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Magnesium in the food chain of plants, animals and man

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In Europe, the weathering soils of basalt, Rotliegende and Upper Triassic produce vegetation with the highest Mg concentration; granite, shell limestone and boulder clay with the lowest. With increasing age the Mg levels in flora decrease. Mg is stored highest by leaf-rich decotyleae and lowest in monocotyleae. Fruits, grain and seeds are poor in Mg, stems, bulbs and buds accumulate more Mg. Leaves incorporate the largest amounts of Mg. Insects and molluscs contain 800-5 000 mg/kg dry matter (DM). Vertebrates (mice, voles, shrews) store only 1 100-1 600 mg Mg/kg DM. The Mg content of processed foodstuffs varies between 20-30 mg/kg DM in starch and sugar and 1 900 mg/kg DM in white beans. Baked goods deliver 150-500 µg Mg/kg DM. Fruits are relatively poor in Mg (150-500 mg/kg DM). Vegetables accumulate between 350 mg/kg DM in mushrooms and 5 000-6 000 mg/kg DM in cucumber, lettuce and spinach. The Mg concentration of animal foodstuffs varies between 15 mg/kg DM in butter and 1 200 mg/kg DM in mutton, chicken, beef, pork, trout, rosefish and cow’s milk. Mg in the leaves of black tea and coffee powder is between 84 and 59% transferred into home made beverages. Mg consumption by adults with self-selected mixed and ovolactovegetarian diets in Germany and Mexico was determined in 21 duplicate portion technique studies on successive days. Women were found to consume 200-300 mg Mg/day, whereas men took in 250-320 mg Mg/day. Female and male ovolactovegetarians eat 375 and 475 mg Mg/day, respectively. The mg consumption by men is 24% higher than of women. Women and men with a mixed diet excreted 65% of the Mg intake through faeces. Omnivores have an apparent absorption rate of 33 and 34%, respectively. Women and men with a mixed diet and a Mg intake of ~200-250 mg/day had an equalised Mg balance. The normative mg requirement of women and men amounts to 200 and 250 mg/day, which is < 3 mg day and kg body weight or a Mg concentration of 650 mg/kg consumed dry matter. People with a genetic Mg homeostasis (Gitelman, Bartter syndrome) have a Mg requirement of 500-1 000 mg/day or more. Toxic hypermagnesemia has only been registered at oral doses of > 2 500 mg Mg/day.

Magnesium metabolism in insulin resistance, cardiometabolic syndrome and type 2 diabetes

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The increasing evidence for the clinical relevance of altered magnesium metabolism to states of altered insulin resistance confirms the role of magnesium deficit as a possible underlying common mechanism of the “insulin resistance” of hypertension and cardiometabolic syndrome. Type 2 diabetes is characterized by cellular and extracellular Mg depletion. Epidemiologic studies showed a high prevalence of hypomagnesaemia and lower intracellular Mg concentrations in diabetic subjects. Insulin and glucose are important regulators of Mg metabolism. Intracellular Mg plays a key role in regulating insulin action, insulin-mediated-glucose uptake and vascular tone. Reduced intracellular Mg concentrations result in a defective tyrosine-kinase activity, post-receptorial impairment in insulin action, and worsening of insulin resistance in diabetic patients. Mg deficit has been proposed as a possible underlying common mechanism of the “insulin resistance” of different metabolic conditions. Low dietary Mg intake is also related to the development of type 2 diabetes. The benefits deriving from daily Mg supplementation in type 2 diabetic patients are supported by studies showing that high daily Mg intakes are predictive of a lower incidence of diabetes. Benefits of Mg supplementation on metabolic profile in diabetic subjects have been found in most, but not all clinical studies, and larger prospective studies are needed to support the potential role of dietary Mg supplementation as a possible public health strategy in diabetes risk.

Assessment of nutritional norms for magnesium fulfilment in food rations used for Polish soldiers’ alimentation within the last 30 years

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The aim of the work was estimation of the fulfilment of nutritional norms for magnesium in the food rations used for Polish soldiers’ alimentation during the last 30 years. Magnesium content was estimated in 1 568 daily food rations planned for soldiers’ nutrition as well as in the rations given for Polish soldiers’ alimentation.
for consumption. Taking magnesium content in post consumption wastes into account, the supply of magnesium in really-eaten rations was assessed as well. It was found that the average magnesium content in daily rations planned for soldiers’ alimentation ranged, depending on the kind of ration, from 402.0 ± 56.3 mg to 616 ± 54.9 mg. The values obtained met from 63.8% to 174.0% of recommended amounts. Magnesium content in the rations given for consumption was lower and amounted from 354.7 ± 63.6 mg to 496.4 ± 78.6 mg, which met from 57.6% to 120.0% of obligatory norms. Rations really eaten delivered from 268.7 mg to 428.7 mg of magnesium. It covered from 46.7% to 98.2% of recommended amounts. Magnesium content in the daily rations depended on the season and ranged from 264.0 ± 47.0 mg in rations served in spring to 480.0 ± 40.0 mg in rations served in autumn. Magnesium supply in food rations planned for the alimentation of Polish soldiers doing military service in the UN Peace keeping missions was higher and amounted as follows: 477.2 ± 70.2 mg in UNDOF (Syria) which was 129% of the norm, 543 ± 56.4 mg in UNIFIL (South Lebanon) which was 146.8% of the norm and 702.3 ± 133.6 mg in KFOR (Kosovo) which was 121.9% of the norm. The main sources of magnesium in the diet were cereal products, potatoes, milk and dairy products. Magnesium shortage in the soldiers’ diet can result from both imperfect menu planning and improper alimentation fulfilment. It should be pointed out that the norms for magnesium which are obligatory in the Polish Army provide for significantly higher values compared to the norms for the Polish population. Therefore values indicated in our research as shortages met the norms in force in Poland in general and do not present any risk of magnesium deficiency occurring among soldiers.

Magnesium, oxidative stress and immune system in athletes

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Athletes should pay extra attention to magnesium status as performing exercise is highly dependent on the regulation of magnesium homeostasis. There is accumulating evidence that exhaustive exercise can lead to considerable magnesium losses. Frequently, these individuals fail to consume a diet that contains adequate amounts of minerals, including magnesium, which leads to marginal nutrient deficiency and results in substandard training and impaired performance. Strenuous physical exercise is also capable of increasing reactive oxygen species (ROS) generation. As magnesium has an important role in the inhibition of ROS induced cell injury, magnesium deficiency is likely to induce oxidative stress, a state where the production of ROS in the body transcends the antioxidant defence capacity. In view of the exposure during exercise, these conditions are prone to increase the generation of reactive oxygen species and decrease the magnesium status. As a consequence, individuals practising exercise are more susceptible to free radical mediated injury. Many aspects of immune function can be depressed temporarily by either a single bout of very severe exercise or a longer period of excessive training. Although the disturbance is usually quite transient, it can be sufficient to allow a clinical episode of infection, particularly upper respiratory tract infections. However, regular and moderate exercise has been reported to improve the ability of the immune system to protect the host from infection. So, the response of the immune system to exercise is varied, with different behaviour for each cell type and dependent on the intensity and duration of the exercise and on the training of the subject. Besides these factors, nutritional deficiencies alter immunocompetence and increase the risk of infection. Magnesium has a strong relation with the immune system in both non specific and specific immune responses and magnesium deficit has been shown to be related to impaired cellular and humoral immune functions. The similarities between exercise-induced alterations in immune function and the changes in immunity caused by a deficiency in magnesium are noteworthy. After a review of the literature, we present our recent data in this field of research.

