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Antibacterial effect of Some New Metal Complexes with Schiff Base Ligands on Gram-positive Bacteria (Staphylococcus aureus) and Gram-negative Bacteria (Pseudomonas aeruginosa)

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Özet

Bu çalışmada HL ligandının nikel(II) ve bakır(II) kompleksleri sentezlendi. HL, 1-naftilamin ve 2-hidroksinaftalin-1-karbaldehitten elde edilen Schiff bazını gösterir. Aynı zamanda H_2L' ligandının nikel(II), bakır(II), kobalt(II) ve çinko(II) kompleksleri de sentezlendi. H_2L', 1,2-bis-(p-aminofenoksi)etan ve 2-hidroksinaftalin-1-karbaldehitten sentezlenen liganddır. HL ve H_2L' ligandlarının Gram-pozitif (Staphylococcus aureus) ve Gram-negatif (Pseudomonas aeruginosa) bakterilerinin gelişimi üzerine etki ve davranışları incelendi. HL nin 0.6, 1.2, 2.4, 4.8 µg gibi ortalama değerdeki dozları 100 mL Mueller Hintor-agar üzerine eklendi, daha sonra Gram-pozitif (Staphylococcus aureus) ve Gram-negatif (Pseudomonas aeruginosa) bakterilerin gelişebildiği gözlemlendi. Diğer taraftan doz arttırıldığında koloni sayısının azaldığı görüldü. Hücre gelişimi her iki tür için de 4.8 µg/100 mL dozda inhibe edildi. Bununla birlikte 0.6 ve 1.2, 2.4 µg/100 mL lik doz aralığında Gram-pozitif (Staphylococcus aureus) ve Gram-negatif (Pseudomonas aeruginosa) bakterilerinin koloni sayılarında belirgin bir düşme saptandğ. HL ve H_2L' Schiff bazı ligandlarının çeşitli komplekslerinin, iki türün gelişimi üzerine birbirinden farklı bir etkisi de yoktu.

Anahtar Kelimeler: Schiff Bazları, Metal Kompleksler, Antibakteriyal Aktiviteler

Abstract

In this study, nickel(II) and copper(II) complexes of HL were synthesized. HL denotes the Schiff base derived from 1-naphtylamine and 2-hydroxynaphthalene-1-carbaldehyde. And also the copper(II), nickel(II), cobalt(II) and zinc(II) complexes of H_2L' were synthesized. H_2L' denotes the Schiff base derived from 1,2-bis-(p-aminophenoxy)ethane and 2-hydroxynaphthalene-1-carbaldehyde. The effects and behaviors of new metal complexes with HL and H_2L' on the development of Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa) were investigated. In the medium ranges such 0.6, 1.2, 2.4, 4.8 µg doses of HL were added into 100 mL Mueller Hintor-agar, then it was observed that Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa) could be germinated. On the other hand, the colony numbers decreased when the dose injection increased. Cell germination was inhibited at 4.8 µg/100 mL dose for the both species. However, a significant decline was observed with the number of colonies at the dose ranges of 0.6 and 1.2, 2.4 µg/100 mL for Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa). There was no distinct point for the effects between various complexes of HL and H_2L' on the development of the two species.

Key Words: Schiff base, transition metal complexes, antifungal activities

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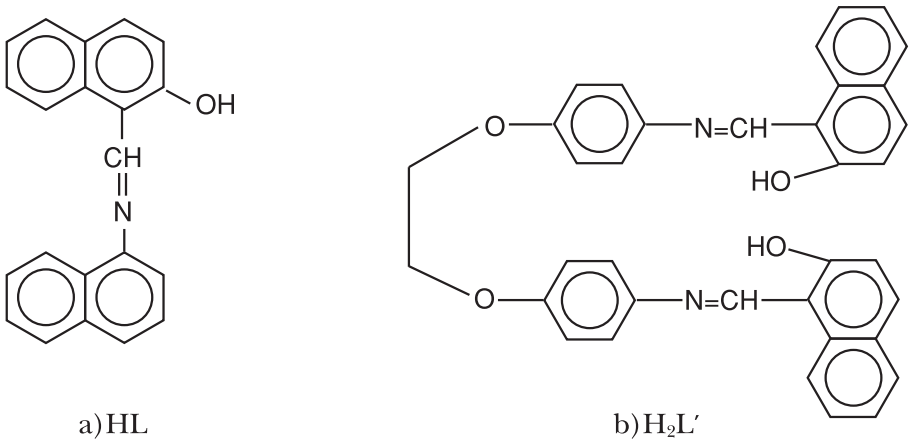
1. Introduction

Schiff bases have been important research fields in medicinal and pharmaceutical chemistry. They represent biological applications with antibacterial [1-2], antifungal [3] and antitumor activities [4]. The poisoning aspects of certain metal ions are investigated in living organisms using these transition metal complexes by determining the action of drugs [5]. Complexes of transition metals involving Schiff bases ligands have found applications towards understanding of many reactions in living processes. In recent years such complexes have been studied as model complexes of biological importance [6-12].

