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Serum and Tissue Concentrations of Magnesium, Calcium, Potassium and Sodium in Rats

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Abstract

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The aim of the study was to analyze concentrations of magnesium in the serum and selected tissues of Wistar rats (erythrocyte, myocardium, rectus abdominis muscle, femoral bone, lung, spleen, small intestine, liver, kidney and uterus in females) and to evaluate the relationships between serum and tissue concentrations of magnesium, calcium, potassium and sodium.

Adult laboratory rats (Wistar strain, n = 39) were studied. The animals were allocated to three groups as follows: females (F; n = 18; body mass, 269 ± 33 g), males I (M I; n = 10; 413 ± 30 g) and males II (M II; n = 11; 633 ± 78 g). The females and males were of the same age (10 – 12 weeks), the males II were older (22 – 24 weeks). Blood was drawn by cardiac puncture under ether anesthesia. After sacrificing the animals under ether anesthesia, tissue samples were collected from the tissues to be studied and analysed for the presence of magnesium, calcium, potassium and sodium. Flame atomic absorption spectrophotometry was used to assess the concentration of magnesium in sera and, after sample mineralization, in all the tissues investigated. For each tissue, ion concentrations were related to wet tissue mass. The results were evaluated by the Mann-Whitney test.

The values of cations were as follows: serum magnesium (mmol/L): F, 0.73 ± 0.11; M I, 0.65 ± 0.04; M II, 0.64 ± 0.05; erythrocyte magnesium (mmol/l): F, 2.23 ± 0.34; M I, 2.25 ± 0.23; M II, 2.25 ± 0.19; myocardial magnesium (mmol/kg): F, 8.37 ± 0.30; M I, 8.40 ± 0.82; M II, 7.19 ± 0.52). Comparison of values for magnesium concentration in the myocardium was: F vs M II, $p < 0.001$; M I vs M II, $p < 0.001$; F vs M I, non-significant.

In conclusion, significant differences in myocardial magnesium concentrations among the groups and non-significant differences in sera and erythrocytes suggest that the actual concentration of intracellular magnesium, i.e. in myocardium and other tissues, cannot be derived from either serum or erythrocyte concentrations. Interestingly, in female rats there was a negative correlation between magnesium and calcium levels in the myocardium, while in both male rat groups (males I and males II) this correlation was positive.

Minerals, myocardium, bone, muscles, erythrocyte, lung, spleen, small intestine, liver, kidney, uterus

The role of magnesium, the second important intracellular cation for the organism, is related to the number of biochemical reactions in which it is involved. Magnesium modulates transport of calcium, potassium and sodium across the cell membrane, constitutes a component of a number of cofactors, activates ATPase controlling metabolic pathways in the cytosol and mitochondria, and is involved in oxidative phosphorylation and protein synthesis (Saris et al. 2000; Touyz 2003). The distribution of magnesium in the organism is not even; nearly two thirds of its total amount are bound to bone and the rest is present in soft tissue, predominantly in skeletal muscles. Plasma and erythrocytes contain only about

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1% of the total body amount of magnesium, which is about an order of magnitude lower than in other tissues (Shils 1999).

It is therefore of great importance to detect magnesium deficiency in the organism (Feillet-Coudray et al. 2003; Gong et al. 2003; Hoane et al. 2003; Lajer et al. 2003; Rude et al. 2003). Some authors recommend the use of magnesium concentrations in serum for assessment of deficiency, but others argue that the loading test will provide more exact results, because in the presence of normal serum values intracellular magnesium may be deficient (Stalnikowitz 2003).

The aim of this study was to assess magnesium concentrations in serum, to compare them with magnesium levels present in selected tissues (erythrocytes, myocardium, skeletal muscle, uterus, lung, spleen, intestine, liver, kidney and bone) and to determine whether there is a relationship between the serum and tissue values in the Wistar rat. The results will be important for clinical evaluation of various human diseases.

Materials and Methods

Thirty-nine Wistar-strain laboratory rats were used in the experiments. They were allocated to three groups; two (females, males I) contained animals of the same age (10 – 12 weeks), and males II group included older rats (22 – 24 weeks). The animals were kept in standard laboratory conditions with *ad libitum* access to water and feed (M1, M3, firm Ing. Máchal, Czech Republic) – Tables 2 and 3.

