



Research Article

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## Synthesis and characterization of some essential amino acid metal complexes having biological activity

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### ABSTRACT

*Metal complexes of the essential amino acids (leucine, methionine)  $[M(L.H_2O)_2]$ , where L (leucine, methionine),  $[M:Co^{+2}, Ni^{+2}, Cu^{+2}, Zn^{+2}, Cd^{+2}]$ , have been prepared from the reaction of chloride-salt of transition metal. With sodium salt of the amino acid. The complexes have been characterized by means infrared spectra and atomic absorption analysis. The IR spectra and atomic absorption analysis show that amino acids act as bidentate ligands. IR spectroscopy confirms the ligand coordination to the metal ions through carboxyl and amine groups. The prepared complexes show poor solubility in water and in the common organic solvents.*

**Keywords:** Amino acid, transition metals, FTIR, complex, leucine, methionine

### INTRODUCTION

Numerous papers have been published on metal complexization of amino acids during the past years because they proved to be useful chelation agents, as anti-inflammatory agent, as antibacterial applied against *Escherichia coli* and *streptococcus pyogenes*, anti-tumor agents against melanoma ...etc.

Twenty natural amino acids comprise the building blocks of proteins, which are chemical species indispensable to perform a large number of biological function, as exemplified by the role of enzymes <sup>(1)</sup>.

From these twenty amino acids, eight are essential and cannot be produced by human body. Leucine and methionine are two of these essential amino acids. When minerals such as zinc, copper, iron and other are chemically bonded to amino acids with at least two bonds from each amino acids, rings of atoms attached to the minerals result and chelation has occurred. Chelation occurs naturally in the body to facilitate transport of minerals across the intestinal wall as part of digestion <sup>(2)</sup>.

It has long been recognized that certain (trace) metals are essential to the health of all living organisms. Such trace metals serve well established functions in enzyme reaction, as components of electrolytes, as binding sites in the transport of oxygen, and as structural components of non-enzymatic macromolecules <sup>(3)</sup>.

Amino acids have been repeatedly shown to produce wide complexes with transition metals repeatedly in the literature <sup>(4)</sup>. All of naturally occurring  $\alpha$ - amino acids bind in what is known as the glycinate way. This means that a

five- membered ring is formed with the metal, amine nitrogen and the carboxylic oxygen. This arrangement is always present for the natural human amino acids even when the side chain has a ligating group. <sup>(6,7)</sup>.

Leucine is branched – chain essential amino acid which means that it cannot be manufactured in the body and must be obtained through dietary sources, Leucine is also available in standalone supplemental form, but should always be taken together with the other two branched – chain amino acids, isoleucine and valine because they work to repair muscles.

Leucine is the most effective branched- chain amino acid for preventing muscle loss because it breaks down and is converted to glucose more quickly than isoleucine and valine. Leucine also promotes the healing of bones, skin, and muscle tissue after traumatic injury, and is often recommended for those recovery from surgery .

Because it is so easily converted to glucose, leucine helps to regulate blood sugar, a deficiency of leucine produces symptoms similar to those of hypoglycemia, which may include headaches, dizziness, fatigue ,depression, confusion, and irritability <sup>(8)</sup>.

Methionine is one of the amino acids containing sulfur, it helps to prevent disorders of the hair, skin and nails, in lowering the cholesterol levels by increasing the liver's production of lecithin and reduces fat build-up in the liver and body <sup>(9)</sup>.

In recent years transition metals amino acids complexes have received much attention because they proved to be useful antibacterial agent <sup>(10)</sup>. Coordination complexes of transition metals have been widely studied for their antibacterial and potential cytotoxic chemotherapeutic agent.

They have been evaluated against several pathogenic fungi and bacteria with promising results. One of the approaches to increase the efficacy of the drugs consists in their modification of physical and chemical factors. In addition to its ability to combat infection or neoplastic disease, these new agents must exhibit selective toxicity, chemical stability, and optimum rates of bio- transformation and elimination <sup>(11)</sup>.

## EXPERIMENTAL SECTION

**Materials:** All chemicals used in this work were analytical analar grade .

**Physical Measurement:** Infrared spectra were recorded for the leucine, methionine, and all the prepared complexes on [FT.IR][ABB-MB 3000] spectrophotometer in the range (4000-400) $\text{cm}^{-1}$ . Spectra were recorded as potassium bromide discs. Melting point was determined using an electrothermal melting point SMP3 Stuart. Metal analysis were measured with (Phoenix-986) atomic absorption spectrophotometer.

