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Synthesis of magnesium complex for medicine application

Abstract

The magnesium methioninate complex was chemically prepared by the addition of magnesium salt to the solution of sodium salt of methionine; the prepared complex was analyzed by reversed phase high performance liquid chromatography (HPLC). The prepared complex was characterized by using appropriate physical measurement, Flame atomic absorption (FAAS), Fourier transformer infrared spectrophotometer (FTIR), melting point (M.P.), (CHN) analyzer. To treatment the deficiency level of magnesium in hypertension and myocardial infarction patients, the complex was formulated at estate of drug medical appliance in Samara as tablet. The present study involved the following groups: (1) 1-100 healthy volunteers (55 men, 45 women) (2) 2-50 patients with myocardial infarction (men) (3) 3-50 patients with hypertension (men). The concentration of magnesium in blood serum was determined by flame atomic absorption spectrophotometer. The results appeared that patients with hypertension and myocardial infarction had lower concentration of magnesium in blood serum as compared with the healthy group. We supplied (21) patients with hypertension and (19) patients with myocardial infarction, with (500mg) Mg(Met)2 tablets for two weeks. The results appeared that the concentration of magnesium in blood serum of hypertension patients were elevated from (10-11mg/ml) to (12-16mg/ml), and for myocardial infarction patients, the concentrations were elevated from (11-12mg/ml) to 17-20mg/ml).

Keywords: magnesium methioniate, HPLC

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Abbreviations: HPLC, high performance liquid chromatography; FAAS, flame atomic absorption; FTIR, fourier transformer infrared spectrophotometer; MP, melting point

Introduction

Epidemiologic evidence suggests that magnesium may play an important role in regulating blood pressure with magnesium deficiency, the walls of the arteries and capillaries tend to constrict a possible explanation for the hypertensive effect. However, foods high in Mg are frequently high in potassium and dietary fiber, which makes it difficult to evaluate the independent effect of mg on blood pressure.[1] A prospective study of more than 30,000 male health professionals found an inverse association between dietary fiber, potassium, magnesium and the development of hypertension over a four- year period.[1] In a similar study of more than 40,000 female registered nurses, dietary magnesium each inversely associated with systolic and diastolic blood pressure in those who did not develop hypertension over the four- year study period. But neither dietary fiber nor Mg was related to the risk of developing hypertension.[2] The risk of developing hypertension in both women and men decreased as serum Mg levels increased.

Studies show higher the death rates from coronary heart disease in areas where the water contains low magnesium levels.[3] Some observational surveys have associated higher blood levels of magnesium with lower risk of coronary heart disease. In addition, some dietary have suggested that a higher magnesium intake may reduce the risk of having a stroke. There is also evidence that low body stores of magnesium increase the risk of abnormal heart rhythms, which may increase the risk of complications after a heart attack. These studies suggest that consuming recommended amounts of magnesium may be beneficial to the cardiovascular system. They have also prompted interest in clinical trials to determine the effect of magnesium supplements on cardiovascular disease.[4]

Magnesium deficiency is also linked to variant angina, a disorder in which heart vessels go into spasm. In 1996, a Japanese study found that men with lower Mg levels had more frequent and sever angina attacks.[5] Result of a meta-analysis or randomized placebo-controlled trials indicated that an intravenous magnesium infusion given early after suspected myocardial infarction could decrease the risk of death.

The most influential study included in the meta-analysis was a randomized placebo controlled trial in 2316 patients and found a significant reduction in mortality (7.8% all-cause mortality in experimental group, 10.3% all-cause mortality in the placebo group) in the group of patients given intravenous magnesium sulfate with 24 hours of suspected myocardial infarction. Fallowing up from one to five years after treatment revealed that the mortality from cardiovascular disease was 21% of the low magnesium treated group.[6]

Magnesium-amino acid complex is the best form of supplemental magnesium, it offers the benefit of fast and complete absorption without interference and without the adverse effects of bowel intolerance. Other forms may take longer or may not work at all if they cannot reach the target cells.[7]

Materials and procedure

Chemicals

The chemicals substances were of highest purity were purchased

from (sigma ,Aldrich), distilled deionized water were used for all research purposes, glassware, tubes, volumetric flask, micropipte, tips and other various glassware were immersed in diluted 5%nitric acidfor 24 hrs, then rinsed with five times with deionized water.

