

N,N'-Bis(salisiliden)-1,2-bis-(*o* - ve *p* - aminofenoksi)etandan elde edilen bazı geçiş metal komplekslerinin biyolojik aktiviteleri

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Özet

Bu çalışma için N,N'-bis(salisiliden)-1,2-bis-(*o*-aminofenoksi)etan (**L₁**) ve N,N'-bis(salisiliden)-1,2-bis-(*p*-aminofenoksi)etan (**L₂**) Schiff bazları sentezlendi. Bu ligandlardan da **L₁**'in Cu(II), Ni(II), Zn(II) kompleksleri, **L₂**'nin Cu(II), Co(II), Zn(II) kompleksleri elde edildi. Sentez sonrası elde edilen bu bileşikler, insanlarda yaygın olarak görülen bulaşıcı bakteriler *E. coli*, *Pseudomonas*, *Acinetobacter* ve *Staphylococcus*'a karşı etkinlikleri incelenmiştir. Her iki ligandın da bakır kompleksleri *Staphylococcus*'a karşı etkili olduğu bulunmuştur. *Staphylococcus*, hastane çevresinde yaygın olarak görülen patojenlerdendir. Bu yüzden bu ligandların bakır kompleksleri (**L₁-Cu** ve **L₂-Cu**) hastane hijyeninde kullanışlı olabileceği düşünülmektedir.

Anahtar Kelimeler: Geçiş metali kompleksi, Antimikrobiyal aktivite

Biological activities of some transition metal complexes derived from N,N'-bis(salicylidene)-1,2-bis-(*o* - and *p* - aminophenoxy)ethane

Abstract

The Schiff base ligands N,N'-bis(salicylidene)-1,2-bis-(*o*-aminophenoxy)ethane (**L₁**) and N,N'-bis(salicylidene)-1,2-bis-(*p*-aminophenoxy)ethane (**L₂**) were synthesized for this study. The Cu(II), Ni(II), Zn(II) complexes of **L₁** and the Cu(II), Co(II), Zn(II) complexes of **L₂** were obtained with various transition metal salts. These compounds were evaluated against to the common infectious bacteria in human such as *E. coli*, *Pseudomonas*, *Acinetobacter* and *Staphylococcus* strains. The copper complexes of both **L₁** and **L₂** were found effective against *Staphylococcus* strains. *Staphylococcus* strains are common pathogens in hospital environment. Thus, their copper complexes (**L₁-Cu** and **L₂-Cu**) may be useful in hospital hygiene.

Keywords: Transition metal complex, Antimicrobial activity

1. Introduction

Through the years, Schiff bases played a central role as chelating ligands in main group and transition metal coordination chemistry [1-4]. Transition metal complexes of tetradentate Schiff base ligands find lots of application fields as model analogues of certain metal enzymes and also in catalysis and materials chemistry [5]. The Schiff base complexes are known showing antifungal activity which is increased by the presence of hydroxy group in the ligand [6,7].

Much attention has been devoted by bioinorganic as well as by medicinal chemists to the relationship between the metal ions and their complexes as antitumour and antibacterial agents [10-16]. In vivo studies have indicated that some biologically active compounds may become more carcinostatic and bacteriostatic upon chelation [11, 17]. Such interactions of transition metal ions with amino acids, peptides and nucleic acids, are of immense biological importance [18-20]. Several reviews showed that the metallo-organic chemistry of such compounds greatly influence their biological action highlighting the catalytic function metals in many biological processes [21-24].

