

An introductory review of resistant starch type 2 from high-amylose cereal grains and its effect on glucose and insulin homeostasis

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Refined carbohydrates result from milling techniques that remove the outer layers of a cereal grain and grind the endosperm into a flour ingredient that is devoid of dietary fiber. Technologies have been developed to produce high-amylose cereal grains that have a significantly higher resistant starch type 2 and thus dietary fiber content in the endosperm of the cereal grain, which has positive implications for human health. A review of the literature was conducted to study the effects of resistant starch type 2 derived from high-amylose grains on glucose and insulin response. While thousands of articles have been published on resistant starch, only 30 articles have focused on how resistant starch type 2 from high-amylose grains affects acute and long-term responses of glucose and insulin control. The findings showed that resistant starch has the ability to attenuate acute postprandial responses when replacing rapidly digestible carbohydrate sources, but there is insufficient evidence to conclude that resistant starch can improve insulin resistance and/or sensitivity.

INTRODUCTION

Objective

The current review article focuses on the effect of resistant starch type 2 from high-amylose cereal grains on specific endpoints related to acute and long-term glucose and insulin responses. While comprehensive review articles exist that discuss the relationship between resistant starch and various metabolic outcomes, 5 types of resistant starch exist, which may elicit different individual responses. In addition, the different types of resistant starch come from various origins, which may influence their metabolic responses. Significant bodies of literature have reported on the discovery of high-amylose grains through various breeding technologies, and their potential impact on human health has been

demonstrated through several clinical studies. However, to the author's knowledge, no comprehensive literature reviews have analyzed these studies and reported on the effects of resistant starch type 2 from high-amylose grains on specific endpoints related to glucose and insulin response.

Resistant starch overview

Starch, the major storage polysaccharide in plants, is composed of two glucose polymers: amylose and amylopectin.¹ Amylose is a minimally branched, linear structure linked by α 1, 4 bonds that is tightly packed within the starch granule found in the endosperm of cereal grains.² Amylopectin is a branched molecule that contains both α 1, 4 and α 1, 6 bonds, yielding a complex

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structure that tends to take up the majority of space in the starch granule of cereal grain endosperm.² Starch is a digestible carbohydrate source that is hydrolyzed by the salivary and pancreatic enzyme, α -amylase.³ As a result of α -amylase activity, starch is broken down into smaller disaccharides and polysaccharides, which are then acted on by brush border enzymes in the small intestine.⁴ Brush border enzymes work to break down disaccharides and polysaccharides into monosaccharides such as glucose, fructose, and galactose, which are then absorbed into the bloodstream.⁴ The release of these monosaccharides into the blood signals endocrine organs such as the pancreas to secrete insulin, which helps deliver glucose into the cells and keeps plasma glucose in the homeostatic range.⁵ The consumption of refined carbohydrates can lead to a rapid rise in plasma glucose, which triggers the pancreas to secrete inappropriately large doses of insulin.⁶ Large surges of glucose and insulin secretions constitute one of many factors that can lead to chronic inflammation, which is known to play a significant role in the development of insulin resistance and subsequent type 2 diabetes.^{7,8} Dietary interventions that can reduce these large surges of glucose and insulin, or that can help enhance glucose uptake and insulin effectiveness, are of interest on account of their ability to prevent and/or control the progression of type 2 diabetes.

Scientists discovered in the late 20th century that some forms of starch pass through the small intestine undigested, thus adding the term “resistant starch” to the definition of dietary fiber, which was previously known as the nondigestible components of plant cell walls.^{9,10} Resistant starch passes through the human small intestine unaffected by α -amylase and other pancreatic enzymes, despite the presence of glucose polymers held together by α 1, 4 and α 1, 6 linkages.¹¹ There are five types of resistant starch defined primarily by their structural properties. Resistant starch type 1, commonly found in whole grains, is resistant to digestion because it is physically inaccessible to enzymes owing to the presence of the bran and germ layers.¹² Resistant starch type 2 is resistant to digestion on account of ungelatinized starch molecules tightly packed in the endosperm, making their accessibility to digestive enzymes minimal¹³; resistant starch type 3 is composed of retrograded amylose, which forms a tight, crystalline structure that is inaccessible to digestive enzymes¹²; resistant starch type 4 is created through chemical modification of starch; and resistant starch type 5 comprises a complex of amylose and lipids which can be found naturally in starch granules or can be created through chemical modification.^{14,15}

