Published in final edited form as:

J Surg Res. 2013 August ; 183(2): 606–611. doi:10.1016/j.jss.2013.02.031.

Lack of Functionally-Active Sweet Taste Receptors in the Jejunum *in vivo* in the Rat

Rizwan M. Chaudhry, MD, Alok Garg, Mohamed M. Abdelfatah, MD, Judith A. Duenes, BA, and Michael G. Sarr, MD

Department of Surgery and Gastroenterology Research Unit, Mayo Clinic, Rochester, MN

Abstract

BACKGROUND—When studied in enterocyte-like cell lines (Caco-2 and RIE cells), agonists and antagonists of the sweet taste receptor (STR) augment and decrease glucose uptake, respectively. We hypothesize that exposure to STR agonists and antagonists *in vivo* will augment glucose absorption in the rat.

MATERIAL/METHODS—30-cm segments of jejunum in anesthetized rats were perfused with iso-osmolar solutions containing 10, 35, and 100 mM glucose solutions (n=6 rats, each group) with and without the STR agonist 2 mM acesulfame potassium (AceK) and the STR inhibitor 10 μ M U-73122 (inhibitor of the PLC pathway). Carrier-mediated absorption of glucose was calculated by using stereospecific and non-stereospecific 14 C-D-glucose and 3 H-L-glucose, respectively.

RESULTS—Addition of the STR agonist AceK to the 10, 35, and 100 mM glucose solutions had no substantive effects on glucose absorption from 2.1 ± 0.2 to 2.0 ± 0.3 , 5.8 ± 0.2 to 4.8 ± 0.2 , and 15.5 ± 2.3 to 15.7 ± 2.7 μ mol/min/30-cm intestinal segment ($p > 0.05$), respectively. Addition of the STR inhibitor (U-73122) also had no effect on absorption in the 10, 35, and 100 mM solutions from 2.3 ± 0.1 to 2.1 ± 0.2 , 7.7 ± 0.5 to 7.2 ± 0.5 , and 15.7 ± 0.9 to 15.2 ± 1.1 μ mol/min/30-cm intestinal segment, respectively.

CONCLUSION—Provision of glucose directly into rat jejunum does not augment glucose absorption via STR-mediated mechanisms within the jejunum in the rat. Our experiments show either no major role of STRs in mediating postprandial augmentation of glucose absorption or that proximal gastrointestinal tract stimulation of STR or other luminal factors may be required for absorption of glucose to be augmented by STR.

Keywords

glucose absorption; sweet taste receptors; SGLT1; GLUT2; acesulfame potassium; U73122; apical translocation

© 2013 Elsevier Inc. All rights reserved.

Address correspondence to Michael G. Sarr, M.D., Gastroenterology Research Unit (GU 10-01), Mayo Clinic, 200 1st St SW, Rochester, MN 55905. Tel: 507-255-5713. Fax: 507-255-6318. sarr.michael@mayo.edu and frank.deborah@mayo.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

The principal energy substrate for humans is glucose, which is absorbed in the small intestine by the intestinal epithelial cells. The majority of glucose absorption occurs via the enterocyte through the action of two, apical, membrane-bound transporter proteins: sodium glucose co-transporter 1 (SGLT1) and glucose transporter (GLUT2). We and others have shown previously that the majority of glucose absorption *in vivo* at postprandial physiologic concentrations (30 mM glucose) occurs via carrier-mediated uptake by GLUT2 [1, 2], although in the mouse others have argued that the majority of postprandial glucose absorption occurs only via SGLT1 [3]. The physiologic mechanisms regulating glucose absorption have been of particular interest and especially with the recent focus in the role of sweet-taste receptors (STRs) [4]. Indeed, STRs are believed to “sense” luminal concentrations of glucose and mediate a signaling pathway to help regulate transporter function in the enterocyte.