Instrumental analysis

Infrared spectra using potassium bromide disc in the range (400-4000) were recorded (a Shimadzu IR Prestige-21 FTIR 8400 S, 2006). The microanalysis (C.H.N, Euro vector EA3000 single V. 3.0 single, at Babel University) was used to determine the percentage of the carbon, hydrogen and nitrogen of the ligand and its complex. Shimadzu model AA670 flame atomic absorption Spectrophotometer has been used to determined magnesium concentration in serum. Connected to a single-slot air/acetylene burner head and attached to a Shimadzu gas- control unit, the data recorded by a Shimadzu graphite printer PR with chart speed 10mm/min. Melting point (M.P.) apparatus of gallen Kamp M.K.B-60 was used to measure the melting point of the complex. This was carried out in the chemistry department, College of Science for women, Baghdad University), high performance liquid chromatography (HPLC), Shimadzu 20A (Japan, Koyot, Co) was used as described in our previous paper.[8]

Synthesis of magnesium methioninate complex

L-methionine (0.98gm, 2mmole) was dissolved in 60ml of deionized water with aqueous solution of sodium hydroxide (0.08gm, 2mmole). The mixture was heated at 60^0C. (0.095gm, 1mmole), then mmole of the magnesium chloride was dissolved in deionized water (10ml) and added to the warm sodium methioninate solution. The mixture was heated at 60^0C with stirrer for 25hr. The solid was then collected by filtration, washed with methanol (10mlx2), dried in vacuum for three hours and then recrystallized from a dry propanol. The white crystals were collected by filtration and then dried in vacuum for four hr.

Yield 64%, m.p. 300^0C

Found: C, %, H, %, N, %, Mg 7.42% Calc. for $C_{10}H_{20}N_2O_4S_2Mg$

C %, H %, N %, Mg 7.58%.

Sample collection and serum preparation

10ml of venues blood sample was drawn aseptically into plastic disposable syringes from each donor and transferred to acid-washed centrifuge tubes provided with plastic caps. Then allowed to stand for 2 hours at room temperature and centrifuged at 3000rpm for 5 min. to separate the serum. Serum was transferred into acid-washed polystyrene tubes and stored in the refrigerator at -20^0C until the day of analysis.

Determination of magnesium in human serum

Serum sample was diluted 25 fold for magnesium assay. Standard solution in the range (2-20µg/ml) magnesium was prepared (1% w/v) and lanthanum chloride was added to sample standard solution to overcome or minimize effects of phosphate and other species on absorbance signal. The instrumental condition for a Shimadzu AA670 flame atomic absorption Spectrophotometer of magnesium as following:

Wavelength (nm) 285.2

Spectral band width (nm) 0.5

Hollow cathode lamp current (mA) 4

Flame type Air/C_2H_2

Fuel/oxidant ratio 1.6/8

Burner height (mm) 6

Burner slot (cm) 10

Result and discussion

Synthesis of the complex

The donors properties of the amino acids methionine, $CH_3SCH_2CH_2CH(NH_2)COOH$ were investigated for a number of transition and nontransition metal ions. Methionine as an anionic ligand (Met), and generally forms neutral complexes, [M(Met)2] and [M(Met)3] were M(II) and M(III) respectively in which the metal attains its usual higher coordination number by linking with the nitrogen atom of the $–NH_2$ group and with oxygen atom of the $–COO^-$ group. Sulfur atom is also a possible ligating site in amino acids containing sulfur atoms.[9] The preparation method of magnesium methioninate complex were performed by the coordination of magnesium ion with oxgen atoms of the $–COO^-$ group of methionine.

Infrared spectra

The infrared spectrum of (methionine) ligand , shows that two peaks at (3225)cm^{-1} and (1612)cm^{-1} were assigned to stretching vibration and bending vibration for the (NH_2) group respectively. The peak appears at (3550)cm^{-1} was attributed to stretching vibration of (O-H). Another set of bands were also observed at (1219)cm^{-1} and (1654)cm^{-1} were due to stretching vibration of (C-O) cm^{-1} and (C=O) cm^{-1} respectively. A strong band was observed at (686)cm^{-1} assigned to the (C-S-C) group of the ligand (Met).[10]