Table 1. Group characteristics of the rats

Group	**Number**	**Age (weeks)**	**Body mass (g)**
Females	18	10 – 12	269 ± 33
Males I	10	10 – 12	413 ± 30
Males II	11	22 – 24	633 ± 78

Table 2. Nutrient composition of the diet

M1	Wheat, soybean meal, soya beans tosted, wheat shoot, defatted milk powder, alfalfa hay, $CaCO_3$, L-lysin, NaCl, ($CuSO_4.5H_2O$), vitamin A, vitamin D_3, vitamin E
M3	Wheat, soybean meal, soya beans tosted, wheat shoot, defatted milk powder, alfalfa hay, $CaCO_3$, L-lysin, NaCl, ($CuSO_4.5H_2O$), vitamin A, vitamin D_3, vitamin E

Table 3. Amounts of nutrient components in 1 kilogram of the diet

Substrats	**M1**	**M3**
Dry matter	12%	12%
Nitrogen substances	225 g	220 g
Fat	35 g	22 g
Fiber	40 g	30 g
Ash	55 g	36 g
Copper	22 mg	25 mg
Vitamin A	30 000 I.E.	20 000 I.E.
Vitamin D_3	2 500 I.E.	2 000 I.E.
Vitamin E (alpha-tocoferol)	120 mg	105 mg

After blood had been drawn for analysis by cardiac puncture, each animal was sacrificed by decapitation under ether anesthesia and samples of the following tissues were collected: myocardium, lung, small intestine, kidney, spleen, liver, skeletal (rectus abdominis) muscle, bone (femur) and uterus in female animals. The samples were weighed and stored at -18 °C.

The blood was processed by a routine method and its hematocrit value was recorded. In addition to the assessment of sodium, potassium, magnesium and calcium in serum, magnesium values in full hemolysed blood were obtained and the magnesium concentration in erythrocytes was calculated as follows:

$$eryMg^{2+} = \frac{hemMg^{2+} - sMg^{2+}(1 - Ht)}{Ht}$$

$eryMg^{2+}$ - magnesium concentration in erythrocytes (mmol/L)
$hemMg^{2+}$ - magnesium concentration in full hemolysed blood (mmol/L)
sMg^{2+} - magnesium concentration in serum (mmol/L)
Ht - hematocrit

The assessment of minerals (sodium, potassium, calcium and magnesium) was performed after mineralization of each sample by flame atomic absorption spectrophotometry in an H 1550 spectrophotometer (Hilger, Great Britain). The mineralization was carried out in a closed system, using the MLS-1200 microwave digestion technique (Milestobe, Italy). The concentrations obtained were related to wet tissue mass.

The results were statistically evaluated using the Mann-Whitney test. For each mineral, correlations between serum and tissue concentrations were calculated on the basis of the correlation coefficient.

This study was approved by the Ethics Committee of the Faculty of Medicine, Masaryk University in Brno.

Results

The values of sodium, potassium, calcium and magnesium concentrations in serum and tissue samples of the female rats (n = 18; 269 ± 33 g) are presented in Table 4. The calculated correlation coefficients were compared with critical values (α) for n = 18 (Table 5).

Table 4. Serum (mmol/L) and tissue values (mmol/kg) in female rats (n = 18)

Tissue	**Mg^{2+}** (mean ± SD)	**Ca^{2+}** (mean ± SD)	**Na^{+}** (mean ± SD)	**K^{+}** (mean ± SD)
Serum	0.73 ± 0.11	2.38 ± 0.37	144.83 ± 1.07	3.67 ± 0.78
Erythrocyte	2.23 ± 0.34			
Myocardium	8.37 ± 0.30	0.6 ± 0.31	39.14 ± 3.17	72.7 ± 4.11
Lung	4.61 ± 0.79	1.89 ± 1.44	56.59 ± 10.57	59.02 ± 9.51
Intestine	8.65 ± 1.80	3.05 ± 2.75	39.52 ± 14.72	59.93 ± 7.08
Kidney	8.44 ± 1.10	4.43 ± 4.10	51.43 ± 9.48	70.10 ± 5.58
Spleen	9.28 ± 1.04	1.48 ± 0.95	28.27 ± 5.64	112.61 ± 14.24
Liver	8.46 ± 0.79	0.93 ± 0.55	22.39 ± 10.04	82.35 ± 10.85
Skeletal muscle	9.84 ± 0.71	0.52 ± 0.35	24.67 ± 2.77	99.48 ± 8.47
Bone	110.28 ± 9.86	2565.42 ± 257.07	121.24 ± 10.17	49.73 ± 6.73
Uterus	4.03 ± 0.73	2.22 ± 1.49	46.64 ± 10.30	49.84 ± 8.09

