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The Effect of Metal Complexes of DL – Methionine on Some Biochemical Parameters

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ABSTRACT

The donor properties of the amino acid Methionine CH3 SCH2 CH2 CH (NH2) COOH (HMt), were investigated for a number of transition Metal Ions , Co(Π) , Ni(Π) , Cu(Π), Zn(Π) , Cd(Π) , Hg(Π) , Pb (Π) .Methionine behaves as on anionic ligand (Mt)and generally forms neutral complexes , M" Mt2 the metal attains its usual higher coordination number by linking with the(N) atom of – NH2 group and with one or both the(O) atom of the – COO- group .In these complexes the (S) atom of the –S CH2 group is still available for coordination. To help in the structural study of Methionine complexes a number of complexes were prepared and investigated .The effect of Methionine with detoxic (Pb, Hg, Cd) on Glutathione s-Transfers and MDA were investigated.

Introduction

The use of chelating agents in biology and medicine has been siad to have only just begun (1). It has been observed recently that metal chelating apparently plays definite role in the cause and treatment of cancer but just how is still matter for conjecture (2, 3). There are indications that some metal chelates of ligands which have anticancer activity are more carcinostatic than the free ligands (3, 4).

DL-Methionine, CH3SCH2CH2CH (NH2) COOH {MtH}, Cannot be synthesized in the body, it is an essential amino acid which must be present in the diet (5).

It is well known that amino carboxylic acid acts as negatively charged chelating ligand toward metal Ions, coordinating both through the –NH2 and the –COO- groups, In contrast only sparce information is available on the donor ability of sulfur - contain amino acid , in which the sulfur atom is also a possible ligating site. For the anion of cysteine –SCH2- CH (NH2) COO-, both sulfur to metal and oxygen to metal bonds have been shown to exist in solid complexes of Zn (Π) ,Cd(Π) , and Hg(Π) ,whereas sulfur and nitrogen appear to be the ligating atoms toward Ni(Π) in aqueous solution (1- 5).

The data available in the literature showed that methionine is capable of coordination through the – S CH2 as well as through the – NH2 and – COO- groups and is potentially tridentate chelating legend. On the other hand, since the (S) atom of this ether group (class b base) differs markedly in its donor properties from the N atoms of an amino group and the(O) atom of acarboxylate group (both class a bases) , methionine may not tend to coordinate with a given metal ion as a tridentate chelating ligand (S,N, and O donor atoms). More likely Methionine could be expected to act as abidentate chelating ligand and use different pairs of different metal atoms (6,7,8).

Experimental

Starting materials- DL-methionine, analytical grade metal salts were used without further purification.

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Preparation and characterization of the complexes

Preparation -1-of the complexes Cu, Ni, Co.

The amino acid (1.3g) and sodium carbonate (0.5g) were dissolved in 70 ml of water at 80 ◦C and the metal nitrate (Hexahydrate)was added with stirring(metal: amino acid mole ratio was (1:2: 3) the resulting solution was concentrated under reduced pressure on a steam bath and then cooled in a refrigerator. after several hours the crystals which formed were filtered off , washed with water and ethanol , and dried in vacuum over P4O10 (9).

Preparation -2- a of the complex Hg ,Cd, pb ,Zn

An ethanol solution of the anhydrous metal chloride was added to ethanol solution of lithium methionainato, and the mixture was refluxed for 3h. the resulting solution was filtered hot and on cooling gave precipitate which was filtered, washed with ethanol, and dried in vacuo over P4O10 (10).

Preparation -2- b

The amino acid was added to a suspension of Li.OH.H2O(slight excess over 1:1 mole ratio in ethanol and stirred at 60 ◦ for 20 min after filtration of the unreacted LiOH.H2O, a solution of the metal perchlorate (Hexahydrate) in ethanol was added slowly . [the metal : amino acid mol ratio was 1:2 for the M"L2 (metal complexes)] the precipitate which formed immediately was filtered washed with ethanol, and dried in vacuo over P4O10(11).

2- Determination of human erythrocyte Malondialdehyde (MDA) (12).

3- Determination of Erythrocyte Glutathione S-Transfers (G.S.T) assay (13).

4- Albino-Swiss- Mice(40), 10 control ,10 Treated with $pbCl_2$, 10 Treated with $HgCl_2$, 10 Treated with $CdCl_2$.

A=Group treated with $pbCl_2$ 200mg, $HgCl_2$ 200mg, $CdCl_2$200mg for one weak.

B= Group treated with methionine 200mg for one weak.

Results and Discussion

Methionine and its alkali metal salts reacted with metal ions which formed complexes containing the negative ligand, CH3SCH2CH2CH(NH2)Coo (Mt). neutral complexes M"Mt2 were generally obtained regardless of the experimental condition (Meta ligand ratio .order of addition of reagents , solvent); however , with Ni(Π) and Cu (Π) different preparative methods yielded cationic, neutral ,or anionic complexes.

