Sodium tungstate decreases sucrase and Na\(^+\)/d-glucose cotransporter in the jejunum of diabetic rats

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Miró-Queralt M, Guinovart JJ, Planas JM. Sodium tungstate decreases sucrase and Na\(^+\)/d-glucose cotransporter in the jejunum of diabetic rats. Am J Physiol Gastrointest Liver Physiol 295: G479–G484, 2008. First published July 10, 2008; doi:10.1152/ajpgi.00566.2007.—Sodium tungstate reduces glycemia and reverts the diabetic phenotype in several induced and genetic animal models of diabetes. Oral administration of this compound has recently emerged as an effective treatment for diabetes. Here we examined the effects of 30 days of oral administration of tungstate on disaccharidase and Na\(^+\)/d-glucose cotransporter (SGLT1) activity in the jejunum of control and streptozotocin-induced diabetic rats. Diabetes increased sucrase-specific activity in the jejunal mucosa but did not affect the activity of lactase, maltase, or trehalase. The abundance and the maximal rate of transport of SGLT1 in isolated brush-border membrane vesicles also increased. Tungstate decreased sucrase activity and normalized SGLT1 expression and activity in the jejunum of diabetic rats. Furthermore, tungstate did not change the affinity of SGLT1 for D-glucose and had no effect on the diffusional component. In control animals, tungstate had no effect on disaccharidase or SGLT1 expression. Northern blot analysis showed that the amount of specific SGLT1 mRNA was the same in the jejunum from all experimental groups, thereby indicating that changes in SGLT1 abundance are due to posttranscriptional mechanisms. We conclude that the antidiabetic effect of tungstate is partly due to normalization of the activity of sucrase and SGLT1 in the brush-border membrane of enterocytes.

SODIUM TUNGSTATE HAS A POWERFUL normoglycemic effect when administered orally. In several induced and genetic animal models of type 1 and 2 diabetes, tungstate restores hepatic glucose metabolism (4, 27), increases β-cell mass (2, 15), stimulates insulin secretion (2, 28), and upregulates glucose transporter expression and translocation in muscle (17).

The antidiabetic effects of tungstate are maintained during long-term treatment (8 mo), and undesirable effects such as hypoglycemic episodes, tungstate intolerance, or adverse toxicological effects do not appear during this time (3). Thus the administration of tungstate offers a novel approach for the long-term management of diabetes.

Despite considerable data on the pharmacological and metabolic effects of tungstate, little information is available on its molecular mechanism of action. Tungstate mimics most of the metabolic effects of insulin and exerts insulin-like actions in primary cultured rat hepatocytes by increasing glycogen deposition (13). The analysis of the effects of this compound on several components of the insulin-signaling transduction cascade demonstrated that they are not mediated by the insulin receptor because the phosphorylation state of this receptor remains unchanged after treatment. In contrast, tungstate activates glycogen synthase and thus glycogen deposition in hepatocytes by stimulating the phosphorylation of extracellular signal-regulated kinases 1 and 2 (ERK1/2) and glycogen synthase kinase-3β at hepatic level (13). Moreover, tungstate also stimulates ERK1/2 phosphorylation in diverse cell types, such as Leydig cells and neurons (1, 19). In the muscle, tungstate induces an increase in glucose uptake (17), and in myotubes this effect is exerted through an ERK1/2-dependent mechanism (18).

To elucidate the effect of tungstate on intestinal function, here we present the first analysis of the action of this compound on intestinal expression of Na\(^+\)/d-glucose cotransporter (SGLT1) and brush-border membrane disaccharidase activities.

The first step in the control of glycemia is the regulation of the transit of dietetic sugars from the intestinal lumen through the enterocytes to the bloodstream. In mammal intestine, d-glucose and d-galactose enter enterocytes through the brush-border membrane mainly via the Na\(^+\)-dependent, high-affinity, low-capacity SGLT1 (32).

In diabetic rats upregulation of SGLT1 increases the capacity of the intestine to absorb monosaccharides (11). In addition, it is well established that diabetes increases mucosal sucrase activity in the rat small intestine (29). Our results indicate that tungstate restores the activity of brush-border disaccharidases and the expression and activity of SGLT1 in rat jejunum.

