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Direct Starch Digestion by Sucrase-Isomaltase and Maltase-Glucoamylase

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Congenital sucrase-isomaltase deficiency (CSID) is an intestinal disease caused by mutations of the SI gene (1–3). The membrane-bound complex (SI) has isomaltase and sucrase activity on the N- and C-terminal subunits, respectively. Both subunits also contribute maltase activities (4), which together with the 2 maltase activities of the maltase-glucoamylase (MGAM) complex digest starch to free glucose. Patients with CSID have reductions of activity or total absence of 1 or both subunits (5–7). In addition to the maldigestion of sucrose, because patients with CSID also have reduced maltase activity, they have maldigestion of starchy foods and may contribute to symptoms of dyspepsia and recurrent abdominal pain (5).

Starchy foods are common carbohydrate sources for human populations. To digest starch to glucose, 6 enzymes, including 2 α-amylases, 2 terminal subunits each of SI and MGAM, are involved. Because the structure of starch is highly correlated to the susceptibility of α-amylase, this lumenal activity plays an important role in digestion. We demonstrated, however, that in addition to α-amylase hydrolysis, SI and MGAM hydrolyze post-α-amylase dextrin to free glucose and determine the digestibility at the brush border. We show that glucogenesis is based on the structure of post-α-amylase dextrin (8). This discovery opens a new approach to controlling glucose delivery from starchy foods to the body. This finding also makes possible the selection of food starches with specific structures from which diets can be designed for patients with CSID who may be able to digest carbohydrates free of symptoms.

Starch is a form of chemical energy storage in plants. Native starches are cold water–insoluble granules with semicrystalline structures (9). Starch granules from various botanical sources have different shapes, sizes, surface pores, and internal channel distributions. Based on the crystalline structures observed in x-ray diffraction, starch granules are classified into A, B, and C types that result from different arrangements of molecules in the granules; they are highly correlated to the susceptibility of α-amylase hydrolysis (10–12). Most A-type granular starches, such as wheat, normal maize, and rice, have a higher susceptibility to α-amylase hydrolysis than B-type starches, such as potato and green banana. C-type starches, such as most of those in beans and seeds, are a mixture of A- and B-type structures (13,14), and their susceptibility to α-amylase is between that of A- and B-type starches (10).

Native starch granules, such as those found in uncooked vegetables, fruits, or low-moisture baked products, are not dominant in human carbohydrate diets. Cooking and other food processing technologies change the native starch molecular form into one that is relatively digestible. When heated with sufficient moisture, starch granules swell, and starch molecules leach out; thus, the starch molecules become more susceptible to digestive enzymes. At this stage, starch molecule properties, such as amylose, amylopectin chain-length, and amylopectin branch-density, are highly susceptible to digestive enzymes. In addition to the starch molecular properties, processes such as cooling and pressure plus other food components also contribute to the different digestibilities of starchy foods (15).

Digestion in the human body is an enzymatic hydrolysis to break down the vast botanical spectrum of starch molecules to a singular molecule, glucose. The first digestive enzyme to attack starchy foods is salivary α-amylase. After mastication, foods are propelled through the gastrointestinal tract and quickly hydrolyzed to dextrins by pancreatic α-amylase within the intestinal lumen. Both SI and MGAM are bound to the small intestine membrane and are the final digestive enzymes to release glucose from starchy foods. All 6 of the human digestive enzymes can cleave the main linkage, α-1,4 glycosidic linkage of starch polymeric molecules (4,16). The N-terminal subunit of SI and the C-terminal subunit of MGAM have additional minor activities on α-1,6 glycosidic branch linkage (17–20). All mucosal enzymes hydrolyze starch from the end of the molecules, but α-amylase can also break the huge molecules by cleaving from the middle and carrying 1 fragment with them when it attacks the next molecular segment (21,22). The endohydrolytic and multiple attack properties quickly break down starch molecules from approximately 10^8 Da (depending upon the botanical source of starch) to dextrins of 342 to 648 Da. The conventional view of starch digestion, therefore, focused on α-amylase hydrolysis, and the role of 4 α-glucosidases to convert post-α-amylase dextrins to glucose. SI and MGAM are the double-headed gatekeepers that regulate production of free glucose for transport through the mucosal sodium-dependent glucose cotransporter-1 gate.

