ACTA SCIENTIFIC MICROBIOLOGY Antimicrobial Activity and Antioxidant Studies of (Z)-2-(2-Methoxybenzylideneamino)- 3-Methylbutanoic Acid with Mixed Ligand Chelates

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Research Article

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Abstract

The present study summarizes the antimicrobial and antioxidant activities of the synthesized Schiff base; (z)-2-(2-methoxybenzylideneamino)-3-methylbutanoic acid (L1) and its Co(II) and Ni(II) complexes. The Schiff base and its chelates were tested for their antimicrobial activities, it is found that the tested compounds are active against microorganisms used (*staphylococcus aureus, Streptococcus pyogenes, Bacillus, Klebsiellapneumonia, Pseudomonas aeruginosa, Escheriehia coli, Aspergillus niger, Penicillium chrysogenum*) when compared with the activity of the reference or standard drugs (Gentamici and Ampicillin). on the other hand, the antioxidant activity was measured with a simple and rapid free radical assay using DPPH. Where he was the higher antioxidant activity of Ni(II) relative to the other synthesized complex.

Keywords: Complexes; Synthesis; Schiff Base; Antimicrobial; Antioxidant

Introduction

Schiff Bases have been known since 1864 when Hugo Schiff reported the condensation of primary amines with carbonyls compounds [1]. Schiff bases are a special class of ligands with a variety of donor atoms exhibiting interesting coordination modes towards transition metals [2].

Schiff Bases are very important due to their simple synthesis, versatility and diverse range of applications of their metal complexes [3-5]. because of the presence of both nitrogen and oxygen donor atoms in the backbones of these ligands, some of these complexes have been exhibited interesting physical, chemical properties and potentially useful biological activities [6,7].

Nickel is usually dipositive in its compounds, but it can also exist in the oxidation states. Besides the simple nickel compounds, or salts, nickel forms a variety of coordination compounds. It is more interesting because the study of the interactions of Ni(II) with Schiff bases offers an opportunity to understand various properties of Ni(II) complexes [8].

Metal complexes of Schiff bases have been extensively investigated because of their medicinall [9,10]. that Schiff bases have been used as chelating ligands in coordination chemistry, in anti-oxidative activity [11].

That free radicals have a great impact on humans in the etiology of various diseases like cancer, liver injury, cardiovascular diseases, diabetes, neurodegenerative and rheumatism diseases, atherosclerosis, autoimmune disorders and aging [11]. During endogenous stimulation of macrophages and leucocytes [12,13], Therefore, antioxidants with free radical scavenging potential may be relevant in the therapeutic and preventions of diseases [14] also they are used as catalyst in medicine like antibiotics such as, antibacterial, antivirus, antifungal and the treatment of cancer also anti-inflammatory agents and in the industry as anticorrosion [15-17]. Presently, synthetic antioxidants are widely used because they are effective and cheaper than natural antioxidants [18].

Methods and Materials

Synthesis and characterization of Schiff base and its chelates:

The synthesis and characterization of these compounds have been reported Figure 1,2 [19].

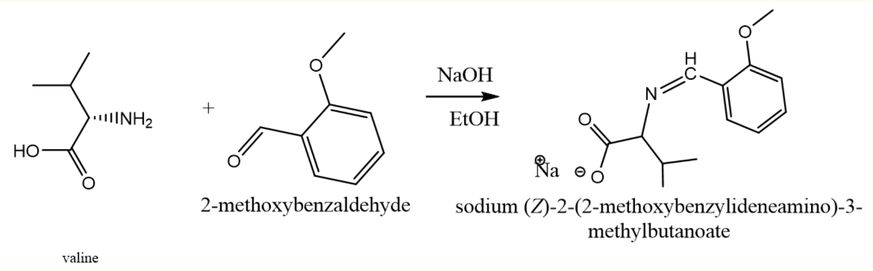

Figure 1: Formation of the Schiff base HL^1.