Explosive magnesium efflux and H$_2$O$_2$ induced apoptosis in quail red blood cells


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Cell volume alteration has been described as a necessary event in cell death, concretely, cell shrinkage during apoptosis and cell swelling during necrosis. In our experiments we employed quail red
blood cells (QRBC) as a cellular model and H2O2 as an apoptotic inducer by reactive oxygen species in order to produce synchronized cell death, letting us study cell volume and ionic fluxes during this process. H2O2 was employed at concentrations (125 and 500 µM) capable of inducing apoptosis in different kinds of cells. For measuring cell volume we employed a Coulter Gen-S (COULTER Corp, Miami, USA). Cell death was confirmed by tripan blue dying and by electrophoretic determination of DNA fragmentation. Magnesium analysis was determined by atomic absorption spectrophotometry (Perkin Elmer 1100 B). All assayed concentrations of H2O2 induced volume changes in QRBC, following the sequence “shrinkage-swelling-shrinkage". H2O2 500 µM developed this volume change more quickly (0 min 155 fl; 3 min 147 fl; 15 min 183 fl; 75 min 127 fl) and swelling was higher. Whereas H2O2 125 µM induced volume changes slowly (0 min 155 fl; 7 min 139 fl; 30 min 170 fl; 120 min 118 fl) and first shrinkage was more pronounced while swelling was smaller. Neither bumetanide nor extracellular potassium changes provoked differences in this phenomenon. Calcium free medium induced a very soft difference. Cells started to be dyed by trypan blue at 120 min (0.5%), and 24 hours later cells continued to shrink, all cells were trypan blue dyed (100%) and DNA fragmentation was verified. In our experiments we found a huge magnesium efflux during the post-shrinkage volume increase and posterior cellular shrinkage. If this phenomenon is necessary in cellular events leading to apoptosis or if this is only a consequence of apoptotic process should be clarified.

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Input of new advances in biology to a better understanding of magnesium needs

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The link between hypomagnesaemia, low magnesium intake and chronic diseases is now well recognized. However, at present it is not well known to what extent currently used magnesium parameters precisely reflect magnesium status and what the respective contribution of nutrition and genetics to magnesium status parameters is. Epidemiological studies evaluating magnesium intake have been carried out in different western populations and support the idea that hypomagnesaemia due to low magnesium intake could be widespread in these populations. Genetic factors are involved in the regulation of magnesium metabolism. However, the causes of inherited hypomagnesaemia, in populations with genetically determined low magnesium status has not been studied, since the study by Henrotte et al. in 1990. This pioneer study reveals a polygenic influence and probably a polymorphism in the genes encoding proteins involved in magnesium handling. Recent advances in molecular genetics have led to the identification of a variety of genes and their encoded proteins involved in human magnesium homeostasis. Different genetic diseases that specially interfere with magnesium (re)absorption and retention have been described. These hereditary disorders of magnesium homeostasis only account for a small subset of hypomagnesaemia, but offer a unique opportunity to study the physiology of magnesium homeostasis. It seems likely that new genes involved in magnesium transport mechanisms will be identified in the near future. In conclusion, molecular genetics has made significant inroads in explaining the basic mechanisms of magnesium homeostasis and will help in the near future to answer key questions: Are we genetically different with regard to magnesium status? Do we have different magnesium needs? Do we have different sensitivities to magnesium deficiency?

Magnesium involvement in bipolar disorders

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In bipolar disorders (BD) there is a diversity of clinical signs with predominance of manic or respective depressive periods. There are divergent data regarding the influence of magnesium and other cations on the pathogeny and evolution of these psychoses. Differences among results could emerge from the existence of 2 types of BD. Some of the authors have reported the absence of any change in plasmatic and spinal fluid concentrations of magnesium in BD and the lack of correlation between concentrations and clinical symptoms (Ramsey et al. 1979, George et al. 1994). Other data sustain the existence of a moderate but significant increase in magnesium concentrations in erythrocytes but only in out patients with mild forms and in conditions of unspecified food intake. In our research, the level of magnesium in erythrocytes in untreated adult patients was significantly decreased during the acute phase of BD type I. Improvement of clinical symptoms
(under treatment with sodium valproate and carbamazepine in therapeutic doses for 4 weeks) was correlated with significantly increasing intra-erythrocyte magnesium concentrations. We consider that decreasing magnesium at neuronal level is involved in the mechanism of BD type I. Our data are in agreement with Chouinard et al. (1990) who show that therapy with magnesium aspartate improved symptoms in BD. Lithium, one of the most used drugs in the therapy of BD, increases the neuronal level of Mg²⁺. In our studies, other “mood stabilizer” drugs also increase intracellular concentrations of Mg²⁺. Calcium antagonists (e.g. verapamil) associated with Mg have a therapeutic benefit in BD. We think that the main pathways of Mg action in BD are: impairment in presynaptic release of glutamate and consequent decreasing stimulation of NMDA receptors. We consider that therapeutic association of Mg²⁺ with mood stabilizers has benefits for patients with BD.

Possible implications of Mg deficiency in the pathogenesis of irritable bowel syndrome – basis of a new therapeutical strategy?

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The role of Mg deficiency (MD) in neuro-muscular diseases, both at the level of striated muscles and that of myocardium, is well known: spasmophilia as well as coronary heart disease, mitral valve prolapse or different arrhythmias are very well researched fields. It’s strange that the implications of MD at the level of smooth muscles are in general less known. For the visceral muscles, data exist about bronchial asthma or neurogenic urinary bladder, and also for the vascular muscles. Regarding the visceral musculature of the digestive tube and biliary tree, few data exist about the implication of MD in the pathogenesis of these diseases. The present paper proposes a theoretical analysis of the MD implications in the pathogenesis of irritable bowel syndrome (IBS) and their practical verification by substitutive Mg therapy.

IBS is characterized by functional disturbances of the gut, especially of the colon, which based on some common pathogenetic links: intensification of segmental contractions, which become painful, and excessive sensibility of intestinal mucosa, respectively. Among the etiological factors which determine these disturbances, stress has an essential role. Taking into consideration the antispastic effect and the positive effect on the increase of cellular excitability level of Mg, its administration in IBS is logical. Likewise, it’s known that MD appears as a consequence of stress, a double relation being evidenced: stress determines MD, which supports stress. So, by substitution therapy with Mg, at least 3 pathogenetic links could be influenced. In our study we analyzed 65 patients in which MD co-existed with different digestive functional disorders, including IBS. After substitution therapy with Mg, MD disappeared in all patients, and the digestive disturbances in 83%.

These results, even though obtained in a group with MD ± IBS and not in a group with IBS ± MD, support the above hypothesis and recommend the continuation of the study.

