ELSEVIER

Journal of Nutritional Biochemistry 15 (2004) 185–189

THE JOURNAL OF Nutritional Biochemistry

Proabsorptive effect of gum arabic in isotonic solutions orally administered to rats: effect on zinc and other solutes

Mahmoud A. Ibrahim[a], Nina Kohn[b], Raul A. Wapnir[a,*]

[a]*Division of Perinatal/Neonatal Medicine, Schneider Children's Hospital at North Shore, North Shore–Long Island Jewish Health System, 300 Community Drive, Manhasset, NY 11030, USA*

[b]*Biostatistics Unit, North Shore–Long Island Jewish Research Institute, North Shore–Long Island Jewish Health System, 300 Community Drive, Manhasset, NY 11030, USA*

Received 22 July 2003; received in revised form 24 October 2003; accepted 12 November 2003

Abstract

We have previously shown that the addition of gum arabic (GA) to oral rehydration solution (ORS) enhances water and electrolyte absorption during jejunal perfusion in rats under anesthesia. This study investigates whether GA by oral administration could be equally effective in rats.

Isotonic solutions containing 25 g/L GA (A_G), or without GA (A_0) were administered via oral tube to lightly anesthetized adult female rats. Similar experiments were conducted with hypertonic solutions containing no GA (B_0), or either 10 (B_{10}) or 50 g/L GA (B_{50}). Blood concentrations of sodium, glucose, glutamate, zinc, and tritiated water were determined at 0, 15, 30, 60, 90, 120, and 180 minutes, and results between treatments were compared. Administration of the isotonic, GA-containing solution (A_G) resulted in a higher blood zinc level than with the isotonic GA-free solution (A_0) from 15 minutes throughout 180 minutes. Blood zinc at 15 minutes (means ± SEM) was as follows: for A_0: 69.3 ± 2.0, for A_G: 83.4 ± 3.5 nmol/L, $P = 0.002$. At 180 minutes, A_0: 52.6 ± 1.8; A_G: 68.1 ± 4.6 nmol/L, $P = 0.004$. The corresponding areas under the curve (AUC) were as follows: for A_0: 10,737 ± 214; for A_G: 13,919 ± 765 nmol × min/L, $P < 0.001$). Glucose, glutamate, sodium, and tritiated water body distribution presented no differences in blood concentrations. For sodium and tritiated water body distribution, there was a significant time effect ($P < 0.0001$). In hypertonic solutions, blood zinc levels declined over time, possibly due to their osmotic, counter-absorptive action, thus obscuring possible opposite effects of GA. GA appears to be an effective enhancer of zinc absorption when orally administered in isotonic solutions to laboratory animals. This proabsorptive capacity could be attributed to some of the physicochemical and biochemical properties of GA and suggest possible applications of GA in liquid formulas and solid food preparations.

Keywords: Zinc; Gum arabic; Intestinal absorption; Diarrhea; Growth

1. Introduction

The limitations of sodium–glucose formulations in oral rehydration solutions (ORS) for the treatment of acute diarrhea have prompted attempts to improve electrolyte and water absorption by introducing additional organic nonelectrolytes, known to be cotransported with sodium. These substances are intended to support the role of glucose in recruiting sodium for transport across the intestinal mucosa. The most extensively tested additives have been the amino acids glycine, alanine, and glutamine. However, none of these additives have provided unquestionable success because of resulting hypertonicity, competition with glucose for the sodium cotransporter, and instability in solution [1–3]. Other avenues to improve ORS rehydration effectiveness and the speed of recovery from diarrheal episodes have included reducing the osmolality, altering the carbohydrate composition, and supplementation with zinc, *Lactobacilli*, and/or soluble fiber [4–6]. Specifically, it has been shown that an ORS supplemented with 40 mg/L of zinc was moderately efficacious in reducing the severity of diarrhea in children [7]. Furthermore, zinc supplementation, in the range of 10–20 mg/day (0.15–0.30 mmol/day), in addition to a standard ORS, was reported to lower the morbidity and mortality of infants and children with diarrheal disease [8, 9].

