Iraqi Journal of Scientific and Industrial Research
Volume 3, Issue (3), July-September 2024, pp. 13-16

Structural Studies of Valine Complexes with Biological Activity

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Abstract

A transition metal ion combination of Ni(II) ion with mixed ligands has been produced, whereby Valine serves as the secondary ligand and 1,10-phenanthroline (phen) in its principal role. The ability of the complex to stop the growth diameter of three different species of fungi - *Aspergillus flavus*, *Aspergillus Niger*, and *Pencillium* was used to measure its antifungal properties at different concentrations.

Keywords: Valine complexes; Antifungal activity: Structural studies; Biological activity

Received: 7 April 2024; **Revised:** 12 July 2024; **Accepted:** 19 July 2024; **Published:** 1 October 2024

1. Introduction

With the advancement in the field of bioinorganic chemistry the role of transition metal complexes as therapeutic compounds is becoming increasingly important. The use of transition metal complexes as therapeutic compounds has become more and more pronounced [1]. Metal ions play an important role in bioinorganic chemistry and metals such as Fe, Co, Ni, Cu, Zn, and Cd may exist in trace amounts in biological systems. Structural studies of the complexes of these metals with biological compounds are extremely important [2]. The study of the coordinated systems metal ion - amino acids has become increasingly important in recently from different points of view. Increasing worldwide interest was confirmed in 1991, when EC countries selected "Biocoordination Chemistry" as one of seven priorities research fields [3]. The ligand 1,10-phenanthroline (phen) as in figure (1) is a strong field bidentate ligand that forms very stable chelates with first row elements of transition metals [4].

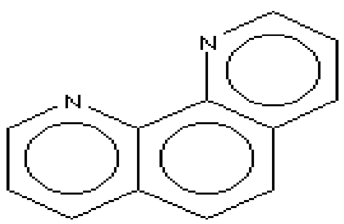

Fig. (1) structure of 1,10-phenanthroline

Although a good number of metal mixed-ligand complexes containing either 2,2'-bipyridine or 1,10-phenanthroline with some other ligands are reported in the literature, there are a few reports on the synthesis and biological activities of metal mixed-ligand complexes containing 2,2'-bipyridine and 1,10-phenanthroline as ligands [5]. The 1,10-phenanthroline (phen) whether in the metal-free state and coordinated to the transition metals disturb the functioning of a wide variety of biological system [6].

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

Compound	Molecular Formula	Molar Mass (g/mol)	Acidity (pKa)	Melting Point (°C)
1,10- phenanthroline	$C_{12}H_8N_2$	180.21	4.27	114-120

Compound	Physical State	Solubility (in water)
1,10- phenanthroline	White Crystalline Powder	Slightly Soluble

Valine is an α-amino acid with the chemical formula $HO_2CCH(NH_2)CH(CH_3)_2$ as Fig. (2). L-Valine is one of 20 protein genic amino acids. This essential amino acid is classified as nonpolar. Valine is branched-chain amino acid. Human dietary sources include cottage cheese, fish, poultry, peanuts, sesame seeds, and lentils [7]. Valine has many properties shown in table (2) [8,9].

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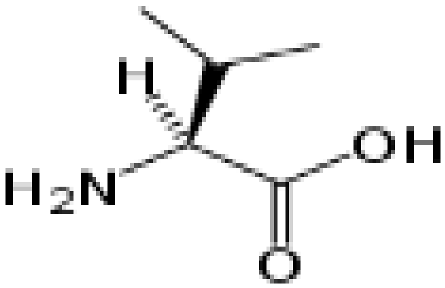

Fig. (2) structure of Valine

Amino acids are organic molecules that constitute a most important part of biological structure and body chemistry. In the amino acids, the amino group is basic portion of the molecule and it is capable of reacting with both organic and inorganic acids to form salts, while the acid portion is capable of reacting with bases [10]. L-Valine complexes belong to non-centrosymmetric space groups and it is an essential criterion for nonlinear optical (NLO) application. L-Valine hydrogen chloride (LVHC) crystal has been formed by combining L-Valine and hydrochloric acid and this complex is found to be a useful NLO material. It has been reported that doping NLO crystals with organic and inorganic impurities can alter various physical and chemical properties and doped-NLO crystals may also find applications in optoelectronic devices like pure NLO crystals [11-14].