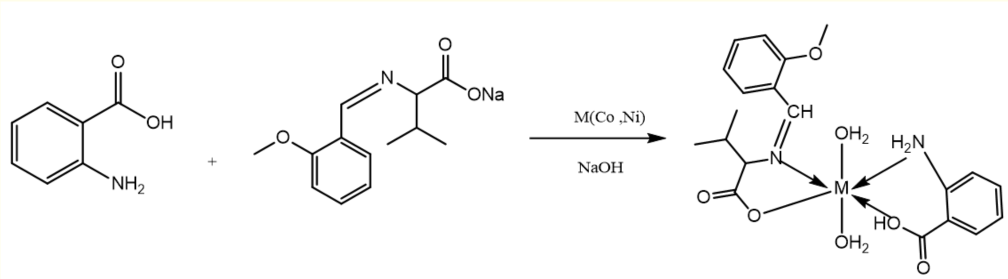

Figure 2: Chemical equations of synthesis chelates.

Biological activity

The bio-activity of the prepared complexes has been examined against the growth of bacteria *in vitro* to evaluate their antimicrobial potential, human pathogenic Gram-Positive and Gram-negative bacteria such as *Staphylococcus aureus, Streptococcus pyogenes, bacillus subtilis Pseudomonas aeruginosa, Klebsiella pneumonia* and *Escherichia coli* and fungal strains: *Aspergillus niger*, *Penicillium chrysogenum* growth. The identity of all the strains was confirmed. For the detection of antibacterial activities and sensitivity spectrum analysis, the disc diffusion method was followed [20,21]. Nutrient Agar (NA) was used as basal medium for culture of test bacteria and N,N Dimethylsulfoxide (DMSO) solvent was used to prepare the desired solution (1%) of the compounds initially.

Nutrient Agar (NA) medium was prepared using the composition; Beef extract (3 g), Peptone (5 g), NaCl (0.5 g), Agar (15 g), Distilled water (1000 mL). 1000 mL of distilled water was taken in a beaker and then 15 g of agar powder, 3 g of beef extract, 5 g of peptone and 0.5 g of NaCl were added slowly in that water and they were mixed thoroughly with a glass rod, heated to boiling for 10 minutes. After 10 minutes of boiling, the medium was transferred in 250 mL conical flasks at the rate of 200 mL per flask. The conical flask was closed with the cotton plug and autoclaved at 121ºC and 15 psi pressure for 15 minutes, then culturing of different microorganisms was per formed [22].

Malt extract medium was prepared using the composition Malt extract 30.000g/l, Mycological peptone 5.000 Agar 15.000g/l and Final pH (at 25°C) 5.4 ± 0.2 Suspend 50.0 grams in 1000 ml distilled water and soak for 15 minutes. Sterilize by autoclaving at 115°C (10 lbs pressure) for 10 minutes [22].

Sensitivity spectrum analysis of bacteria and fungi: was placed 10 μL from 2% solution of test complexes in the holes. 0.2 mL of the suspension of test organism was taken in sterilized glass Petri dish of 100 cm diameter. A plates was also maintained in each case with solvent. The plates were kept for 24 h at 35ºC for growth of bacteria and 27 C of fungi. were observed at 24 h interval for two days. The activity was determined by measuring the diameter of the zone of inhibition in mm, and the zones of inhibition were measured around well. Gentamicin was used as negative control, and Ampicilin was used as positive control.

Antioxidant activity

The ability of Schiff bases and their metal complexes to scavenge free radicals is an important property [22] presently a number of Schiff-base metal complexes have been investigated as antioxidants.

Scavenging activity measurements of 1,1-Diphenyl-2-picrylhydrazyl (DPPH) Radical

The antioxidant activity of the suggested drugs was studied using spectrophotometric technique with 1,1-diphenyl-2-picrylhydrazyl(DPPH) method. This compound is known as a stable readily accessible free radical. It gives a purple solution in methanol solvent. The complexes' DPPH radical scavenging potentials were evaluated as mentioned in [23]. The tested drugs are prepared in different concentrations. Spectrophotometrically at 517 nm, the absorbance of the mixture produced from mixing DPPH and each drug was measured. All tested analysis was performed in triplicate. Ascorbic acid (Vit. C) was taken as the standard drug. All tested analysis was performed in triplicate. DPPH radical scavenging activity (%) was calculated.