Increasing the consumption of resistant starch is of interest owing to the ability of this starch to enter the large intestine and undergo fermentation by resident bacteria.¹¹ One group of by-products generated from bacterial fermentation include the short-chain fatty acids butyrate, propionate, and acetate.¹¹ The synthesis and release of short-chain fatty acids decrease the pH of the colon, which subsequently helps to maintain a healthy bacterial population and prevent the overgrowth of harmful classes of bacteria such as *Enterobacteriaceae* and *Clostridia*.¹⁶ Aside from their cumulative effects, individual short-chain fatty acids also play major roles in a variety of mechanisms. Butyrate is the main fuel source for colonic epithelial cells and has antineoplastic effects in the colon.¹⁷ Propionate may play a role in regulating glucose homeostasis in humans, as in-vitro studies have shown it increases insulin-mediated glucose uptake into adipocytes.¹⁸ Acetate is an energy source for peripheral tissues and plays a role in cholesterol synthesis.¹⁹ Resistant starch also has a prebiotic effect and can stimulate the growth of many beneficial bacterial genera, such as *Bifidobacterium*.²⁰ In addition to its ability to function as a fermentable fiber and a prebiotic, resistant starch is known to play a role in improving postprandial glucose response, postprandial insulin response, and insulin sensitivity, with mechanisms suggested to be both dependent and independent of the by-products of bacterial fermentation.^{21–23}

Importance of fiber in the diet

The current recommendations for dietary fiber consumption are primarily based on evidence indicating its protective effect in preventing the development of cardiovascular disease.²⁴ The consumption of soluble fiber from oat beta-glucan decreases serum low-density lipoprotein (LDL)-cholesterol and serum total cholesterol, both of which are essential for cardiovascular health and preventing disease.²⁵ Additionally, diets higher in soluble fiber are associated with decreases in blood pressure.²⁵ There is strong evidence that reducing body weight, increasing physical activity, and consuming soluble and/or insoluble dietary fiber decrease the risk of developing type 2 diabetes.^{26–28} Moreover, it has been suggested that soluble and/or insoluble fiber consumption may play a role in preventing type 2 diabetes through the ability of fiber to increase satiety, slow nutrient release into the body, and decrease body weight.^{29,30} Diets that contain a mixture of insoluble and soluble fibers have been shown to decrease fasting insulin and improve insulin sensitivity, both of which have positive implications for decreasing the risk of developing type 2 diabetes.³¹

Recommendations for dietary fiber consumption vary by organization, but the adequate intake as recommended by the Institute of Medicine is 25 g/d for females and 38 g/d for males, yet the average intake in US adults is 15–16 g/d.²⁴ Because of the concerning deficiency in the majority of the American population and the role dietary fiber plays in human health, the 2015–2020 Dietary Guidelines for Americans declared dietary fiber as a nutrient of public health concern, prompting many food organizations to rethink their strategy around dietary fiber.³² Existing technologies allow the food industry to add supplemental, isolated fiber to food products, but there are still many consumers who fall short of the recommendations. To encourage the consumption of more dietary fiber, high-amylose grains that can be milled into refined flour and inherently contain high levels of resistant starch type 2 have been developed to deliver similar taste, texture, and visual appeal to refined cereal grains while maintaining the amount of fiber needed to potentially decrease the risk of chronic disease.

Cereal chemistry overview

Conventional cereal grains have three main layers that make up a whole grain – the germ layer, bran layer, and endosperm – all of which have unique nutritional profiles. The bran and germ layers contain nutrients such as vitamin E, vitamin B6, minerals, phytoestrogens, antioxidants, and fiber, whereas the endosperm contains mostly digestible starch.³³ Within the endosperm, the starch granule typically contains more than 70% amylopectin and less than 30% amylose. To create refined flour, whole grains go through milling technologies that separate out the fiber-rich bran and germ portion and mill down the starchy endosperm to create a very functional, yet nutrient poor, food ingredient. Targeting biochemical pathways that increase the amylose content within a starch granule allows for the synthesis of high-amylose grains that contain more resistant starch type 2, and consequently more dietary fiber, in refined flour.

