

Research Article

Synthesis, Characterization, and Biological Activity of Nickel (II) and Palladium (II) Complex with Pyrrolidine Dithiocarbamate (PDTC)

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The synthesis of square planar Ni(II) and Pd(II) complexes with pyrrolidine dithiocarbamate (PDTC) was characterized by elemental, physicochemical, and spectroscopic methods. Two complexes were prepared by the reaction of nickel acetate and palladium acetate with pyrrolidine dithiocarbamate (PDTC) in 1 : 2 molar ratio. The bovine serum albumin (BSA) interaction with complexes was examined by absorption and fluorescence spectroscopic techniques at pH 7.4. All the spectral data suggest that coordination of the pyrrolidine dithiocarbamate (PDTC) takes place through the two sulphur atoms in a symmetrical bidentate fashion. All the synthesized compounds were screened for their antimicrobial activity against some species of pathogenic bacteria (*Escherichia coli*, *Vibrio cholerae*, *Streptococcus pneumoniae*, and *Bacillus cereus*). It has been observed that complexes have higher activity than the free ligand.

1. Introduction

The dithiocarbamate stoichiometry has much external consideration in recent years due to its ability to act as a bidentate ligand [1–3]. Dithiocarbamates such as diethyl dithiocarbamates and pyrrolidine dithiocarbamate display cytotoxic properties and they have been used to fight against metal poisoning [4–6]. The complexes are thermodynamically stable, so they are used as chelating agent for the extraction of trace metals [5, 7]. Metal complexes of dithiocarbamate present a wide range of applications in agriculture, medicine, industry, and analytical and organic chemistry [2, 7]. The dithiocarbamate complexes are commercially important because they are used in rubber vulcanization process [8].

The metal complexes show enhanced biological activities such as antibacterial, antimalarial, and fungicidal activities compared to free ligands due to drop in polarity of metals after complexation [9, 10]. Dithiocarbamates from nickel group that is of platinum (II) and palladium (II), as well as of

isoelectronic gold (III), showed remarkable antitumor properties [11]. Particularly, nickel (II) and palladium (II) play an important role in both fundamental research and application of their physical properties. Nickel and palladium complex with pyrrolidine dithiocarbamate (PDTC) has been studied extensively.

Herein, we report an account of Ni and Pd (II) complex with formulae $[\text{Ni}(\text{PDTC})_2]$ and $[\text{Pd}(\text{PDTC})_2]$ synthesized. The BSA binding study of the complexes has been performed spectroscopically. The PDTC and its metal (II) complexes show antibacterial activities screened by disc diffusion method beside some variety of pathogenic bacteria.

2. Experimental

2.1. Materials and Physical Measurements. Nickel acetate and palladium acetate (E. Merck) were distilled before use. Solvents (methanol, ethanol, DMF, chloroform, etc.) were purified by standard methods. Ammonium dithiocarbamate

TABLE 1: Elemental analysis of **L** (PDTC) and its complexes.

Formula	Comp.	MW	MP (°C)	Colour	Found (calculated)%			
					C	H	N	M
C ₅ H ₈ NS ₂	L	164	144	White	36.58 (36.64)	4.87 (4.95)	8.53 (8.59)	—
C ₁₀ H ₁₆ N ₂ S ₄ Ni	1	350.69	268	Light green	34.21 (34.42)	4.56 (4.73)	7.92 (7.96)	16.73 (16.84)
C ₁₀ H ₁₆ N ₂ S ₄ Pd	2	398.42	308	Yellow	30.12 (30.26)	4.01 (4.07)	7.02 (7.09)	26.71 (26.79)

(Aldrich) was used as received without further purification. The elemental (C, H, and N) analyses were performed on a Perkin-Elmer model 2400 elemental analyzer. Nickel and palladium were analyzed by Varian atomic absorption spectrophotometer (AAS) model-AA55B, GTA using graphite furnace. Electronic absorption spectra were carried out on a SHIMADZU UV-1800 spectrophotometer. The fluorescence spectrum of albumin was obtained in the Fluorimeter (Hitachi-2000) with thermostat. IR spectra were recorded using a Perkin-Elmer FTIR model RX1 spectrometer. Molar conductance values (μ) were measured in systronics conductivity meter 304 model in DMF solvent. The concentrations of BSA were determined from optical density capacity, using the values of molar absorptivity of $\epsilon_{280} = 44\,720$ and $35\,700\text{ M}^{-1}\text{ cm}^{-1}$.