MATERIALS AND METHODS

Animals and experimental design. Male Wistar rats of 200 g body wt were purchased from Harlan Ibérica (Barcelona, Spain). They were housed in conditions of stable humidity (50%) and temperature (22°C) with a 12:12-h light-dark cycle. Rats were allowed to eat (Panlab A04 diet, Reus, Spain) and drink ad libitum and were divided into two groups. One group (control rats) received a single streptozotocin (STZ) injection (60 mg/kg body wt ip in 50 mM sodium citrate, pH 4.5) to induce diabetes. The other group (control rats) were injected with citrate buffer. Tail-blood glucose levels were measured 7 days after STZ injection and only animals with serum glucose levels above 16.5 mM were used (26).

Treatment began 7 days after STZ injection. Both control and diabetic animals were then subdivided into two groups: tungstate treated and untreated. Treated groups received a solution of 2 mg/ml of sodium tungstate instead of drinking water throughout the treatment period. This dose has been shown to be optimal in previous studies (2, 4). Treatment was carried out for 30 days. Body weight,

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food, and water intake and glyceremia were measured in the morning (9:00–10:00 h) three times per week.

At the end of the experiment, rats were fasted for 12 h and then anesthetized with ketamine (90 mg/kg body wt im) plus xylazine (10 mg/kg body wt im) and killed by decapitation. Jejunum was removed, flushed with ice-cold saline, and immediately used to prepare brush-border membrane vesicles (BBMVs).

All protocols used in this study were approved by the ethical committees of the Universitat de Barcelona and the Autonomous Government of Catalonia (Departament d’Agricultura, Ramaderia i Pesca, Generalitat de Catalunya) for the use and handling of experimental animals.

**Disaccharidase activities.** The activity of brush-border sucrase, lactase, maltase, and trehalase (glycosidases EC 3.2.1.48, EC 3.2.1.23, EC 3.2.1.20, EC 3.2.1.28, respectively) was assayed on isolated vesicles and jejunal mucosa following Dahlqvist (10).

**Cell isolation.** Enterocytes were isolated from the jejunum of two rats as described previously (5). The pooled intestine was incubated in a medium containing 80 mM NaCl, 3 mM K2HPO4, 20 mM Tris-HCl (pH 7.4), 37 mM mannitol, 0.1 mM EGTA, 27 mM trisodium citrate, and 1 mg/ml BSA. Incubation was maintained for 100 min at 25°C to isolate enterocytes from the entire villus. Cell viability was assayed by Trypan blue exclusion. Total RNA was extracted from the enterocytes.

**RNA extraction and northern blot analysis.** For the Northern blot analysis of SGLT1 mRNA, we used enterocytes instead of mucosa to avoid interferences with other cells of the intestinal wall. Total RNA was isolated from enterocytes, as described by Chomczynski and Sacchi (7). RNA was quantified by spectrophotometric analysis at 260 nm. Samples were loaded on a formaldehyde-agarose gel (15 μg total RNA/lane) and transferred to a nylon membrane (Nytran 0.45, Schleicher and Schuell, Dassel, Germany). Specific mRNA was detected using a 3.1-kb EcoRI fragment from pMJC424 plasmid encoding rabbit jejunal SGLT1. Probes were labeled with α-32P-dCTP (deoxy-cytidine triphosphate) by random priming (Random primer DNA labeling mix, Biological Industries, Kibbutz, Israel). Blots were normalized by rehybridization with a plasmid encoding for the 18S ribosomal protein. Autoradiograms were quantified by scanning densitometry.