Chemosensing of intestinal luminal nutrients is a topic of tremendous interest recently. Chemoreceptors appear to have a function in controlling both food intake and nutrient absorption. In the gastrointestinal tract, enteroendocrine cells and enterocytes are considered the main cells active in sensing the luminal concentration of sugars [5, 6]. Glucose sensing in the intestine of animals may occur through a monosaccharide sensor located on the luminal surface of the intestinal brush border; this “sensor” is distinct from SGLT1 [7], an apical membrane-bound hexose transporter that accounts for the majority of glucose absorption at lesser intraluminal concentrations of glucose (<30 mM glucose) *in vivo* [1]. Limited work in rats *in vivo* suggests that SGLT-3, an apical membrane protein with low affinity for glucose, may be responsible for sensing glucose [8].

Multiple groups have been investigating the combined roles of STRs in glucose sensing and the subsequent marked postprandial stimulation of glucose absorption at the level of intestinal epithelial cell. The mammalian tongue contains taste receptors that sense various compounds ingested (bitter, sweet, salty, and sour). Interestingly, the same receptor complex responsible for sweet taste sensing found on the tongue has been identified in intestinal epithelial cells [9]. Specifically, the heterodimer T1R2 + T1R3 responsible for sugar sensing of the tongue is also present on enteroendocrine cells and enterocytes. This STR appears to use a G-protein-linked signaling pathway involving α -gustducin, the β 2 isoform of phospholipase C (PLC), inositol 1,4,5 triphosphate (IP3), and transient receptor potential channel M5 (TrpM5) as signaling elements for the translocation of GLUT2 to the apical membrane of the enterocyte to increase absorptive capacity for glucose [6, 9, 10].

Preliminary work in our laboratory explored the role of artificial sweeteners and the STR pathway in glucose uptake into Caco-2, RIE-1, and IEC-6 cells in culture. In these studies, the addition of the artificial sweetener acesulfame potassium (AceK) at low concentrations failed to increase carrier-mediated glucose uptake in the cells at glucose concentrations 25 mM, whereas at a greater glucose concentration (30 mM), glucose uptake was augmented [11]; moreover, inhibiting the presumed PLC-mediated STR pathway with U-73122 (a specific PLC inhibitor) decreased carrier-mediated uptake of glucose at glucose concentrations exceeding the uptake capacity of SGLT1. These experiments in cell culture suggested that the T1R2 + T1R3 receptor located at the apical membrane of intestinal epithelial cells was involved importantly in augmenting glucose uptake.

Our aim in this present work was to explore whether activation of STRs using an artificial sweetener would increase jejunal absorption of glucose in a rat model *in vivo* that we have validated previously. Our prior work in the rat *in vivo* (as well as in cell culture using rat enterocytes) showed an impressive augmentation of glucose absorption mediated by GLUT2

when the jejunum was exposed to high concentrations of glucose. We also wanted to investigate whether PLC played a role *in vivo* in this augmentation of carrier-mediated absorption of glucose at physiologic concentrations of glucose by inhibiting the G-protein coupled receptor/PLC pathway using U-73122. Our hypothesis was that stimulation of STRs directly in the jejunum *in vivo* would increase carrier-mediated glucose absorption at all luminal concentrations of glucose, while inhibition of PLC would inhibit glucose absorption at glucose concentrations >25 mM.

METHODS

All experiments were conducted after approval by our Institutional Animal Care and Use Committee and in accordance with the guidelines of the National Institute of Health for the humane use and care of laboratory animals.

Design

Experiments of intestinal perfusion in rats were conducted *in vivo* to compare glucose absorption from isosmolar solutions containing 10, 35, and 100 mM glucose before and after addition of the potent artificial sweetener AceK (Sigma Aldrich, St. Louis, MO) [11, 12]. In separate experiments, we added the well-established PLC inhibitor, U-73122 hydrate (Sigma Aldrich), to the same glucose-containing perfusates [11, 12]. By measuring absorption of ^{14}C -D-glucose and ^3H -L-glucose, we were able to determine separately the contribution of the stereospecific, carrier-mediated (^{14}C) absorption of glucose and the non-stereospecific, non-carrier mediated (^3H) absorption of glucose under each condition.