From a comparison between the FTIR spectra of the ligand and its complex in Table 1 showed the following observations: (1) An appreciable difference in the absorption of (NH_2) group of the complex, which observed as a broad band at (3324)cm^{-1} and (1608) cm^{-1} belong to stretching and bending vibrations respectively. This shift confirms the ligand coordinate with Mg ion through nitrogen atom of amine group. (2) No appreciable change in the absorption of (CH_2-S-CH_3) group of the complex, A strong band was observed at (686)cm^{-1} assigned to the (CH_2-S-CH_3) group, which exclude the coordination of (S) atom of the (-SCH_3) group to metal in the prepared complex. (3) Disappeared of the (OH) group band in IR spectrum of the complex, and new band appeared at (443)cm^{-1} which belong to (Mg-O) bond.[11] (4) There is appreciable change in absorption of the stretching vibration symmetrical of (COO^{-1}) at 1250cm^{-1} and (1581) cm^{-1} of the complex. This change confirms the ligand coordinate with Mg ion through the oxygen atom of carboxylic group. From these observations it is indicated that the ligand (met) coordinate with Mg ion through oxygen atom of carboxylic group and nitrogen atom of amine group as bidentate chelating. The IR data of the ligand and its complex is illustrated in Table 1.

Table 1 The most diagnostic FTIR bands of ligand and its complex in (cm^{-1})

Group	Ligand	Complex
(N-H) stretch	3225	3324
(N-H) bend	1612	1608
(C=O)	1654	1581
(C-O)	1219	1250
(C-H)	2920	2947
(C-S)	686	686
(Mg-O)	-	443
(O-H)	3550	-

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Estimation of magnesium in healthy groups

The magnesium concentrations were measured in healthy volunteers of both sexes between 20 over 60 years. The results show a slightly decrees in magnesium with increase ages for both sexes. Also, the results observed no significant difference between the magnesium concentration in male and female volunteers, as seen in Tables 2-4 they show a comparison between concentration of magnesium in both sexes at various between 20 over 60 years.

Table 2 Magnesium concentration ranges in male blood serum of various healthy volunteers

Age	No	Range µg/ml	Mean±SD
20-30	8	8.7-22	15.21±2.2
31-40	12	8.5-25	16.10±2.3
41-50	15	7.9-23	14.60±3.6
51-60	10	8.2-24	15.20±2.6
Over 60	10	8.0-21	14.20±3.1
	55		n.s.

Table 3 Magnesium concentration ranges in female blood serum of healthy various volunteers

Age	No	Range µg/ml	Mean±SD
20-30	8	8.6-21	14.30±2.6
31-40	10	8.4-20	15.60±2.9
41-50	7	7.6-22	13.30±2.1
51-60	12	7.4-21	15.80±3.6
Over 60	8	7.0-21	14.90±3.1
	45		n.s.

Table 4 Comparison of magnesium concentration in blood serum of healthy adult of both sexes

Age	Male (mean) µg/ml	Female (mean) µg/ml	P-value
20-30	15.21±4.2	14.30±2.6	n.s.
31-40	16.10±3.2	15.60±2.9	n.s.
41-50	14.60±3.6	13.30±2.1	n.s.
51-60	15.20±2.6	15.80±3.6	n.s.
Over 60	14.20±3.1	14.90±3.1	n.s.

Estimation of magnesium in patient groups

Magnesium methioninate supplementation: In several reports,[12,13] it is confirmed that the magnesium concentrations below 15µg/ml were not enough to activate more than 300 enzyme in human beings. Therefore, a supplementation of magnesium to human body was highly recommended, the best magnesium formula for supplementation, magnesium-amino acid chelate in absorption through interinestind trace.

Therefore, we suggest the used of magnesium methioninate formula is suggested to treat the magnesium deficiency in measured blood serum of hypertension patients and myocardial infarction patients. The recommended supplement helps recover the normal range of magnesium within two weeks.[14] Therefore 21 hypertension patients and 19 myocardial infarctions patients were supplied with 500mg magnesium methioninate tablet (formulated in estate for drugs and medical appliance, Sammara, IRAQ).

From the results, it is observed that the magnesium level of hypertension patients elevated from (11-11.5µg/ml) to (16.5-21.2µg/ml) after supplying these patients with 500mg tablets for 15 days, while the magnesium level of myocardial infarction patients were elevated from (11-11.9µg/ml) to (17.26-20.1µg/ml) after supplying these patients with 500mg tablets for 15 days. The results are shown in Table 7 & Table 8.

