MAGNESIUM SUPPLEMENTATION AND MICROELEMENT HOMEOSTASIS

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Magnesium participates in numerous enzymatic reactions in the human body and it has an essential role in maintaining the antioxidant system. Our purpose was to investigate the effect of magnesium on element content in blood. Male Wistar rats were divided into four groups. The animals in group I. were fed with normal diet, the animals in group II. were fed with normal diet and treated with magnesium polygalacturonate (200 mg Mg/kg body weight ad libitum daily). The animals in group III. were fed with fat rich diet containing cholesterol (2.0%), sunflower oil (20%) and cholic acid (0.5%) added to the control diet. The animals of group IV. were fed with fat-rich diet and magnesium polygalacturonate. The rats were kept on the diets for 9 days. The element concentration (Al, As, B, Ba, Ca, Cd, Co, Cr, Cu, Fe, K, Li, Mg, Mn, Ni, P, Pb, S, Si, Sn, Sr, Ti, V, Zn) of blood samples was determined with an ICP-OES after digestion with a mixture of nitric acid and hydrogen peroxide. The results show that the concentration of several elements changed significantly in both magnesium-treated groups, nevertheless the alteration was different in the control and hyperlipidemic groups. It has been concluded that high amount of magnesium supplementation alters the metal ion homeostasis in short-term experiment. Although some favourable effects were found in the hyperlipidemic group by magnesium polygalacturonate treatment, it is worth to note that supplementation with magnesium should be carried out carefully especially in metabolic diseases.

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Introduction

Magnesium is essential for the function of living organisms. It has structural roles in bone, cell membranes and chromosomes. Active transport of several ions as potassium and calcium through cell membranes needs magnesium. Magnesium is required for muscle contraction, the function of the heart and nerve cells and for the metabolism of carbohydrates and fats to produce energy in magnesium-dependent biochemical reactions. Magnesium plays a key role in more than 300 enzymatic reactions in the body. [1, 2]

Metabolic pathways, which consume energy, require magnesium in a complex form with adenosine triphosphate (MgATP), and MgATP stores the energy in phosphate bonds. Magnesium is essential in the synthesis and metabolism of carbohydrates, lipids, proteins, and nucleic acids, for example, for synthesizing DNA and RNA in mitochondria. [2, 3] Magnesium is also required for the synthesis and maintenance of the antioxidant defence system, including enzymes and antioxidant molecules. [4, 5]

Low magnesium intake is a risk factor in the development of several diseases e.g., diabetes, ischemic heart disease, severe retinopathy and causes reduced magnesium content in cells.[6,7,8] Magnesium supplementation may have protective effect on the development of different diseases and may increase magnesium concentration and insulin sensitivity. [9,10]

Hypomagnesemia is one of the common features of obesity, liver diseases as fatty liver, alcoholic and other cirrhosis. In these diseases decrease in the magnesium level in serum, erythrocyte, lymphocyte, liver tissues, heart muscle, skeleton muscle and bone is a well-known symptom. [11, 12, 13]

The absorption of magnesium depends on several factors. In general 30-40% of the daily dietary intake of magnesium is absorbed in the small intestine. In case of low magnesium intake, absorption rate may be as high as 75%, and if the intake is high, the absorption rate may be reduced to 25%. The presence of calcium and other divalent cations, as well as phosphorus, fat, lactose, influences also the rate of magnesium absorption. [14]

The low magnesium absorption in jejunum and ileum causes low magnesium status in several diseases. Increased urinary magnesium excretion also contributes to latent magnesium deficiency. The first sign of magnesium deficiency is the low level of serum Mg (hypomagnesemia). [15, 16]

Alimentary induced hyperlipidemy and consecutive development of fatty liver is a suitable experimental model for studying liver damage and metal element homeostasis, therefore our aim was to study the effect of supplementation of Mg in polygalacturonate form on metal element homeostasis in hyperlipidemic rats.

