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Comparison of penetration rates of magnesium through the rat ileum for selected organic salts

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Magnesium is necessary for growth and many basic functions of living organisms [1, 2]. The deficiency of magnesium in humans could be treated by a proper diet or medication [3–5]. Many magnesium preparations are administered prophylactically as well as for curative purposes in magnesium deficiency [4, 5]. The absorption rates of magnesium are relatively low: only 30–40% of the dose are absorbed in the ileum [6, 7]. Usually, magnesium in preparations contain inorganic compounds e.g.: chloride, oxide, carbonate, sulphate or organic salts e.g., asparaginate, lactate, gluconate, citrate, and ascorbate.

Fumarates of selected elements were applied for therapeutical purposes, e.g., ferrous fumarate in anemias caused by a deficiency of iron. The ferrous fumarate was characterised by the lowest toxicity and a high bioavailability among the studied iron preparations [8, 9]. Magnesium fumarate has a magnesium content higher then magnesium gluconate (ca. 17.6% vs. 5.9%). The mentioned salt rejoins curative properties of magnesium and fumaric acid [10]. Up to now, no wide use of magnesium fumarate in supplementation therapy is reported in the accessible literature.

The intention of our study was to compare *in vitro* the penetration rates of magnesium available from the organic magnesium salts: fumarate and gluconate and the inorganic magnesium chloride. An apparatus containing a segment of reversed rat's ileum introduced into the circulating 0.9% sodium chloride aqueous solution was used for measuring the penetration rate of magnesium through the ileum.

The penetration rates of magnesium in %, determined for the studied solutions containing various magnesium concentrations after two hours of the experiment time are presented in the Table. The higher absorption rate of magnesium was observed for the fumarate solutions in comparison to the gluconate and chloride solution. Differences between the penetration rates of magnesium gluconate and fumarate were statistically significant ($p < 0.05$) in comparison to magnesium chloride. The penetration process of magnesium had higher velocity at the beginning of the experiment. The total quantity of magnesium absorbed decreased with a decrease in the concentration difference of magnesium in the two liquids used in the *in vitro* system: the stationary liquid containing magnesium salt and the eluent. According to published data [11, 12], a higher bioavailability and a lower toxicity were observed for the organic magnesium compounds. Szyszka *et al.* [12] assumed that no preference for any of the studied magnesium salt was observed. Preparations of magnesium characterised by an increased availability and low side effects could be very appreciated. In such cases the therapeutic dose might be decreased considerably. Magnesium fumarate fulfills these demands and could be introduced for magnesium deficiency therapy in humans.

The results of the magnesium absorption measurements carried out *in vitro* indicated that the absorption rate from magnesium fumarate solution is 5.4% higher than from the magnesium gluconate, and 17.3% higher than from magnesium chloride solutions. In the studied concentration range no influence of the magnesium dose on the absorption rate was observed.

Table: Parameters describing Mg^{2+} ions absorption from magnesium preparation in a small intestine

Magnesium solution		Amount of absorbed Mg^{2+} ions after 120 min (%)	W (%)	K (min^{-1})	$t_{50\%}$(min)
Magnesium concentrations (mM)	Magnesium salts				
0.82	Magnesium fumarate	47.80 ± 1.24*	2.59	0.006253	110.84
0.82	Magnesium gluconate	45.60 ± 1.36*	2.98	0.005958	116.31
0.82	Magnesium chloride	39.40 ± 1.07	2.72	0.005077	136.51
4.20	Magnesium fumarate	47.10 ± 1.99*	4.24	0.006170	112.32
4.20	Magnesium gluconate	44.50 ± 2.02*	4.55	0.005745	120.63
4.20	Magnesium chloride	39.60 ± 1.42	3.59	0.005131	135.07
8.10	Magnesium fumarate	48.20 ± 1.20*	2.49	0.006274	110.45
8.10	Magnesium gluconate	46.40 ± 1.30*	2.80	0.006019	115.14
8.10	Magnesium chloride	40.10 ± 1.28	3.21	0.005194	133.43

* $p < 0.05$ compared with magnesium chlor

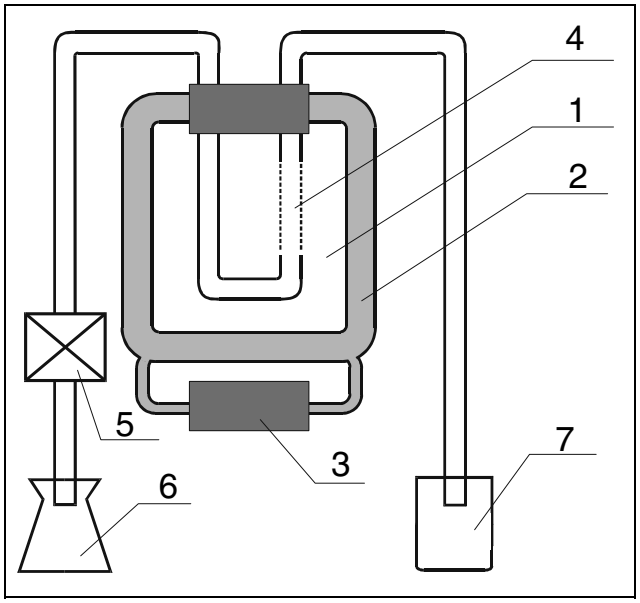

Fig. 1: Apparatus for determination of drug penetration through the studied membranes
Legend: 1 – glass chamber; 2 – water mantle; 3 – thermostatic unit (type 304); 4 – the membrane studied (the reversed primary segment of the rat's ileum, Wistar race); 5 – peristaltic pump (type 324 Zalimp, Unipam, Warsaw, Poland); 6 – container of the eluent (0.9% aqueous sodium chloride solution); 7 – waste container.

Experimental

The following substances were used for investigations: magnesium fumarate (obtained from the Nitrogen Plant, Kedzierzyn-Koźle, Poland), sodium chloride, magnesium chloride (from POCH, Gliwice, Poland), and magnesium gluconate (from Fluka, Switzerland). The magnesium concentration was measured by atomic absorption spectrometry using standard solutions of magnesium chloride obtained from the Polish Committee for Standardisation, WZORMAT.

Adult male Wistar rats with a mean body weight of 370 g were used for the experiments. The experiments were performed with 54 animals. The small intestine was removed under Halothane anesthesia, cleaned with 0.9% saline solution and connected to the flow apparatus immediately. Each experiment was carried out with fresh segment of ileum. The penetration measurements were carried on *in vitro* in the flow apparatus, presented in the Fig. [13].

In the glass chamber containing 30 ml of the studied drug dissolved in 0.9% NaCl aqueous solution the primary, a reversed segment of the rat ileum was placed. The eluent was composed of the aqueous solution containing 0.9% NaCl and circulated through the ileum at a rate of 1.2 ml/min during 2 h.

The temperature was stabilised at 37 ± 1 °C. The fractions were collected every 15 min and their magnesium content was measured by atomic absorption spectrometry at a wavelength of 285.2 nm. The limit of detection was below 0.007 μg/ml. Measurements of the magnesium penetration were carried out using the following magnesium salts: fumarate, gluconate and chloride for three concentrations: 0.82; 4.2 and 8.1 mM/l Mg. The measurements were repeated six fold in order to minimise statistical errors. Standard deviation (SD) and variation (W) were determined. The t-test of Student was used in order to assess the statistical significance of data obtained.

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