Table (2) different properties of Valine

Compound	Molecular Formula	Density (g/cm^3)	Molar Mass (g/mol)	Melting Point (°C)
Valine	$C_5H_{11}NO_2$	1.316	117.15	298 decomposition

Compound	Acidity (pKa)	Solubility (in water)
Valine	2.32 (carboxyl), 9.62 (amino)	Soluble

Aspergillus Niger or *A. Niger* is a fungus and one of the most common species of the genus *Aspergillus*. It causes a disease called black mold on certain fruits and vegetables such as grapes, onions, and peanuts, and is a common contaminant of food. It is ubiquitous in soil and is commonly reported from indoor environments, where its black colonies can be confused with those of Stachybotrys (species of which have also been called "black mould") [15]. Some strains of *A. Niger* have been reported to produce potent mycotoxins called ochratoxins [16], but other sources disagree, claiming this report is based upon misidentification of the fungal species. Recent evidence suggests some true *A. Niger* strains do produce ochratoxin A. [17].

Aspergillus flavus is a saprotrophic and pathogenic [18] fungus with a cosmopolitan distribution [19] *A. flavus* infections can occur while hosts are still in the field (pre-harvest), but often show no symptoms (dormancy) until post-harvest storage and/or transport. In addition to causing pre-harvest and post-harvest infections, many strains produce significant quantities of toxic compounds known as mycotoxins, which when consumed are toxic to mammals [20].

Species of *Pencillium* are ubiquitous soil fungi preferring cool and moderate climates, commonly present wherever organic material is available. Saprophytic species of *Pencillium* and *Aspergillus* are among the best-known representatives of the Eurotiales and live mainly on organic biodegradable substances. Commonly known as molds, they are among the main causes of food spoilage, especially species of subgenus *Pencillium* [21]. Many species produce highly toxic mycotoxins. The ability of these *Pencillium* species to grow on seeds and other stored foods depends on their propensity to thrive in low humidity and to colonize rapidly by aerial dispersion while the seeds are sufficiently moist [22].

2. Materials and Methods

2.1 Preparation of complex

Complex was prepared in general method of mixed ligands metal complexes [23,24] with preparation a solution of 1,10- phenanthroline (0.180 g, 1 m.mol) in aqueous ethanol (1:1:10 ml) and solution of L-Valine (0, 234, 2 m.mol) in aqueous ethanol (1:1:10 ml) containing sodium hydroxide (0.08, 2 m.mol) 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] as Scheme (1). The above solution was stirred for 1houre and allowed to stand for overnight. The product formed was filtered off, washed with aqueous ethanol (1:1 ml) and dried in air.

2.2 Antifungal activity test

Fungi were obtained from the University of Mustansiriyah and diagnosed based on the taxonomic keys in Domch&Gamas. The antifungal activity was determined on the potato dextrose agar which it was solidify. According to the manufacturer's instructions Attended by dissolving 39 g of powdered middle-ready and as directed by the manufacturer in 1000 ml of distilled water and acidic function seized to 5.6 and infertility medium, added 1ml of prepared complex and added the media after let go solidifies. The percentage of inhibition was measured by the following equation:

$$\text{percentage of inhibition} = \frac{\text{The growth of fungus on the control medium - The growth of fungus on the Medium with complex}}{\text{The growth of fungus on the control media}} \times 100$$

3. Results and Discussion

Generally, the complexes were prepared by reacting the respective metal salts with the ligands using 1:1:2 mole ratio, i.e., one mole of metal salt: one mole of 1,10-phenanthroline and two moles of sodium valinate.

The synthesis of mixed ligand Metal complexes may be represented as follows

$2Val\ H + 2NaOH \rightarrow 2Val^- Na^+ + 2H_2O$

$2Val^- Na^+ + phen + MCl \rightarrow [M:(Val):(phen)] + 4H_2O + NaCl$

where phen is 1,10-phenanthroline and Val H is amino acid L-valine)

The formula weight, molecular weight, color and melting points are given in table (3).

Based on the physicochemical characteristics (table 3), it was found that all the complexes were non-hygroscopic, stable at room temperature.