Table 5. Values of correlation coefficients for serum and tissue concentrations in female rats (n = 18)

	Myocardium	**Intestine**	**Muscle**	**Kidney**	**Spleen**	**Liver**	**Bone**	**Lung**	**Uterus**	**Erythrocyte**
Magnesium										
Serum	**0.70**	-0.36	0.21	**0.75**	-0.18	0.46	-0.43	0.13	**0.48**	**0.72**
Potassium										
Serum	-0.18	**0.48**	-0.06	**-0.47**	-0.45	**-0.58**	-0.12	0.11	-0.19	
Calcium										
Serum	**-0.66**	**-0.59**	**-0.70**	**-0.50**	**-0.59**	**-0.80**	-0.07	**-0.70**	-0.39	
Sodium										
Serum	-0.29	-0.19	0.24	0.28	0.05	-0.11	-0.10	-0.39	-0.04	

For n = 18, **α ≥ 0.47** ($p < 0.05$); **α ≥ 0.59** ($p < 0.01$)

The values of sodium, potassium, calcium and magnesium concentrations in serum and tissue samples of the two male groups (males I, n = 10, 413 ± 30 g; males II, n = 11, 633 ± 78) and the relevant correlation coefficients compared with critical values (α) are presented in Tables 6, 7, 8 and 9.

Table 6. Serum (mmol/L) and tissue values (mmol/kg) in male rats I (n = 10)

Tissue	**Mg^{2+}** (mean ± SD)	**Ca^{2+}** (mean ± SD)	**Na^{+}** (mean ± SD)	**K^{+}** (mean ± SD)
Serum	0.65 ± 0.04	2.21 ± 0.09	143.80 ± 1.64	4.14 ± 0.20
Erythrocyte	2.25 ± 0.23			
Myocardium	8.40 ± 0.82	1.48 ± 0.35	41.53 ± 2.17	66.77 ± 6.52
Lung	4.78 ± 0.70	3.54 ± 1.14	65.94 ± 5.51	61.13 ± 10.76
Intestine	5.98 ± 1.61	3.08 ± 1.26	46.79 ± 6.09	72.65 ± 6.66
Kidney	6.23 ± 0.60	1.40 ± 0.22	57.44 ± 2.98	69.94 ± 7.47
Spleen	9.62 ± 0.96	2.41 ± 0.79	31.02 ± 1.17	97.59 ± 15.06
Liver	5.43 ± 1.26	1.44 ± 0.39	26.46 ± 2.87	95.46 ± 7.83
Skeletal muscle	9.24 ± 0.53	0.80 ± 0.22	21.05 ± 1.28	100.48 ± 3.72
Bone	116.30 ± 25.27	2759.14 ± 373.48	146.35 ± 32.98	47.92 ± 11.59

Table 7. Values of correlation coefficients for serum and tissue concentrations in male rats I (n = 10)

Tissue	**Myocardium**	**Intestine**	**Muscle**	**Kidney**	**Spleen**	**Liver**	**Bone**	**Lung**	**Erythrocyte**
Magnesium									
Serum	0.21	0.42	-0.05	-0.10	0.02	0.36	-0.13	0.20	-0.58
Potassium									
Serum	-0.37	-0.34	0.01	0.16	0.03	-0.01	0.15	0.44	
Calcium									
Serum	0.18	-0.08	-0.14	-0.03	-0.10	0.27	0.30	0.34	
Sodium									
Serum	-0.40	-0.58	-0.43	-0.13	0.07	0.21	-0.24	-0.06	

For n = 10. **$\alpha \geq 0.63$** ($p < 0.05$); **<u>$\alpha \geq 0.76$</u>** ($p < 0.01$)

