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Nickel Complex Antifungal Evaluation with Mixed Ligands

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Abstract
Valine has been synthesized as a secondary ligand and 1,10-phenanthroline (phen) as a primary ligand in a mixed ligands transition metal ion complex of Ni(II) ion. The antifungal properties of the complex were assessed by measuring its capacity to stop the growth diameter of three different fungus species: Aspergillus flavus, Aspergillus Niger, and Pencillium. Various doses of the complex were used.

Keywords: Antifungal activity; Metal complexes; Biochemistry; Mixed ligands

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1. Introduction

Since bioinorganic chemistry has advanced, transition metal complexes have played an ever-more-important role. Bioinorganic chemistry relies heavily on metal ions, and biological systems may contain trace levels of metals like Fe, Co, Ni, Cu, Zn, and Cd. It is crucial to conduct structural analyses of the metal complexes with biological substances [1]. Recently, the study of the coordinated systems between metal ions and amino acids has gained importance from various perspectives. When "Biocoordination Chemistry" was chosen as one of seven priority research subjects by electroconductivity (EC) countries in 1991, the growing global interest was validated [2]. The strong field bidentate ligand 1,10-phenanthroline (phen), as shown in figure (1), produces extremely stable chelates with transition metal first row elements [3].

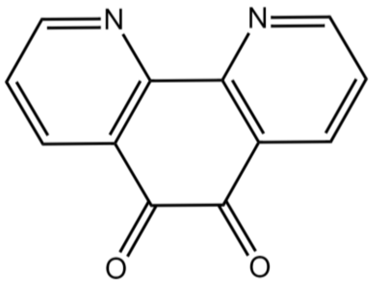


Fig. (1) Structure of 1,10-phenanthroline

While there are many reports in the literature about metal mixed-ligand complexes with either 2,2'-bipyridine or 1,10-phenanthroline and other ligands, there aren't many about the synthesis and biological activities of metal mixed-ligand complexes with 2,2'-bipyridine and 1,10-phenanthroline as ligands [4]. Whether in the metal-free state or in combination with transition metals, 1,10-phenanthroline (phen) disrupts the operation of numerous cellular systems [5].

Figure (2) shows that valine is an α-amino acid with the chemical formula $HO_2CCH(NH_2)CH(CH_3)_2$. One of the twenty proteinogenic amino acids is L-valine. Non-polar is the classification given to this important amino acid. Lentils [6], peanuts, sesame seeds, salmon, poultry, and cottage cheese are examples of foods that humans eat. Valine has a lot of different qualities [7,8].

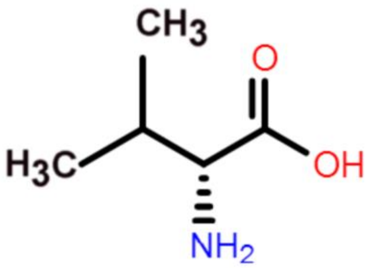


Fig. (2) Structure of Valine

The chemical compounds known as amino acids are crucial to bodily chemistry and biological structure. Both organic and inorganic acids can react with the basic amino group of the amino acid molecule to generate salts, while bases can react with the acid part [9]. The non-centrosymmetric space groups that L-valine complexes belong to are a crucial need for nonlinear optical (NLO) applications. Combining L-valine with hydrochloric acid yields the L-valine hydrogen chloride (LVHC) crystal, which is a valuable NLO material [10-13].

A fungus, Aspergillus Niger, is one of the most prevalent species in the Aspergillus genus. It is frequently found in food and produces a disease called black mold on some fruits and vegetables, including peanuts, onions, and grapes. It is found in soil everywhere and is frequently recorded from indoor settings, where its black colonies might be mistaken for those of Stachybotrys, a species that has also been referred to as "black mold" [14].

Some authors dispute this assertion, stating that the fungus species was misidentified. However, some strains of A. Niger have been documented to produce strong mycotoxins known as ochratoxins [15]. Some genuine A. Niger strains may produce ochratoxin A, according to recent data.

A saprotrophic and harmful fungus, Aspergillus flavus is found throughout the world. Prior to post-harvest storage and/or transportation, A. flavus infections can happen while hosts are still in the field (pre-harvest), although they frequently don't exhibit any symptoms (dormancy). Numerous strains not only cause illnesses before and after harvest, but they also create large amounts of mycotoxins, which are harmful to mammals when consumed [16].