Magnesium and endothelium dependent relaxation

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The major relaxing agents released by the endothelium, e.g. nitric oxide (NO), prostacyclin (PGI₂) and the so-called endothelium-derived hyperpolarizing factors (EDHF: epoxy-eicosatrienoic acids, K⁺, H₂O₂, atrial natruretic peptide C, etc.) act via diverse mechanisms to decrease cytosolic calcium in smooth muscle cells and calcium sensitivity of the contractile mechanism. All of them determine smooth muscle hyperpolarization by activating various K⁺ channels (voltage-dependent Kir and Kv; ATP-dependent K ATP, calcium-dependent KCa), thereby reducing calcium influx via L-type channels. Moreover, potential membrane perturbations propagate electrotonically from the endothelium to the muscle layer via gap junctions and the EDHF phenomenon frequently involves activation of the endothelial KCa with low and intermediate conductance. Within our traditional interest in vascular physio-pharmacology we are intensifying research devoted to the way this complicated endothelio-muscular communication network is used within endothelium-dependent relaxation (EDR), be it induced by vasoactive agents, flow-dependent, or longitudinally propagated. Despite wide investigation regarding the influence of Mg²⁺ upon vascular smooth muscle, few studies analyze the impact of Mg²⁺ upon EDR. This is surprising, because Mg²⁺ interferes with NO release and multiple studies describe the influence of both intra- and extra-cellular Mg²⁺.
upon K+ channels which are clearly involved in EDR. We review existing data on Mg2+ and EDR and we emphasize that they cannot be easily extrapolated, because EDR mechanisms are highly variable with species, age, sex, hormonal status, vascular territory and calibre, vasodilating agent, and pre-existing tone. We are currently using a combined experimental approach (chronic versus acute; in vivo versus in vitro) to investigate the effects of Mg2+ upon EDR in rats and humans and the mechanisms involved. As shown in our study presented at this symposium, chronic Mg2+ may enhance the preservation of EDR in resistance arteries of 1-NAME treated rats by promoting the EDHF mechanism. Moreover, our preliminary data indicate that the manipulation of extracellular Mg2+ may change the relative contribution of NO and EDHF to EDR.

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**In vitro antioxidant activities of magnesium compounds**

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In the human body several enzymatic reactions are magnesium dependent and magnesium plays a basic role in the maintenance of the antioxidant system. The effect of magnesium on the antioxidant system is indirect, although a direct effect has also been published. Our purpose was to examine the free radical scavenging activity of some magnesium compounds. Inorganic salts (e.g. MgCl2) and organic complexes (e.g. Mg-gluconate) were also studied. The antioxidant/pro-oxidant effects were determined with the chemiluminometric method (H2O2/•OH-microperoxidase-luminol) and hem (iron) mediated LDL (low density lipoprotein) oxidation (LDL-hem-H2O2). It has been stated that the chemiluminescence method and LDL oxidation measurement is applicable in the presence of magnesium salts and complexes. Most of the compounds do not generate free radicals and the antioxidant/pro-oxidant effect depends on the quality of the ligand and the concentration applied. In the concentration range used, some representatives of the magnesium compounds (MgO, Mg-gluconate) showed radical generating activity measured with chemiluminescence method whereas the LDL oxidation was not affected. Magnesium citrate and malate proved to be the antioxidant measured with the chemiluminescence method and they accelerated the LDL oxidation in the system and in the concentration applied. According to the results, some of the magnesium compounds studied have free radical (H2O2/•OH) scavenging activity although they do not affect the lipid peroxidation directly in the LDL fraction.

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**Magnesium in acute brain injury**

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A number of studies have now supported a role for magnesium as a neuroprotectant following acute brain injury. Our own studies have established that both brain and blood free magnesium decline after traumatic brain injury (TBI), and that administration of magnesium salts early after trauma increases the free magnesium concentration in brain, and results in an associated improvement in both motor and cognitive outcome as well as a reduction in post-traumatic depression/anxiety. A number of reports have suggested that the improvement in functional outcome is due, in part, to the ability of magnesium to reduce blood brain barrier permeability and subsequent oedema formation after trauma. Since aquaporin water channels have been recently implicated in oedema formation, we chose to examine the effects of magnesium on aquaporin-4 channels (AQP-4) after TBI. Adult male, Sprague Dawley rats were injured using the 2-metre impact acceleration model of diffuse TBI. After injury, animals were treated with either 30 mg/kg magnesium sulphate at 30 min after injury, or equal volume saline vehicle. At 5h, which corresponded to the point of maximum oedema formation, animals were killed and their brains fixed for histological examination of AQP-4. There was a profound reduction in AQP-4 electron density in vehicle-treated animals, coincident with an increase in AQP-4 immunoreactivity in subependymal and subpial glia limitans, suggesting a redistribution of AQP-4 channels from perivascular cell processes to the glia limitans. Small vacuoles also appeared in perivascular astrocytes indicating incipient cellular oedema. Administration of magnesium at...
30 min after injury resulted in a restoration of AQP-4 channels within 4 h of administration, and an associated pronounced perivascular astrocyte swelling. The pronounced astrocyte swelling was interpreted as precocious astrocytic oedema formation drawn from extracellular fluid, presumably as an early adaptive response for resolution of oedema through the vascular network. It is of interest here that endothelial cells of brain capillaries at this time point also showed increased AQP-4 immunoreactivity. We conclude that magnesium may decrease brain oedema formation after TBI by restoring the polarized state of astrocytes with preferential distribution of AQP-4 channels to perivascular foot processes.

Magnesium and cardiac arrhythmias

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Heart disease represents the leading cause of death. The mechanism of the cardiac death is usually arrhythmia. Sometimes, the victims are suffering from mild heart disease or even considered healthy. Fatal arrhythmias express the electrical instability of the myocardium which is the consequence of magnesium deficit, catecholamine excess or toxic agents, sometimes in combination. Because the myocardium is globally affected, different forms of supraventricular and ventricular rhythm disturbances are noticed. Some distinctive traits of the arrhythmias caused by magnesium deficit are discussed. One of them is the relapsing tendency. In these cases, the administration of magnesium over a long duration proved to be beneficial. An advantage of magnesium as an antiarrhythmic agent is its safety in administration if the renal function is conserved. Magnesium is not only antiarrhythmic but also a cardioprotective agent.

Serum magnesium in patients with acute ischemic stroke

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Magnesium (Mg) has important effects within the vascular system. Magnesium deficiency has been shown to trigger vasoconstriction and enhance vascular endothelial injury, thus promoting the development and progression of atherosclerosis. However, it is still not completely known whether low serum Mg also promotes the occurrence of stroke. We hereby intended to investigate Mg levels in serum in the early stages of stroke and to evaluate the relationship between serum Mg concentration and the development of neurological deficits. The study included forty patients with stroke (26 women and 14 men), mean age 56 ± 4 years, without any other serious injuries. Twenty-one healthy subjects, sex- and age-matched were selected as controls. The serum Mg concentrations were measured by colorimetry on a Hitachi 917 autoanalyzer. Serum levels of Mg were checked on admission, and at 48 hours after the onset of ischemic stroke. Using NIHSS, the neurological deficit was assessed on the 1st day, and 48 hours later. Statistical analysis was performed using the Student t test. The results confirm that there is a relationship between a low Mg concentration in serum at 48 hours after onset of ischemic stroke and the intensity of the neurological deficit. Mean value was 1.39 ± 0.213 mmol/L (on admission), 1.47 ± 0.181 mmol/L (at 48 hours after the onset of stroke) versus 1.66 ± 0.138 mmol/L (in controls). Severity of paresis degree was higher in the patients with low Mg levels (p < 0.05). The serum Mg concentration has been suggested to possibly affect the neurologic state. A decrease in the serum Mg concentration indicates the severity of the injury. A Mg substitution therapy may be useful.