2.2. Preparation of [Ni(PDTC)₂] (1) and [Pd(PDTC)₂] (2). To prepare these complexes, **1** and **2**, a common procedure was followed as described below, using nickel acetate for complex **(1)**, palladium acetate for complex **(2)**, and the organic ligand (**HL**) in stoichiometry ratio (1:2). A methanolic solution of **L** (0.082 g) was mixed with 0.07121 g of nickel acetate and 0.0561 g of palladium acetate with stirring condition and the mixture was refluxed for 3 hours. After the completion of the reaction, the reaction mixture was cooled down to room temperature and precipitate was filtered, dried, and recrystallized from methanol to give pure product.

2.3. BSA Binding Experiments. The BSA binding interactions between complexes were performed by absorption spectra and fluorometric titration in presence of phosphate buffer at pH 7.4. The aqueous solution of protein was titrated by addition of the proper concentration of the solution complexes. For every addition, the mixture solution was shaken and sanctioned to rise for 20 minutes, and then the fluorescence intensities were calculated with an excitation wavelength of 280 nm.

2.4. Antimicrobial Screening. The antibacterial screening effects of the compounds were tested against four bacterial strains, namely, *Escherichia coli*, *Vibrio cholerae*, *Streptococcus pneumoniae* (Gram-negative bacteria), and *Bacillus cereus* (Gram-positive bacteria) [12, 13]. The antibacterial activities of complexes **1** and **2** were done in DMF solvent. The solutions of ligand and complexes **1** and **2** were added to the agar plates. The DMF solvent was used as a negative control. Incubation of the plates was done at 37°C for 24 hours; inhibition of

the organisms was measured and used to calculate mean of inhibition zones in millimetres.

2.5. Theoretical Methodology. The density functional theory (DFT) calculations were performed in the gas phase using the B3LYP (Becke three-parameter Lee-Yang-Parr) exchange correlation functional [14]. The basis set LanL2DZ was used to palladium (II) complex for all atoms. All calculations were approved using the GAUSSIAN 09 program with the support of the Gauss View visualization program [15].

3. Results and Discussion

3.1. Synthesis and Characterization of Complexes 1 and 2. The square planar nickel (II) and palladium (II) complex was obtained in good yield from the reaction of the metal acetate with organic moiety **L** (PDTC) in the methanol medium (1:2) ratio. The organic molecule **L** acts as bidentate ligand through S, S- donor centres. The molar conductivity values for complexes **1** and **2** (Λ_0 , $\text{ohm}^{-1}\text{ cm}^2\text{ mol}^{-1}$) are 48 and 52 at 300 K, indicating that complexes are nonelectrolyte in DMF solution. The elemental analysis of **L** and complexes (given in Table 1) is reliable with the designed results from the empirical formula of each compound. All the complexes are air-stable, nonhygroscopic, partly soluble in ethanol and methanol, and soluble in acetonitrile, DMSO, and DMF and are monomeric in nature.

3.2. Infrared Spectra. The IR data of the ligand (Figure 1) pyrrolidine dithiocarbamate (PDTC) shows several bands at 1454, 939, 827, and 2968 cm^{-1} due to C-N, C=S, C-S, and C-H bond stretching vibrations in the solid state, respectively [16]. These bands are shifted to lower frequency on complexation with different stoichiometry ratio. New vibrations at 428–442 cm^{-1} for complexes **1** and **2** are not present in the free ligand. The new stretching frequency of $\nu(\text{M-S})$ bond in complexes **1** and **2** at 428 cm^{-1} and 442 cm^{-1} confirmed the involvement of only sulphur atom (Figures 2 and 3) in chelation with metal ions [17].