Starch synthesis occurs through a series of biochemical reactions within the endosperm of a cereal grain. Sucrose is delivered to the cytosol of the developing endosperm as a result of photosynthesis or recirculation of carbohydrates, and activates the starch synthesis pathway.³⁴ The enzymatic degradation of sucrose in the cytosol ultimately yields glucose-1-phosphate, which is transported into the developing endosperm amyloplast through a hexose phosphate transporter.³⁴ Adenosine diphosphate glucose pyrophosphorylase (ADP-glucose pyrophosphorylase) activity is found in both the plastids and cytosol of the developing cereal grain.³⁵ ADP-glucose pyrophosphorylase and ATP (adenosine

triphosphate) work to break down glucose-1-phosphate to form ADP-glucose, which is used by multiple enzymes to elongate glucose polymers, thus initiating the synthesis of amylose and amylopectin.³⁶ The enzyme granule-bound starch synthase (GBSS) forms amylose by binding to the ADP-glucose substrate and adding additional glucose residues.³⁴ Multiple different starch synthase (SS) enzymes initiate amylopectin development by removing glucosyl units from ADP-glucose and transferring them to the non-reducing end of the glucan chains.³⁵ Additional starch branching enzymes (SBEs) and starch debranching enzymes are required to complete the synthesis of amylopectin.³⁴ SBEs cleave the α 1, 4 linkages within the glucan chains created by SS enzymes and subsequently add the cleaved portion back onto an adjacent glucan chain to create branch points linked by α 1, 6 bonds.³⁷ Starch debranching enzymes formalize the structure of amylopectin by hydrolyzing excessive α 1, 6 linkages.³⁴ Throughout the starch synthesis pathway, the generation of substrates for one enzymatic pathway is achievable via the enzymatic activity of a different pathway. This dynamic cycle leads to the synthesis of starch molecules in the cereal grain endosperm, which act to store energy for the plant.³⁵

Breeding technologies have facilitated the production of grain varieties incorporating alterations in the starch synthesis pathway that favor the synthesis of amylose and thus resistant starch type 2. A variety of mechanisms have been identified for increasing the amylose content of cereal grains. The most successful mechanisms involve suppressing or reducing the activity of the SBE enzymes, which can result in increases of amylose of 50% or more. In addition to the increases in amylose, alterations in the starch synthesis pathway concurrently yield amylopectin structures with high degrees of polymerization ($DP > 20$ times the standard), which form stable double helices and can resist enzymatic digestion, thus contributing to the resistant starch content.^{38,39} A summary of the explored mechanisms and the generated amylose contents in different cereal grains is shown in [Table 1](#).^{2,40–47}

METHODS

The electronic search engines utilized in this literature review were PubMed, Medline, Google Scholar, and ScienceDirect. The search terms for relevant articles published in peer-reviewed journals were: “high amylose wheat,” “high amylose rice,” “high amylose barley,” “high amylose corn,” “wheat GBSS,” “wheat SS,” “wheat SBE,” “rice GBSS,” “rice SS,” “rice SBE,” “barley GBSS,” “barley SS,” “barley SBE,” “corn GBSS,” “corn SS,” “corn SBE,” “high maize, glucose,” “high amylose wheat, glucose,” “high amylose rice, glucose,” and “high

Table 1 An overview of high-amylose grains generated through alterations in starch synthesis pathways of cereal grains and their respective amylose contents

Cereal grain	Original amylose content in starch, %	Alteration in starch synthesis pathway	Amylose content in high-amylose starch, %
Wheat	~25	Overexpression of GBSS	30 ⁴⁰
Wheat	~25	Suppression of SSIIa	37 ⁴¹
Wheat	~25	Reduction in both SBEIIa and SBEIIb	65–85 ²
Rice	~20	Suppression of SBEIIb	28 ³⁸
Rice	~20	Suppression of SSIIIa	30 ³⁸
Rice	~20	Suppression of SSIIIa + SBEIIb	45 ³⁸
Rice	~20	Suppression of SBEI + SBEIIb	65 ³⁹
Corn	~30	Suppression of SBEIa	No impact ⁴²
Corn	~30	Suppression of SBEIIb	>60 ⁴³
Corn	~30	Suppression of SBEIIb, addition of modifier genes	>80 ⁴⁴
Barley	~25	Suppression of SBEIIa or SBEIIb	30–40 ⁴⁵
Barley	~25	Suppression of the <i>amo1</i> gene, which negatively regulates GBSS, SS, and SBE	50 ⁴⁶
Barley	~25	Reduction in SBEIIa and SBEIIb	>70 ⁴⁵
Barley	~25	Suppression of SSIIa	>71 ⁴⁷

Abbreviations: GBSS, granule-bound starch synthase; SBE, starch branching enzyme; SS, starch synthase.