**Synthesis of metals amino acid complexes:** The purpose of the study was to obtain neutral complexes of  $[\text{M}(\text{L}.\text{H}_2\text{O})_2]$  type ,where  $\text{M}=\text{Co}^{+2}, \text{Ni}^{+2}, \text{Zn}^{+2}, \text{Cd}^{+2}, \text{Cu}^{+2}$ , L=ligand (leucine, methionine) at PH=8-10, in the presence of strong basis (NaOH) to obtain the ionization conditions of the amino acid (leucine, methionine).

The complexes were prepared following the procedure:

(2) mmols of leucine or methionine were dissolved in (20) ml distilled water and for deprotonation of the leucine and methionine (0.33)ml(30%) NaOH was added <sup>(12)</sup>.

Then (1)mmole of the metal chloride was dissolved in (2)ml of distilled water, and was added to the deprotonated amino acid solution under stirring for several minutes. The precipitate was filtered off ,washed with water several times, and dried in air.

## RESULTS AND DISCUSSION

The metal ions complexes theoretical concentration have similar values with those of the synthesized complexes. Which demonstrates the complete reaction took place table (1).

The qualitative differences between the infrared spectrum of the free amino acid leucine, methionine, leucine complexes, and methionine complexes are discussed in order to ascertain ligand to metal ions bonding modes. The characteristic infrared bonds which are assigned to most significant functional groups of the amino acids and its metal ion complexes are summarized in tables (2) and (3).

The infrared spectra of the leucine and metal ion complexes had indicated presence of broad band at the range (2624-3070) $\text{cm}^{-1}$  which are attributed to stretching vibration of  $\text{NH}_2$  amino group, and this band confirmed by the appearance of bending vibration band  $\nu_b\text{NH}_2$  at 1514 $\text{cm}^{-1}$  such values were reported in literature <sup>(13)</sup>.

A broad band at (2624-3070) $\text{cm}^{-1}$  are assigned to stretching vibration of amino group in free amino acid, represented of two well-resolved band at 3366 and 3281 $\text{cm}^{-1}$  for cobalt complex, (3368 and 3277) $\text{cm}^{-1}$  for nickel complex, (3300 and 3244) $\text{cm}^{-1}$  for copper complex and (3351 and 3254) $\text{cm}^{-1}$  for cadmium complex. This observation proved involvement amino group in the coordination in the metal ions.

The band at 1514 $\text{cm}^{-1}$  in the spectrum of the leucine which is assigned to the bending vibration of N-H band, shift to lower wave number about (42-47) $\text{cm}^{-1}$  in the spectra of metal complexes confirming coordination through nitrogen to the metal ion in these complexes. These observation are in an agreement with that reported in the literature <sup>(14)</sup>.

The absence of ( $\text{NH}_3^+$ ) vibration at 2131 $\text{cm}^{-1}$  in the spectra of leucine-metal ion complexes comparison to the free ligand (leucine) is another valuable proof of the involvement of  $\text{NH}_2$  group coordination <sup>(15)</sup>.

The infrared spectrum of the leucine exhibit sharp bands at 1584 $\text{cm}^{-1}$  attributed to stretching mode of carbonyl group which is confirmed by the appearance of medium intensity band at 1408 $\text{cm}^{-1}$  assigned to  $\text{COO}^-$  asymmetric vibration. These bands shifted to higher frequency by (7-38) $\text{cm}^{-1}$  in the spectra of the metal complexes of cobalt, nickel, zinc, cadmium and copper complexes confirming coordination through carbonyl group. These observation are in an agreement with reported in the literature <sup>(16)</sup>.

In the water containing complexes  $[\text{ML}_2.\text{xH}_2\text{O}]$ , bands due to  $\nu(\text{OH})$  and  $(\text{OH})$  are present in the range (3300-3500) $\text{cm}^{-1}$  (broad) and near (860-840) $\text{cm}^{-1}$  (weak) respectively suggesting the presence of coordinated water, these results are in an agreement with literature <sup>(14)</sup>.