3.3. Electronic Absorption Spectral Study. At room temperature, electronic absorption spectra of PDTC and complexes (**1** and **2**) were recorded in DMF solvent (given in Figure 4). The spectra of the ligand (**L**) pyrrolidine dithiocarbamate exhibit main peaks: at 354 nm. The peaks were attributed to $\pi \rightarrow \pi^*$ transitions, respectively [18]. The absorption spectra of the nickel (II) complex exhibit broad bands at 325 nm and 387 nm attributed to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition; again, the

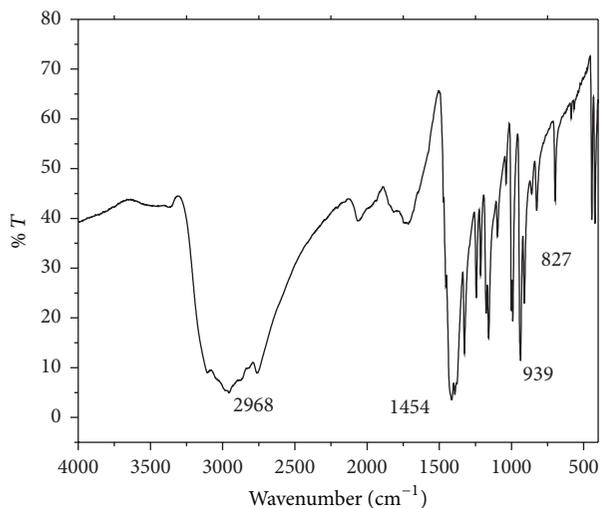


FIGURE 1: IR spectrum of ligand L (PDTC).

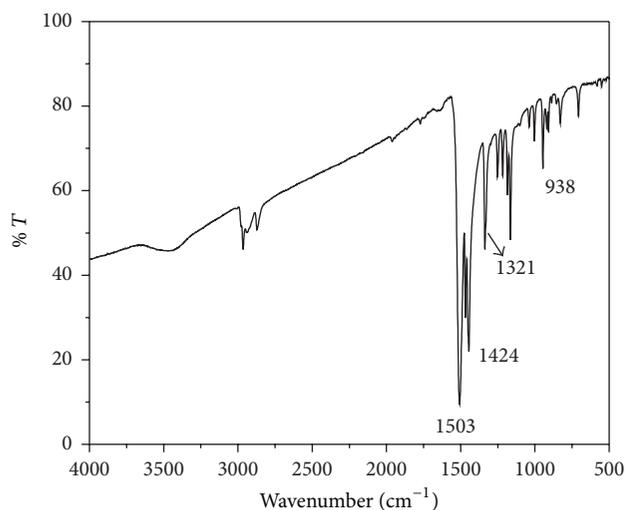
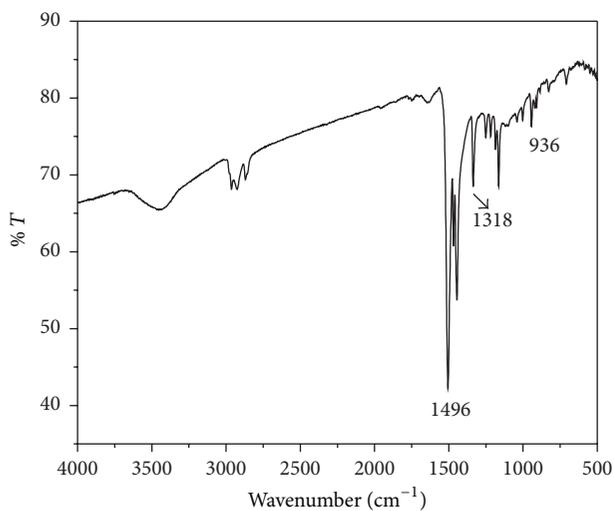
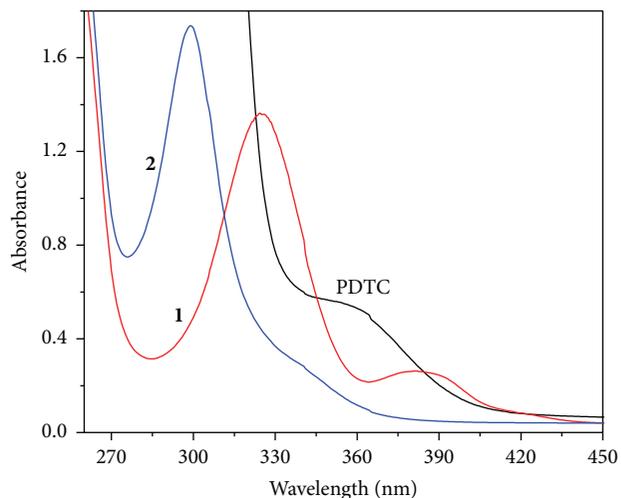
FIGURE 2: IR spectrum of $[\text{Ni}(\text{PDTC})_2]$ complex.FIGURE 3: IR spectrum of $[\text{Pd}(\text{PDTC})_2]$ complex.