Preparation of *In Vivo* Model of Perfusion

We used male Lewis rats (Harlan, Indianapolis, IN) weighing 200-300g with free access to water and standard rat chow (5001 Rodent Diet, PMI Nutrition International, LLC, Brentwood, MO, USA). The rats were acclimated to our rodent facility for at least 5 days before study and maintained in 12:12-h dark-light controlled environment (6:00 AM lights on, 6:00 PM lights off). Rats were anesthetized initially using 2% inhaled isoflurane for induction followed by intraperitoneal injection of sodium pentobarbital (50 mg/kg) for maintenance. Rats were kept on a warmed mat during the operation and the subsequent intestinal perfusion experiment to prevent hypothermia as before [1]. After a short, mid-ventral celiotomy, a 30-cm segment of proximal jejunum was isolated beginning 5 cm distal to the duodenojejunal junction. The bowel was ligated both proximal and distal to the test segment to avoid spillage of intestinal contents into the abdomen during the experiment and to prevent proximal or distal small bowel content from entering the test segment. This 30-cm test segment of jejunum was then cannulated with Silastic® tubing proximally (I.D.=0.035 in) and distally (I.D.=0.118 in) and secured with a purse string suture. First, 30 ml of warmed Ringer's lactate was flushed through the jejunal segment to evacuate all intraluminal content. All the perfusion experiments were carried out between 8:00-11:00AM to avoid problems of interpretation related to the diurnal variation in expression of hexose transporters.

Conduct of Experiments

All experiments were conducted in anesthetized rats. Rats were randomized into six groups of six rats each after placement of the infusion and effluent catheters and closure of the abdomen with 4-0 silk suture. The groups were the following: Group 1: 10 mM glucose with 2 mM AceK (the STR agonist), Group 2: 35 mM glucose with 2 mM AceK, Group 3: 100 mM D-glucose with 2 mM AceK, Group 4: 10 mM glucose with 10 μM U-73122 hydrate (the PLC inhibitor), Group 5: 35 mM glucose with 10 μM U-73122 hydrate, and Group 6: 100 mM glucose with 10 μM U-73122 hydrate.

The rats lay on their sides for the duration of the infusion. The rats were kept anesthetized with additional doses of pentobarbital if needed. The 2-h experiments were conducted using our well-established, *in vivo* rat model described previously [1]. The first hour of perfusion served as the baseline control period, after which the test agent was infused at a constant concentration in the infusate for the entire second hour of infusion (test period). U-73122 hydrate was solubilized in 0.1% ethanol. The doses of AceK and U-73122 hydrate were selected specifically based on our experiments in cell culture model [11] as well as in other previous, well-validated *in vivo* studies [12]. In addition to the 2 mM concentration of AceK, we conducted experiments on two rats with a greater concentration of AceK (10mM) to see if a greater dose would change our results. All infusate solutions were isosmolar and made up by altering the concentration of NaCl according to the glucose concentration. The warmed solutions (37°C) were infused into the test segment proximally at a constant rate of 1ml/min; effluent was collected from the distal end at 10-min intervals. Thus, the enterocytes were exposed luminally to the STR agonist and to the PLC inhibitor for the entire second hour of the infusion. Based on our previous studies [1] with isosmolar solutions containing radiolabeled polyethylene glycol (³H-PEG, a nonabsorbable marker) to determine the time taken to reach a steady state, we validated that a steady state is established in this model within 10-15 min [1].

The volume of effluent/10-min interval was measured, samples of which were mixed with 5ml of counting cocktail (Opti-Fuor, Perkin-Elmer, Shelton, CT). Two samples were collected for each 10-min effluent, and counts were obtained using a dual isotope, liquid scintillation algorithm on a Beckman LS60000 SC counter (Fullerton, CA). The mean of both the samples was used as final disintegrations/min (DPM)/sample. Carrier-mediated glucose uptake was calculated as total uptake (¹⁴C-D-glucose) minus passive uptake (³H-L-glucose) for each sample and expressed in $\mu\text{mol}/\text{min}/30\text{-cm}$ segment of bowel.

