J. Dairy Sci. 100:1–21
https://doi.org/10.3168/jds.2016-12122

A mechanistic model of small intestinal starch digestion and glucose uptake in the cow

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ABSTRACT

The high contribution of postruminal starch digestion (up to 50%) to total-tract starch digestion on energy-dense, starch-rich diets demands that limitations to small intestinal starch digestion be identified. A mechanistic model of the small intestine was described and evaluated with regard to its ability to simulate observations from abomasal carbohydrate infusions in the dairy cow. The 7 state variables represent starch, oligosaccharide, glucose, and pancreatic amylase in the intestinal lumen, oligosaccharide and glucose in the unstirred water layer at the intestinal wall, and intracellular glucose of the enterocyte. Enzymatic hydrolysis of starch was modeled as a 2-stage process involving the activity of pancreatic amylase in the lumen and of oligosaccharidase at the brush border of the enterocyte confined within the unstirred water layer. The Na^+-dependent glucose transport into the enterocyte was represented along with a facilitative glucose transporter 2 transport system on the basolateral membrane. The small intestine is subdivided into 3 main sections, representing the duodenum, jejunum, and ileum for parameterization. Further subsections are defined between which continual digesta flow is represented. The model predicted nonstructural carbohydrate disappearance in the small intestine for cattle unadapted to duodenal infusion with a coefficient of determination of 0.92 and a root mean square prediction error of 25.4%. Simulation of glucose disappearance for mature Holstein heifers adapted to various levels of duodenal glucose infusion yielded a coefficient of determination of 0.81 and a root mean square prediction error of 38.6%. Analysis of model behavior identified limitations to the efficiency of small intestinal starch digestion with high levels of duodenal starch flow. Limitations to individual processes, particularly starch digestion in the proximal section of the intestine, can create asynchrony between starch hydrolysis and glucose uptake capacity.
Key words: starch digestion, small intestine, glucose uptake, mechanistic model

INTRODUCTION

The need to satisfy the energy requirements of high-genetic merit dairy cows during early lactation often results in the feeding of substantial quantities of starch rich concentrate. Coupled to this is the use of high-starch corn silages as a main or primary forage component in many dairy production systems (Khan et al., 2015). The fate of dietary starch is highly variable and depends on many factors, including starch type, processing, and interaction with other diet components (Mills et al., 1999a,b; Patton et al., 2012; Moharrery et al., 2014) as well as maturity of corn at harvest (Hatew et al., 2016; Peyrat et al., 2016); this has significant implications for the productive capacity of the dairy cow (Nocek and Tamminga, 1991).

Previously, we developed a model for lactate metabolism in the rumen with a view to address the issue of rumen acidosis (Mills et al., 2014). Whereas starch may be highly degraded by rumen microorganisms, up to 50% may escape undegraded to the small intestine, in particular with corn, sorghum, and legumes (Mills et al., 1999a; Larsen et al., 2009), depending on the ration. The digestion of starch within the small intestine, followed by the absorption of the released glucose, may avoid the inefficiencies of rumen fermentation (Waldo, 1973; Huntington et al., 2006; Reynolds et al., 2014). Digestion of up to 2.5 kg/d of starch in the small intestine of lactating dairy cows has been reported (Reynolds et al., 2014); however, starch reaching the small intestine is by nature less digestible than starch digested in the rumen. As starch flow to the small intestine increases, starch digestibility in the small intestine decreases, and