Disappearances of the ( $\text{NH}_3^+$ ) vibration in the spectra of complexes and appearances two bands to amino group and two bands to carboxyl group in further to appearances band indicated presence of coordinated water, these data indicate octahedral structure around metal ions.

In the spectrum of methionine, broad band at about (3235-2618) $\text{cm}^{-1}$  correspond to the  $\nu_{\text{N-H}}$  stretching vibration. This band appear in the spectra of the complexes at 3447  $\text{cm}^{-1}$  for CuII, 3455 $\text{cm}^{-1}$  for ZnII and at 3478 $\text{cm}^{-1}$  for Cd II complexes. These shifted indicates the involvement of  $\text{NH}_2$  group in the metal ligand, in further confirming coordination through amino group absence of  $\text{NH}_3^+$  vibration band 2101 $\text{cm}^{-1}$  in the spectra of complexes of methionine comparison to the free amino acid is another valuable proof of the involvement of the  $\text{NH}_2$  group coordination.

A sharp band at 1580 $\text{cm}^{-1}$  which is attributed to the  $\nu(\text{C=O})$  stretching vibration in methionine spectrum these band shifted to higher frequency for complexes of methionine about (23-58) $\text{cm}^{-1}$ , this shifted indicated that carboxyl group was involved in covalent bonding to metal ions.

The infrared spectra of copper, nickel, cobalt, zinc and cadmium complexes show weak absorption band near 563, 568, 572, 561, 553 $\text{cm}^{-1}$  which are attributed to (M-O) band while (M-N) frequencies were identified at (500-400) $\text{cm}^{-1}$ . These bands support the coordination through both nitrogen atoms of amino group and carboxyl group of the amino acid to the metal ion <sup>(17)</sup>.

**Table (1): Metal ions complexes concentration obtained by means of atomic spectroscopy and some physical properties of leucine complexes**

Proposed formula	Formula Weight	Colour	Yield %	Melting point °C	Metal	
					Theoretical	Synthesized
Cu(L.H <sub>2</sub> O) <sub>2</sub>	359.54	Blue	72.0	260 dec.	17.6	18.0
Co(L.H <sub>2</sub> O) <sub>2</sub>	354.9	Pink	62.02	280 dec.	16.5	16.5
Ni(L.H <sub>2</sub> O) <sub>2</sub>	354.7	light- green	74.35	265 dec.	16.5	16.0
Zn(L.H <sub>2</sub> O) <sub>2</sub>	361.37	White	72.6	290 dec.	18.0	18.5
Cd(L.H <sub>2</sub> O) <sub>2</sub>	408.4	White	93.0	280 dec.	27.5	28.0

**Table 2: Some important IR bands of leucine and their metal complexes**

compound	$\nu_{as}(\text{COO})^-$	$\nu_{st}(\text{C=O})$	$\nu_b(\text{NH}_2)$	$\nu_{st}(\text{NH}_2)$
leucine	1408	1584	1514	3070-2624 (br)
Co.leucine	1410	1591	1472	3366,3281,2957(sh)
Ni.leucine	1414	1591	1472	3551-3277(br) 2955(sh)
Zn. leucine	1410	1622	1471	3459(br) 2957(sh)
Cd.leucine	1400	1591	1560	3472(br) 3351,3254,2961(sh)
Cu.leucine	1397	1618	1472	3416(br) 3244,2960(sh)

*as=asymmetric, br=broad, b=bending, st=stretching, sh=sharp*

**Table 3: Some important infrared bands of methionine and their metal complexes**

compound	$\nu_{as}(\text{COO})^-$	$\nu_{st}(\text{C=O})$	$\nu_b(\text{NH}_2)$	$\nu_{st}(\text{NH}_2)$
methionine	1414	1580	1514	3547-3420(br) 2946-2919(br)
Co.methionine	1384	1627	1530	3632(sh) 3551-3474(br)
Ni.methionine	1407	1619	—	3644(sh) 3416(br)
Cd.methionine	1410	1638	1568	3547-3420(br) 2973(sh)
Zn.methionine	1391	1603	1507	3505,3455,3324,2919(sh)
Cu.methionine	1395	1619	—	3447-3229(br) 2919(sh)

*as=asymmetric, br=broad, b=bending, st=stretching, sh=sharp*

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