Analysis of Data

A 20-min period was allowed for establishment of a steady state at the beginning of the experiment (first hour) and again after the addition of the test agent at the start of the second hour. Therefore, each experiment consisted of a 40-min period of baseline absorption in the absence of the STR agonist or PLC inhibitor (experiment time 20-60 min) and another 40 min of test period (experiment time 80-120 min) when the infusate contained either the STR agonist (AceK) or the PLC inhibitor (U-73122) at a continuous constant concentration. Samples were collected at 10-min intervals for each 40-min period of the experiment. The values for each of the four, separate 10-min samples were meaned in each animal, and an overall mean absorption/10 min was calculated for each of the groups of 6 rats for statistical analysis.

Statistical Analyses

All statistical analyses were performed using paired Student's t-tests to compare parametric data between groups. A p value 0.05 was considered significant. All data are reported as the mean values $\pm$ standard error of the mean (SEM); n values are numbers of rats.

RESULTS

Addition of an Artificial Sweetener (Figure 1)

Contrary to our hypothesis, addition of the potent STR agonist AceK did not augment carrier-mediated glucose absorption at any of the concentrations of glucose infused (10, 35, or 100 mM). When evaluated at the 10 mM glucose solution, when most of the carrier-mediated glucose absorption should have been mediated by SGLT1 and not GLUT2 based on our prior work both *in vivo* and in cell culture [1, 13], AceK had no effect on glucose

absorption from baseline (2.1 ± 0.2 to 2.0 ± 0.3 $\mu\text{mol}/\text{min}/30\text{cm}$; $P=\text{NS}$). Next, we evaluated the solution containing an intermediate concentration of glucose (35 mM), a concentration which in cell culture was great enough to stimulate some translocation of GLUT2 to the apical membrane of enterocyte-like cells (and increased carrier-mediated uptake of glucose via a GLUT2-mediated mechanism) [13]; when the 35 mM glucose solution was infused, again in contrast to our hypothesis, AceK had no additive effect on carrier-mediated uptake, and a functionally insignificant, decrease in carrier-mediated absorption occurred (from 5.8 ± 0.2 to 4.8 ± 0.2 $\mu\text{mol}/\text{min}/30\text{cm}$; $p=0.01$). Finally, during the 100 mM glucose infusion, when carrier-mediated glucose absorption was markedly increased by a GLUT2-mediated mechanism as we have shown previously *in vivo* in this model [1], the STR agonist AceK had no additive effect on carrier-mediated absorption (from 15.5 ± 2.3 to 15.7 ± 2.7 ; $p=\text{NS}$).

There was no effect of AceK on passive, non-carrier-mediated absorption of glucose during any infusion (^3H -glucose; data not shown). Of note, when we increased the concentration of AceK to 10 mM, we again were unable to elicit an augmentation of glucose absorption at the 10 mM glucose concentration ($n=2$; data not shown).

Addition of PLC inhibitor (Figure 2)

We next evaluated the effect of U-73122, a PLC βII inhibitor, because we have shown in cell culture of rat enterocytes that the effect of STRs appears to be mediated via a PLC- βII pathway [11]. At the least glucose concentration evaluated (10 mM), when we would not have expected STRs to augment the carrier-mediated glucose absorption, no effect of U-73122 was seen (from 2.3 ± 0.1 to 2.1 ± 0.2 $\mu\text{mol}/\text{min}/30\text{cm}$; $p=\text{NS}$). When we evaluated the greater glucose concentrations (35 mM and 100 mM) when our prior work suggested the recruitment of GLUT2-mediated uptake/absorption, in contrast to our hypothesis of a role for STR in sensing luminal glucose and thereby augmenting glucose uptake in the enterocyte by stimulating GLUT2 translocation to the apical membrane of the enterocyte, U-73122 had no inhibitory effect on the increase in carrier-mediated glucose absorption (from 7.7 ± 0.5 to 7.2 ± 0.5 $\mu\text{mol}/\text{min}/30\text{cm}$ and 15.7 ± 0.9 to 15.2 ± 1.1 $\mu\text{mol}/\text{min}/30\text{cm}$; $p=\text{NS}$).

Passive uptake of glucose was unaffected by U-73122 at any glucose concentration (data not shown).