Central anti-arhythmic action of magnesium

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The anti-arhythmic effect of magnesium on the arrhythmias caused by high doses of cardiotonic as well as the anti-arhythmic effect upon myocardial infarction is well known. In this paper I analyze the central anti-arhythmic effects of some magnesium salts. The tests were made on white rats of both sexes, weighing between 180-240 g, anesthetized with ethylic urethane. The lateral cerebroventricle was tackled stereotaxically. The compounds investigated were injected with a modified Hamilton microsyringe. The following were recorded: the electroencephalogram (EEG),
the electrocardiogram (EKG) and the respiratory movements. The experiment was made both in spontaneous respiration and in artificial ventilation. It was established that the administration of low doses causes bradycardia. In high doses (81, 29 x 10 moles) it causes the modification of the EEG and cardiac arrhythmias which depress respiratory moments. Magnesium thiosulphate induces similar modifications. If artificial breathing was installed, the antihomogenous modifications did not occur. This proves that the magnesium, which induced depression of respiratory moment, caused the arrhythmias. The magnesium salts administered in low doses prevented the antihomogenous effects of sodium glutamate, of desimpramine and of calcium chloride if these substances were administered intracerebroventricularly. The antiarrhythmic effects of magnesium salts may be explained by antagonisation of the antihomogenous effects of the calcium ions, which are responsible in the last analysis for the arrhythmias caused by the substances mentioned above.

In conclusion, the magnesium salts antagonize the antihomogenous effects of some antihomogenous compounds. Administered in high doses, these salts may induce cardiac arrhythmias. In urethane anesthetized rats, the intracerebroventricular administration of very high doses of magnesium sulphate and magnesium thiosulphate induced cardiac arrhythmias. These cardiac rhythm disorders were probably caused by some respiratory depression. In lower non-arrhythmogenic doses, both magnesium salts prevented the central arrhythmonic activity of sodium glutamate, calcium chloride and desimpramine.

**Magnesium deficiency detected in several elderly persons**

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The importance of magnesium in the pathophysiology of elderly people has been evaluated by scientists all over the world. The nutritional deficiencies were considered to be more pronounced in institutionalized than in free-living aged groups. It seems to be well established in the medical literature that magnesium does not constitute an *elixir vitae*. Conversely, magnesium deficit may play a role in the pathophysiology of ageing. We determined in 80 elderly persons, 40 men and 40 female, between 60-70 years of age, the serum Mg level, by using the laboratory atomic spectrophotometry technique. The deficiency levels were correlated with their pathology stage. As controls we used the Mg values determined in 80 adults with a normal medical status. The media value for the Mg determined in the control adults presented a statistical significance, which was higher than the media value in the elderly tested group (p < 0.001). Magnesium deficit participates in the clinical pattern of the ageing group, particularly in neuromuscular, cardiovascular and renal symptomatologies. Ageing remains a well determined risk factor for magnesium deficit. Supplementation with oral magnesium (5 mg/kg/d) was able to overcome the magnesium deficiencies under 1.50 mg/mL, in 6 men and 18 females from the ageing group tested. That improved the biological status of these 24 elderly persons.

**Beneficial pharmacological effects of magnesium supplementation in pediatric patients receiving chronic anticonvulsant monotherapy**

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Although magnesium is a trace element found in small amounts in the human body, it has obvious structural and functional importance, being related to various physiological functions, including the control of neuronal excitability. To evaluate the implications caused by chronic anticonvulsant monotherapy on magnesium serum concentration in epileptic patients, we studied the magnesium serum concentrations of a randomized trial of 55 patients - 30 female and 25 male, aged 9-16 years, (study group). The clinical diagnosis was made according to the criteria of the International League against Epilepsy and encephalographic records. The patients had received anticonvulsant monotherapy for at least two years, and all of them were examined during interictal periods. The epileptic patients were classified in three subgroups, according to their anticonvulsant monotherapy: carbamazepine (n = 23), valproic acid (n = 22), and relatively new anticonvulsants,
such as oxcarbazepine, lamotrigine and topiramate (n = 10).
The results were compared to 55 age-matched healthy subjects (control group). We assessed magnesium serum levels in all subjects with an atomic absorption spectrophotometer and results were calculated in µg/mL. For comparison of means, the Student’s test was used. Results and discussion: the mean magnesium concentrations in epileptic patients were significantly reduced (91.50 ± 35.30 µg/mL) versus controls (122.40 ± 45.50 µg/mL), and the lowest levels were reached in the subgroup receiving valproic acid therapy.
The present study indicates that chronic anticonvulsant therapy leads to a diminished magnesium status that may increase the risk of epileptic crises. Therefore, magnesium supplementation is mandatory in epileptic patients.

Nutrition in early childhood and some dental problems

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Teeth are the “living” memory of the diet consumed whether it is an adequate one or it is unbalanced. The purpose of this study was to assess the nutrition of a group of children and its impact on their dental health status. In this study we analyzed by statistical method the nutrition of 30 children from a foster home with ages between 14-42 months. Nutritional inquiries were performed over one year, divided into three stages: in the middle of autumn, at the end of winter and at the end of spring (cumulated interval of time 30 days). After one year, all the children were examined by the medical dentist in order to assess their oral health status. Results: among the well-known risk factors for dental health we can mention: carbohydrates (the average intake was in excess, with 10.73% than the recommendations), fats (in excess with over 20%), severe iron deficiency (on average with 46.3% less), magnesium (on average with 10.69% less). Even though the calcium, phosphorus and vitamin C intakes were normal, at the clinical examinations we found occlusive decay in 40% of the children and 25% of all the decay was located on tooth 85, respectively. 46.87% on teeth 84, 75, 74 in equal distribution. From the total number of decays, 84.37% were identified in children under 3 years old. Spaces between teeth were identified in 46.67% of all the children. The most frequent location of the spacing process was between teeth 51-61 (22.44%) and teeth 81-71 (12.24%). 57.14% of all the spacing processes were found in children under 2½ years old. Another aspect followed was the occlusional type of the oral cavity. 46.67% of all the children had no occlusional deficiency, 6.67% had a cap occlusion and in 30% the occlusion was absent. The type of respiration was oral in 16.67% of all the children. Nutrition plays a key role in teeth appearing and developing, but the dental health status is also determined by the care for oral hygiene. These two environmental factors have a common ground: the family.

Serum magnesium level in bitumen exposed workers

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Occupational exposure to bitumen fumes has a lot of harmful health effects. It produces ocular and dermal irritative and respiratory affections. Malignant outcomes with different localization have also been reported following long time occupational exposure to bitumen. In a cross sectional epidemiological study the health status of a group of road pavers was investigated in order to find the connection between the biochemical changes and the morbidity pattern, focusing on blood Ca and Mg levels. A group of 75 subjects exposed to bitumen by road paving activities was investigated by a complex protocol, including clinical, biochemical, haematological and immunological examination. The employees had a mean age of 35.7 ± 9.8 years, a mean service length of 12.9 ± 10.5 years and an average length of bitumen exposure of 6.3 ± 2.9 years. The results were compared with those of a control matched group having the same age and smoking habits. Serum magnesium was determined with commercial kits provided by Randox Laboratories Ltd (Antrim, UK). The results were statistically analyzed through usual methods (Student’s t-test, χ2-test, Pearson’s correlation coefficient). Average magnesium level in bitumen-exposed workers was significantly lower than in controls (t = 2.65, p < 0.01). 18.6% of subjects had abnormal low magnesium levels, in 9.5% of cases hypomagnesaemia was associated
ABSTRACTS

with normal low serum calcium level. 12% of subjects with low magnesium levels had a decreased content of reduced and total glutathione in whole blood. In exposed subjects, the serum magnesium level correlated inversely with the length of bitumen exposure ($r = 0.27, p < 0.01$), suggesting an occupational causality of this imbalance. The incidence of the affections where magnesium deficit is responsible for the aetiology is higher in the subgroup of exposed workers with hypomagnesaemia. In bitumen exposed workers the loss of serum magnesium seems to be occupationally related. This deficit is also in strong correlation with the detoxifying mechanisms involved in the organism's protection against the complex occupational risks encountered by these employees.