FIGURE 4: UV-Vis spectra of ligand (PDTC) and its corresponding complexes 1 and 2.

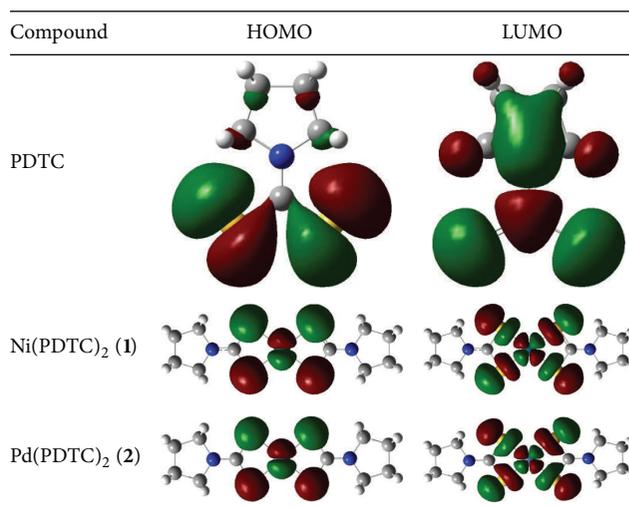


FIGURE 5: Some selected molecular orbitals of PDTC and its complexes 1 and 2.

palladium (II) complex presents broad bands at 298 nm and 342 nm accredited to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition.

3.4. Electronic Structure. Full geometry optimization of L and its complexes was approved by density functional theory (DFT) at the B3LYP level in their ground state and the frontier orbitals of HOMO and LUMO of L and its complexes are given in Figure 5. Thus, it is inferred that in HOMO of L electrons are localised on C-S group but in complex electrons are localised on metal and C-S group. In LUMO, electrons are largely localized on pyrrole ring and S group. The HOMO-LUMO energy difference of PDTC in ground state is 0.16574 eV but in complexes energy gap is 0.0211 eV and 0.01919 eV for 1 and 2, respectively.

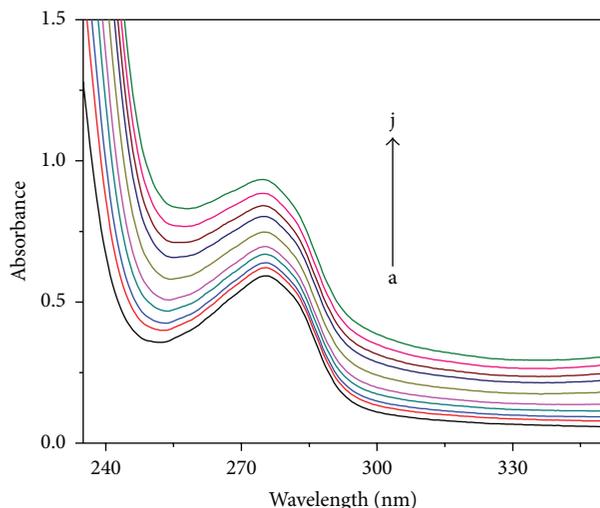


FIGURE 6: Absorption spectrum of nickel complex (1) with BSA at 280 nm in phosphate buffer. Arrow indicates increase of the concentration of complex (1).