DISCUSSION

Our study was designed to investigate the role of jejunal STRs in sensing increases in luminal concentration of glucose and thereby stimulating mechanisms mediated by intracellular PLC to augment glucose absorption. Our experiments were based on our previous *in vivo* experiments [1] showing augmented glucose absorption in the rat model mediated by GLUT2 and complemented by our cell culture work using rat enterocytes [11, 13] showing that STR agonists augment enterocyte uptake of glucose mediated by a PLC-dependent mechanism. In contrast to our hypothesis and prior *in vivo* work by others [12, 14], we were not able to demonstrate a direct effect on augmentation of glucose absorption when the potent STR agonist AceK was added to the infusate. In fact, during the intermediate glucose concentration (35 mM), when we would have expected the most evident effect of the potent STR agonist AceK, we found no increase in luminal, carrier-mediated glucose absorption when AceK was added and again, somewhat surprisingly, no effect during the 100 mM glucose solution.

Our findings are in stark contrast to what we observed when the human-derived Caco-2 cells, and the rat enterocyte cell lines RIE1, and GLUT2-transfected IEC-6 cells were exposed to an artificial sweetener [11]. In this prior cell culture study, we demonstrated increases in glucose absorption at glucose concentrations >25 mM when these enterocyte-

like cell lines were exposed to similar “luminal” concentrations of AceK for five minutes. Consistent with our cell culture studies, Kellett’s group has shown that the addition of sucralose, another albeit less potent STR agonist, increased glucose uptake in their *in vivo* rat preparation at lesser concentrations of glucose (<50 mM) [12, 14]. Although they focused on sucralose in their experiments, they also showed that AceK at similar concentrations (1 mM vs 2 mM in our study) exhibited similar efficacy to sucralose in its effect on glucose absorption [12].

We do not know why our *in vivo* experiments differ from our cell culture work and from the *in vivo* work of another laboratory. In our isolated segment of jejunum, similar to the preparation studied by Kellett’s group, we purposely excluded the stomach and duodenum completely from exposure to the sweet taste pharmacologic agents, and the luminal secretions from the foregut do not mix with our infusate in the jejunal study segment. The exposure of receptors in the tongue and gastroduodenum to these agents and the presence of foregut secretions may be necessary for the activation of the cellular component of the STR pathway in jejunal enterocytes *in vivo*, although the effect of STR agonists and antagonists had measureable effects on enterocyte-like cells in culture [11] and *in vivo* [12]. Prior work with Western blotting and immunocytochemistry revealed that the translocated intimin receptor (Tir) proteins (part of the STR complex) are expressed in rat jejunum in Paneth cells, and solitary chemosensory cells, but also at the apical membrane of enterocytes [12]. Similarly, we probed rat enterocytes and also could find Tir receptors (unpublished data). Although secretions from the stomach and/or duodenum may play a role in orchestrating the activity of Tir proteins between these three, different enteric cell lines, at present, there are no data to support or even suggest this interaction. Indeed, our cell culture work [11] showed the effect of a STR agonist to be effective in rat enterocytes without associated enteroendocrine cells or related neurohumoral effects. Finally, Raybould [15] and Shirazi-Beechey et al [16] have shown an interaction between taste receptors and visceral afferent nerves; while this interaction may have been disrupted in our anesthetized rats, we must point out that a marked increase in carrier-mediated glucose absorption was present in our prior *in vivo* study [1] and the current study when the luminal glucose concentration was increased, presumably via a GLUT2-mediated mechanism based on our prior work [1].

STRs are also present elsewhere in the alimentary tract [7]. The tongue of mammals contains the same, G-protein coupled taste receptor complex (i.e. T1R) as is found in the mucosa of the upper gut. Stimulation of taste receptors on the tongue may be necessary to activate maximally the taste receptors in the jejunum, possibly via a central neural mechanism. Indeed, Giduck et al showed that stimulating the rat oropharynx with sucrose produced an increase in intestinal glucose absorption compared to rats that received no oral stimulation [17]. Because we studied anesthetized rats, our experimental design may have altered the normal absorptive stimuli in the jejunum *in vivo*, yet the effect of STR agonists and PLC-BII inhibitors was evident in our cell culture studies [11]. We point out, however, that a similar lack of effect of STR agonists has also been described in both diabetic and normal human subjects, further questioning the physiologic role of STR in augmenting glucose uptake in the gut [18-20] as our current study shows.