Result and Discussion

1. Antimicrobial activity of the Schiff base and its chelates: Susceptibilities of pathogenic bacterial isolation and used Schiff base (HL1),Co(II) and Ni(II) chelates and anthranilic acid HL2, were investigated by measuring their inhibitory, The effect were as follows Co(II)-Complex (*E.coli, S. pyogenes S. aureus. K.pneumonia. B. subtilis, P. aeruginosa A. niger and P. chrysogenum*) Ni(II)-Complex (*E.coli, S. pyogenes s. aureus. B. subtilis, P. aeruginosa A. niger* and *P. chrysogenum*) Schiff bases (*K. pneumonia, E. coli, S. pyogenes* and *A. niger*).

The results in Table 1, Figure 3 and plate 1 show that Co(II) complex had strong antimicrobial activity on growth of the microbial isolates, the highest activity (32 mm inhibition zone diameter) against *E. coli* and *K. pneumonia* followed (24mm inhibition zone diameter) against *S. pyogenes*. followed by Ni(II) complex had an inhibition effect against the growth S. aureus and E. coli (28 and 20 mm inhibition zone diameter, respectively.), while *P. aeruginosa*, non-sensitive to Ni(II) complex., In contrast reference [24,25] mentioned that most of the Ni (II_complex compound have no or little antibacterial activities against selected human pathogenic bacteria.

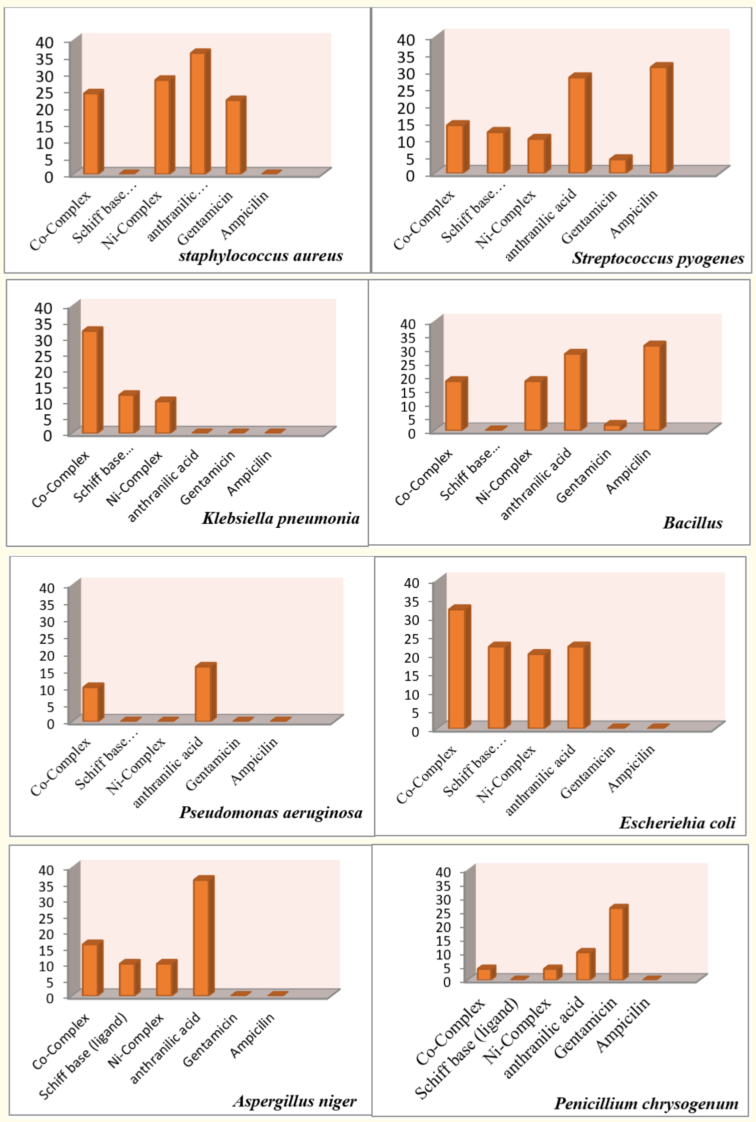

Figure 3: Zone of inhibition produced by the synthesized compounds; Schiff base (ligand), anthranilic acid, Co(II) and Ni(II) chelates against Gram-Positive and Gram-negative antimicrobial species.