In preceding studies we have shown that gum arabic

* Corresponding author. Tel.: (516) 562-3889; Fax: (516) 562-1170.
E-mail address: rwapnir@nshs.edu (R.A. Wapnir).

0955-2863/04/$ – see front matter
doi:10.1016/j.jnutbio.2003.11.003

(GA) improved small intestinal absorption of water, glucose, and electrolytes in normal rats, and more so under conditions mimicking diarrheal diseases [10–12]. The beneficial effects of GA have been associated with its nitric oxide (NO) scavenging property [13], its indirect modification of basolateral membrane potassium channels [14], and its enhancement of intestinal paracellular transport [15, 16].

We have shown that rats with osmotic-secretory diarrhea induced by oral magnesium citrate and phenolphthalein had a faster recovery when presented with an ORS containing GA than with either a plain ORS or water [12]. These data suggest that GA could be similarly effective when consumed orally as much as when directly introduced distally from the stomach, as done in the studies of intestinal perfusions under anesthesia [10–16]. To verify these results, the experiments presented here were intended to determine whether different types of solutes and water were more rapidly absorbed from solutions containing GA than in the absence of this additive. The tests were conducted by tube administration into the stomach of rats of preparations with or without GA, and monitoring the absorption rate via sequentially determined blood concentrations.

2. Methods and materials

2.1. Experimental animals

We used female Sprague-Dawley rats with an initial weight of 150–170 g, purchased from Taconic Farms (Germantown, NY) and acclimated in the animal facility for at least 48 hours before the experiments. Solid food (Rodent Chow, Harlan-Teklad, Madison, WI) was withheld overnight from animals to be used the following morning. The test solutions were administered under CO_2 anesthesia using a 3-inch stainless steel feeding tube (Yale 16) attached to a 3-mL syringe.

2.2. Test solutions

Two types of solutions were used. Type [A_0] was isotonic and contained 75 mmol/L D-glucose, 60 mmol/L NaCl, 25 mmol/L Na glutamate, and 15 mmol/L zinc chloride. The GA-containing version of this solution [A_G] contained 25 mg/mL of GA plus the remaining components. The hypertonic test solution [B_0] was similar to a preparation for a glucose tolerance test and contained 2.78 mol/L (500 mg/mL) D-glucose, 2.5 mmol/L zinc chloride, and 5 mmol/L Na glutamate. The same solution was also prepared with additions of either 10 [B_{10}] or 50 mg/mL [B_{50}] GA. All formulas also contained ± 70 kBq/L of ^3H_2O and were administered by oral tube at a dose of 1 mL/100 g body weight. The precise volume introduced was determined by weighing the syringe before and after intubation and fluid delivery. The specific gravity of the solutions was taken into consideration to calculate the volume.

2.3. Experimental procedure and assays

Before administering the solutions orally the animals were anesthetized by CO_2 and a baseline blood specimen of 0.3–0.4 mL was obtained from the suborbital sinus. After the oral dose of each solution, also given under anesthesia (as indicated in "Experimental animals" section), blood samples of 0.3–0.4 mL were obtained from the same route at 15, 30, 60, 90, 120, and 180 minutes. The samples were collected in heparinized tubes and the amount collected was determined by weighing. After the last blood drawing, the rats were euthanized by CO_2 overdose. The protocol described above was approved by the Institutional Animal Care and Utilization Committee. Whole blood specimens were deproteinized with two volumes of 1.1 mol/L $HClO_4$. The samples were centrifuged at $600 \times g$ and the supernatants neutralized with an equal volume of ice-chilled 2.0 mol/L K_2HPO_4. After centrifugation at $600 \times g$ and 4°C, the supernatants were used for the assays described below.