We wanted to determine if AceK, a well-documented, potent STR agonist, would increase glucose absorption at concentrations of glucose that do not of themselves stimulate an increase in glucose uptake by GLUT2 as we have shown previously in this rat model [1]. We found no evidence for such augmentation by GLUT2-mediated transport in the 10 mM glucose solution where the majority of uptake would otherwise be by SGLT1 [1]. Similarly, we wanted to determine if AceK would further augment glucose absorption at concentrations of luminal glucose (35 and 100 mM) that themselves increase glucose absorption via an SGLT1-dependent mechanism that increases GLUT2 translocation to the

apical membrane of the enterocyte and thereby augments glucose uptake [1, 13]. We chose 35 mM glucose as a concentration at which maximal glucose uptake (and GLUT2 apical translocation) would not have been achieved. Again, in contrast to our hypothesis, we found no evidence for such augmentation of glucose absorption *in vivo* in our rat model; either this proposed mechanism mediated by STRs is not active in the rat jejunum or, less likely, the 35 mM and 100 mM glucose concentrations had already lead to maximal stimulated glucose uptake.

Our study has several limitations. The rats were anesthetized, yet the jejunal study segment was perfused naturally by the rat circulation, similar to the preparation by Mace et al [12]; why our results differ we cannot explain despite the marked increase in glucose absorption that occurs with increased concentration of glucose (>30 mM) in both our work and that of Mace et al [12]. Second, we only evaluated in depth one concentration of AceK and U-73122 in six rats/group. These doses are well supported, both in our cell culture work [13] and in the literature both *in vitro* and *in vivo* [2, 12]. In addition, because the effect of these agents appear to be mediated within the enterocyte, the constant continuous presence of the STR agonist and the PLC antagonist was maintained in the infusate throughout the experimental period; therefore, the enterocytes were exposed continuously to these agents; parenteral administration was not used. Because we were surprised by the lack of effect of AceK at the well-established dose of 2 mM, we also tried a greater dose (10 mM) and similarly found no effect on glucose uptake.

In summary, we were unable to confirm our hypothesis nor show that the concomitant addition of an artificial sweetener or a STR antagonist (PLC inhibitor) had any substantive effect on enteric, carrier-mediated glucose absorption in a live, albeit anesthetized animal model at low (10 mM), intermediate (35 mM), or high (100 mM) luminal concentrations of glucose. If artificial sweeteners do augment glucose absorption after a meal, which we were not able to reproduce with our *in vivo* model of the isolated jejunum, our findings suggest that the effects occur independent of isolated stimulation of STRs in the jejunum in the rat. These observations may have important, relevant physiologic and nutritional implications in the management and prevention of diabetes and obesity. Further work in this compelling field is necessary to better understand the actual role of enteric STRs in glucose absorption.

Acknowledgments

This work was supported in part by a grant from the National Institutes of Health (DK39337 – MG Sarr).

References

1. Chaudhry RM, Scow JS, Madhavan S, et al. Acute enterocyte adaptation to luminal glucose: a posttranslational mechanism for rapid apical recruitment of the transporter GLUT2. *J Gastrointest Surg.* 2012; 16:312–9. [PubMed: 22068967]
2. Kellett GL, Helliwell PA. The diffusive component of intestinal glucose absorption is mediated by the glucose-induced recruitment of GLUT2 to the brush-border membrane. *Biochem J.* 2000; 350(Pt 1):155–62. [PubMed: 10926839]
3. Gorboulev V, Schurmann A, Vallon V, et al. Na(+)-D-glucose cotransporter SGLT1 is pivotal for intestinal glucose absorption and glucose-dependent incretin secretion. *Diabetes.* 2012; 61:187–96. [PubMed: 22124465]
4. Sbarbati A, Osculati F. The taste cell-related diffuse chemosensory system. *Prog Neurobiol.* 2005; 75:295–307. [PubMed: 15882778]
5. Sternini C, Anselmi L, Rozengurt E. Enteroendocrine cells: a site of 'taste' in gastrointestinal chemosensing. *Curr Opin Endocrinol Diabetes Obes.* 2008; 15:73–8. [PubMed: 18185066]
6. Merigo F, Benati D, Cristofaletti M, et al. Glucose transporters are expressed in taste receptor cells. *J Anat.* 2011; 219:243–52. [PubMed: 21592100]