Table 1. Weight (g) of different organs and body of rats (n=10)

	Control		Control+ Mg-treated		Hyperlipidemic		Hyperlipidemic + Mg-treated		Significance at *P*<0.05 by ANOVA
	Main	SD	Main	SD	Main	SD	Main	SD	
Liver (g)	11.71	1.44	11.76	1.03	14.38	1.06	13.84	1.16	Sign.
Heart (g)**	0.89	0.12	0.93	0.15	0.90	0.08	0.78	0.10	Sign.
Lung (g)	1.28	0.37	1.55	0.49	1.13	0.09	1.13	0.11	Sign.
Spleen (g)	0.70	0.13	0.61	0.11	0.66	0.14	0.61	0.13	Not sign.
Thymus (g)**	0.46	0.15	0.52	0.12	0.50	0.09	0.94	0.07	Sign.
Kidney (g)	0.99	0.10	1.05	0.13	1.00	0.08	0.94	0.10	Not sign.
Body weight (g)**	314.5	18.36	322.4	12.38	294.0	11.2	269.9	14.6	Sign.

** significant difference between hyperlipidemic and hyperlipidemic+Mg-treated group at *P*<0.05 (Student-t test)

Table 2. Rutin parameters in sera of rats (n=10)

	Control		Control +Mg-treated		Hyperlipidemic		Hyperlipidemic + Mg-treated		Significance at *P*<0.05 by ANOVA
	Main	SD	Main	SD	Main	SD	Main	SD	
UA (μmol/L)	114.6	20.4	115.6	34.0	131.0	31.4	113.6	18.5	Not sign.
GGT (U/L)	0.125	0.820	0.600	1.260	0	1.050	1.20	1.750	Not sign.
Triglicerid (mmol/L)**	1.22	0.42	1.47	0.44	0.57	0.28	0.86	0.30	Sign.
GPT (U/L)	65.43	18.60	62.00	22.83	76.20	19.75	54.67	21.00	Not sign.
GLUC (mmol/L)	7.63	0.98	8.44	0.75	8.57	0.66	7.87	0.68	Sign.
T-bilirubin (mmol/L)	1.25	0.63	1.22	0.67	1.11	0.60	0.89	0.93	Not sign.
Albumin (g/L)*	28.25	1.06	31.00	1.05	32.50	1.51	32.50	1.09	Sign.
BUN (mmol/L)	5.01	0.68	5.57	0.72	4.09	0.66	4.26	0.72	Sign.
ALP (U/L)**	584.9	102.0	561.8	50.1	1458	43.2	1217	166	Sign.
Total protein (g/L)	50.75	2.75	52.38	1.41	54.10	2.42	55.70	2.21	Sign.
Creatinin (μmol/L)	35.38	1.51	36.70	3.12	43.10	2.06	41.00	3.02	Sign.
GOT (U/L)	123.4	45.9	133.4	22.1	145.8	43.2	126.5	38.5	Not sign.
Cholesterol (mmol/L)*	1.67	0.38	2.11	0.34	5.48	1.83	4.49	1.38	Sign.
Amylase (U/L)**	2520	512	2771	175	4094	1082	3234	284	Sign.

* significant difference between control and control+Mg-treated group at *P*<0.05 (Student-t test); ** significant difference between hyperlipidemic and hyperlipidemic+Mg-treated group at *P*<0.05 (Student-t test)

Experimental

Materials

Basic magnesium-polygalacturonate from pectin (a component of higher order plants) was produced by In Vitro Kft according to a patent and the permission of OÉTI. [1, 17, 18] Several methods were applied for the characterization of the magnesium polygalacturonate, e.g. elemental analysis, infrared spectroscopy, thermogravimetry. [18] The magnesium content of magnesium poligalacturonate was 7.2%.