Glucose was determined by a spectrophotometric method (Sigma 510-DA; Sigma-Aldrich, St. Louis, MO); sodium and zinc were assayed by atomic absorption spectrophotometry using external standards (Varian SpectrAA-10; Varian Analytical Instruments, Walnut Creek, CA); and glutamate was determined by an enzymatic method [17]. For estimation of water absorption using the isotope dilution method, counts of ^3H_2O (Packard 1900TR; PerkinElmer Life Sciences, Boston, MA), minus background, were extrapolated to total body water, assuming it was 55% of body weight. If necessary, data were corrected from the actual dose administered to 1 mL/100 g body weight.

2.4. Statistical analyses

Data were analyzed using three methods. Repeated measures analysis of variance (RMANOVA), where solution type was the between subjects effect and time was the within subjects effect, was used to examine the relationship between solution and time for each solution. Significant interactions were assessed using pairwise comparisons at each time point within the RMANOVA model (SAS Institute Inc., Cary, NC). The area under the curve (AUC) calculations were based on the trapezoidal method for each rat, and the differences between the two treatments with isotonic solutions (type A) were analyzed by ANOVA. Graphic representation of results was done with Sigmaplot® (SPSS Inc., Chicago, IL). Trends were evaluated using the Cuzick test based on Wilcoxon's approach [18].

3. Results

3.1. Isotonic solutions

Absorption of one of the solutes, zinc, showed that the A_G solutions yielded consistently higher blood zinc concen-

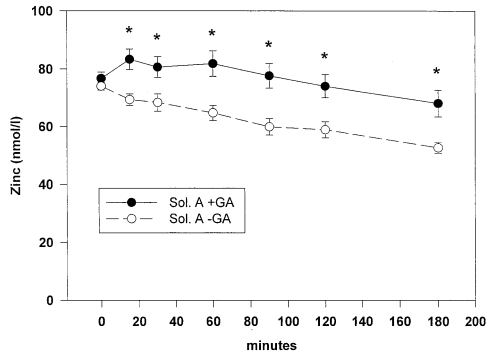

Fig. 1. Blood zinc concentrations after oral administration of isotonic solutions (type A) containing (+GA) or omitting 25 mg/mL of GA (-GA). The error bars represent the SEM. The asterisks denote significant differences ($P< 0.05$) at various time points as determined by RMANOVA. The AUC for both series of data was significantly different ($P< 0.001$). The number of animals for each data point was between 10 and 13 and is the same as in Table 1.

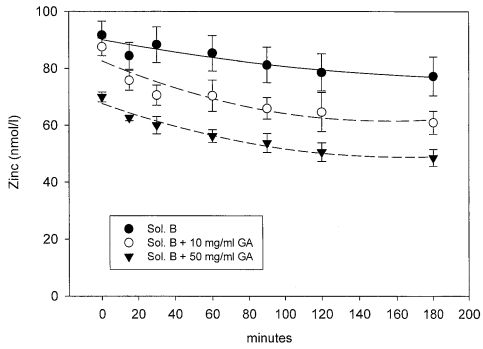

Fig. 2. Blood zinc concentrations after oral administration, via intubation of hypertonic solutions containing no GA (Sol. B), or the same solution with either 10 or 50 mg/mL of GA. The graphic representation follows the features described under Fig. 1. The number of rats included in each time point varied between five and nine and is stipulated in Table 2.

trations than with the GA-free A_0 solutions from 15 minutes onward (Fig. 1). The greater AUC of A_G solutions was consistent with a greater absorption rate (A_0: 10,737 ± 214; A_G: 13,919 ± 765 nmol × min/L, $P< 0.001$). Glucose and glutamate, two other components in the isotonic solutions, showed no differences in blood concentrations over time. The omission or inclusion of GA produced no differences (Table 1). Throughout the 180 minutes of the experiment, tritiated body water distribution was similar after administration of either the A_0 or the A_G solutions. The same was found for blood sodium levels. However, in both cases there was a significant time effect (RMANOVA, $P < 0.0001$) consistent with a progressive increase in blood sodium concentrations in the course of the sample collection period (Table 1).