**Preparation of BBMVs.** BBMVs were prepared from the jejunum by a double MgCl2 precipitation method (24). Jejunal mucosa was scraped and homogenized, MgCl2 was added to a final concentration of 10 mM, and the mixture was stirred for 20 min. The suspension was then centrifuged at 3,000 g for 15 min and the supernatant was centrifuged at 30,000 g for 20 min. The resulting pellet was resuspended in 100 mM mannitol, 2 mM HEPE-Tris (pH 7.4), 0.41 mM LiNO3 and homogenized with a glass-Teflon pestle (30 strokes). The suspension was stirred again with 10 mM MgCl2 for 15 min and centrifuged at 4,300 g for 20 min. The supernatant was finally centrifuged at 30,000 g for 30 min and the final pellet was homogenized with a 27-gauge needle in a medium containing 300 mM mannitol, 20 mM HEPE-Tris (pH 7.4), 0.1 mM MgSO4, and 0.41 μM LiNO3 with a protein concentration of 15–20 mg/ml. The vesicles were stored in liquid N2 and used in the next 3 days. During this time, their integrity and functionality were maintained by proportional weighting to the data. Kinetic parameters with experimental fluxes were roughly proportional to their values, and the specific activity of inward concentration gradient of 100 mM Na+. The substrate concentrations used for the kinetic analysis of α-glucose uptake by BBMVs ranged from 0.01 to 75 mM. The osmolality of intra- and extravesicular media was kept constant at 320 mosmol/kg by adjusting the total sugar concentration with mannitol.

**Phlorizin binding.** The specific steady-state phlorizin binding to SGLT1 was assayed to determine the correlation between α-glucose transport rate and the number of SGLT1 transporters present in BBMVs, as described by Garriga et al. (16). The specific binding is expressed as pmol of phlorizin bound per mg of protein at a concentration of 50 μmol/l (Bmax).

**Western blot analysis of SGLT1.** SGLT1 protein abundance in BBMVs of rat jejunum was measured by Western blot analysis, as previously described (16). Blots were incubated with a rabbit polyclonal antibody raised against the synthetic peptide corresponding to amino acids 564-575 of the deduced amino acid sequence of rabbit intestinal SGLT1 at a 1:5,000 dilution for 16 h at 4°C. In simultaneous experiments, nitrocellulose membranes were incubated with the same antibody adsorbed with the antigenic peptide (1 mg/ml). Hybridization bands were quantified by scanning densitometry.

**Immunohistochemical localization of SGLT1.** Small fragments of jejunum were fixed in Bouin’s solution for 24 h at room temperature, washed, dehydrated in graded ethanol series, and embedded in paraffin wax (Vogel Histo-Comp, melting point 56°C) at 60°C for 20–24 h. Sections (5 μm each) were cut with a microtome and mounted on slides.

Deparaffinized rehydrated sections were treated with 3% hydrogen peroxide and 10% methanol in 10 mmol/l PBS (pH 7.2) for 10 min to inhibit tissue peroxidase. Slides were incubated with a rabbit polyclonal anti-SGLT1 antibody (1:150) overnight at 4°C. After being washed in PBS, the sections were incubated with peroxidase-conjugated goat anti-rabbit IgG (1:50) for 1 h and developed with 0.025 mg/ml 3,3′-diaminobenzidine tetrahydrochloride and 0.03% hydrogen peroxide in PBS. Slides were counterstained with Harris hematoxylin solution, dehydrated, cleared in xylene, and mounted in a synthetic resin (a mixture of divinylurea, triscrylil phosphates, and xylene).

In parallel experiments, sections were incubated with the antibody previously adsorbed with the corresponding antigenic peptide, to confirm the specificity of the immunostaining obtained.

**Chemicals.** Sodium tungstate was from Carlo Erba (Milan, Italy). STZ and other unlabeled reagents were purchased from Sigma (St. Louis, Mo.). d-[1-U-14C]glucose (specific activity 251 mCi/mmol) and [3H]phlorizin (specific activity 46.4 Ci/mmol) were purchased from New England Nuclear Research Products (Deirheim, Germany). The final activity of labeled substrates in the incubation medium was 0.5–2 μCi/ml. α-32P-dCTP (specific activity 3,000 mCi/mmol) was purchased from Amersham Ibérica (Madrid, Spain).

**Kinetic analysis.** Total α-glucose fluxes from at least four independent experiments were analyzed by nonlinear regression using the Biosoftware EnzFitter program (Cambridge, UK). As the errors associated with experimental fluxes were roughly proportional to their values, we applied proportional weighting to the data. Kinetic parameters were evaluated by systematically testing different model equations corresponding to one or two Michaelian components plus a linear nonspecific component.