Combination therapy is used to expand the antimicrobial spectrum, minimize toxicity, and prevents the emergence of resistant mutants during therapy and to obtain synergistic antimicrobial activity. Methicillin-resistant Staphylococcus aureus (MRSA) causes many problems in public health not only to its common occurrence (<1 80%) but also because it has become resistant to almost all the currently available antibiotics except teicoplanin and vancomycin. Its susceptibility to vancomycin has recently decreased and vancomycin-intermediate and -resistant S. aureus (VISA and VRSA) have been found in an increasing number of countries. This makes the discovery of alternative antibiotics and chemotherapeutics particularly important [13-17].

Continuing our work [11,12] on Schiff base compounds of transition metals, we report here the antifungal activities of the some metal complexes with two Schiff base ligands derived from condensation of 1-naphtylamin and 2-hydroxynaphthalene-1-carbaldehyde (HL), or 1,2-bis-(p-aminophenoxy)ethane with 2- hydroxynaphthalene-1-carbaldehyde (H_2L') (Fig. 1).



a) HL b) H_2L'

Fig.1. Schiff Base Ligands
a) HL: 2-hydroxynaphthalene-1-carbaldehydene1-naphtylamin
b) H_2L': N,N 2-bis(-2-hydroxynaphthalene-1-carbaldehydene)-1,2-bis-(p-aminophenoxy)ethane.

2. Experimental

All the chemicals were obtained from Aldrich and used without further purification. HL, H_2L' ligands and their corresponding complexes were prepared according to literature procedure [11-12].

2.1. Synthesis of Ligands (HL and H_2L')

Schiff bases were derived from condensation of stoichiometric amounts of analytically pure 1-naphtylamin and 2-hydroxynaphthalene-1-carbaldehyde (HL), or 1,2-bis-(p-aminophenoxy)-ethane with 2-hydroxynaphthalene-1-carbaldehyde (H_2L') in absolute ethanol, in the usual way. The mixtures were heated under reflux on a water bath until the appearance of shining yellow crystals. The crude products were recrystallized from ethanol [11-12].

2.2. Preparation of Complexes

The following general procedure was used to prepare all the complexes. A solution of metal salt in 95 % ethanol (10 mmole) was mixed with the Schiff base ligands 95 % ethanol (10 mmole or 20 mmole) 1:2 or 1:1 (M:L) ratios and contents were refluxed in 50 mL ethanol in a water bath for 2-3 hours. The refluxed solution was then poured into ice cold water when a colored solid separation out which was isolated by filtration and washed with ether, recrystallized in absolute ethanol and dried in vacuum at room-temperature [11-12] (Fig. 2.).