Magnesium influence on rats with nickel excess administration

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We tested the magnesium effect on toxic doses of nickel at the level of rat kidney tissue. We used for this study 3 groups of white Wistar rats, which were kept in similar experimental conditions and received the same food. Ten adult male rats formed each group, with a weight between 200 and 250 g. The first group was the control which received no substance. The second group received NiCl$_2$ 0.1 mEq/kg weight/day, intraperitoneal administration, unique daily dose, for 3 weeks. The third group received NiCl$_2$ 0.1 mEq/kg weight/day, intraperitoneal administration, unique daily dose, 3 weeks and magnesium acexamate, 0.5 mEq/kg weight/day, intraperitoneal administration, unique daily dose (magnesium was administrated with 1 hour before the administration of NiCl$_2$). After 10 days, half of the animals of each group were anesthetized with Pentobarbital and slaughtered by cutting the carotid arteries. After 21 days, the remaining animals were anesthetized with Pentobarbital and slaughtered by cutting the carotid arteries. Morphopathological microscopic examinations of the lungs, livers, kidneys and testicles were performed for each animal. The prolonged administration of nickel produces variable injuries to lungs, liver, kidneys and testicles. Our study proves that the magnesium partly decreases these injuries, but was not able to counteract them entirely.

Magnesium content in the diets used for patients staying in the military institute of aviation medicine hospital in Warsaw

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Following proper nutrition rules helps keep good health for many years. Proper nutrition is particularly important for hospitalized patients. Adjusting alimentation to the patient’s current metabolic and clinical condition is crucial, however, it is still underestimated. The diet of hospitalized patients should only be a modification of the proper diet of healthy people. The aim of the work was the estimation of the magnesium content in the standard and light diets used for nutrition of patients staying in the Military Institute of Aviation Medicine Hospital in Warsaw. Material for examination consisted of 80 daily diets, half of them were standard and the other half, light ones. The diets served to patients from January to October 2006 underwent examination. Samples of these diets were homogenized, mineralized in the muffle furnace at a temperature of 450°C, and then dissolved in 1% nitric acid. Magnesium content was indicated by atomic absorption spectrometry, using the FAAS flame technique and the AAS AVANTA Σ (GBC) spectrometer. The analyses were done in standard conditions in acetylene-air flame. The average magnesium content in the standard diet given for consumption was $229.7 \pm 37.6$ mg. The lowest magnesium content was found in July (204.5 mg) and the highest one in January (294.3 mg). Average magnesium content in the standard diet met 79.2% and 63.8% of the recommended Polish norm for women and men staying in hospitals, respectively. A lower magnesium content amounting to $153.9 \pm 29.7$ mg was found in the light diet. The lowest magnesium content was found in July (116.8 mg) and the highest one in January (187.9 mg). Average magnesium content in the light diet met 53.0% and 42.8% of the recommended norm respectively. Research carried out revealed that diets used for alimentation of patients in Military Institute of Aviation Medicine
did not meet the requirements for magnesium. Huge differences in the magnesium content in the planned diets, in particular months, testify to inappropriate menu planning. Differences between magnesium content in planned and food rations given result from wrong execution of patients’ alimentation in hospital.

**Magnesium, lead and delta-aminolevulinic acid dehydratase activity in vitro**

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Magnesium (Mg) is present in abundance in organisms and is one of the most essential elements for metabolism and vital processes. Some data show that magnesium ions interact (non-specific competition) with bivalent lead (Pb) ions. Lead impairs the delta-aminolevulinic acid dehydratase (delta-ALAD) activity by replacing zinc ions on the active centre of enzymes, and thus changing the spatial conformation. Sufficient magnesium concentrations may even stimulate the activity of delta-ALAD. The aim of present research was to investigate whether magnesium may protect delta-ALAD activity upon lead impact. We investigated whether $201.01 \mu M \text{Mg}^{2+}$ (MgSO$_4$) additives 20 min preceding the $0.04-80.45 \mu M \text{Pb}^{2+}$ (Pb(CH$_3$COO)$_2$) exposure, and $2010.14 \mu M \text{Mg}^{2+}$ (MgSO$_4$) additives 20 min preceding the $0.04-840.54 \mu M \text{Pb}^{2+}$ (Pb(CH$_3$COO)$_2$) exposure respectively, may protect haeme enzyme delta-ALAD activity upon lead inhibition in human erythrocytes *in vitro*. The results showed that $201.01 \mu M \text{Mg}^{2+}$ prevented enzyme inhibition only up to a lead concentration of $0.56 \mu M \text{Pb}^{2+}$. Preceding saturation with magnesium ions at a concentration of $2010.14 \mu M \text{Mg}^{2+}$ significantly protected enzyme activity on $0.04-840.54 \mu M \text{Pb}^{2+}$ exposure. Mean delta-ALAD activity was 27.23% higher with magnesium additives as compared to no magnesium additives on the basis of $0.04-840.54 \mu M \text{Pb}^{2+}$ exposure. Moreover, research showed that the protection effect on the erythrocyte enzyme activity *in vitro* was due to magnesium ions but not sulphate (MgSO$_4$ *versus* MgO) ions. Further studies will be undertaken to find out the threshold concentrations at which advanced supplementation with magnesium ions protects delta-ALAD activity on lead impact.

**The influence of magnesium and other bivalent cations on the effect of montelukast sodium in experimental thermoalgesia**

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We tested the influence of magnesium, zinc and copper on montelukast (MK, antagonist of cysteinyl leukotriene receptor type 1) effects in experimentally-induced thermoalgesia. We worked on 5 groups of 10 adult, Wistar rats, which received: group I-control; group II: MK (10 mg/kg) unique administration; group III: MgCl$_2$ (1 mmol/kg/day) i.p., 3 days and MK (10 mg/kg) unique administration on the 3rd day; group IV: ZnCl$_2$ (0.1mmol/kg/day), i.p., 3 days and MK (10 mg/kg) unique administration on the 3rd day; group V: copper acetate (0.05 mmol/kg/day), i.p., 3 days and MK (10 mg/kg) unique administration on the 3rd day. We determined the thermoalgesic sensitivity (TS) using a tail flick analgesia meter, initially, 3 days after cation administration and 3 hours after MK administration. The results were statistically interpreted using the t test. Our data show that MK has a statistically significant reduction of TS *versus* control group ($3.76 \pm 1.04 \text{s} *versus* 1.81 \pm 0.98 \text{s}, p < 0.05$). Copper administration does not significantly change the MK effect on TS. Magnesium decreased mildly (but not significantly) the effect of MK on TS. Zinc decreased TS and significantly prolonged the time of tail flick. Co-administration of zinc and MK statistically significantly decreased TS of the group which received only MK ($2.51 \pm 0.21 \text{s} *versus* 3.76 \pm 1.04 \text{s}, p < 0.05$) and increased the thermoalgesic effect of MK.

**Magnesium concentration in patients with secondary Raynaud's syndrome**

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Raynaud’s disease, or secondary Raynaud’s syndrome, presents with similar symptoms in association with one or more systemic disease(s), the most common of which is connective tissue disease. We suggest the use of syndrome in place
of disease or phenomenon, and it is this terminol-ogy which will be used in the presentation. The purpose of this study was to investigate serum magnesium levels in 128 patients with secondary Raynaud’s syndrome and 46 healthy subjects age-and sex-matched and to ascertain the potential role as marker for this pathology. Analyses were performed using a Hitachi 917 autoanalyser (colorimetric method). Statistical analysis was performed using the Student t test. Magnesium levels were significantly lower in serum of patients with secondary Raynaud’s syndrome than in controls. Mean value was 1.19 ± 0.202 mmol/L (on admission) versus 1.47 ± 0.128 mmol/L (in controls); p < 0.05. The decreased levels of Mg in the serum of patients with secondary Raynaud’s syndrome may suggest involvement of Mg in pathogenesis of vasospasm.