Received October 7, 2016.
Accepted January 23, 2017.
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limits may exist to the capacity of the small intestine for enzymatic hydrolysis of starch or glucose uptake by epithelial tissue (Mills et al., 1999b; Huntington et al., 2006; Reynolds et al., 2014). Subsequently, excessive fermentation in the hindgut of starch that escapes digestion in the small intestine may negatively affect fiber digestion and may have negative effects on absorption of microbial LPS (Li et al., 2012). Published data regarding glucose flux across the small intestine in cattle shows highly variable results depending on diet fed or level of postruminal glucose infusion (Huntington and Reynolds, 1986; Reynolds et al., 1988; Reynolds et al., 1991). Patton et al. (2012) compared several models on accuracy of prediction of postruminal starch digestion. Even with the large intestine compensating for part of the variation in starch digestion in the small intestine, they still obtained substantial prediction errors of 15% and over 20% of observed means for corn starch and non-corn starch, respectively. Hence, room for improvement of prediction of intestinal starch digestion exists. Complementary to improving empirical models (which include fractional rates of passage and digestion; e.g., Patton et al., 2012), is the study of factors that underlie such variation. The objective of the present study was to construct a mechanistic model that could be used to simulate the digestive metabolism of NSC flowing through the small intestine of the dairy cow.

MATERIALS AND METHODS

Our model is based on principles advanced by Mills et al. (1999b) and is illustrated in Figure 1. The level of aggregation adopted to describe the biological processes was similar to that used in previous modeling studies for the rumen and large intestine (Mills et al., 2014). Hence, the model can be considered alone as a tool for small intestinal starch digestion or as an element within a larger model of nutrient digestion and utilization in the dairy cow. The model consists of 3 principal sections representing the duodenum, jejunum, and ileum, between which parameters describing enzyme activity, metabolite transport, and intestinal physiology were varied according to literature values. These sections are further subdivided into subsections (2 in duodenum, 15 in jejunum, and 30 in ileum; see below for discussion), representing shorter lengths of intestine within which the state variables are represented. Division into subsections facilitates the simulation of digesta flow within each section (i.e., within duodenum, jejunum, or ileum) as well as between sections. Equations representative of the model and abbreviations used to define model entities are listed in the Appendix. Associated parameters describing properties of the model and their values are given in Table 1. All pools are expressed in moles, with volume in liters and time in hours. The flow equations are described by Michaelis–Menten or mass action forms. To describe NSC in molar terms, molecular mass of nonpolymerized and polymerized glucose is assumed to be 180 and 162, respectively. It is assumed that oligosaccharide resulting from starch hydrolysis contains an average of 5 glucose molecules.

Parameterization: Intestinal Size and Digesta Passage

In the absence of other experimental observations, the length of the small intestine was set according to the observations of Gibb et al. (1992) for dairy cows at different stages of lactation. Whereas duodenal length is well characterized within the literature, the proportion of total length attributable to the jejunal and ileal sections is less clear, with particularly little data available in the cow. Madge (1975) cites the ratio of duodenal, jejunal, and ileal length as 1:4:7; however, most experimental observations for biological activity at these 3 points relate to measurements taken well within the bounds of the respective sections. Therefore, location-dependent parameters were set according to observed data for the mid duodenum, mid jejunum, and terminal ileum (0.9 of ileal length). These parameters were extrapolated in a linear fashion between these 3 points. The proportions of small intestinal length accounted for by the duodenum, jejunum, and ileum were set at 0.02, 0.35, and 0.63, respectively. For the volume and surface area calculations, the small intestine was treated as a cylinder of diameter 5 cm across all sections (Braun et al., 1995).

Duodenal nutrient inputs are determined by the composition of infusate or of duodenal nutrient flow reported in the investigations being used for model simulations. Passage of digesta between the intestinal sections and subsections was represented as a fractional rate (k_p), assuming mixing within each section due to myoepithelial contractions (Ruckebusch, 1988). Fractional passage rate between the luminal pools was a function of total mean retention time (**MRT**) for the small intestine. The total MRT in the small intestine was dependent on k_p and intestinal length. Where experimental observations are lacking, k_p was set according to Cant et al. (1999), who observed a rate of 16 m/h in a mature dairy heifer (507 kg). Whereas, in reality, passage along the small intestine is pulsatile (Ruckebusch, 1988), for simplicity the model assumes a continuous digesta flow between the luminal pools of the intestinal subsections.

Small intestinal digesta volume was set at 13% of theoretical lumen volume (12.5 L for a dairy cow with small intestinal length assumed to be 48 m; Gibb et al., 1992). Water absorption was assigned a fractional rate