Starch is thus classified into rapidly digestible, slowly digestible, and resistant starch, based on the reaction of combined pancreatic α-amylase and fungal glucoamylase (fungal glucoamylase is commonly used in in vitro systems to convert the dextrins to glucose) (23). We found, however, that human α-glucosidases do not only simply convert post-α-amylase dextrins to glucose but also react with starch or dextrin molecules in a more complicated

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The study was supported by the Whistler Center for Carbohydrate Research at Purdue University.

The authors report no conflicts of interest.

DOI: 10.1097/01.mpg.0000421414.95751.be

TABLE 1. Relative direct α-glucogenesis from starch by individual recombinant mucosal α-glucosidases

	Ct-SI	Nt-SI	Ct-MGAM	Nt-MGAM
Native granular starch	6.2 ± 0.7	0.8 ± 0.1	5.0 ± 0.3	0.3 ± 0.4
Cooked starch	28.9 ± 2.8	20.2 ± 3.2	76.0 ± 1.7	24.2 ± 0.9

Ct-MGAM = C-terminal subunit of maltase-glucoamylase; Ct-SI = C-terminal subunit of sucrase-isomaltase; Nt-MGAM: N-terminal subunit of maltase-glucoamylase; Nt-SI = N-terminal subunit of sucrase-isomaltase; both Nt-SI and Nt-MGAM are human recombinant enzymes; both Ct-SI and Ct-MGAM are mouse recombinant enzymes. The value presents the released glucose (micrograms) from 100 μg starch. Native granular starch was incubated with individual α-glucosidase of 200 U for 48 hours, and cooked starch was incubated with enzymes of 100 U for 24 hours. Values are mean ± standard deviation in triplicate analysis.

manner, depending on the chemical structure of starch or dextrin (24). In other words, α-amylase is not the only digestive enzyme to determine the glucose generation rate, and the chemical structure of starch or post-α-amylase dextrin affects the glucogenesis at the brush border.

METHODS

Normal maize starch, including native granular starch and cooked starch, were incubated with individual mucosal α-glucosidase subunits in the in vitro system to examine the glucogenesis as described previously (24). Briefly, native granular starch and cooked starch were incubated with individual α-glucosidases of 200 and 100 U, respectively, at 37°C. The incubation time of granular starch and cooked starch was 48 and 24 hours, respectively, because of the relatively higher glucogenesis of cooked starch. The released glucose amount and residual structure were measured (24).

RESULTS

Table 1 shows that individual α-glucosidases released glucose from both native granular starch and cooked starch in different proportions.

DISCUSSION

Our study confirms that α-amylase is not the only enzyme to hydrolyze starch. Native granular and cooked starches were directly digested to glucose by all 4 mucosal α-glucosidases without the participation of α-amylase. A proposed scheme of starch digestion by the both α-amylase and mucosal α-glucosidases is shown in Figure 1. Although native granular starch is less susceptible to digestive enzymes than other starch forms, each mucosal α-glucosidase activity liberated free glucose. The most surprising finding, however, arose from cooked starch; all 4 mucosal α-glucosidases liberated 20% to 80% (anhydroglucose amount/starch dry weight) glucose from starch in the in vitro system. All 4 of the mucosal α-glucosidases are assayed as maltase in Dahlqvist biopsy assays (25). The minor activity on the α-1,6 glycosidic linkage does not completely explain the large starch digestion capability. SI is known to be responsible for the digestion of sucrose in the human body (16), and sucrose is the energy precursor of starch in plants; thus, SI may have enabled normal cooked starch digestion. MGAM regulates the total starch digestion, but the slower SI plays a complementary role.