Animal experiment

Male Wistar rats (n=40; 150-200 g bw) were divided into four groups. The animals in group I were fed with normal diet from BIOFARM FARM PROMT Kft (BFP, Gödöllő, Hungary). The animals in group II were fed with normal diet and treated with magnesium polygalacturonate (200 mg Mg/kg body weight ad libitum). The animals in group III were fed with diet rich in fat contained cholesterol (2.0%), sunflower oil (20%) and cholic acid (0.5%) added to the control BFP. The animals of the IVth group were fed with fat rich diet and magnesium polygalacturonate (200 mg Mg/kg body weight ad libitum). The rats were kept on the above diets for 9 days. All experiments were performed with the permission of the Animal Health and Food Control Station (MÁB 1.81.4/2006).

The rats were anaesthetized with Nembuthal (35 mg/kg) and were exsanguinated from the abdominal vein. The liver was removed and washed. The rat bodyweight and the different organs were measured by gravimetry.

Hyperlipidemy was proved by elevated serum lipid parameters.

Rutin laboratory parameters

The next routine laboratory parameters were obtained with the use of a Hitachi 717 analyser: alkaline phosphatase (ALP), amylase, glucose, total bilirubin (T-bilirubin), albumin, total protein, blood urea nitrogen (BUN), serum triglycerides (TG), cholesterol (CHOL), uric acid (UA), creatinine, gamma glutamyl transferase (GGT), glutamate-oxaloacetate transaminase (GOT), glutamate-pyruvate aminotransferase (GPT).

Measurement of elements

Element concentration (Al, As, B, Ba, Ca, Cd, Co, Cr, Cu, Fe, K, Li, Mg, Mn, Ni, P, Pb, S, Si, Sn, Sr, Ti, V, Zn) of the

Table 3. Element content (μg/g) in blood of rats (n=10)

	Control		Control+Mg-treated		Hyperlipidemic		Hyperlipidemic + Mg-treated		Significance at P<0.05 by ANOVA
	Main	SD	Main	SD	Main	SD	Main	SD	
Al**	11.73	6.76	12.63	5.10	14.00	4.25	23.25	7.48	Sign.
As	1.96	0.47	2.10	0.34	1.94	0.32	2.15	0.38	Not sign.
B**	28.89	16.38	21.52	6.19	25.30	8.96	59.48	17.48	Sign.
Ba**	0.0690	0.019	0.0638	0.02	0.0744	0.0298	0.161	0.118	Sign.
Ca*	144.7	17.08	53.78	4.78	60.30	8.31	57.63	15.39	Sign.
Cd*,**	0.0061	0.0004	0.0139	0.0019	0.0121	0.0051	0.0052	0.0015	Sign.
Co	0.011	0.008	0.007	0.0007	0.016	0.016	0.015	0.007	Not sign.
Cr*	0.0641	0.0706	0.120	0.018	0.144	0.089	0.093	0.036	Sign.
Cu*,**	0.704	0.104	0.830	0.093	0.915	0.177	0.777	0.087	Sign.
Fe*	521.6	53.5	422.8	133.9	473.2	73.7	488.2	172.7	Not sign.
K*,**	1873	99	1587	123	1716	278	2005	301	Sign.
Li	2.01	0.32	2.07	0.25	2.00	0.33	1.66	0.54	Sign.
Mg	44.03	4.03	43.50	3.63	42.04	6.97	43.84	5.69	Not sign.
Mn	0.0116	0.0081	0.0094	0.0121	0.0065	0.0048	0.0476	0.1175	Sign.
Ni*	0.142	0.061	0.035	0.011	0.121	0.186	0.125	0.215	Not sign.
P*	596.8	72.4	477.8	55.4	481.9	88.4	458.1	99.1	Sign.
Pb*	0.259	0.085	1.16	1.08	0.447	0.340	0.225	0.109	Sign.
S	1498	347	1728	242	1638	235	1614	336	Not sign.
Si*,**	78.12	37.60	127.9	25.89	140.4	25.60	42.97	33.63	Sign.
Sn	0.181	0.129	0.211	0.125	0.212	0.111	0.135	0.123	Not sign.
Sr*	0.074	0.0168	0.0476	0.0079	0.073	0.0179	0.0906	0.0793	Not sign.
Ti	0.302	0.244	0.174	0.113	0.217	0.08	0.184	0.120	Not sign.
V	0.0298	0.0102	0.026	0.0062	0.0237	0.007	0.0228	0.0024	Not sign.
Zn	4.14	0.48	4.95	0.58	5.15	1.00	4.78	0.69	Sign.