3.5. BSA Protein Binding Experiments

3.5.1. *Absorption Characteristics of BSA with Complexes 1 and 2.* BSA gives absorption band at 280 nm due to the aromatic tryptophan and tyrosine residues. The absorption spectra of BSA in the absence and presence of complexes 1 and 2 were studied at different concentrations. We observed that absorption of BSA increases frequently upon increasing the concentration of the complex, indicating the formation of a ground state complex [19, 20]. As dynamic quenching does not affect the absorption spectrum of quenching molecule, the observed changes in presence of complex could be indicating static quenching interaction between complex and serum albumin. The absorption spectra of BSA with complexes 1 and 2 are given in Figures 6 and 7. The apparent association constant (K_{app}) determined the complex with BSA using the Benesi-Hildebrand equation [21]

$$\frac{1}{(A_{obs} - A_0)} = \frac{1}{(A_c - A_0)} + \frac{1}{K_{app}(A_c - A_0)} [\text{comp}], \quad (1)$$

where A_{obs} indicates observed absorbance of the solution having different concentrations of the complex at 280 nm, A_0 is the absorbance of BSA, A_c is the absorbance of complex at 280 nm, and K_{app} represents the apparent association constant. The enrichment of absorbance at 280 nm was due to adsorption of the surface complex, based on the linear relationship between $1/(A_{obs} - A_0)$ and reciprocal concentration of the complex. The apparent association constant (K_{app}) for complexes 1 and 2 was $3.18 \times 10^4 \text{ M}^{-1}$ ($R = 0.9884$) and $3.47 \times 10^4 \text{ M}^{-1}$ ($R = 0.9869$) indicating complexes are strongly bound with BSA protein.

3.5.2. *Fluorescence Quenching of BSA by Complexes 1 and 2.* The emission spectra of BSA in presence of different concentrations of complexes 1 and 2 were recorded in the wavelength range 295–530 nm by exciting the protein at

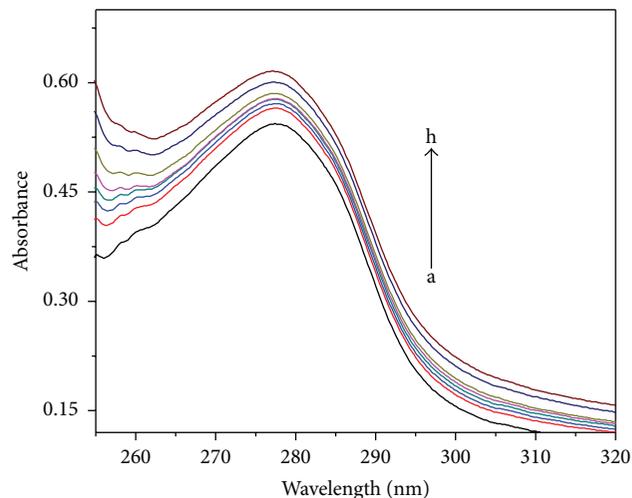


FIGURE 7: Absorption spectrum of palladium complex (2) with BSA at 280 nm in phosphate buffer. Arrow indicates increase of the concentration of complex (2).

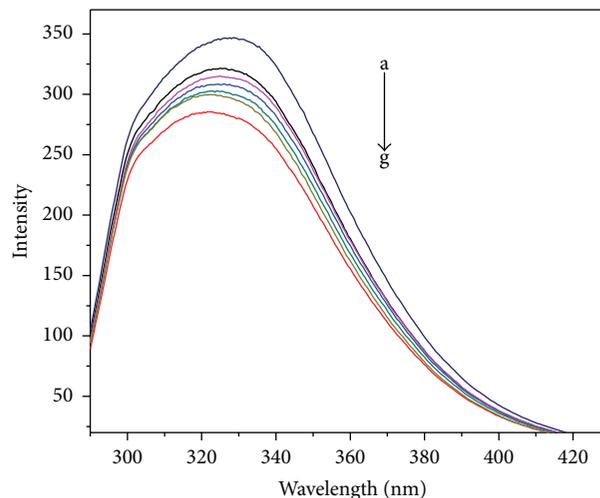


FIGURE 8: Fluorescence emission spectra of BSA with complex 1 in phosphate buffer. The concentration of complex varied from 0.0 to $3.2 \times 10^{-6} \text{ ML}^{-1}$.