amylose barley, glucose.” Appropriate articles, their relevant references, and cereal chemistry textbooks were analyzed for inclusion in this review. To be included for analysis, sources had to be written in English and contain relevant information, consisting of clinical research conducted in humans pertaining to glucose and insulin homeostasis in response to treatments containing resistant starch type 2 that was derived from a high-amylose cereal grain. Additionally, the intervention had to include a high-amylose cereal grain that contained at least a 50% increase in amylose within the starch component of the respective grain. This is because cereal grains are raw agricultural ingredients and it can be difficult to differentiate between high-amylose grains that have been developed and bred for increased amylose content and natural variations in crop conditions that result in increased amylose content. Relevant end points derived from the analyzed research were predominantly related to acute or long-term markers of glucose and insulin response. These included, but were not limited to, postprandial glucose, postprandial insulin, fasting glucose, fasting insulin, insulin resistance, and/or insulin sensitivity. Articles were excluded if they met any of the following exclusion criteria: (1) there was no identification of the type of resistant starch (1–5) used in the intervention; (2) the resistant starch type 2 intervention was not derived from a high-amylose cereal grain; (3) the primary intervention was not resistant starch type 2; (4) the resistant starch type 2 intervention was combined with another intervention; or (5) the endpoints were not centered on glucose and/or insulin responses.

RESULTS AND DISCUSSION

Resistant starch type 2 from high-amylose grains has been shown to play a role in improving end points

related to acute glucose and insulin responses and long-term effects of glucose and insulin control. End points obtained after short-term and long-term interventions related to acute glucose and insulin responses include postprandial peak glucose, postprandial glucose and insulin at specific points in time, and the incremental area under the curve (iAUC) for postprandial glucose and insulin. These types of end points provide information on the ability of resistant starch to influence the immediate metabolism of glucose after consumption. While this is important for outcomes relating to short-term metabolic health, these end points fail to provide insight into the long-term effects of the ability of resistant starch to improve insulin sensitivity by enhancing the mobilization and utilization of glucose. Examples of end points obtained after intervention studies that relate to the long-term effects of glucose and insulin control include fasting blood glucose, insulin resistance as measured by the Homeostatic Model of Assessment (HOMA), insulin sensitivity as measured by the frequently sampled intravenous glucose tolerance test (FSIVGTT), and insulin sensitivity as measured by the euglycemic-hyperinsulinemic clamp. These end points provide a better indication of how resistant starch influences the body’s ability to metabolize glucose, which is an essential mechanism for improving insulin resistance and sensitivity.

The initial search terms described in the “Methods” section resulted in thousands of articles, but only 30 articles met the inclusion criteria and were included for analysis in this literature review. Because acute glucose and insulin responses and the long-term effects of glucose and insulin control may be interpreted differently, the included studies were divided into these two categories of end points.

Resistant starch and its effect on acute markers of glucose and insulin response

Table 2^{39,48–62} describes the analyzed studies that observed the acute effects of resistant starch. Table 2 includes details on the resistant starch dose, control dose, participant characteristics, study characteristics, and the comprehensive results reported.

Two studies looked at how resistant starch supplementation from high-amylose cornstarch may influence acute postprandial metabolites when the resistant starch dose was adjusted to match the control for available carbohydrate. Neither study showed a significant improvement in the acute postprandial glucose or insulin response.^{50,59} Another two studies looked at different doses of high-amylose corn that provided less available carbohydrate than the control or provided equal amounts of available carbohydrate as the control in order to understand whether the effects of resistant starch depended on the quantity of available carbohydrate entering the small intestine or the overall quantity of resistant starch.^{51,58} The results from the first of these two studies showed that the resistant starch treatment with the least amount of available carbohydrate yielded significant improvements in postprandial glucose and insulin response compared to the control, whereas the treatment with equal available carbohydrates yielded no significant differences compared to the control.⁵⁸ The results from the second study showed that both resistant starch treatment doses resulted in significant reductions in postprandial glucose, postprandial insulin, and iAUC for postprandial glucose and insulin compared to the control.⁵¹ However, this study used arepas made from high-amylose corn flour as the delivery format, and it is possible that the two different doses of resistant starch both yielded improvements in postprandial metabolites owing to the decreased rate of enzymatic digestion through the unexpected formation of amylose-lipid complexes in the arepa-making process.⁵¹