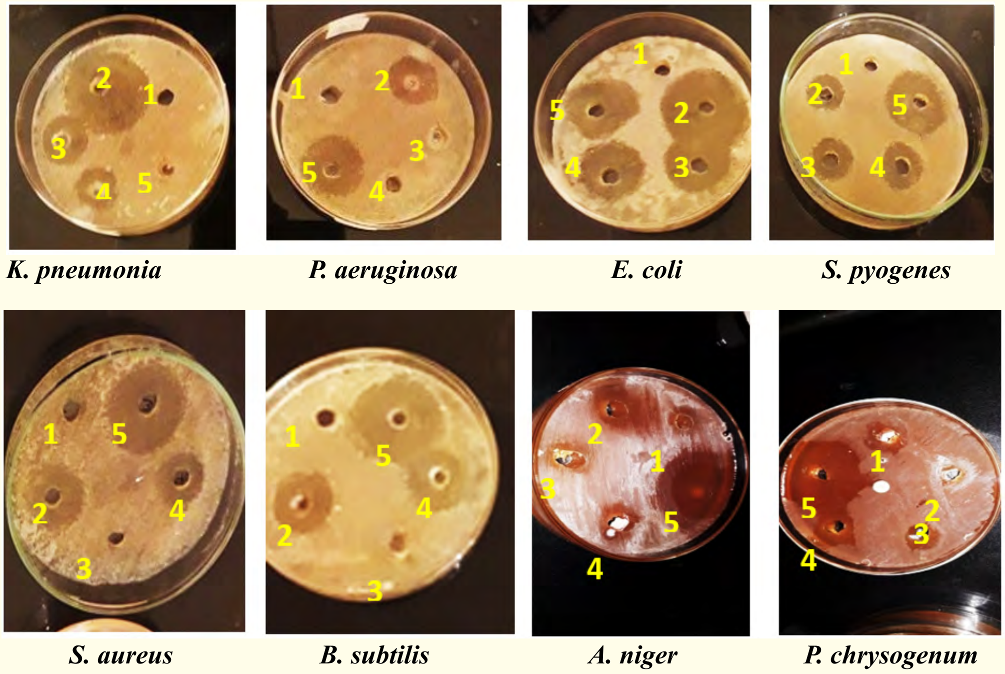

Plate 1: Inhibition Zone produced by the synthesized Schiff base (ligand), anthranilic acid, Co(II) and Ni(II) chelates against Gram-Positive and Gram-negative bacteria and fungi. 1:DMSO control, 2: Co-Complex, 3: Schiff base (L1), 4: Ni-Complex, 5: anthranilic acid L2.

Micro-organisms		Inhibitory Zones (mm)					
		Co-Complex	Schiff base (L1)	Ni-Complex	anthranilic acid L2	Standard antibiotics	
						Gentamicin	Ampicilin
Gram(ve$^-$)	*Staphylococcus aureus*	24	-	28	36	22	-
	Streptococcus pyogenes	14	12	10	28	4	31
	Bacillus subtilis	18	-	18	28	1	31
Gram(ve$^+$)	*Klebsiella pneumonia*	32	12	10	-	-	-
	Pseudomonas aeruginosa	10	-	-	16	-	-
	Escheriehia coli	32	22	20	22	-	-
Fungi	*Aspergillus niger*	16	10	10	36	-	-
	Penicillium chrysogenum	4	-	4	10	26	-

Table 1: Antimicrobial activities of the compounds compared with Standard antibiotics.

On the other hand Schiff base (HL1) had antimicrobial activity on growth of *E. coli* and *P. chrysogenum* (22 mm inhibition zone diameter). While, they showed a good inhibition against microorganism as compared to standard drugs. This is consistent with reference [2,3] Schiff base shown to been exhibited a broad range of biological activities against fungi, bacteria and malarial, antiproliferative, anti-inflammatory, antiviral and antipyretic.