3.2. Hypertonic solutions

Body distribution of labeled tritiated water presented a significant time effect (RMANOVA, $P < 0.0001$), although there were no differences among the three hypertonic solutions: either without GA (B_0), or with either 10 mg/mL (B_{10}) or 50 mg/mL (B_{50}) of the additive (Table 2). Because these solutions contained no sodium, this electrolyte was not monitored during the experiments. The administration either of the hypertonic solutions B_0, B_{10}, or B_{50} produced significant differences in glucose concentrations over time. Glutamate, however, showed a marginal time effect (RMANOVA, $P= 0.0459$), although there were no differences among solutions. The B_0 solution showed a decreasing trend over time (Cuzick test, one-tailed, $P = 0.0279$); however, neither the B_{10} nor the B_{50} solutions exhibited significant variations over the 3-hour period. In contrast, zinc concentrations were different as time went on after the oral administration (RMANOVA, $P = 0.0154$) (Fig. 2). Pairwise comparisons revealed that plasma concentrations of zinc with the B_0 solution were significantly higher than with the B_{50}. There were no differences between the results of B_{10} and B_{50} solutions.

Table 1
Total body water distribution, blood sodium, glucose, and glutamate after administration of isotonic solutions without (A_0) or with 25 mg/mL (A_G) GA

	Treatment	Initial	15 min	30 min	60 min	90 min	120 min	180 min
Total body water % of ^3H_2O dose (n)	A_0	—	36.3 ± 4.0 (13)	41.9 ± 3.6 (13)	44.4 ± 3.7 (13)	48.2 ± 3.6 (13)	50.7 ± 3.5 (13)	52.0 ± 3.5 (13)
	A_G	—	34.2 ± 3.9 (13)	40.0 ± 3.7 (13)	44.8 ± 3.7 (13)	47.8 ± 4.6 (12)	49.2 ± 4.2 (12)	48.4 ± 5.4 (11)
Blood sodium mmol/L (n)	A_0	88.3 ± 3.7 (13)	92.1 ± 1.8 (12)	95.1 ± 2.0 (13)	97.2 ± 2.4 (12)	94.4 ± 2.1 (12)	101.6 ± 3.1 (12)	102.0 ± 3.1 (11)
	A_G	92.4 ± 2.3 (12)	102.6 ± 6.7 (12)	105.8 ± 6.1 (13)	105.2 ± 6.0 (12)	111.6 ± 8.4 (11)	112.9 ± 7.6 (12)	117.9 ± 8.3 (10)
Blood glucose mmol/L (n)	A_0	2.51 ± 0.11 (13)	3.50 ± 0.13 (13)	4.13 ± 0.37 (13)	3.60 ± 0.14 (13)	3.77 ± 0.15 (13)	4.83 ± 0.15 (13)	5.03 ± 0.33 (13)
	A_G	2.22 ± 0.16 (13)	3.86 ± 0.17 (13)	3.93 ± 0.16 (13)	4.34 ± 0.32 (13)	4.82 ± 0.44 (12)	5.07 ± 0.44 (12)	5.74 ± 0.66 (11)
Blood glutamate nmol/L (n)	A_0	245 ± 39 (13)	204 ± 19 (13)	215 ± 24 (13)	235 ± 22 (12)	220 ± 29 (13)	235 ± 30 (13)	232 ± 29 (12)
	A_G	182 ± 20 (13)	208 ± 34 (13)	228 ± 33 (13)	222 ± 33 (13)	227 ± 45 (12)	217 ± 34 (12)	206 ± 46 (11)

All values are means ± SEM.
A very significant time effect ($P < 0.0001$) was observed for tritiated water body distribution and blood sodium.

