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Synthesis, spectral studies and biological evaluation of 2-aminonicotinic acid metal complexes

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ABSTRACT

We synthesized 2-aminonicotinic acid (**2-ANA**) complexes with metals such as Co(II), Fe(III), Ni(II), Mn(II), Zn(II), Ag(I),Cr(III), Cd(II) and Cu(II) in aqueous media. The complexes were characterized and elucidated using FT-IR, UV–Vis, a fluorescence spectrophotometer and thermo gravimetric analysis (TGA). TGA data showed that the stoichiometry of complexes was 1:2 metal/ligand except for Ag(I) and Mn(II) where the ratio was 1:1. The metal complexes showed varied antibacterial, fungicidal and nematicidal activities. The silver and zinc complexes showed highest activity against *Bacillus subtilis* and *Bacillus licheniformis* respectively. *Fusarium oxysporum* was highly susceptible to nickel and copper complexes whereas *Macrophomina phaseolina* was completely inert to the complexes. The silver and cadmium complexes were effective against the root-knot nematode *Meloidogyne javanica*.

1. Introduction

Metal-based compounds have received great attention in medicinal chemistry and have been widely studied in modern medicine for the diagnosis and treatment of different human malignancies. For instance, metallo-pharmaceutical agents have been described for the treatment of cancer, arthritis, manic depression, and for use as anti-microbial and anti-parasitic agents [1,2]. Pyridines have been extensively studied for their biological and physiological activities. For example, nicotinic acid has been assessed for its antibacterial properties [3] and as an anti-hyperlipidemic agent raising HDL cholesterol level to reduce cardiovascular risks [4,5]. Nicotinamide and isonicotinamide were also found to have an antifungal and antimicrobial activity [6]. Transition metal complexes are widely used as potential therapeutics [7], they are useful in health and skin care [8]. Many researchers reported biological activities of Cd complexes such as anti-cancer [9], cytotoxicity, antibacterial and antifungal activities [10–12].

Nicotinic acid and its derivatives constitute important ligands in coordination chemistry and have been extensively used as medicinal agents. Morsy et al., [13] reported the preparation of silver complexes with nicotinate ligands and studied their antibacterial activities against antibiotic-resistant pathogens.

Soil-borne plant pathogens are equally important as they affect plant cultures with economic, social and environmental implications. Many soil-borne plant pathogens cause severe damage to different vegetable crops and pulses by reducing crop yield and quality of bioproducts. The soil-borne plant pathogens including nematodes, fungi and some bacteria infect plant roots causing disruption of absorption and translocation of nutrients and water from the soil resulting in mortality. Nematodes, including plant parasitic nematodes, are among the most abundant macro and micro fauna of soil. Of these plant parasitic nematodes, the root-knot nematodes (*Meloidogyne* spp.) are the most destructive. They are widely distributed and reproduce on over 2000 species of plants [14].

Root-knot nematodes (*M.* species) are obligate parasites and cause root cells to become giant and multinucleated. *Macrophomina phaseolina* is another pathogen that causes rotting of roots, stem and pods of hundreds of cultivated plant species [15].

M. phaseolina has a wide distribution and it can survive in soil and dead plant debris for several years by forming sclerotia. Symptoms including appearance of lesions on roots, stem and other parts of plants which result in stunted growth, yellowing of leaves and reduction in yield [16]. Similarly, *Fusarium* species are also very common plant

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pathogens that cause root and stem rot and wilt diseases on a variety of crop plants. Symptoms include yellowing of lower leaves and wilting.

In this work, we report the synthesis of metal complexes of 2-aminonicotinic acid (**2-ANA**). The complexes were characterized by different spectroscopic techniques and their inhibitory effect was evaluated against bacteria, fungi and nematode.

2. Experimental

2.1. Materials and chemicals

All chemicals were of analytical reagent grade and were used without further purification. 2-Aminonicotinic acid, dimethyl sulfoxide (DMSO) and metal salts Co(II), Fe(III), Ni(II), Mn(II), Zn(II),Ag(I),Cr(III), Cd(II), and Cu(II) in the form of hydrated chloride or nitrate salts were purchased from Sigma-Aldrich and BDH. Melting points of the complexes were determined on a Gallenkamp apparatus and reported as uncorrected.

2.2. General procedure for the preparation of 2-aminonicotinic acid (*2-ANA*) metal complexes

2 mmol (0.28 g) of **2-ANA** and 2 mmol (0.11 g) of potassium hydroxide were stirred in deionized water for 30 min. To this mixture, an aqueous solution of metal salt (0.5 mmol) was added and the mixture was stirred for 30 min. The precipitate formed was filtered, washed several times with water, dried and stored in a silica gel desiccator.

2.3. Characterization

Infrared (IR) spectra of ligand and their metal complexes were recorded on a Nicolet Impact 410 FT-IR spectrometer (4000–400 cm^{-1}) as a potassium bromide (KBr) pellet with 4 cm^{-1} resolution. UV–Visible spectra of compounds were recorded on a CARY 50 spectrophotometer using dimethyl sulfoxide (DMSO) as a blank. Absorption and emission spectra were recorded on a CARY 50 spectrofluorometer in DMSO, using a 10 mm quartz cell. Thermal analysis was carried out on a Shimadzu thermo gravimetric analyzer (TGA). The sample (5.00 mg) was heated in corundum crucibles up to 600 °C, with a heating rate of 20 °C min^{-1} in air. The products of decomposition were calculated from TG curves. The temperature ranges were determined by means of a thermoanalyzer data processing module.