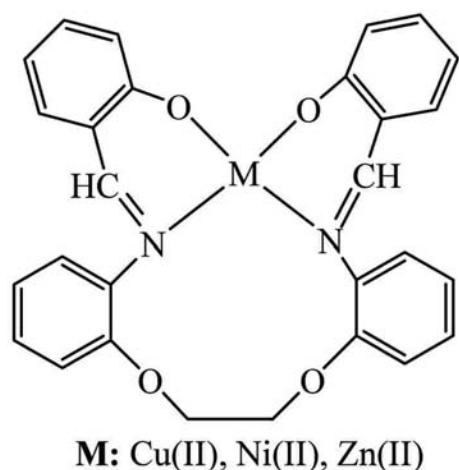


Figure 1. Suggested Structure of the Tetrahedral Zn(II) and Ni(II) and Square-planar Cu(II) Complexes of the Ligand L_1

The development of bacterial resistance to available antibiotics and increasing incidence of multiresistant bacterial infections in hospitals and in the community has necessitated the search for new antibacterial agents to treat the bacterial infection.

In this paper, the title Schiff bases and their metal chelates were evaluated for their antibacterial activity against the strains *E. coli*, *Pseudomonas*, *Acinetobacter* and *Staphylococcus*. These bacteria are very common in hospital environment. Effectiveness to these bacteria is very important for hospital hygiene. Different anti-septic agents are available for hospital usage but all of them have some disadvantages also. The Schiff bases and their Cu(II), Co(II), Zn(II) and Ni(II) complexes could be valuable materials for hospital usage.

2. Experimental

2.1. Synthesis of L_1 and its Complexes

N,N' -Bis(salicylidene)-1,2-bis-(*o*-aminophenoxy)ethane (L_1) and its Cu(II), Ni(II) and Zn(II) complexes were synthesized by the method described in the literature [8].(Figure 1)

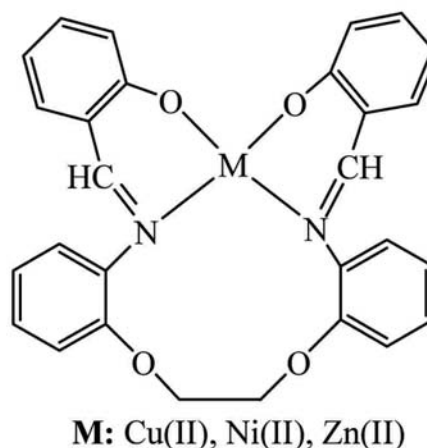


Figure 2. Suggested Structure of the Tetrahedral Co(II), Zn(II) and Square-planar Cu(II) Complexes of the Ligand L_2 (N,N' -bis(salicylidene)-1,2-bis-(*p*-aminophenoxy)ethane)

2.2. Synthesis of L₂ and its Complexes

N,N'-Bis(salicylidene)-1,2-bis-(*p*-aminophenoxy)ethane (L₂) and its Cu(II), Co(II) and Zn(II) complexes were synthesized by the method described in the literature [8]. (Figure 2)

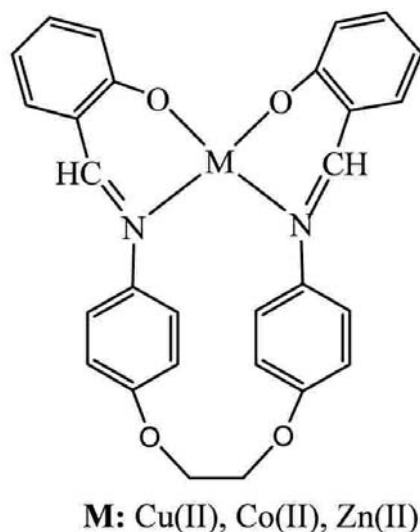


Figure 2. Suggested Structure of the Tetrahedral Co(II), Zn(II) and Square-planar Cu(II) Complexes of the Ligand L₂ (N,N'-bis(salicylidene)-1,2-bis-(*p*-aminophenoxy)ethane)

3. Results and Discussion

3.1. The Effect of Schiff Base and Complexes on Bacteria

The antimicrobial activities of the complexes and ligands were screened by adapted qualitative, diffusimetric methods (i.e. distribution of the tested solutions on filter paper disks, in agar wells or in spots on solid media that have been inoculated with test microbial strains) and quantitative methods based on serial two-fold dilutions of the tested compounds in order to establish the corresponding Minimal Inhibitory Concentrations (MIC). Four bacterial strains, i.e. *P. aureginosa*, *Acinetobacter spp.*, *E. coli* and *Methicillin-sensitive Staphylococcus aureus*, freshly isolated from patients with infections from the Clinical Microbiology Laboratory at Dicle University Hospital and identified by conventional methods were cultivated on solid media and incubated at 37

°C for 24 hours prior to testing.