Table 2
Total body water distribution and blood glutamate after administration of hypertonic solutions without or with 10 mg/mL (B_{10}) or 50 mg/mL (B_{50}) GA

	Treatment	Initial	15 min	30 min	60 min	90 min	120 min	180 min
Total body water % of ^3H_2O dose (n)	B_0	—	21.7 ± 4.5 (9)	29.3 ± 5.2 (9)	40.2 ± 5.0 (9)	47.9 ± 6.7 (9)	52.8 ± 5.0 (9)	58.9 ± 5.4 (9)
	B_{10}	—	20.8 ± 4.3 (8)	29.6 ± 5.2 (8)	43.5 ± 5.0 (8)	44.6 ± 7.4 (8)	60.4 ± 3.7 (8)	60.2 ± 6.9 (8)
	B_{50}	—	23.8 ± 1.6 (9)	30.9 ± 2.7 (9)	40.2 ± 3.3 (9)	50.3 ± 3.9 (9)	57.1 ± 4.1 (9)	60.5 ± 3.0 (9)
Blood glutamate nmol/L (n)	B_0	300 ± 65 (6)	273 ± 40 (6)	240 ± 36 (6)	234 ± 40 (6)	228 ± 18 (5)	237 ± 39 (6)	211 ± 35 (6)
	B_{10}	373 ± 73 (9)	307 ± 51 (8)	303 ± 72 (8)	350 ± 79 (9)	309 ± 88 (7)	281 ± 48 (8)	268 ± 34 (9)
	B_{50}	417 ± 50 (6)	335 ± 13 (5)	327 ± 12 (6)	317 ± 14 (6)	339 ± 31 (6)	289 ± 20 (6)	264 ± 53 (6)

All values are means ± SEM.

A very significant time effect ($P < 0.0001$) was observed for tritiated water body distribution but no differences among solutions. There was a marginal time effect ($P = 0.0459$) for blood glutamate and a specific decrease trend over time ($P = 0.0279$) for the B_0.

4. Discussion

We found that GA added to an isotonic solution produced higher serum zinc levels from the first sampling after oral tube delivery of the solutions throughout the end of the experiment, as compared to the solutions without GA, a result consistent with a more rapid rate of zinc uptake and distribution. Peak blood zinc concentrations in the presence of GA were achieved after 15 minutes and a progressive decline occurred thereafter. Rats given solutions omitting GA showed a decline in blood zinc concentrations throughout the experimental period, an effect attributable to the volume expansion associated with the fluid administration in the oral load.

Because zinc was included in the solutions as a soluble, ionized salt, it may have reached the circulation via bulk paracellular transport [19, 20]. As opposed to other ingredients of the isotonic solutions, zinc was added at a relatively high concentration, purposely elevated to facilitate discrimination of a GA effect. In contrast, what could be considered an indicator of bulk transport, the body distribution of tritiated water, exhibited no differences between treatments, possibly because water equilibration process may proceed independently of membrane translocation of a hydrated divalent cation such as zinc. This indicates that, under the conditions of the experiments, that is, when orally ingested in isotonic solution, GA does not affect fluid movement. This stands in contrast to some of the data previously obtained using rat intestinal perfusions, particularly in models of gastrointestinal dysfunction, where net water absorption was increased [11]. Although there were no differences in blood sodium levels attributable to GA, the time pattern for sodium consistently paralleled that of zinc. There has been some previous evidence that zinc may be at least partially cotransported with sodium [21]. Given the presence in these solutions of a much larger glucose concentration, it is not possible to elucidate whether zinc cotransport is operational in these experiments, or whether sodium is mostly involved in glucose translocation by the SGLT1 transporter [22]. GA has been shown earlier to enhance sodium absorption in rat jejunum, particularly under conditions mimicking chronic diarrhea [10, 11]. Oral administration of a solution of modest sodium concentration, in the presence of glucose, does not provide optimal conditions to discriminate whether GA could produce sodium absorption enhancement.

The understanding of mediated zinc transport in the gastrointestinal tract has been better defined in recent studies. The divalent cation transporter-1 transporter is a transmembrane polypeptide found in the crypts and lower villar cells of the duodenum, capable of translocating several divalent metals including zinc [23, 24]. Another group of zinc carriers involved in cellular zinc uptake are the ZIP transporters. Several of the members of the ZIP family of transporters have been identified in plants and certain animal cells, including the Caco-2 intestinal cell line [25]. The ZIP transporter family (ZRT, IRT-like proteins) may be involved in releasing zinc or sequestering zinc within cells [24]. The ZnT1 transporter is located apically adjacent to the brush borders, whereas the ZnT4 transporter is located at both the apical and basolateral membranes [24]. From the data obtained in the present studies, it cannot be determined whether a specific zinc transporter may be operational under the experimental conditions.