2.4. Biological cultures

Bacteria used for present study were isolated from the rhizosphere of cultivated plants and identified as *Bacillus subtilis* (BSER) and *Bacillus licheniformis* (BLF1). Fungi namely *Fusarium oxysporum* and *M.phaseolina* were isolated from the soil of Department of Botany experimental field, University of Karachi. Root-knot nematodes were extracted from the roots of egg plants maintained in culture.

2.5. Antibacterial activity

Antibacterial activity of metal complexes was tested by a disc diffusion technique [17]. Bacterial cells were spread on the surface of LB (Lysogeny Broth) agar plate; prepared 6 mm diameter discs were dipped in the solution of the complexes and placed on inoculated agar surface. Plates were incubated for 24 h at 37 °C in the dark, the zone of growth inhibition was measured in millimeter around each of the antibiotic disc, after incubation.

2.6. Fungicidal activity

Antifungal activity was carried out by an agar dilution method [18]. 100 μL of each metal complex was added to sterilize Petri plates (having 9 mm of internal diameter) after pouring Potato Dextrose agar (PDA). About 10 mL of PDA was poured in each Petri plate and rotated well before solidification. A 6 mm pure culture disc was placed at the center of the plate and incubated at 30 °C for 4–7 days (depending upon tested fungi). Fungal redial growth was measured in mm after incubation and data of % inhibition by metal complexes were calculated.

2.7. Nematicidal activity

Nematicidal activity of complexes was assessed against the second stage juveniles of root-knot nematodes, *Meloidogyne javanica*. Egg masses were directly picked from roots with the help of fine needle under a stereomicroscope and transferred into cavity blocks containing sterilized distilled water. After hatching, the number of juveniles was maintained around 25–35 J2/mL. The metal complexes were diluted to 1000 ppm in the nematode suspensions. The number of dead juveniles was counted after 24, 48 and 72 h of exposure. Cavity blocks without metal complexes and with juveniles only were considered as controls. Each treatment was repeated thrice. Nematodes were considered dead if they did not move when probed with a fine needle [19]. Data of dead juveniles were calculated and showed in mortality %.

3. Results and discussion

3.1. Characterization

The physical properties and spectral data of the ligand (**2-ANA**) and its metal complexes are presented in Table 1 and the proposed structure is shown in Fig. 1. Most of the complexes were colored, stable in air and soluble in DMSO. The proposed formulae of the complexes are in accordance with the elemental analysis presented in Table 2.

In order to find out the coordination sites in the **2-ANA** that may involve in complexation, the IR spectral data of **2-ANA** and its metal complexes are compared and summarized in Table 1. The position and intensities of the peaks are expected to change upon complexation. The IR spectrum of the free ligand showed characteristic bands at 1709 and 3246 cm^{-1} due to carboxylic and amino group stretching modes respectively. In the complex spectra, the bands due to carboxylic group were shifted to lower frequency as compared with the free ligand suggesting that carboxylic group is coordinated to the metal ions. The stretching band of the primary amine group also shifted to higher frequencies in most cases suggesting that the $-NH_2$ group is also involved in coordination. The peaks are sharp indicating that there is no intra/inter molecular hydrogen bonding in the solid state of the complexes. Thus it indicates that the carboxylate oxygen and the primary amino group of **2-ANA** are chelated to the metal ions (Fig. 1). It is further noted that the IR spectra of the complexes are similar indicating that the coordination nature of the complexes is the same.

The UV–Vis absorption spectra of the ligand and metal complexes were recorded in water and DMSO respectively at 1.18 mM

Table 1
Analytical and physical data of 2-aminonicotinic acid and its metal complexes.

Complexes	Formula	Color	Solubility	m.p (°C)	λ_{max} (nm)	υ (cm^{-1})	
						C = O	NH
ANA	$C_6H_6N_2O_2$	White	H_2O	298 °C	318	1709	3246
1	$Co(ANA)_2$	Purple	DMSO	>300 °C	338	1626	3404
2	$Fe(ANA)_2 \cdot 3H_2O$	Buff	DMSO	>300 °C	335	1705	3258
3	$Ni(ANA)_2 \cdot H_2O$	Green	DMSO	>300 °C	337	1670	3437
4	$Mn(ANA) \cdot 3H_2O$	White	DMSO	>300 °C	326	1624	3402
5	$Zn(ANA)_2$	White	DMSO	>300 °C	336	1629	3392
6	Ag(ANA)	White	DMSO	>300 °C	331	1625	3427
7	$Cr(ANA)_2 \cdot H_2O$	Green	DMSO	>300 °C	335	1707	3258
8	$Cd(ANA)_2$	White	DMSO	>300 °C	329	1624	3398
9	$Cu(ANA)_2 \cdot H_2O$	Green	DMSO	>300 °C	338	1702	3392