**Statistical analysis.** Results are expressed as means ± SE. The effects of STZ-induced diabetes were analyzed comparing results of control and diabetic animals by an ANOVA using the SPSS-10.0 software (SPSS). To analyze the effects of tungstate treatment, the results of the treated (control and diabetic) groups were compared with the untreated (control and diabetic) groups by ANOVA followed by Scheffé’s post hoc test. Differences were considered significant at P < 0.05.
The results demonstrated the effectiveness of tungstate treatment on blood variables and physical status. After 30 days of treatment, glycemia in diabetic rats decreased significantly (from 32.4 ± 2 to 8.36 ± 0.6 mM), although it remained slightly higher than in their non-diabetic counterparts. Tungstate did not modify blood glucose concentration in control rats (4.49 ± 0.1 vs. 4.99 ± 0.3 mM) (Table 1). Untreated diabetic rats increased food and liquid consumption. Tungstate treatment reduced both variables. Table 1 summarizes blood variables and physical status of all experimental groups.

Disaccharidase activities. The specific activity of sucrase increased in diabetic rats (Table 2). Oral tungstate did not affect this parameter in control rats, but it normalized this activity in diabetic animals. In contrast, there were no differences in the amount of SGLT1 mRNA between experimental groups (Table 3). The total fluxes from each experiment were resolved into a saturable (SGLT1-mediated) and a linear component, and the resulting values were subjected to ANOVA. This revealed two patterns: the first, including control (untreated and treated) plus treated diabetic rats, was characterized by high mediated transport rates ($V_{\text{max}}$). The second pattern (untreated diabetic group) was characterized by significantly higher $V_{\text{max}}$. The Michaelis constants ($K_m$) calculated for all experimental conditions ranged from 0.25 to 0.29 mM, without differences between groups. The linear component allowed the calculation of the diffusion constants ($D_0$) for d-glucose, which were between 19.5 and 24.8 nl·mg protein$^{-1}$·s$^{-1}$, without statistical differences between groups.

Phlorizin binding measurements. The specific binding of phlorizin ($B_{50}$) for all experimental groups is shown in Table 3. The effects of diabetes and tungsten treatment on $B_{50}$ paralleled the changes observed in $V_{\text{max}}$. Both variables showed a linear correlation defined by the equation $y = 2.415x - 13.17$ ($r = 0.9961$).

SGLT1 immunoblotting. In all groups, the antibody recognized a protein of ~75 kDa. The relative abundance of SGLT1 in the treated diabetic group approximately doubled that of the other three groups (Fig. 2). When the antibody was preadsorbed with the antigenic peptide, no hybridization signal was detected.

Immunohistochemical SGLT1 detection. There was positive staining in villus-attached enterocytes in all four groups (Fig. 3). The immunoreaction was uniformly localized in the brush-border membrane of the enterocytes along the total length of the villus, whereas no staining was seen in mucus-secreting goblet cells. No staining was observed in the epithelial cells when the tissue slides were preadsorbed with the antigenic peptide (data not shown). An increase in the length of the villi in the STZ-induced diabetes rats was detected. This increase was normalized by tungsten treatment.

Table 1. *Serum glucose, body weight, and intake of fluid, food, and tungstate in treated and untreated control and diabetic rats*