In the experiments presented here, it was of interest that zinc given orally in hypertonic solutions produced a decline in blood zinc concentrations in the course of the 3-hour sampling period. The data showed comparable behavior for the three hypertonic solutions. The group of rats fed the hypertonic solution with 50 g/L GA (B_{50}) had different initial values than the B_0 (hypertonic, no GA) and the B_{10} (hypertonic, 10 g/L GA), although the time sequence patterns were similar. It may be possible that the “dumping” effect of hypertonicity, pulling fluid into the gastrointestinal tract, is strong enough to overcome any proabsorptive effect of GA, which would tend to direct fluid from lumen to serosa. The significant differences observed between the isotonic and hypertonic solutions in tritiated water distribution at 15 and 30 minutes, regardless of the presence of GA, support this contention. The much lower percentage of tritiated water in the B_0, B_{10}, and B_{50}, than in the A_0 or A_G

at those times (Tables 1 and 2) is consistent with this possibility.

Glutamate presented no significant differences at any time in blood levels, after administration via gastric tube of isotonic or hypertonic solution, either containing or omitting GA. Glutamate has active transport systems with either sodium-dependent or sodium-independent carriers [26, 27]. Under the current experimental conditions it is apparent that the contents of the intestinal lumen neither affect the rate of glutamate transport nor modulate the activity of the transmembrane carriers. No interaction between zinc and either sodium or glutamate could be ascertained.

It is of potential clinical interest that GA apparently enhances zinc absorption, in view of the role of zinc supplementation in chronic and acute diarrhea of infancy and childhood. Hence, in addition to its general proabsorptive properties, GA may specifically improve the absorption of a mineral element with a well documented role in the physiopathology of chronic diarrhea of childhood, a condition documented to be aggravated in overt or subclinical zinc deficiencies [7–9]. In conclusion, the addition of GA to orally ingested isotonic solutions produces changes in the rate of zinc absorption consistent with a facilitation of its uptake. To a limited extent, other test solution constituents respond favorably to the addition of GA. These results support the hypothesis attributing proabsorptive properties to this natural soluble fiber. Additional studies will be needed to confirm further the potential of GA as an additive in special diets or liquid formulas, and to explore the possibility that other mineral elements or poorly absorbed medications may be more effectively assimilated in conjunction with GA use.

Acknowledgments

This work was supported in part by a grant of the North Shore-Long Island Jewish Research Institute.