The results of the quantitative assays showed that the tested compounds exhibited variable MIC_s and selective antimicrobial activity, depending on the microbial strains. The Schiff base ligands L₁ and L₂ and their various complexes Cu(II), Co(II), Zn(II) and Ni(II) complexes have been evaluated for their antibacterial activity against *P. aureginosa*, *Acinetobacter spp.*, *E. coli* and *Methicillin-sensitive Staphylococcus aureus* (MSSA) strains. The lowest concentration of compound that completely inhibited microbial growth rate was considered to be the MIC expressed in µg/mL. The L₁ and its complexes were found to be ineffective against *P. aureginosa*, *Acinetobacter spp.* and *E. coli* in 0.1 µg/mL. Its copper complex was found to be effective against *Staphylococcus* stains, but the nickel (II) and zinc complexes of the L₁ ligand were found ineffective against *Staphylococcus* strains at 0.1 µg/mL. (Table 1) The L₂ and its complexes were found to be ineffective against *P. aureginosa*, *Acinetobacter spp.* and *E. coli* in 0.1 µg/mL, too. The copper complex of L₂ was found to be effective against *Staphylococcus* stains. On the other hand the cobalt(II) and zinc(II) complexes of the L₂ were found ineffective against *Staphylococcus* strains at 0.1 µg/mL. (Table 2)

3.1.1. Antibacterial Studies of L₁ and Its Complexes

All bacterial strains were obtained from patients samples from the Clinical Microbiology Laboratory at Dicle University Hospital. The antibacterial susceptibility tests were performed according to standard microbiological methods [9].

3.1.2. Antibacterial Studies of L₂ and its Complexes

All bacterial strains were obtained from patients samples from the Clinical Microbiology Laboratory at Dicle University Hospital. The antibacterial susceptibility tests were performed according to standard microbiological methods [9].

Table 1. Antimicrobial activity of N,N'-bis(salicylidene)-1,2-bis-(*o*-aminophenoxy) ethane (L₁) Schiff Base complexes against some bacteria.

Compounds	<i>P. aureginosa</i>		<i>E. coli</i>		<i>Acinetobacter spp.</i>		<i>MSSA</i>	
	x	y	x	y	x	y	x	y
(MIC)	x	y	x	y	x	y	x	y
Ligand (L ₁)	a	b	a	b	a	b	a	b
L ₁ -Cu(II)	a	b	a	b	a	b	b	b
L ₁ -Zn(II)	a	b	a	b	a	b	a	b
L ₁ -Ni(II)	a	b	a	b	a	b	a	b

x = 0.1 µg/mL, y = 1 µg/mL, a = growth, b = non-growth

Table 2. Antimicrobial activity of N,N'-bis(salicylidene)-1,2-bis-(*p*-aminophenoxy) ethane (L₂) Schiff Base complexes against some bacteria.

Compounds	<i>P. aureginosa</i>		<i>E. coli</i>		<i>Acinetobacter spp.</i>		<i>MSSA</i>	
	x	y	x	y	x	y	x	y
(MIC)	x	y	x	y	x	y	x	y
Ligand (L ₂)	a	b	a	b	a	b	a	b
L ₂ -Cu(II)	a	b	a	b	a	b	b	b
L ₂ -Zn(II)	a	b	a	b	a	b	a	b
L ₂ -Ni(II)	a	b	a	b	a	b	a	b

x = 0.1 µg/mL, y = 1 µg/mL, a = growth, b = non-growth

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