Free ligand chelates HL2 had activity against *S. aureus* and *A. niger*, *S. pyogenes* and *B. subtilis*.

The some bacteria under study were highly sensitive to ampicilin (31 inhibition zone diameter) against *S. pyogenes* and *B. subtilis*. While, antibiotics did not effect on *E. coli, P. aeruginosa* and *K. pneumonia*. This is consistent with reference [5]. the S. aureus strain showed resistance to the effect of ampicillin. Gentamicin (26 and 22 inhibition zone diameter) against *P. chrysogenum* and S. aureus, respectively.

DPPH free radical-scavenging assay

The antioxidant activity was measured with a simple and rapid free radical assay using DPPH. The DPPH is able easily to accept an electron or hydrogen atom (proton) to become a stable diamagnetic molecule. Thus, the loss of the DPPH transition signal intensity in the presence of antioxidants is clearly directly proportional with the concentration (or number) of protons accepted. As shown in Figure 4, the Schiff base has the higher antioxidant activity than its complexes. It can be explained due to the presence of the carboxylic group can dissociate easily and inhibit the working of the free radical. The previous explanation depends on the principle of acceptance of DPPH hydrogen atom (proton) to become a stable diamagnetic molecule. We noticed the higher antioxidant activity of Ni(II) relative to the other synthesized complex. We can suggest this higher reactivity due to the easier proton dissociation of coordinated water molecule in case of Ni(II) complex due to its smaller size with increasing its effective nuclear charge facilitates the proton loss.

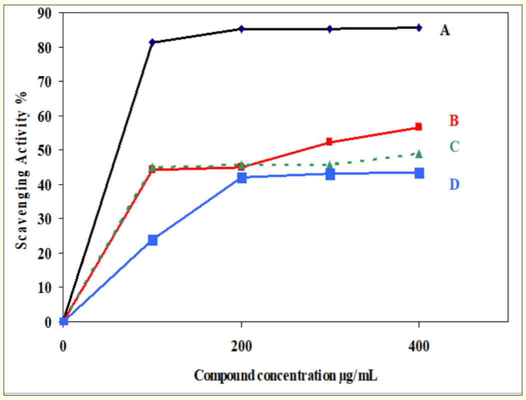

Figure 4: Antioxidant using DPPH.

Conclusion

In present study each of Co(II) and Ni(II) chelates, Schiff base(HL1) and anthranilic acid (HL2) have been evaluated against human eight pathogenic microorganisms such as *E.coli, S. pyogenes s. aureus. K. pneumonia. B. subtilis, P. aeruginosa A. niger* and *P. chrysogenum*. and compared with antibiotics.

Most of the prepared compounds Co(II)-Complex, anthranilic acid and Ni-Complex have considerable inhibition capacity on growth against selected human pathogenic bacteria and fungi. On the other hand, Schiff base (L1) have little antibacterial activities against selected human pathogenic bacteria and fungi. Also the antibiotics apenicillin and gentamycin have a different effect against gram positive bacteria. While the gram negative bacteria showed high resistance. The present study reveals that Co-Complex compounds a highest effective against Gram-positive, Gram- negative bacteria and Fungi. *K. pneumonia. E.coli, S. aureus. B. subtilis, A. niger S. pyogenes. P. aeruginosa* and *P. chrysogenum* also higher than the activity of commonly used antibiotics such as Gentamicin, followed by L2 and Ni-Complex. On the other hand, Schiff bases (L1) were not effective against *S. aureus, B. subtilis* and *P. aeruginosa* while activity of antibiotics Ampicilin was higher than the activity of used L1. These results may be explained on the bases that the metal complexes penetrate more easily through the bacterial cell wall, due to the protein denaturation of the Co-Complex, destruction the bacterial cell wall. In conclusion Schiff bases and their chelates are a class of compounds with literature evident pharmacological importance and applications. Schiff base and their Ni(II) chelates displayed good antioxidant properties.

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