Table 5 Magnesium concentration ranges in males blood serum of hypertension patients

Age	Range µg/ml	Mean	No.
20-30	11.0-12.00	11.60±1.00	7
31-40	10.8-14.50	11.00±0.90	11
41-50	11.0-16.00	12.60±0.78	14
51-60	11.2-17.00	11.70±0.92	9
Over 60	11.0-12.50	11.50±1.00	9
			50

Table 6 Magnesium concentration ranges in males blood serum of myocardial infaraction patients

Age	Range µg/ml	Mean	No.
20-30	10.0-15	11.2±1.2	9
31-40	11.0-14	11.8±1.3	12
41-50	10.0-16	11.9±1.25	8
51-60	11.5-15	12.0±1.60	10
Over 60	10.5-12	11.0±1.50	11
			50

Table 7 Magnesium concentration range in males blood serum of various hypertension patients after supplying them with 500 mg magnesium methioninate tablet for 15 days

Age	Range µg/ml	mean	No.
20-30	15.0-16.0	15.8±0.12	3
31-40	16.0-17.6	17.0±0.21	6
41-50	16.5-18.2	18.0±0.25	7
51-60	16.0-18.5	18.2±0.31	5
			21

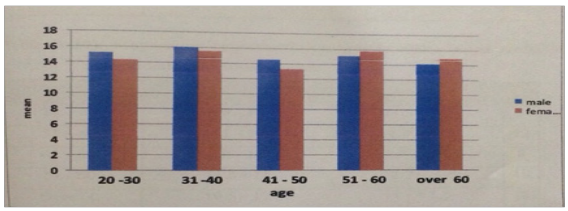

Table 8 Magnesium concentration range in male blood serum of various myocardial infarctions after supplying them with 500mg magnesium methioninate tablet for 15 days

Age	Range µg/ml	mean	No.
20-30	14-17.2	16.0±0.27	4
31-40	18-21.0	18.2±0.31	6
41-50	17-22.0	19.2±0.42	4
51-60	17-21.0	20.1±0.39	5
			19

Magnesium recovery study

Recovery study of magnesium is explained in Table 9 recovery % and RSD% is ranging from 98.60% to 101.40% and 1.61% to 3.23% respectively.

Table 9 Analytical recovery of magnesium added to serum

Added µgml in final volume	Found µg/ml	Expected µg/ml	Recovery %	RSD %
0	19.95	-	-	2.51
5	24.88	24.95	98.60	1.61
11	31.10	30.95	101.40	3.23
15	34.94	34.95	99.93	2.50

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None.

Conflict of interest

The author declares that there is no conflict of interest.

References

1. Ascherio A, Rimm ER, Giovaannucci EL. A prospective study of nutritional factors and hypertension among us men. *Circulation*. 1992;85(5):1475–1484.
2. Ascherio A, Hennekens C, Willett WC. A prospective study of nutritional factors and hypertension among us women. *Hypertension*. 1997;27(5):1065–1072.
3. Eisnberg MJ. *Am Heart J*. 1999;124(2):544–566.
4. Goto K. Magnesium deficiency detected by intravenous loading test in variant angina pectoris. *Am J Cardiol*. 1990;65(11):709–712.
5. Brodsky MA. Magnesium therapy in new-onset atrial fibrillation. *Am J Cardiol*. 1994;73(16):1227–1229.
6. Woods KL, Fletcher S, Roffe C, et al. Intravenous magnesium sulphate in suspected acute myocardial infarction: results of the second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). *Lancet*. 1992;339(8809):1553–1558.
7. Wester PO. Magnesium. *Am J Clin Nutr*. 1987;45(5 Suppl):1305–1312.
8. Mahmoud WA, Abid FM, Mahdi ZA. *Inter J of Sci Res*. 2014;3(9).
9. Mcauliffe CM, Quagliano JV, Vallarino LM. *Inorganic Chemistry*. 1966;5(11):1996–2003.
10. Pavia, Lamoman, Kriz, et al. Spectroscopy. Brooks/Cole. 2007.
11. Lever AB. *Inorganic Electronic Spectroscopy*. 2nd edition. Elsevier: New York; 1986.
12. Altura BM, Altura BT. 1980.