Effects of magnesium sulphate on immobilization-induced gastric ulcerations in rat
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Magnesium compounds are widely used in ulcer treatment. Moreover, magnesium salts also have gastro-protective effects on some experimental ulcer models. Therefore, we followed the effects of magnesium sulphate in acute gastric ulcerations occurring with immobilization in rats. We worked on male albino Wistar-Bratislava rats weighing 70-100 g, kept in standard lab environment and alimentation. Five groups of 10 animals were formed, and fasted for 12 hours. The first group was free moving, the other groups were immobilized on wood in a dorsal position for 12 hours. The second group received i.p. saline, the other groups received 0.5; 1 and 2 mmoles/kg magnesium sulphate in a volume of 2 mL/kg, 20 minutes before immobilization. Treatments were repeated after 6 hours. After sacrifice and collecting stomachs, we examined the incidence, number, type and gravity of gastric lesions. Null hypothesis was rejected at p < 0.05 at all parametric and non-parametric statistical analysis. Free moving rats had no gastric lesions. Immobilization causes hemorrhagic ulcerations in all animals. At the before mentioned 3 doses of magnesium sulphate the total number of mucosal lesions is unaffected, compared to the immobilized and saline treated group. At the highest dose of magnesium sulphate, gastric ulcerations are confluent and more severe. Magnesium sulphate administered i.p. in 2 doses of 0.5 and 1 mM/kg had no influence whatsoever on gastric ulcerations. The dose of 2 mmoles/kg had an aggravating effect on gastric lesions.

Magnesium effect on the interaction of statin molecules with an immobilized phosphatidylcholine monolayer
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High plasma cholesterol has been acknowledged, since mid-20th century, as a major heart disease risk factor. Several studies have demonstrated that magnesium deficit is an important factor in the physiology of the cardiovascular apparatus and the pathogenesis of cardiovascular diseases. More recently, drugs such as statins or 3-Hydroxy-3-MethylGlucaryl Co enzyme A Reductase (HMG-CoA R) inhibitors have been widely used for reducing the circulating atherogenic lipid fractions and decreasing cardiovascular morbidity and mortality. In this work, the effect of the magnesium cation on the passive diffusion of these drugs through the cellular membrane was analyzed. For this, the interaction of five statin molecules (pravastatin, mevastatin, atorvastatin, simvastatin and fluvastatin) with a phosphatidylcholine monolayer, that was immobilized to porous silica particles and packed into a stainless column cartridge, was studied, using dynamic elution techniques. This immobilized lipid monolayer, (i.e. Immobilized Artificial Membrane [IAM]), provides a biophysical model system with which to study the binding of these drugs to a lipid membrane. An analysis of the thermodynamics (i.e. enthalpy [AH°], entropy [AS*]) of the interaction of the statin molecules with the immobilized phospholipid monolayer was carried out at all the magnesium cation concentrations in the medium. These data showed that, at all the
magnesium cation concentrations, the statin-biomimetic phosphatidylcholine monolayer binding was enthalpically controlled. Indeed, the $\Delta H^\circ$ and $\Delta S^{*\circ}$ values were negative due to van der Waals interactions and hydrogen bonding between the statin molecules with the polar head groups of the phospholipid monolayer. However, the increase of the statin-IAM association, with the Mg$^{2+}$ concentration increases, was associated with an increase of these thermodynamic data. These changes are consistent with the formation of hydrophobic bonds of these drugs with the lipid monolayers which were enhanced with magnesium cations. Also, it appeared that a Mg$^{2+}$ supplementation (Mg$^{2+}$ concentration range 0-2.60 mmol/L, including its biological concentration range i.e., 0.75-0.90 mmol/L) could probably increase the statin passive diffusion into hepatocytes and thus their biological effects, i.e. their pharmacological actions.

Mineral waters as a good source of magnesium - Polish mineral waters from southern Poland (Nowy Sacz Region)

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In 2002 the Standing Committee on the Food Chain and Animal Health voted in favour of a Commission proposal to strengthen the legislation in force on natural mineral waters. The proposal established maximum concentration for a series of substances of natural origin that may pose long term health risks at high concentrations, and reinforces the labelling provisions applicable to natural mineral waters. The new rules on labelling applied as of 1 January 2004. FDA regulates bottled water as a food and in Title 21 of the Code of Federal Regulations (21 CFR) and other regulations, the mineral water must contain no less than 250 parts per million (ppm) total dissolved solids; it must come from a geologically and physically protected, underground water source, and it must contain no added minerals. According to Polish regulations low mineralized waters contain less than 500 mg/L dry matter (d.m.) medium – 500-1 500 mg/L d.m. and high mineralized water above 1500 mg/L d.m. Magnesium as magnesium ion (Mg$^{2+}$) in underground water occurred in smaller amounts than calcium ion, because of its lesser dissemination in nature. In some mineral waters originating from such regions as Muszyna, Krynica, Zegiestow (Poland) the magnesium ion outweighs the calcium ion. Magnesium in underground waters has its sources in sedimentary stones: dolomites (calcium-magnesium carbonate) and magnesites (magnesium carbonates), as well as easily dissolved sulphates. According to the Polish law, waters coming from 70 sites in Poland, many of them in Nowy Sacz region, belong to the remedial waters. The mineral waters containing more than 1000 mg solid components in 1 L of water are divided among others for: magnesium bicarbonate or magnesium chloride or magnesium sulphate waters. Taking into account the dietary habits in different regions in Poland and availability of mineral water sources it maybe concluded that drinking one bottle (1.5 L) of mineral water a day it is easily possible to meet the recommended values for men, 350 mg/day and for women, 300 mg/day.

Magnesium in drinking water of the public systems and wells - possible effects on health

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Many studies support a statistic correlation between a reduced level of the magnesium and total hardness in the drinking water and higher cardiovascular disease mortality, and also the possibility of supplementing the drinking water with magnesium. Tap water was more effective in meeting magnesium requirements than dietary supplementation. It is possible, then, that waterborne magnesium could correct an insufficient dietary magnesium level. The aim of the study was to analyse the Mg, Ca, Ca/Mg and total hardness in the drinking water of the Pascani, Hirlau and Tg. Frumos areas of Iaşi district. The mineral macroelement concentrations: Mg, Ca, Ca/Mg and total hardness was measured in 62 samples of the drinking water, 38 of the public systems and 24 samples of wells, in two periods of the year, July and October. The calculation of probability to determinate the size of the water sample in the three cities was used. The chemical analyses of the samples point out a low degree of mineralization and fixed residuum, on average below 500 mg/L, variations of the Ca, Mg, total hardness concentration. Magnesium average concentration was higher
in the well water of Tg. Frumos and Hirlau city. The average of magnesium concentration in deep water of Pascani and Tg. Frumos city was lower. With respect to the total hardness in drinking water of the public system, the variation limits ranged between 13.2-16.28 °G and the average was higher in the well water of the three cities. The Ca/Mg ratio was higher in the drinking water of the public system with a variation between 2.91-16.84, and in the well water between 0.7-8.49. The drinking waters represent a source of essential elements for consumers.