Table 8. Serum (mmol/L) and tissue values (mmol/kg) in male rats II (n = 11)

Tissue	**Mg^{2+}** (mean ± SD)	**Ca^{2+}** (mean ± SD)	**Na^{+}** (mean ± SD)	**K^{+}** (mean ± SD)
Serum	0.64 ± 0.05	2.57 ± 0.15	144.1 ± 2.40	4.70 ± 0.39
Erythrocyte	2.25 ± 0.19			
Myocardium	7.19 ± 0.52	0.77 ± 0.24	39.26 ± 2.42	60.27 ± 4.22
Lung	1.06 ± 0.20	2.42 ± 1.04	54.96 ± 8.77	46.61 ± 5.89
Intestine	0.82 ± 0.12	1.23 ± 0.28	40.17 ± 8.00	63.19 ± 6.65
Kidney	7.74 ± 0.67	0.80 ± 0.35	40.79 ± 3.62	67.46 ± 6.94
Spleen	7.57 ± 0.32	1.53 ± 0.43	34.80 ± 1.78	96.93 ± 8.76
Liver	9.59 ± 0.19	1.64 ± 0.51	32.83 ± 3.97	90.76 ± 5.75
Skeletal muscle	9.13 ± 1.72	0.61 ± 0.09	22.84 ± 2.07	92.02 ± 9.01
Bone	133.67 ± 14.56	5385.51 ± 717.07	213.1 ± 27.2	35.82 ± 8.11

The results of statistical evaluation (Mann-Whitney test), with levels of statistical significance *p*, are presented in Tables 10, 11, 12 and 13.

In addition to the importance of correlations between the serum and tissue concentrations, correlations amongst individual cations in tissues also play an important role. A good example is the myocardium, in which the relation between magnesium and calcium concentrations showed a marked difference between male and female animals.

Table 9. Values of correlation coefficients for serum and tissue concentrations in male rats II (n = 11)

Tissue	Myocardium	Intestine	Muscle	Kidney	Spleen	Liver	Bone	Lung	Erythrocyte
Magnesium									
Serum	0.35	0.51	0.55	**0.60**	0.42	0.04	0.55	0.31	-0.06
Potassium									
Serum	0.36	-0.13	-0.11	-0.20	-0.36	0.12	0.43	-0.14	
Calcium									
Serum	0.13	0.22	0.04	0.02	-0.31	0.01	-0.16	-0.27	
Sodium									
Serum	-0.26	-0.09	0.15	0.12	**-0.71**	0.03	0.01	-0.57	

For n = 11. **$\alpha \geq 0.60$** ($p < 0.05$); **$\alpha \geq 0.74$** ($p < 0.01$)

Table 10. Statistical evaluation of magnesium concentration

	females vs males I	females vs males II	males I vs males II
Serum	ns	ns	ns
Erythrocyte	ns	ns	ns
Myocardium	ns	$p < 0.001$	$p < 0.001$
Lung	ns	$p < 0.001$	$p < 0.001$
Intestine	$p < 0.01$	$p < 0.001$	$p < 0.001$
Kidney	$p < 0.001$	ns	$p < 0.001$
Spleen	ns	ns	$p < 0.001$
Liver	$p < 0.001$	$p < 0.001$	$p < 0.001$
Skeletal muscle	$p < 0.05$	ns	ns
Bone	ns	$p < 0.05$	$p > 0.01$

Mann-Whitney test, *p* – level of statistical significance, ns - non-significant

Table 11. Statistical evaluation of calcium concentration

	females vs males I	females vs males II	males I vs males II
Serum	ns	ns	ns
Myocardium	$p < 0.05$	ns	$p < 0.01$
Lung	$p < 0.01$	ns	$p < 0.01$
Intestine	ns	ns	$p < 0.01$
Kidney	$p < 0.01$	$p < 0.001$	$p < 0.01$
Spleen	$p < 0.01$	$p < 0.001$	$p < 0.001$
Liver	ns	$p < 0.01$	ns
Skeletal muscle	ns	ns	$p < 0.05$
Bone	ns	$p < 0.001$	$p > 0.001$

Mann-Whitney test, *p* – level of statistical significance, ns - non-significant

The negative correlation in the male rats contrasted with the positive correlation in the female rats (Fig. 1).

