DTA/TG HIGH RG 2/S thermal analyser. All compounds at different concentrations were performed. Potato dextrose agar medium was prepared by using potato, dextrose, agar-agar and distilled water. Appropriate amount of the compounds in DMSO was added to potato dextrose agar medium in order to get a concentration of 100 and 200 µg/mL of compound in the medium.

2.4. Antimicrobial activity

2.4.1. Antifungal screening

Preliminary antifungal screenings of the prepared compounds at different concentrations were performed. Potato dextrose agar medium was prepared by using potato, dextrose, agar-agar and distilled water. Appropriate amount of the compounds in DMSO was added to potato dextrose agar medium in order to get a concentration of 100 and 200 µg/mL of compound in the medium.
The medium was poured into a set of two Petri plates under aseptic conditions in a laminar flow hood. When the medium in the plates was solidified, a mycelial disc of 0.5 cm in diameter was cut from the periphery of the seven days old culture and it was aseptically inoculated upside down in the center of the Petri plates. These treated Petri plates were incubated at 26 ± 1 °C until fungal growth in the control Petri plates was almost complete. The mycelial growth of fungi (nm) in each Petri plate was measured [22].

2.4.2. Antibacterial screening

The paper disc diffusion method was used to screen the antibacterial activity of the prepared compounds and performed by using Mueller Hinton agar (MHA). The ligand and its complexes were carried out according to the National Committee for Clinical Laboratory Standards Guidelines. Bacterial suspension was diluted with sterile physiological solution to 108 cfu/mL (Turbidity = McFarland standard 0.5). One hundred microliters of bacterial suspension were swabbed uniformly on the surface of MHA and the inoculum was allowed to dry for 5 minutes. Sterilized filter paper discs (Whatman No. 1, 6 mm in diameter) were placed on the surface of the MHA and soaked with 20 µL of a solution of each sample. The inoculated plates were incubated at 37 °C for 24 h in the inverted position. The diameters (mm) of the inhibition zones were measured [23].

3. Results and discussion

3.1. Synthesis

The synthesis of ligand containing an imidazole ring is outlined in Scheme 1. The corresponding palladium (II) and platinum (II) complexes were obtained in two steps. In the first step, the ligand was synthesized by condensing equimolar quantities of thiosemicarbazide with 4-imidazole carboxaldehyde in ethanol: water mixture. In the second step, the prepared ligand was refluxed with metal salt in 1:2 M ratio, to lower and higher frequencies on the coordination of the ligand has been assigned to \( \nu(NH) \) [18,24-25]. This evidence indicates the noncoordination of the NH\(_2\) group on the metal ion [10,18,26,27]. The electronic spectra of 4-ITSC showed that a strong absorption band at 313 nm. This band assigned to the \( \pi \rightarrow \pi^* \) transition of the azomethine group [24,25]. The intra-ligand transitions for Pd (II) complex were observed 226, 313, 376 nm and for Pt (II) complex was observed in 210, 226, 265 nm and these bands are mainly due to \( \pi \rightarrow \pi^* \) and \( n \rightarrow \pi^* \) transitions [24,25].

The \( ^1 \)H and \( ^{13} \)C NMR spectra and chemical shift values of the ligand and corresponding metal complexes were record in DMSO-\( d_6 \) solvent. The \( ^1 \)H NMR of 4-ITSC ligand and its metal complexes show signal at \( \delta 8.2, 8.5, \) and 8.6 ppm have been assigned to \( \delta (NHCS) \) protons and the signals at \( \delta 7.3, 7.4 \) and 7.2 ppm have been assigned to \( \delta (CSNH2) \) protons. The signals at \( \delta 8.2, 8.1, \) and 8.2 ppm assignable to azomethine protons (CH=N). The downfield chemical shift in the spectra of Pd(II) and Pt(II) complexes indicate the coordination through the azomethine nitrogen to the metal atom resulting in the formation of a coordinate N→M linkage and all imidazole ring protons were observed in the expected regions [18,24-28].

3.2. Antimicrobial activity

The synthesized compounds were screened in \( \text{vitro} \) for their antibacterial activity against four pathogenic bacteria; \( Bacillus cereus, \) \( Staphylococcus aureus, \) \( Escherichia coli, \) Salmonella typhimurium and one fungus; \( Candida albicans \) at a concentration of 100 and 200 µg/mL with DMSO as the solvent. The results showed that the tested compounds possess moderate antimicrobial activity against most of the tested organisms, as shown in Table 2.
In similar previous studies, the evaluation of antibacterial activity of the synthesized compounds exhibit a moderate inhibitory effect on the microbial proliferation and only against some Gram-positive bacteria [18,20,21,23,25,28]. The palladium complex was more effective against E. coli than standard drug.

4. Conclusion

In this study, condensation reaction was adopted for preparing a new Schiff base ligand; 4-imidazolecarboxaldehyde thiosemicarbazone. The ligand and its metal complexes were fully characterized by several techniques and the antibacterial and antifungal activities of the ligand and its metal complexes were also evaluated.

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Disclosure statement

Conflict of interests: The authors declare that they have no conflict of interest.

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Table 2. Antimicrobial activity of synthesized thiosemicarbazone and its complexes.

| Compound | Concentration (μg/mL) | Diameter of inhibition zone (mm) |
|----------|----------------------|----------------------------------|
|          | Gram+ve bacteria     | Gram-ve bacteria                 | Fungi                     |
|          | E. coli              | S. aureus                        | E. coli                  | S. typhi                 | C. Alibicans |
| 4-FTSC   | 100                  | 10                               | 07                       | 07                      | 06          | 06          |
|          | 200                  | 10                               | 11                       | 12                      | 10          | 09          |
| Pd(4-FTSC)Cl₂ | 100              | 11                               | 09                       | 16                      | 11          | 09          |
|          | 200                  | 12                               | 12                       | 19                      | 14          | 10          |
| Pt(4-FTSC)Cl₂ | 100              | 11                               | 11                       | 11                      | 11          | 11          |
|          | 200                  | 12                               | 12                       | 12                      | 13          | 11          |
| Gentamicin | 200                | 20                               | 14                       | 17                      | 16          | -           |

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