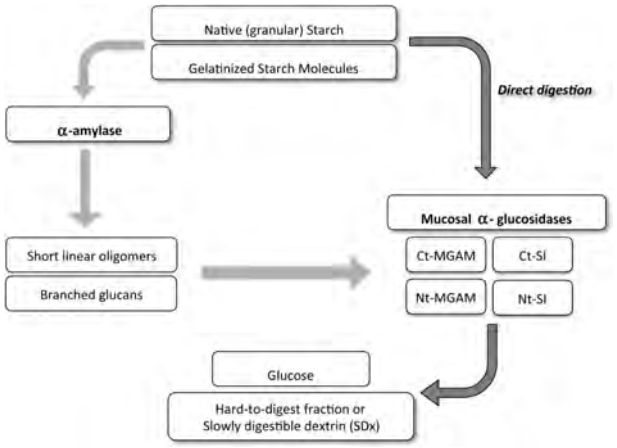

FIGURE 1. The proposed scheme of starch digestion by the digestive enzymes in the body.

The finding of the direct starch digestion activity by all 4 mucosal maltases (α-glucosidases) demonstrates the importance of both SI and MGAM on starch digestion when lumenal α-amylase is absent or has poor activity. For example, SI and MGAM are the key enzymes that digest starch for the young infant before pancreatic α-amylase secretion matures in the body. Young infants without SI must rely on MGAM to digest starch, but MGAM activity may be depressed if digestion produces large quantities of maltotriose and maltotetraose, which are normally hydrolyzed by SI. Healthy young infants with developmental α-amylase delay may be able to digest starch, but young infants with CSID may have symptoms that result from maltotriose- (G3) and maltotetraose (G4)-suppressed MGAM activity.

CONCLUSIONS

Our study was designed to develop a methodology that can predict types of starchy foods that cause fewer CSID symptoms. In older children (or adults), with the full development of pancreatic α-amylase, G3 and G4 become the primary glucans in the lumen. For patients who have CSID, however, MGAM is the only α-glucosidase complex to convert post-α-amylase dextrins to glucose. Nevertheless, the activity of MGAM is regulated by the post-α-amylase dextrins, G3 and G4, which exert what is known as the ''brake effect'' (26,27). When rapidly digestible starches (definition is based on the susceptibility to α-amylase (23)) are fed, pancreatic α-amylase quickly breaks down starch molecules and generates large amounts of G3 and G4 that depress MGAM activity and may result in the poor digestion of post-α-amylase dextrins. The nondigested post-α-amylase dextrin becomes a substrate for colonic fermentation and leads to severe CSID symptoms. Thus, from the enzyme digestion mechanism, slowly digestible starches will introduce post-α-amylase dextrins to the small intestine at a relatively low rate, and have less impact on MGAM activity. As mentioned, the starch digestion rate is correlated to the starch chemical structures. The difference in chemical structures arises from the different botanical sources and food processing techniques (8). In the human body, SI and MGAM are involved in both direct starch and post-α-amylase dextrin digestion. Evidence from the digestion study on post-α-amylase dextrins (data not shown) suggests that the

chemical structure of post-α-amylase dextrin affects the rate of glucose production at the brush border, and the effect on individual α-glucosidase digestion is altered (8). Overall, the digestion capability of SI and MGAM is affected by the chemical structure of carbohydrates. Thus, in addition to controlling the amount of carbohydrate consumed, patients with CSID do have a choice of different types of starchy foods. Future clinical studies will attempt to increase those choices.

Acknowledgments: The authors thank Dr Lyann Sim at University of Toronto (currently at Carlsberg Research Center, Copenhagen, Denmark), Dr David Rose at University of Waterloo, Mr Stephen E. Avery, and Dr Roberto Quezada-Calvillo (currently at Universidad Autonoma de san Luis, Mexico) at the Baylor College of Medicine (Houston, TX) for preparing the mucosal enzymes.

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Inhibition of Maltase-Glucoamylase Activity to Hydrolyze α-1,4 Linkages by the Presence of Undigested Sucrose

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The digestion of glycemic carbohydrates (predominantly starch and sucrose) to monosaccharides (eg, glucose, fructose) is finally carried out by the mucosal α-glucosidases in the small intestine. They are located in the brush border membrane of the small intestine and are made up of maltase-glucoamylase (MGAM) and sucrase-isomaltase (SI) complexes. These complexes have 2

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The authors report no conflicts of interest.

DOI: 10.1097/01.mpg.0000421415.95751.f7