Discussion

The concentration of magnesium in serum had a similar value in all three groups of rats, whereas its concentrations varied in the tissues tested as well as amongst the animal groups. This supports our view that the value of magnesium concentration in serum cannot be taken as an indicator of the presence of intracellular magnesium, i.e., of its reserves in tissues (Holtmeier 1995; Morii et al. 2002). Similar findings were made for the other cations studied.

Table 12. Statistical evaluation of sodium concentration

	females–males I	females–males II	males I–males II
Serum	ns	ns	ns
Myocardium	ns	ns	ns
Lung	$p < 0.01$	ns	$p < 0.001$
Intestine	ns	ns	ns
Kidney	ns	$p < 0.05$	$p < 0.001$
Spleen	$p < 0.001$	$p < 0.001$	$p < 0.001$
Liver	ns	$p < 0.01$	$p < 0.01$
Skeletal muscle	$p < 0.001$	ns	$p < 0.05$
Bone	ns	$p < 0.001$	$p > 0.001$

Mann-Whitney test, *p* – level of statistical significance, ns - non-significant

Table 13. Statistical evaluation of potassium concentration

	females–males I	females–males II	males I–males II
Serum	$p < 0.001$	$p < 0.001$	$p < 0.001$
Myocardium	$p < 0.05$	$p < 0.001$	ns
Lung	ns	$p < 0.001$	$p < 0.001$
Intestine	$p < 0.001$	ns	$p < 0.01$
Kidney	ns	ns	ns
Spleen	$p < 0.01$	$p < 0.001$	ns
Liver	$p < 0.01$	ns	ns
Skeletal muscle	ns	$p < 0.05$	$p < 0.01$
Bone	ns	$p < 0.01$	$p < 0.05$

Mann-Whitney test, *p* – level of statistical significance, ns - non-significant

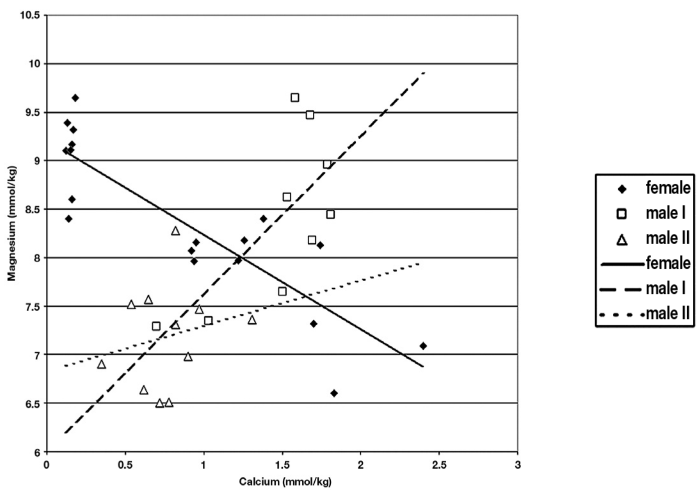

Fig. 1. Myocardium; correlations between concentrations of magnesium and calcium (mmol/kg)

The role of magnesium in the development of cardiovascular disease is a current topic of discussion. In relation to this, our results of the correlation between magnesium and calcium in the myocardium, which differed in males and females, suggest a new line of investigation. While in the female rats the correlation between these two cations was clearly negative, in the male rats of both age categories it was not so explicit. This suggests that the male myocardium may operate under factors different from those influencing the female myocardium. Varying concentrations of magnesium in the matrix of cardiac myocytes affect, for instance, metalloproteinase-2 involved in some cardiac diseases (Yue et al. 2004). These facts may play an important role not only in relation to disease prognosis (but also in a different reaction to ion substitution, including that of magnesium). In connection with cardiac diseases it is often reported that a decrease in potassium is accompanied by that of magnesium; the low levels of intracellular magnesium and potassium may induce an increased calcium and sodium input in the cell, which results in significant electrophysiological and mechanical changes (Picard et al. 2002; Touyz 2003). These may be associated with acute coronary syndrome and a frequent occurrence of arrhythmias (Maciejewskij et al. 2003). Some authors relate administration of magnesium to a reduced frequency of cardiovascular disease (Abbot 2003; Vaskonen 2003). Others show better clinical outcomes in patients who, during coronary artery reconstruction, received magnesium for improvement of reperfusion in the myocardium (Nakashima et al. 2004). These results are colaborated by the LIMIT-2 study, in which improvement was found within 28 days as well as after 2 to 7 years (Woods and Fletcher 1992; 1994).