<table>
<thead>
<tr>
<th></th>
<th>Serum Glucose, mM</th>
<th>Body Weight, g</th>
<th>Food Intake, g·kg$^{-1}$·day$^{-1}$</th>
<th>Fluid Intake, ml·kg$^{-1}$·day$^{-1}$</th>
<th>Tungstate Intake, mg·kg$^{-1}$·day$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>4.5 ± 0.1</td>
<td>320 ± 1</td>
<td>72.7 ± 2</td>
<td>107.1 ± 3.3</td>
<td></td>
</tr>
<tr>
<td>Treated</td>
<td>5.0 ± 0.1</td>
<td>284 ± 15</td>
<td>62.5 ± 1.7</td>
<td>76.6 ± 3.3</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetic rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Untreated</td>
<td>32.4 ± 2</td>
<td>208 ± 9</td>
<td>180.1 ± 0.8</td>
<td>845.4 ± 20.1</td>
<td></td>
</tr>
<tr>
<td>Treated</td>
<td>8.4 ± 0.6</td>
<td>211 ± 15</td>
<td>105.9 ± 1.8</td>
<td>185.6 ± 5.4</td>
<td>206.8 ± 6.9</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE for 15 rats. Serum glucose values and body weight are those at the end of the experiment. Food, fluid, and tungstate intake are the average consumption of the treatment period. Statistical analysis vs. $^a$: $^b$P < 0.05; $^c$P < 0.01; $^d$P < 0.001; $^e$P < 0.0001.

Table 2. *Disaccharidase activity in jejunal mucosa of control and diabetic rats treated with tungstate or left untreated*

<table>
<thead>
<tr>
<th></th>
<th>Sucrase, nkat/mg protein</th>
<th>Lactase, nkat/mg protein</th>
<th>Maltase, nkat/mg protein</th>
<th>Threalse, nkat/mg protein</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>1.54 ± 0.18</td>
<td>0.27 ± 0.06</td>
<td>12.72 ± 0.90</td>
<td>1.00 ± 0.01</td>
</tr>
<tr>
<td>Treated</td>
<td>1.61 ± 0.16</td>
<td>0.26 ± 0.05</td>
<td>11.69 ± 0.83</td>
<td>1.01 ± 0.19</td>
</tr>
<tr>
<td><strong>Diabetic rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>2.96 ± 0.26</td>
<td>0.27 ± 0.05</td>
<td>14.56 ± 1.11</td>
<td>0.96 ± 0.11</td>
</tr>
<tr>
<td>Treated</td>
<td>1.61 ± 0.42</td>
<td>0.32 ± 0.05</td>
<td>14.44 ± 1.06</td>
<td>1.01 ± 0.20</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 separate experiments. Statistical analysis: $^b$P < 0.05 vs. $^a$.
DISCUSSION

Sodium tungstate normalizes glycemia in STZ-diabetic rats and has been proposed for the oral treatment of diabetes mellitus type 1 and 2 (2–4, 15). Here we studied the effects of sodium tungstate on the intestinal disaccharidases and SGLT1 transporter activities in the jejunum of control and STZ-induced diabetic rats.

The STZ treatment induced polydipsia and polyphagia as well as an increase in serum glucose levels (5.5-fold), as previously described (4, 26). These effects were partially reversed by tungstate treatment. In control rats, treatment with this compound did not lead to hypoglycemia and induced a reduction of 11% in body weight. This effect can be explained by the recent finding that oral administration of tungstate significantly decreases body weight gain and adiposity in obese rats without modifying caloric intake, intestinal fat absorption, or growth rate (8).

The increase in sucrase activity observed in the jejunal mucosa of diabetic rats could contribute to hyperglycemia. Augmented sucrase activity in diabetic rats has been attributed to the lack of insulin. Tandon et al. (30) offered two possible explanations for this increase. First, since insulin inhibits sucrase activity, deficiency of this hormone may increase this activity. Second, the higher glucose transport in diabetes may also stimulate sucrase activity. In our study, oral administration of sodium tungstate significantly reduced sucrase activity in diabetic rats. This reduction indicates lower levels of absorbable glucose obtained from carbohydrate digestion, thus leading to reduced blood glucose levels. This reduction may ameliorate the diabetic state (25, 33) and could explain the lowered blood glucose levels observed in treated diabetic rats. In diabetic rats, intestinal absorption of glucose increases as a result of a rise in the number of glucose transporters (14, 31). Our results confirm that diabetes increases the activity and expression of SGLT1 in rat jejunum. Tungstate did not affect this transporter in control rats, but there was a marked reduction in the activity and abundance of SGLT1 in the brush-border membrane of diabetic animals. The correlation between

Table 3. V_{max}, K_{m}, and K_{d} of α-glucose uptake across BBMVs, and B_{50} to BBMVs from jejunum of control and diabetic rats treated with tungstate or left untreated