Magnesium and mitral valve prolapse
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Mitral valve prolapse (MVP) is one of the most common cardiac abnormalities (up to 10% of the population). Described in the 1960s by Barlow (South Africa), the idiopathic (primary) MVP, that represents 95% of MVP cases, is an expression of a collagen weakness. J. Durlach, pointing out the frequent association between spasmophilia and MVP suggested that both are related to a prolonged Mg deficit. In this paper this hypothesis is developed. Not only a Mg deficit, but also genetic (familial) and other environmental factors, mainly stress, are considered. Important prophylactic and therapeutic consequences of this ethiopathogenic concept are discussed. Mg supplementation detains the key role in both these aspects.

The values of calcium: magnesium ratio in drinking water. Significance for human health
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Several epidemiologic studies have shown an association between calcium (Ca), magnesium (Mg) and coronary disease mortality and morbidity. Drinking water is an important vehicle for the supply of minerals, especially macronutrients (Ca, Mg). Hard waters can supply 9 to 29 percent of the daily Mg intake. Because of metabolic antagonism between Ca and Mg, the ratio between these two minerals in drinking water is of considerable importance. Theoretical deviation of the recommended Ca to Mg ratio in water (2: 1) has a negative effect on health in both directions. The aim of our study was to determine the Ca and Mg concentrations in drinking water (tap water, springs, well waters and mineral waters) to calculate Ca:Mg ratio. In order to assess water quality, other inorganics were analyzed using standard laboratory methods. Water samples were collected from taps in urban and rural areas (total 75 samples), springs (n = 20), well waters from rural areas of Moldova territory (n = 80) and mineral waters distributed in Romania (n = 20) and in other countries (n = 30). The results shows that the Ca:Mg ratio ranged between 0.65 to 6.59 in tap water, 0.65 to 6.11 in springs, 0.53 to 3.79 in well waters and 0.49 to 4.65 in mineral waters. Only 28.13 percent of the drinking water samples had the recommended Ca:Mg ratio. The findings of a positive correlation between cardiovascular mortality and the estimated Ca:Mg ratio of diet (water) suggest that a high Ca:Mg ratio in the diet may be harmful. Any definitive conclusions and recommendations cannot be drawn from the data available. A low water Mg:Ca ratio has always been associated with a low water Mg level and the water Mg level has proved to play an important role in risk reduction of cardiovascular disease.

Effects of chronic L-NAME and magnesium upon arterial blood pressure and in vitro vascular reactivity in rats
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Despite wide investigation of the influence of Mg2+ upon vascular smooth muscle, few studies have analyzed the impact of magnesium on endothelium-dependent relaxation (EDR). Chronic inhibition of nitric oxide synthase (NOS) is well known to induce hypertension in various animal models including rats. There are indications that the Mg2+ load does not influence the development of higher arterial pressure but may reduce this effect at a later stage. Besides this, we studied the influence of chronic Mg2+ on the acute effects of two antihypertensive agents in L-NAME hypertension. We used 24 male Wistar rats, divided into 4 groups, which received (1 mL saline solution i.p. twice a day): isotonic NaCl (control group, A), isotonic MgCl2 1 mmol/kg/day (Mg group, B), and L-NAME
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40 mg/kg/day, either in NaCl solution (l-NAME group, C) or in MgCl$_2$ solution (combined group, D). Arterial blood pressure and heart rate were measured with a tail cuff sphygmomanometer. Single dose rilmenidine (1 mg/kg i.p.) and captopril (50 mg/kg i.p.) were given to assay their acute effects (10, 20 and 30 min. after injection). The animals were sacrificed afterwards, for in vitro evaluation of vascular reactivity using isometric myography of rings from the aorta and first order branches of the mesenteric artery. l-NAME induced hypertension, starting the third day, reached 135 ± 3.5 mmHg versus 104 ± 3.8 mmHg (p < 0.01) in 14 days. This was not altered by concomitant i.p. MgCl$_2$ (126 ± 4.3 mmHg, day 14) and could be normalized acutely by i.p. rilmenidine (97 ± 7 mmHg after 30') or captopril (104 ± 5.3 mmHg after 30'), but this effect tended to be reduced by chronic MgCl$_2$ treatment (103 ± 5.6 and 116 ± 5.1 mmHg respectively). In vitro data indicate that chronic Mg$^{2+}$ promotes the partial preservation of EDR in resistance arteries of l-NAME treated animals, by fostering the endothelium derived hyperpolarizing factor (EDHF). Our combined experimental approach brings new evidence regarding the effects of Mg$^{2+}$ upon EDR and the mechanisms involved.

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Neuroprotective properties of 6-hydroxyflavanone in two murine models of epilepsy: magnesium deficiency-dependent audiogenic seizure and pentylentetrazole tests

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Flavonoids which are brought by food, possess antioxidant properties and could interfere on central GABAergic pathways. In the present work, we studied the neuroprotective/anticonvulsant properties of three flavonoid compounds, 6-hydroxyflavanone (6HFN), 6-hydroxyflavone (6HF) and flavanone (FN) in two murine models of epilepsy: the Magnesium Deficiency-Dependent Audiogenic Seizure (MDDAS) test and the pentylentetrazole (PTZ)-induced seizure test. The MDDAS test allows the detection of the main anti-epileptic drug (AED) mechanisms of action (voltage-dependent sodium channel inhibition or GABAergic pathway activation and/or antioxidant/anti-inflammatory effects), whereas the PTZ test mainly targets the GABA$_A$ pathway. Neurotoxicity was studied by using the rotarod test. In the PTZ test, the efficient dose (ED$_{50}$) i.e. the doses protecting 50% of mice with normal magnesium input against seizures, were 5.5 and 13.5 mg.kg$^{-1}$ for 6HFN and 6HF respectively, whereas FN was rather proconvulsant. In the MDDAS test, 6HFN protected 50% of magnesium-deficient mice tested at a dose of 32 mg.kg$^{-1}$, whereas the ED$_{50}$ of 6HF and FN were 72 and 58 mg.kg$^{-1}$ respectively. The MDDAS pattern measured with 6HFN ED$_{50}$ was different from those classically observed with the reference AEDs, but the decrease in seizure duration suggests a GABAergic mechanism. The toxic doses (TD$_{50}$) determined by using the rotarod test were > 200, 150 and 80 mg.kg$^{-1}$ for 6HFN, 6HF and FN respectively. The only molecule giving an interesting protective index (PI = TD$_{50}$/ED$_{50}$) was 6HFN, which had a PI of 35.7 in the PTZ test and 6.2 in the MDDAS test. Among the three flavonoids, HFN was the best anti-epileptic drug, acting mainly through the GABAergic reinforcing effect.

Neuroprotective potential of chronic rapeseed oil diet in magnesium-deficient mice, evaluated by audiogenic seizure test

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Omega3 alphanlinolenic acid [18:3n-3, ALA] is relevant in preventing brain dysfunctions. It represents 9% of rapeseed oil but is absent in omega6 rich sunflower or corn oils. The audiogenic seizure (MDDAS) test has been validated in magnesium-deficient-mice individually exposed to a calibrated sound stimulus. It presents 4 successive phases: (i) Wild Running Latency (WRL), (ii) Wild Running (WR), (iii) Tonic Seizure (TS) and (iv) Recovery (R) the durations of which may indicate the underlying mechanisms of compounds tested. Two groups of mice (n = 8) were fed magnesium-deficient diets containing 5% vegetable oils, either omega6 (sunflower: corn 1:3) or omega3 (rapeseed) for 32 days. They were afterwards subjected to the MDDAS test.