Our results show that serum levels of magnesium have no relation to magnesium concentrations in the myocardium. The term normomagnesemia should refer only to physiological serum levels and not to an overall magnesium status indicating no deficit of this ion. Different concentrations of the other cations in the tissues investigated and the fact that, in each animal group, an increased level of magnesium was associated with different levels of the other cations in the studied tissues are findings of great clinical importance. They may explain inconsistencies and controversies in the interpretation of the effects of magnesium substitution in prevention or therapy of various diseases.

In this study the concentrations of magnesium, potassium, calcium and sodium in selected tissues of adult Wistar rats were evaluated and compared with those found in serum. The serum levels of magnesium did not correspond to those found in the tissues studied and, in many instances, this was also true for the other cations investigated. This shows that interrelationships of tissue ion concentrations are very complex and that the importance of this issue warrants further study.

Sérové a tkáňové koncentrace hořčíku, vápníku, draslíku a sodíku u potkanů

Cílem předkládané práce byla analýza aktuální koncentrace hořčíku v séru a v jednotlivých tkáních (erytrocyt, srdce, kosterní sval - přímý břišní, kost - femur, plíce, slezina, střevo, játra, ledviny a samic děloha) a zhodnocení vztahů mezi sérovou koncentrací a tkáňovou koncentrací u potkana kmene Wistar u kationtů hořčíku, vápníku, sodíku a draslíku.

Laboratorní výsledky byly získány u dospělého laboratorního potkana kmene Wistar (n = 39). Zvířata byla rozdělena do tří skupin – na skupinu samic (F; n = 18, hmotnost 269 ± 33 g), samců I. (M I; n = 10, 413 ± 30 g) a samců II (M II; n = 11, 633 ± 78 g). Skupina samic a samců I. byla stejného stáří (10 – 12 týdnů), skupina samci II. byla starší (22 – 24 týdnů). Krev byla zvířatům odebrána punkcí z intrakadriálního přístupu v éterové anestezii. Po usmrcení v éterové anestezii byly získány vzorky studovaných tkání na analýzu hořčíku, vápníku, draslíku a sodíku. Metodou plamenové atomové absorpční spektrofotometrie, byla stanovena koncentrace iontů v séru a po mineralizaci jednotlivých vzorků i v ostatních studovaných tkáních. Stanovené koncentrace kationtů byly vztaženy k vlhké hmotnosti tkáně. Výsledky byly hodnoceny Mann-Whitneovým testem.

Koncentrace Mg^{2+} v séru (mmol/l): F, 0,73 ± 0,11; M I, 0,65 ± 0,04; M II, 0,64 ± 0,05; koncentrace Mg^{2+} v erytrocytu (mmol/l): F, 2,23 ± 0,34; M I, 2,25 ± 0,23; M II, 2,25 ± 0,19; koncentrace Mg^{2+} v myokardu (mmol/kg): F, 8,37 ± 0,30; M I, 8,40 ± 0,82; M II, 7,19 ± 0,52. Statistická významnost koncentrace Mg^{2+} v myokardu: F vs M II, $p < 0{,}001$; M I vs M II, $p < 0{,}001$; F vs M I, ns. Nález signifikantně rozdílných koncentrací hořčíku v myokardu při statisticky nepřítomných rozdílech v koncentraci hořčíku v séru i erytrocytu ukázal, že ani sérové koncentrace hořčíku, ani erytrocytární koncentrace nevypovídají o skutečném stavu intracelulárních koncentrací hořčíku a to nejenom v myokardu, ale i v dalších studovaných tkáních. Zajímavý je nález negativní korelace mezi koncentrací Mg^{2+} a Ca^{2+} v myokardu u potkanů – samic, naopak u potkanu samců I i samců II jsme nalezli mezi oběma ionty pozitivní korelaci.

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