There are Pencillium species everywhere there is organic matter, and they are common soil fungi that prefer cool, moderate conditions. Aspergillus and Pencillium saprophytic species, which are among the most well-known members of the Eureptiles, primarily use organic, biodegradable materials for their survival. Molds, also referred to as molds, are one of the primary causes of food spoiling, particularly those belonging to the Pencillium subgenus [17-19]. Highly poisonous mycotoxins are produced by numerous species. Given their inclination to flourish in low humidity and to quickly expand by aerial dispersion while the seeds are suitably moist, certain Pencillium species are able to grow on seeds and other stored foods [20,21].

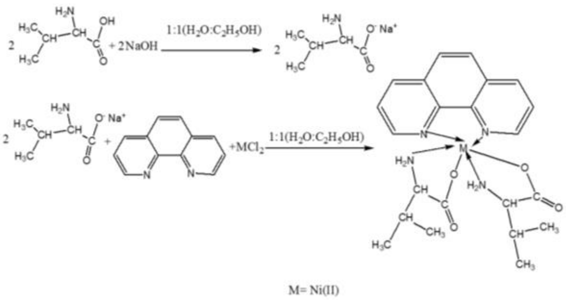
2. Materials and Methods

2.1 Preparation of complex

A solution of 1,10-phenanthroline (0.180 g, 1 m.mol) in aqueous ethanol (1:1:10 ml) and a solution of L-Valine (0,234, 2 m.mol) in aqueous ethanol (1:1:10 ml) containing sodium hydroxide (0.08, 2 mmol) were added simultaneously to a solution of $NiCl_2.6H_2O$ (1 m.mol) in aqueous ethanol (1:1:10 ml) in the stoichiometric ratio [2Val:M: phen] (scheme 1). After being agitated for an hour, the aforementioned solution was let to stand overnight. After filtering off the result, it was cleaned with a 1:1 ml aqueous ethanol and allowed to air dry [22,23].

2.2 Antifungal activity test

Fungi were acquired from Mustansiriya University and identified using Domch & Gama's taxonomic keys. Agar mechanics made of potato dextrose were used to measure the antifungal activity. In compliance with the manufacturer's recommendations As instructed by the manufacturer, 39 g of middle-ready powder was dissolved in 1000 ml of distilled water, infertile medium, and acidic function seized to 5.6. One milliliter of the prepared complex was then added, and the media was introduced once the let-go solidified. The percentage of inhibition was measured by equation (1).



Scheme (1) Preparation of the Complex [Ni(Val)$_2$(phen)]

3. Results and Discussion

A 1:1:2 mole ratio was typically used to create the complexes, meaning that one mole of metal salt was reacted with one mole of 1,10-phenanthroline and two moles of sodium valinate. Making a mixed ligand synthesis One way to depict metal complexes is as follows:
From 2Val H + 2NaOH to 2Val-Na^+ + H_2O

Where phen is 1,10-phenanthroline and Val H is the amino acid L-valine, 2Val-Na+ + phen + MCl_2 → [M (Val)$_2$(phen)] + 4H_2O + NaCl.

The formula weight, color, melting temperatures, and molecular weight are listed in Table 3.

Table (3) Different properties of complex

Compounds	M. Wt	Color	M.P (de) °c	% Metal Theory
[Ni(phen)(Val)$_2$]	471.18	Light green	273	12.46

The physicochemical properties (table 3) revealed that every combination was stable at room temperature and non-hygroscopic.

According to the results of the antifungal activity of various concentrations on complex [Ni(Val)$_2$(Phen)], the concentration 0.01M is the best among the concentrations, with a diameter in cm unit of growth Aspergillus Niger a solid medium 1.5 cm and Pencillium 2.6 cm while a growth Aspergillus flavus 1.2 cm. In contrast, the concentration 0.001M had a range of effects from weak to had to grow Aspergillus Niger as it reached a diameter of growth 2.5 cm.

Finally, the concentration 0.0001M had no effect on Pencillium in the growth zone, which was 4 cm, while Pencillium 3.8 cm had a large effect on Aspergillus flavus as the growth zone was 2.6 cm in comparison to the control media in the growth of three fungi.