7. Dyer J, Vayro S, Shirzai-Beechey SP. Mechanism of glucose sensing in the small intestine. *Biochem Soc Trans.* 2003; 31:1140–2. [PubMed: 14641013]
8. Freeman SL, Bohan D, Darcel N, et al. Luminal glucose sensing in the rat intestine has characteristics of a sodium-glucose cotransporter. *Am J Physiol Gastrointest Liver Physiol.* 2006; 291:G439–45. [PubMed: 16675747]
9. Bezencon C, le Coutre J, Damak S. Taste-signaling proteins are coexpressed in solitary intestinal epithelial cells. *Chem Senses.* 2007; 32:41–9. [PubMed: 17030556]
10. Li X, Staszewski L, Xu H, et al. Human receptors for sweet and umami taste. *Proc Natl Acad Sci U S A.* 2002; 99:4692–6. [PubMed: 11917125]
11. Zheng Y, Sarr MG. Effect of the artificial sweetener, acesulfame potassium, a sweet taste receptor agonist, on glucose uptake in small intestinal cell lines. *J Gastrointest Surg.* 2013; 17:153–8. [PubMed: 22948835]
12. Mace OJ, Affleck J, Patel N, et al. Sweet taste receptors in rat small intestine stimulate glucose absorption through apical GLUT2. *J Physiol.* 2007; 582:379–92. [PubMed: 17495045]
13. Zheng Y, Scow JS, Duenes JA, et al. Mechanisms of glucose uptake in intestinal cell lines: role of GLUT2. *Surgery.* 2012; 151:13–25. [PubMed: 21943636]
14. Mace OJ, Lister N, Morgan E, et al. An energy supply network of nutrient absorption coordinated by calcium and T1R taste receptors in rat small intestine. *J Physiol.* 2009; 587:195–210. [PubMed: 19001049]
15. Raybould HE. Gut chemosensing: interactions between gut endocrine cells and visceral afferents. *Auton Neurosci.* 2010; 153:41–6. [PubMed: 19674941]
16. Shirazi-Beechey SP, Moran AW, Batchelor DJ, et al. Glucose sensing and signalling; regulation of intestinal glucose transport. *Proc Nutr Soc.* 2011; 70:185–93. [PubMed: 21450125]
17. Giduck SA, Threatte RM, Kare MR. Cephalic reflexes: their role in digestion and possible roles in absorption and metabolism. *J Nutr.* 1987; 117:1191–6. [PubMed: 3302135]
18. Grotz VL, Henry RR, McGill JB, et al. Lack of effect of sucralose on glucose homeostasis in subjects with type 2 diabetes. *J Am Diet Assoc.* 2003; 103:1607–12. [PubMed: 14647086]
19. Mezitis NH, Maggio CA, Koch P, et al. Glycemic effect of a single high oral dose of the novel sweetener sucralose in patients with diabetes. *Diabetes Care.* 1996; 19:1004–5. [PubMed: 8875098]
20. Ma J, Chang J, Checklin HL, et al. Effect of the artificial sweetener, sucralose, on small intestinal glucose absorption in healthy human subjects. *Br J Nutr.* 2010; 104:803–6. [PubMed: 20420761]

Figure 1.

Addition of acesulfame potassium t 1 hour did not decrease absorption at any of the tested glucose concentrations (10, 35, and 100 mM glucose).

Figure 2.

Addition of U-737122 (PLC β II inhibitor) had no effect on glucose absorption over the spectrum of different concentrations (10, 35, and 100 mM glucose)