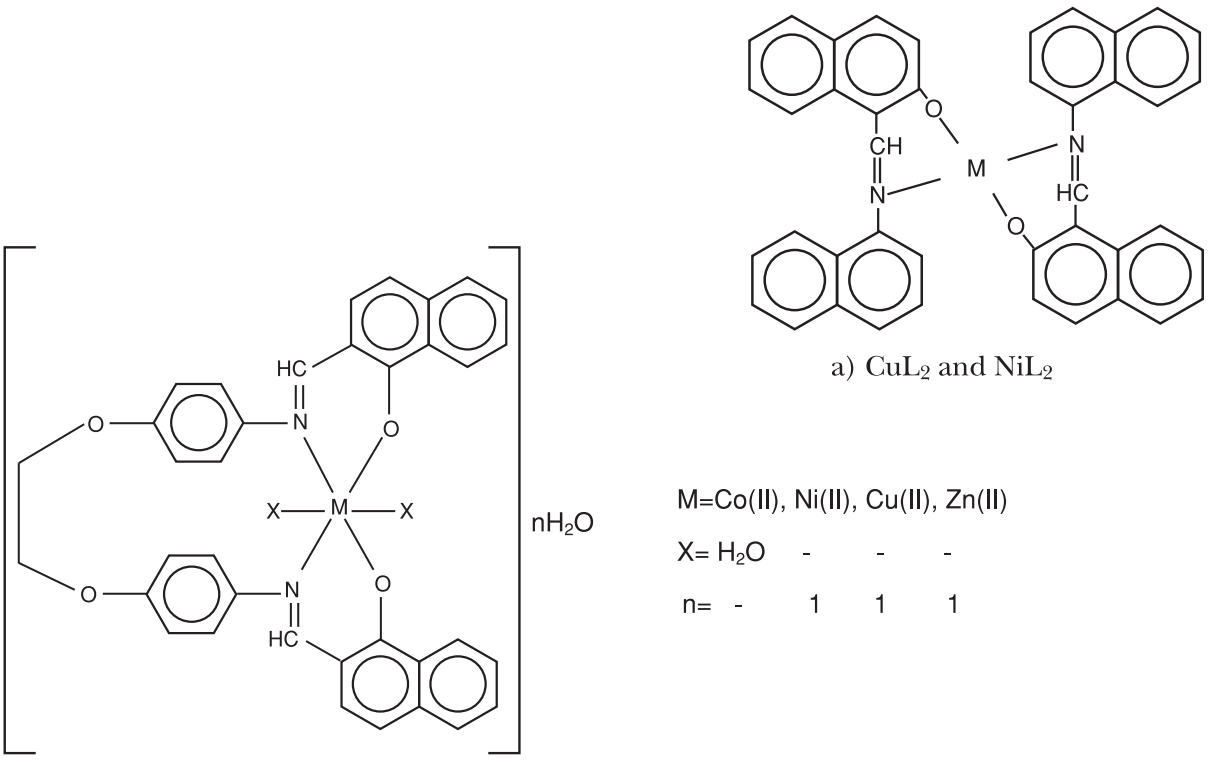


Figure 2. Suggested structure of square-planar NiL_2, CuL_2, CuL′ and NiL′ and the tetrahedral ZnL′ and octahedral $CoL'2H_2O$ complexes.

2.3. Preparation of Microbial Culture

In this study, Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa) were used as the test organisms in an antibacterial study. Bacteria were inoculated into Mueller Hintor-agar (Oxoid). The Schiff base complexes were added in this base media at concentrations of 0.6 μg/100 mL, 1.2 μg/100 mL, 2.4 μg/100 mL, and 4.8 μg/100 mL. Schiff base complexes were not added to the control media. The bacteria were incubated for 24 hour, at 37 °C and bacteria were incubated one day at 37 ± 2 °C. The inoculated bacteria colonies were evaluated one day later. The numbers of bacteria colonies were measured. The experimental trials were made three times. And also the pure water was used as a solvent during the antibacterial studies. The nutrient substances which bacterium could be grown were made in a soluble phase with pure water. Therefore no additive interaction with water was observed.

3. Results and Discussion

All compounds were tested for their antibacterial activity in vitro against Gram-positive bacteria (Staphylococcus aureus)) and Gram-negative bacteria (Pseudomonas aeruginosa) (Table 1).

The effect of ligand H_2L' and its complexes such as Co, Zn, Cu, Ni on Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa) was observed as cell germination at the dosen of 0.6, 1.2 and 2.4 μg/100 mL. However, a decrease was noticed in colony numbers parallel to the increasing dose, with respect to control, but cell germination was not observed at 4.8 μg/100 mL. The effect of Ligand HL and its complexes such as Cu and Ni on Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa) was observed as cell germination at the dosen of 0.6, 1.2 and 2.4 μg/100 mL. However, a decrease was noticed in colony numbers parallel to the increasing dose, with respect to control, but cell germination was not observed at 4.8 μg/100 mL. In literature, it is maintained that ligands and their metal complexes are considerably active against Bacillus megaterium and Candida tropicalis, but that the effect of metal complexes are stronger with respect to ligands [18-20]. It was also reported that ligands and their metal complexes are active against Escherichia coli, Barilum sp and Pseudomonas acurtuginan, while that Cu are more effective. Moreover Cu complex of ligands were reported to be inhibiting active agents against bacteria and fungus [19-21]. It was also determined that ligands could produce an inhibiting effect on the development of Aspergillus niger, Penisilium rubrum and Aspergillus ferreus [22]. It was also established that ligands had an antibacterial effect at 100 ppm concentration and that they had an antifungal effect [23-24].

It was reported that free ligands and their complexes are considerably active against Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa). Nevertheless in view of the antimicrobial activity of the molecule, metal complexes were found to be more active with respect to ligands [4, 18, 25-28].

In our study, it was determined that H_2L' and HL were effective against Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria and that the complexes such as Cu, Ni, Co and Zn increased this efficiency but that this effect statistically was not significant.

Table 1 Antibacterial Activity Data for the Schiff bases and their complexes on Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Pseudomonas aeruginosa)

Compounds	**Concentrations (μg/100 mL)**				
	Control	0.6 μg/100 mL	1.2 μg/100 mL	2.4 μg/100 mL	4.8 μg/100 mL
HL	100%	75 colonies	50 colonies	25 colonies	Non growth
CuL_2	100%	75 colonies	50 colonies	25 colonies	Non growth
NiL_2	100%	75 colonies	50 colonies	25 colonies	Non growth
H_2L'	100%	75 colonies	50 colonies	25 colonies	Non growth
CuL′	100%	75 colonies	50 colonies	25 colonies	Non growth
CoL′	100%	75 colonies	50 colonies	25 colonies	Non growth
ZnL′	100%	75 colonies	50 colonies	25 colonies	Non growth
NiL′	100%	75 colonies	50 colonies	25 colonies	Non growth

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