Table (3) different properties of complex

Compound	Molecular Weight	Color	Melting Point (°C)	% Metal Theory
[Ni(phen)(Val)2]	471.18	Light Green	273	12.46

The results of the antifungal activity of different concentrations of complex [Ni(Val)2(phen)] on the radial growth of plant pathogenic fungi compared with the control, the concentration 0.01M is the best among the concentrations, where it was diameter in cm unit of growth *Aspergillus Niger* a solid medium 1.5cm and *Pencillium* 2.6cm while a growth *Aspergillus flavus* 1.2cm while the concentration 0.001M was ranged affect between weak and had to growth of *Aspergillus Niger* as reached diameter of growth 2.5cm, and *Pencillium* 3.8cm to a high effect on *Aspergillus flavus* as growth zone was 2.6cm compared with the control media in growth of three fungi, finally the concentration 0.0001M was absent in effect on *Pencillium* in growth zone was 4cm Equal with control medium and semi-absent effect on *Aspergillus Niger* in growth zone was 3.8cm Comparison with control medium which stood at 4cm while effect on *Aspergillus flavus* was highest and it was growth zone 3.4cm Comparison with control medium which stood at 4cm.

Although the *Aspergillus flavus* was the best among the three fungi in growth in the control media, but it was most sensitive direction of the chemical complex. The results were viewed in table (4).

Table (4) antifungal activity of different concentration of complex on radial growth rate of *Aspergillus Niger, Aspergillus flavus, Pencillium sp.*

Fungi	Control (cm)	Complex Concentration (mol/L)	Growth Diameter (cm)	% Inhibition
Aspergillus Niger	4	0.01	1.5	62.5
		0.001	3.5	12.5
		0.0001	3.8	5
Aspergillus flavus	5	0.01	1.2	76
		0.001	2.6	48
		0.0001	3.4	32
	6	0.01	2.6	35
Pencillium sp.		0.001	3.8	5
		0.0001	4	0

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

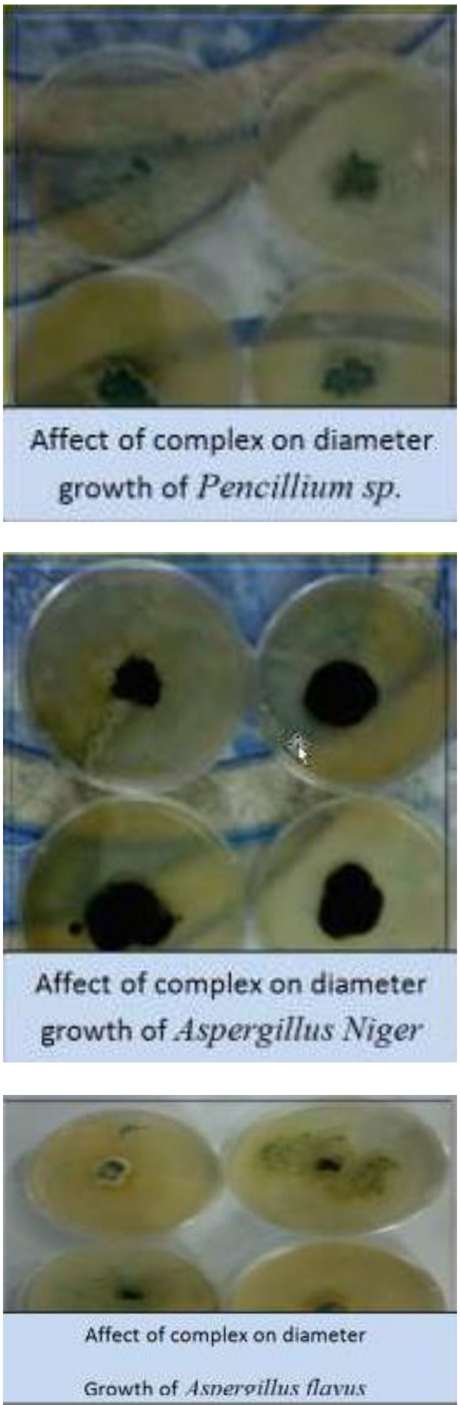

Fig. (3) Effects the different concentrations of complex on types of fungi

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 ISSN (print) 2079-4630 (online) xxxx-xxxx