280 nm and represented in Figures 8 and 9. As seen, with increasing the concentration of the complex, the fluorescence intensities of the proteins are repeatedly decreased. The fluorescence quenching is described by the Stern-Volmer relation [22]:

$$\frac{F_0}{F} = 1 + K_{sv} [Q], \quad (2)$$

where F_0 and F indicate the fluorescence intensities in the absence and presence of quencher, respectively. K_{sv} is a linear Stern-Volmer quenching constant; Q is the concentration of quencher. In case of fluorescence quenching of BSA, a linear plot between I_0 and I against [complex] was obtained. K_{sv} calculated from the slope are 3.41 M^{-1} ($R = 0.9836$) and 3.58 M^{-1} ($R = 0.9847$) for complexes 1 and 2, respectively. The binding constant values suggest that complexes strongly

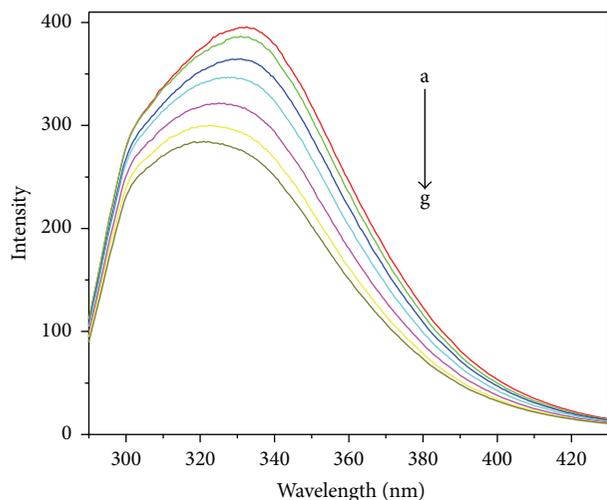


FIGURE 9: Fluorescence quenching spectra of BSA with complex 2 in phosphate buffer. The concentration of complex varied from 0.0 to $3.4 \times 10^{-6} \text{ M L}^{-1}$.

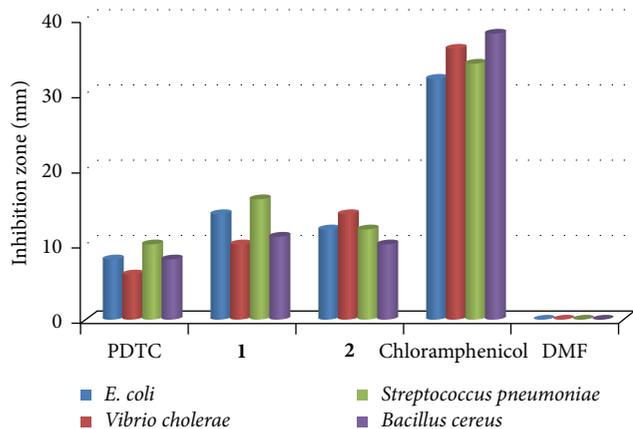


FIGURE 10: Antibacterial activity of ligand and its complexes (1 and 2).

bind to albumins. The linear Stern-Volmer plots indicate quenching mechanism either static or dynamic.

3.6. Antibacterial Activity. Determination of antimicrobial activity against specific pathogens is essential for proper therapy. The antibacterial activity was studied by agar disc diffusion method and comparison with standard antibiotic chloramphenicol is shown in Figure 10. From this experiment, it is contingent that complexes have more activity than free ligand [23, 24]. The complexes are highly active due to increasing the delocalization of pi-electrons into the hole chelate ring, indicating increase in its lipophilicity. All the results indicate that chelation improved the antibacterial activity compared to the ligand.

4. Conclusion

Four coordinated square planars of Ni (II) and Pd (II) compound are synthesized and characterized by various

spectroscopic tools. The compounds are strongly bound with BSA protein investigated by spectroscopic methods. The quenching constant value indicated that complexes have good binding with BSA through a static quenching mechanism. The biological data suggested that ligand and its metal (II) complexes displayed promising antibacterial activity compared to known antibiotic drug.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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