* significant difference between control and control+Mg-treated group at P<0.05 (Student-t test); ** significant difference between hyperlipidemic and hyperlipidemic+Mg-treated group at P<0.05 (Student-t test).

blood samples was determined with an ICP-OES (inductively coupled plasma optical emission spectrometer). Type of instrument: Spectro Genesis ICP-OES (Kleve, Germany). After digestion of the samples with a mixture of nitric acid and hydrogen peroxide (10 + 5 mL) and dilution with double distilled water to 25 mL, concentration of elements was determined. [19]

Statistical analysis

Means and standard deviations (SD) were calculated from the results. For comparison of the means of the four groups, one way analysis of variance (ANOVA) was used and for determination of the difference between two groups, the Student t-test was used by GraphPAD software version 1.14 (1990). Significance was determined as P<0.05.

Results

The magnesium supplementation affects the body weight of rats and the weight of different organs (Table 1). The measured weights are significantly different in the four groups (ANOVA, P<0.005) instead of spleen and kidney. The weights in control groups did not change, while in the hyperlipidemic groups significant changes were observed for heart, thymus and bodyweight. Nevertheless the difference was larger between the control and hyperlipidemic groups than between the control and control-treated or hyperlipidemic and hyperlipidemic-treated groups.

The routine laboratory parameters showed that significant changes were observed in triglyceride, glucose, albumin, BUN, total protein, creatinine, GOT, cholesterol, ALP and amylase content between the four groups calculated by ANOVA test (Table 2). The magnesium supplementation hardly changed the routine parameters of rats in the control group, significant elevation was only seen in albumin and cholesterol levels, while in the hyperlipidemic group the level of triglyceride, ALP and amylase changed significantly. Similarly to the weights of organs, the difference was larger between control and hyperlipidemic groups than between the control and control-treated or hyperlipidemic and hyperlipidemic-treated groups.

The element concentration changes in the whole blood were significant in the four groups for Al, B, Ba, Ca, Cd, Cr, Cu, K, Li, Mn, P, Pb, Si and Zn by the method of ANOVA. Significant changes in the concentration of Ca, Cd, Cr, Cu, Fe, K, Ni, P, Pb, Si and Sr were also observed between the control group and control-treated group (Student's t probe), while the concentration of Al, B, Ba, Cd, Cu, K and Si showed significant alteration between the hyperlipidemic and hyperlipidemic-treated group (Table 3). In this sort time experiment high amount of magnesium changed the metal ion homeostasis, whilst the magnesium concentration in the blood did not change significantly.

Discussion

For magnesium supplementation several magnesium products are available in the market. For the animal experiment magnesium polygalacturonate was selected because of its favourable absorption property proved by human studies. [20] The most important benefit of magnesium polygalacturonate is that the carrier is of natural origin. According to acute oral toxicological investigation, these complexes are nontoxic even in high concentration (LD_{50} > 5000 mg/kg body weight). By oral application of the complexes, no side effects have been observed so far. [20] This natural origin may be the cause of results that magnesium concentration in blood did not increase. The concentration of several elements changed significantly in both magnesium-treated groups, nevertheless the alterations were different in the control and hyperlipidemic groups.

It has been concluded that high amount of magnesium supplementation changes the metal ion homeostasis in short-term experiment. Although some favourable effects were found in the hyperlipidemic group by magnesium-treatment, it is worth to note that supplementation with magnesium should be carried out carefully especially in metabolic diseases. Similar results were found for magnesium supplementation with magnesium malate in rat experiment. [21, 22] The cause of this may be that both magnesium compounds have natural origin and the uptake occurs similar absorption in the intestine. [23]

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