The metal-methionine complexes (Table 1) are crystalline, have rather high decomposition temperatures are stable to air, and, with after exception, are. Stable to moisture. Most of these complexes, once, isolated as solids, are insoluble in all solvent and consequently their structural study had to be limited to the solid state. For this reason, and because of the complexity of their infrared spectra the geometric (cis – Trans) form of the complexes was not investigated.

Complexes with legend ML2 (L =Mt and M=Co (Π), Ni (Π) and Cu (Π)

The magnetic moment (Table1) and visible spectra of the Co (Π) ,Ni (Π) and Cu (Π) methionine complexes , M Mt2 , indicate that the control metal ion is six – coordinated with a high-spin, essentially octahedral, configuration. Therefore in these complexes each methionine anion ligates through three sites, and the tow most likely possibilities are

1-Coordination via the N and S atoms and O atom of the –coo- group.

2-Coordination via the N atom and both O atom of the –coo- group.

The infrared spectra of the methionine (Table Π) are very similar and the following are of interest.

1-The anti symmetric and symmetric carboxylate stretching vibration (coo-) of the methionine.

2-The sodium salt of methionine have three medium, well- resolved absorption bands between 3410 and 3274 cm-1 ,all of which shift upon deuteration of the –NH2 group .for this reason a well defined trend in the υ(NH2) frequencies is not observable for the M Mt2 complexes, although there is a general lowering of the absorption rang .the range of the υ (NH2) absorption for the Cu (Π) complexes (3290- 3130 cm-1) is about 100 cm lower then for the other complexes (3370-3270 cm-1), suggesting that the M-N band is- as expected – strongest for Cu(Π) .

3-Should the S atom of the –S CH3 group

coordinate to the metal in the complexes of methionine, a regular shift of GS stretching mod, which in aliphatic sulfide appear a weak band in the 600-700 cm reign.

Could not be identified with certainty in the spectra several other modes absorb in the some region .However, indirect evidence that the S atom of methionine is not involved is coordination is the fact that the deformation vibration of –CH2 group. Zinc (Π) , cadmium (Π) , mercury (Π) and led (Π) complexes.

These post- transition metal ions form , with methionine complexes. That type ML2 , insoluble. In all solvent . the infrared spectra of the complexes show that both the – NH2 and – coo- groups are coordinated; the range of absorption of the υ(NH2) modes indicates that Hg (Π)forms the strongest M-N bond. While the values of Δυ(coo-) indicate that the strength of M- O bond decreases in the order Pb > Zn>Hg> Cd the similarity between the methionine complexes is very marked and indicates that the sulfur atom of methionine is not in rolved in coordination even for these heavy post- transition metals, which may be expected to have an affinity for the –SCH2 group . these complexes may than be considered to be structurally similar to ML2 complexes of the first –row transition metals(9,14).

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Table (1): Formulas, analytical data. and some properties of the metal complexes of methionine.

complexes	color	mp orde tamp c	meff B.M	prep method
(Co Mt_2)n	pinlc	285	4.91	1
(Ni Mt_2) n	Light blue	>300	3.18	1
(Cu Mt_2)n	Deep blue	270	2.05	1
(Zn Mt_2)n	White	280		2
(Cd Mt_2)n	White	214		2
(Hg Mt_2)n	Yellow	120		2
(Pb Mt_2)n	White	214		2

21.

Table (2): Formulas, analytical data. infrared absorption frequencies(cm-1) of properties of complexes of methionine.

complexes	$\upsilon(NH_3)^+$ $\upsilon(NH_2)$	$\delta(NH_3)^+$ $\delta(NH_2)$	$\upsilon(coo^-)$ antisym	$\upsilon(coo^-)$ sym
(Co Mt_2)n	3360_{sh}, 3342_s, 3272_s	1565_{sh}	1587_s	1410_m

(Ni Mt_2) n	**3338_m ,3276_m**	**1587_s**	**1617_s**	**1399_m**
(Cu Mt_2)n	**3280_s, 3236_s, 3136_w**	**1574_s**	**1621_s**	**1400_s, 1392_s**
(Zn Mt_2)n	**3314_s, 3292_s, 3250_s, 3154_m**	**1572_m**	**1610_s**	**1334_m2**
(Cd Mt_2)n	**3330_m, 3247_w, 3200_{sh}**	**1570_m**	**1500_s**	**1410_m**
(Hg Mt_2)n	**3157_m, 3090_m**	**1573_s**	**1597_s**	**1400_s**
(Pb Mt_2)n	**3315_s, 3250_s, 3160_w**	**1553_s**	**1629_s**	**1400_s**

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Table (3): Erythrocyte G.S.T activity in-patients (pbCl2) and control group before and after treatment with methionine.

NO.	T.TEST	±S.D	mean G.S.T U.g-1Hb	SUBJECT
10		**±0.075**	**0.95**	**Control**
10	**P<0.01**	**±0.42**	**1.44**	**(A)before treatment**
10	**N.S**	**±0.12**	**1.06**	**(B) after treatment**

A=Group treatment pbCl2 200mg for 1 weak.
B= Group treatment methionine 200mg for 1 weak.
Table 3 A Group showed Increased Erythrocyte G.S.T activity in –patients
(pbCl2) comparative with control group.
B Group showed decreed Erythrocyte G.S.T activity in –patients
(pbCl2) comparative with A group(14).