Aspergillus Niger in the growth zone was affected by semi-absent and equal to control media by 3.8 cm. 3.4 cm was the growth zone where Aspergillus flavus was most affected, compared to 4 cm for the control medium. Comparing the control medium, which was 4 cm

Even though Aspergillus flavus outperformed the other two fungus in terms of growth in the control conditions, it was the chemical complex's most sensitive direction. The findings were displayed in tables (4,5,6).

Table (4) Effect of complex on *Aspergillus Niger*

Fungi	Control (cm)	Conc. of complex Mol/lit	Growth Diameter (cm)	Inhibition (%)
Aspergillus Niger	4	0.01	1.5	62.5
		0.001	3.5	12.5
		0.0001	3.8	5

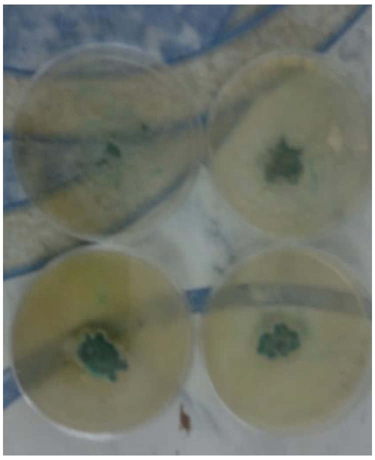
Table (5) effect of complex on *Aspergillus flavus*

Fungi	Control (cm)	Conc. of complex Mol/lit	Growth Diameter (cm)	Inhibition (%)
Aspergillus flavus	5	0.01	1.2	76
		0.001	2.6	48
		0.0001	3.4	32

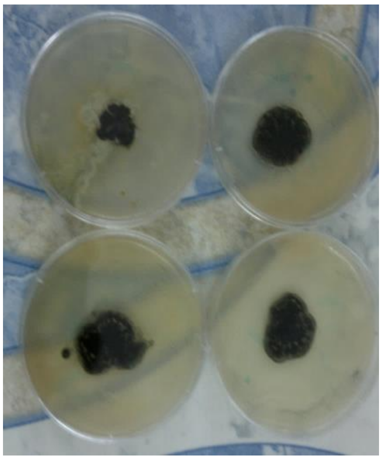
Table (6) effect of complex on *Pencillium sp.*

Fungi	Control (cm)	Conc. of complex Mol/lit	Growth Diameter (cm)	Inhibition (%)
Pencillium sp.	6	0.01	2.6	35
		0.001	3.8	5
		0.0001	4	0

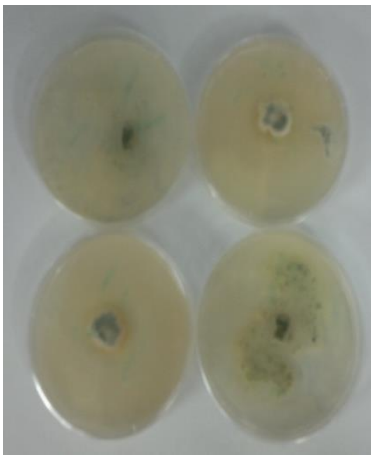
The results of affect the different concentrations of complex on two plant pathogenic fungi show below in Fig. (3)



(a) Effect of complex on diameter growth of *Pencillium*



(b) Effect of complex on diameter growth of *Aspergillus Niger*



(c) Effect of complex on diameter Growth of *Aspergillus flavus*
Fig. (3) Effects of different concentrations of complex on types of fungi

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Table (1) different properties of 1,10-phenanthroline

Compound	Molecular formula	Physical State	Molar mass g mol^{-1}	Solubility (water)	Acidity (pK$_a$)	Melting point (°C)
1,10-phenanthroline	$C_{12}H_8N_2$	White crystalline powder	180.21	Slightly soluble	4.27	114 - 120

Table (2) different properties of Valine

Compound	Molecular formula	Density g/cm^3	Molar mass g mol^{-1}	Solubility (water)	Acidity (pK$_a$)	Melting point °C
Valine	$C_5H_{11}NO_2$	1.316	117.15	soluble	2.32 (carboxyl) 9.62 (amino)	298 decomp.

$$\text{Inhibition (\%)} = \frac{\text{The percentage growth of fungus on the control medium} - \text{The percentage of growth of fungus on the medium with complex}}{\text{The growth of fungus on the control medium}} \times 100\% \quad (1)$$