References

[1] Michell AR. Oral rehydration for diarrhoea: symptomatic treatment or fundamental therapy. J Comp Pathol 1998;118:175–93.
[2] Duggan C. Glutamine-based oral rehydration solutions: the magic bullet revisited? J Pediatr Gastroenterol Nutr 1998;26:533–5.
[3] Rhoads M. Management of acute diarrhea in infants. J Parenter Enter Nutr 1999;23:S18–9.
[4] Bhan MK. Current and future management of childhood diarrhoea. Int J Antimicrob Agents 2000;14:71–3.
[5] Wapnir RA. Recent progress and future aims in the formulation and use of oral rehydration solutions. Int Pediatr 2000;15:205–14.
[6] Farthing MJ. Oral rehydration: an evolving solution. J Pediatr Gastroenterol Nutr 2002;34:S64–7.
[7] Bahl R, Bhandari N, Saksena M, Strand T, Kumar GT, Bhan MK, Sommerfelt H. Efficacy of zinc-fortified oral rehydration solution in 6- to 35-month-old children with acute diarrhea. J Pediatr 2002;141: 677–82.
[8] Bhandari N, Bahl R, Taneja S, Strand T, Molbak K, Ulvik RJ, Sommerfelt H, Bhan MK. Substantial reduction in severe diarrheal morbidity by daily zinc supplementation in young North Indian children. Pediatrics 2002;109:e86.
[9] Baqui AH, Black RE, El Arifeen S, Yunus M, Chakraborty J, Ahmed S, Vaughan JP. Effect of zinc supplementation started during diarrhoea on morbidity and mortality in Bangladeshi children: community randomized trial. Br Med J 2002;325:1059.
[10] Wapnir RA, Teichberg S, Go JT, Wingertzahn MA, Harper RG. Oral rehydration solutions: enhanced sodium absorption with gum arabic. J Am Coll Nutr 1996;15:377–82.
[11] Wapnir RA, Wingertzahn MA, Moyse J, Teichberg S. Gum arabic promotes rat jejunal sodium and water absorption from oral rehydration solutions in two models of diarrhea. Gastroenterology 1997;112: 1979–85.
[12] Teichberg S, Wingertzahn MA, Moyse J, Wapnir RA. The effect of gum arabic in an oral rehydration solution on recovery from diarrhea in rats. J Pediatr Gastroenterol Nutr 1999;29:411–7.
[13] Rehman R, Wingertzahn MA, Harper RG, Wapnir RA. Nitric oxide scavenging by a soluble fiber: implications in gastrointestinal disease. J Invest Med 2000;48:215A.
[14] Rehman K, Wingertzahn MA, Harper RG, Wapnir RA. Proabsorptive action of gum arabic: regulation of nitric oxide metabolism in the basolateral potassium channel of the small intestine. J Pediatr Gastroenterol Nutr 2001;32:529–33.
[15] Wingertzahn MA, Teichberg S, Wapnir RA. Stimulation of non-sodium dependent water, electrolyte and glucose transport in rat small intestine by gum arabic. Digest Dis Sci 2001;46:1105–12.
[16] Rehman KU, Wingertzahn MA, Teichberg S, Harper RG, Wapnir RA. Gum arabic (GA) modifies paracellular water and electrolyte transport in the small intestine. Digest Dis Sci 2003;48:755–60.
[17] Bernt E, Bergmeyer H-U. L-glutamate determination with glutamate dehydrogenase. In: Bergmeyer, editor: Methods of Enzymatic Analysis. New York: Academic Press, 1965. p. 384–91.
[18] Cuzick J. A Wilcoxon type test for trend. Stat Med 1985;4:87–90.
[19] Pappenheimer JR, Reiss KZ. Contribution of solvent drag through intercellular junctions to absorption of nutrients by the small intestine of the rat. J Membr Biol 1987;100:123–36.
[20] Sadowski DC, Meddings JB. Luminal nutrients alter tight-junction permeability in the rat jejunum: an *in vivo* perfusion model. Can J Physiol Pharmacol 1993;71:835–9.
[21] Wapnir RA, Lee S-Y, Stiel L. Intestinal absorption of zinc: sodium-metal-ligand interactions. Biochem Med Metab Biol 1989;42:146–60.
[22] Shirazi-Beechey SP. Molecular biology of intestinal glucose transport. Nutr Res Rev 1995;8:27–41.
[23] Harris ED. Cellular transporters for zinc. Nutr Rev 2002;60:121–4.
[24] Liuzzi JP, Bobo JA, Cui L, McMahon RJ, Cousins RJ. Zinc transporters 1, 2 and 4 are differentially expressed and localized in rats during pregnancy and lactation. J Nutr 2003;133:342–51.
[25] Reeves PG, Briske-Anderson M, Johnson L. Pre-treament of Caco-2 cells with zinc during the differentiation phase alters the kinetics of zinc uptake and transport. J Nutr Biochem 2001;12:674–84.
[26] Christensen HN. Role of amino acid transport and countertransport in nutrition and metabolism. J Physiol Rev 1990;70:43–77.
[27] Munck LK, Munck BG. Amino acid transport in the small intestine. J Physiol 1994;43:335–46.