Table (4): Erythrocyte G.S.T activity in-patients (HgCl2)and control group before and after treatment with methionine.

NO.	T.TEST	± S.D	Mean G.S.TU. g-1Hb	SUBJECT
10		**±0.077**	**0.95**	**Control**
10	**P<0.01**	**±0.40**	**1.42**	**A**
10	**N.S**	**±0.21**	**0.99**	**B**

A=Group treatment HgCl2 200mg for 1 weak.
B= Group treatment methionine 200mg for 1 weak.
Table 4 A Group showed Increased Erythrocyte G.S.T activity in –patients
(HgCl2) comparative with control group.
B Group showed decreed Erythrocyte G.S.T activity in –patients
(HgCl2) comparative with A group (19).

Table (5): Erythrocyte G.S.T activity in-patients (CdCl2) and control group before and after treatment with methionine.

NO.	T.TEST	±S.D	mean	SUBJECT
			GST	
10		**±0.12**	**0.95**	**Control**
10	**P<0.001**	**±0.94**	**1.75**	**A**
10	**P<0.05**	**±0.87**	**1.06**	**B**

A=Group treatment CdCl2200mg for 1 weak.
B= Group treatment methionine 200mg for 1 weak.
Table 5 A Group showed Increased Erythrocyte G.S.T activity in –patients
(CdCl2) comparative with control group.
B Group showed decreed Erythrocyte G.S.T activity in –patients
(CdCl2) comparative with A group(16).

Table (6): Erythrocyte (MDA) levels as an index of lipid peroxidation in patients (pbCl2) and control group before and after treatment with methionine.

NO.	T.TEST	±S.D	Mean MDA nmol/gHb	SUBJECT
10		**±0.076**	**0.45**	**Control**
10	**P<0.001**	**±0.97**	**1.55**	**A**
10	**P<0.05**	**±0.27**	**0.87**	**B**

A=Group treatment pbCl2200mg for 1 weak.
B= Group treatment methionine 200mg for 1 weak.
Table 6 A Group showed Increased Erythrocyte MDA lipid peroxidation in –patients(pbCl2) comparative with control group.
B Group showed decreed Erythrocyte MDA lipid peroxidation in –patients
(pbCl2) comparative with A group.

Table (7): Erythrocyte (MDA) levels as an index of lipidperoxidation in patients(HgCl2) and control group before and after treatment with methionine.

NO.	T.TEST	± S.D	Mean MDA nmol/gHb	SUBJECT
10		**±0.15**	**0.46**	**Control**
10	**P<0.001**	**±0.48**	**1.78**	**A**
10	**P<0.05**	**±0.82**	**0.88**	**B**

A=Group treatment HgCl2 200mg for 1 weak.
B= Group treatment methionine 200mg for 1 weak.
Table 7 A Group showed Increased Erythrocyte MDA lipid peroxidation in –patients(HgCl2) comparative with control group.
B Group showed decreed Erythrocyte MDA lipid peroxidation in –patients
(HgCl2) comparative with A group.

Table (8): Erythrocyte (MDA) levels as an index of lipidperoxidation in patients(CdCl2) and control group before and after treatment with methionine.

NO.	T.TEST	±S.D	mean MDA	SUBJECT
10		**±0.15**	**0.45**	**Control**
10	**P<0.001**	**±0.97**	**1.76**	**A**
10	**P<0.05**	**±0.26**	**0.83**	**B**

A=Group treatment CdCl2200mg for 1 weak.

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B= Group treatment methionine 200mg for 1 weak.
Table 8 A Group showed Increased Erythrocyte MDA lipid peroxidation in –patients(CdCl2) comparative with control group.
B Group showed decreed Erythrocyte MDA lipid peroxidation in –patients
(CdCl2) comparative with A group(17, 20).

تأثير معقدات الحامض الاميني الميثيونين مع أنواع من العناصر النزرة على بعض المتغيرات البايوكيميائية.

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الخلاصة

تتضمن الدراسة تأثير معقدات الحامض الاميني الميثيونين مع أنواع من العناصر النزرة الانتقالية مثل عنصر الكوبلت، النيكل، النحاس، الزنك، الكادميوم، الزئبق، الرصاص حيث ان الحامض الاميني المثيونين يرتبط بأواصر تناسقية مع عدد من الذرات مثل ذرة النايتروجين الموجودة في مجموعة الأمين .ومع ذرة الاوكسجين الموجودة في مجموعة الكاربوكسيل. ومع ذرة الكبريت الموجودة في مجموعة الثايول. وتم دراسة تأثير معقد ت الحامض الاميني المثيونين مع العناصر الرصاص والزئبق والكادميوم. على بعض المتغيرات البايوكيميائية والإنزيمية مثل إنزيم الكلوتاثايون اس_ ترانسفريز والمالون داي الديهايد.