<table>
<thead>
<tr>
<th></th>
<th>V_{max}, pmol α-Glucose/mg protein/ s</th>
<th>K_{m}, mM</th>
<th>K_{d}, nl/mg protein/ s</th>
<th>B_{50}, pmol Phz/mg protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>77.5 ± 6.7^a</td>
<td>0.29 ± 0.05</td>
<td>22.3 ± 6.3</td>
<td>39.1 ± 4.7^a</td>
</tr>
<tr>
<td>Treated</td>
<td>82.6 ± 2.9^a</td>
<td>0.25 ± 0.07</td>
<td>19.5 ± 1.2</td>
<td>38.6 ± 7.3^a</td>
</tr>
<tr>
<td>Diabetic rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>189.9 ± 15.6^b</td>
<td>0.25 ± 0.08</td>
<td>21.5 ± 0.7</td>
<td>86.5 ± 2.8^b</td>
</tr>
<tr>
<td>Treated</td>
<td>71.9 ± 15.5^a</td>
<td>0.28 ± 0.14</td>
<td>24.8 ± 2.8</td>
<td>39.2 ± 6.9^a</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 separate experiments. V_{max}, maximal transport rates; K_{m}, Michaelis constant; and K_{d}, diffusion constant; BBMVs, brush-border membrane vesicles; B_{50}, specific phlorizin binding. Statistical analysis: ^b^P < 0.05 vs. a.
the decrease of the maximal \( \text{D-glucose} \) transport rates in BBMVs and the number of SGLT1 indicates that the tungstate-induced reduction in the transport of \( \text{D-glucose} \) in diabetic animals is due to a decrease in the number of SGLT1.

Tungstate treatment did not alter the affinity of SGLT1 for \( \text{D-glucose} \) (\( K_m \)). This observation contrasts with what occurs when diabetic animals are treated with vanadate (22). Vanadate-supplemented rats show a decrease in \( K_m \), which indicates increased affinity of the glucose transporter for \( \text{D-glucose} \) (22). In our study, the unchanged \( K_m \) indicates that tungstate does not induce alterations in the structure or composition of the brush-border membrane. This conclusion is supported by the absence of effects in the diffusional component of \( \text{D-glucose} \) transport across BBMVs.

Helliwell et al. (20) proposed that the \( \text{D-glucose} \) transporter present in the basolateral membrane of enterocytes or GLUT2 is also expressed in the apical membrane of jejunal rat enterocytes as a result of increased trafficking of GLUT2 in the STZ-diabetic intestine. However, in our studies, GLUT2 was not found in BBMVs (data not shown). One explanation might be that in our experimental conditions the rats were starved for 12 h and therefore the rapid regulation of \( \text{D-glucose} \) transport, described by Kellet’s group, was abolished.

Moreover, our results from immune staining of SGLT1 showed that the protein is present in the brush border membrane of absorptive epithelial cells. The increased size of villi observed in rats with STZ-induced diabetes was normalized by tungstate treatment.

It has recently been described (23) that sweet taste receptors and the G protein gustducin exert control on SGLT1 mRNA and protein. However, in our experiments, the amount of specific mRNA did not vary significantly between experimental groups. Therefore, the mechanism by which tungstate regulates SGLT1 probably differs from that of the taste receptors. The changes in transport and number of transporters that we have observed cannot be explained by the induction or repression of the SGLT1 gene but rather suggest that tungstate does not regulate SGLT1 transcriptionally. The same has been shown for insulin (21). Therefore, tungstate, like insulin, exerts its effects at the posttranscriptional level. There is ample evidence that tungstate does not induce the activation of the insulin receptor and that its mechanism of action involves the phosphorylation of ERK1/2 rather than the classical PI3K pathway activated by the hormone. It is therefore tempting to speculate that tungstate also exerts its insulin-like effects through the activation of ERK in enterocytes.
In summary, our results show that oral tungstate normalizes the levels and activity of apical SGLT1 and mucosal sucrase activity. These effects limit the entry of sugars into the body, which could contribute to the antidiabetic effects of tungstate.

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