Omega3 alphanlinolenic acid [18:3n-3, ALA] is relevant in preventing brain dysfunctions. It represents 9% of rapeseed oil but is absent in omega6 rich sunflower or corn oils. The audiogenic seizure (MDDAS) test has been validated in magnesium-deficient-mice individually exposed to a calibrated sound stimulus. It presents 4 successive phases: (i) Wild Running Latency (WRL), (ii) Wild Running (WR), (iii) Tonic Seizure (TS) and (iv) Recovery (R) the durations of which may indicate the underlying mechanisms of compounds tested. Two groups of mice (n = 8) were fed magnesium-deficient diets containing 5% vegetable oils, either omega6 (sunflower: corn 1:3) or omega3 (rapeseed) for 32 days. They were afterwards subjected to the MDDAS test.
Their spontaneous locomotor activity (for 3 min), showed that magnesium deficiency induced central nervous hyperexcitability in the omega6 but not in the rapeseed group (152.7 ± 37.9 versus 97.0 ± 22.5). In the MDDAS test, the mice responses differed with the diets: 1) The number of convulsive mice was lower in the rapeseed group (50%) as compared to the omega6 group (100%). In addition, all the mice convulsing in the rapeseed group recovered whereas 50% died in the omega6 group. 2) The pattern of seizures was different. The time periods of the first two phases of the audiogenic test increased significantly in the rapeseed group: WRL and WR were 6.7 ± 5.5 and 3.7 ± 0.5 sec versus 4.0 ± 1.4 and 2.3 ± 0.4 sec respectively in the omega6 group, and TS decreased slightly while R remained similar in the two groups. These differences are indicative of an inhibiting effect of the rapeseed oil on seizures, mediated partly by Na+ voltage-dependent channels but the global pattern is rather GABAergic. To conclude, chronic consumption of rapeseed oil could help to reduce neuronal disorders observed in magnesium-deficient mice, an animal model of audiogenic seizures.

The modifications of plasma, erythrocyte and urinary magnesium in diabetic patients compared to non-diabetic ones

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The values of plasma, erythrocyte and urinary magnesium are different in diabetic patients compared with non-diabetic ones, the degree of metabolic control being an important factor implicated in magnesium value modifications. We studied 180 diabetic patients and a control group of 70 non-diabetic patients. For all patients we determined through spectrophotometric method the following: plasma, erythrocyte and urinary Mg. The degree of metabolic control was calculated by the values of glycaemia and Hb A1c. The prevalence of subnormal plasma Mg is significantly greater in type 1 DM compared with type 2 DM (p < 0.04) and strongly increased in type 1 DM compared with the control group (p < 0.001). The prevalence of lower erythrocyte Mg is greater in type 1 DM compared with type 2 DM, but without significant differences (p > 0.05). The urinary magnesium presents a prevalence of significantly increased values in type 1 DM patients compared with type 2 DM (p < 0.05) and significantly bigger between type 1 DM and the control group (p < 0.04). In type 1 diabetic patients, the magnesium deficit was present in 20% of those with good metabolic control, in 63.6% of those with medium metabolic control and in 75% of those metabolically uncontrolled. In type 2 DM patients, the magnesium deficit was present in 14.55 of the well controlled ones, in 58.5% of those with a medium control and in 73.1% of those insufficiently metabolically controlled. Conclusions: 1) The prevalence of magnesium deficit is greater in diabetic patients compared with the non-diabetic ones and in type 1 DM compared with type 2 DM. 2) The prevalence of magnesium deficit increases at the same time as the decrease of metabolic control, from good to insufficient.

The correlation between magnesium deficit and insulinoresistance

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The magnesium (Mg) ion is a cofactor of insulin activity, and its deficit is associated to insulin resistance and the presence of insulin resistance will induce a decrease of Mg penetration into the cells. The magnesium deficit determines an increase in insulin secretion. We studied 250 obese patients who presented insulin resistance and a control group consisting of 100 non-obese without insulin resistance. The patients were between 30 and 60 years old. In all patients we measured: plasma Mg, erythrocyte Mg and urinary Mg using the spectrophotometric method. In all patients the insulin resistance was detected through the HOMA method. Patients with obesity and insulin resistance presented an Mg deficit in a percentage of 68% while the control group presented only 25%. The prevalence of magnesium deficit was 2.7 times greater in the patients with increased secretion of insulin compared to the patients without this increase. (p < 0.001) Mg deficit was shown as an increase in plasma and erythrocyte Mg and as an increase of the urinary one. In patients with insulin resistance a dominant decrease of the intra-erythrocyte Mg at 56% was noted, and in those without insulin resistance the deficit of intra-erythrocyte magnesium was noted at 24%. We see lower average values for plasma and erythrocyte magnesium in the patients with obesity and insulin resistance compared with the non-obese patients. Also, the urinary elimination is increased in the obese patients compared with the non-obese ones. The
patients with obesity and insulin resistance presented a significantly increased magnesium deficit prevalence compared with the ones without insulin resistance. The most exact parameter showing the presence of magnesium deficit was the decreased erythrocyte magnesium.

Factors influencing magnesium nutritional status in apparently healthy pregnant women
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Literature provides evidence that an inadequate magnesium (Mg) nutritional status may be involved in several disorders that can occur during pregnancy. We aimed to identify socioeconomic, dietary, environmental factors associated with Mg status in an apparently healthy pregnant women group.

The group investigated involved 433 pregnant women, 18-39 years of age, in different stages of pregnancy. Serum and erythrocyte Mg levels were determined. The women were asked about their socio-economic status (residence, marriage, parity, religion, education, employment, income), the frequency of food consumption and 24 h recall of food intake, smoking habits, physical activity, mineral supplements. Stress was investigated using a questionnaire with 20 items. The total energy and energy of the main nutrients were estimated. The relationships between Mg and different factors were investigated using the Pearson correlation index (r), ANOVA test and “chi squared” test. The relationships of Mg with factors that are not dependent on the gestational age were followed using values of Mg levels adjusted by this parameter. The Mg level is directly related to total and animal lipids and proteins and indirectly related to calories, carbohydrates, vegetal lipids, potatoes, coffee, excess bread consumption (p < 0.05 in all cases). Serum Mg level was negatively related with stress (p = 0.012). No relation was found between the Mg level and smoking habits. The erythrocyte Mg level was indirectly associated with daily walking distance (p = 0.027). The women supplemented with calcium, zinc, iron but also Mg had lower Mg serum or erythrocyte Mg levels (p < 0.050 in all cases). The adjusted Mg levels were higher in the married women (p = 0.034), the orthodox ones (p = 0.025) and in those with a higher income (p = 0.030). Our study on healthy pregnant women emphasized that Mg levels correlated or were associated with diet, socio-economic status (marriage, religion, and income), stress and physical activity and with mineral supplements. Some recommendations were elaborated.

Magnesium status in dialysed chronic kidney diseases
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Trace element status in kidney diseases has become a subject of discussion for clinicians. The serum magnesium level was determined by using the spectrophotometer laboratory technique for 60 patients with between 1-19 years of dialysis. The ages of these patients, M and F, was between 40-73. The clinical disorders they presented were: chronic obstructive nephropathy, kidney sclerosis, glomerulonephritis, and other chronic kidney problems. 50% of them had several risk factors for kidney pathology and 18 of these were heavy smokers. The aim of this preliminary study was to assess the serum magnesium level in connection with the particular kidney pathology. The data shows almost reference values of the different medical situations.