Six studies examined the effect of resistant starch supplementation from high-amylose corn on postprandial glucose and insulin responses when matched to the control for the quantity of total carbohydrate in the test meal. All studies, except one,⁵² found significant improvements with resistant starch supplementation in terms of postprandial glucose and insulin response.^{48,53,57,60,62} A study involving healthy adults found no differences in acute glucose or insulin response after the subjects consumed resistant starch meals, but this study was uniquely designed to deliver equal amounts of total carbohydrate and total fiber from other food sources, which may have influenced the ability of resistant starch to elicit a unique outcome.⁵² Behall and Hallfrisch studied various doses of

resistant starch from high-amylose cornstarch in healthy adults and found that breads made with cornstarch containing more than 50% amylose, and thus at least twice the resistant starch content, yielded significantly lower peak glucose concentrations ($P < 0.003$).⁴⁸ In addition, breads made with the highest doses of resistant starch resulted in a significantly lower 2-hour iAUC glucose (13.4 g dose only; $P < 0.0001$) and 2-hour iAUC insulin (11.5 g and 13.4 g dose; $P < 0.0001$).⁴⁸ Hospers et al studied two different doses of resistant starch in pasta meals made with high-amylose cornstarch in healthy males and found that the 2 resistant starch meals yielded significantly lower postprandial glucose (30, 60 minutes; $P < 0.03$, $P < 0.034$) and insulin responses (60, 120, 180 minutes; $P < 0.01$, $P < 0.001$, $P < 0.001$) than the control subjects.⁵³ Luhovyy et al studied the effects of consuming cookies made with 2 different doses (22.2 g vs 11.1 g) of resistant starch from high-amylose corn flour once a week for 3 weeks in healthy male participants.⁵⁷ The two different doses of resistant starch both yielded significantly lower post-treatment iAUC glucose (0–120 minutes; $P < 0.0001$), post-second-meal iAUC glucose (120–200 minutes; $P < 0.0001$), and cumulative iAUC glucose (0–200 minutes; $P < 0.0007$) than the control subjects.⁵⁷ In addition, the high-dose resistant starch treatment (22.2 g) yielded a significantly lower peak glucose concentration than the control group at 30 minutes ($P < 0.05$).⁵⁷ Another study, conducted by Noakes et al, found that overweight individuals who consumed a diet high in resistant starch from high-amylose cornstarch on a daily basis for 12 weeks had significantly lower postprandial glucose at 45 minutes ($P < 0.03$) after a meal tolerance test, though there was no effect on iAUC glucose (105 minutes), compared to the control group.⁶⁰ The results of the meal tolerance test also showed that at 75 minutes, the resistant starch group had a significantly lower postprandial insulin concentration, and the iAUC insulin (105 minutes) was significantly lower, compared to the control group ($P < 0.001$, $P < 0.01$).⁶⁰ Zafar found that consuming beverages formulated with 75 g amylose from high-amylose cornstarch yielded a significantly lower 2-hour iAUC glucose than the control beverage and the beverage containing 38 g amylose from high-amylose cornstarch ($P < 0.05$, $P < 0.05$).⁶²

Another study examined the effect of resistant starch supplementation from high-amylose rice on postprandial glucose and insulin response when matched to the control for the quantity of total carbohydrate in the test meal. When consuming meals made with high-amylose rice, healthy participants had significantly lower peak glucose values ($P < 0.05$) and 90-, 120-, and 240-minute iAUC glucose than when they consumed meals made with wild-type rice ($P < 0.05$,

Table 2 Characteristics of the studies that investigated acute markers of glucose and insulin response

Reference	Study characteristics	Participants	Results
Behall and Hallfrisch (2002) ⁴⁸	The intervention tested 2.0 g, 3.8 g, 8.2 g, 11.5 g, or 13.4 g RS from high-amylose cornstarch. The control was a glucose solution. Breads were formulated to match the control for total CHO.	Healthy participants (13 male, 12 female) aged 38–43 y. Participants consumed each test product on 6 different days.	Peak PP glucose concentration for breads made with 8.2 g, 11.5 g, or 13.4 g RS were significantly lower than breads made with 2 g or 3.8 g RS ($P < 0.003$). Two-hour iAUC PP glucose for the 13.4-g RS group was significantly lower than for the 2 g, 3.8 g, or 8.2 g RS group ($P < 0.0001$), but was not different with the 11.5 g dose. PP insulin at $t = 30$ min was significantly lower after a 13.4-g RS dose than after all the other tests ($P < 0.001$). PP insulin at $t = 60$ min was significantly lower after an 11.5-g and 13.4-g RS dose than after all the other tests ($P < 0.001$). Two-hour iAUC insulin was significantly lower after an 11.5-g and 13.4-g RS dose ($P < 0.0001$).
Belobrajdic et al (2018) ⁴⁹	The intervention tested 3.2 g or 4.7 g RS from high-amylose wheat flour. The control was 50 g glucose, 0.3 g or 0.4 g RS, from common wheat. Breads were not formulated to match the control for total or available CHO.	20 healthy participants (5 male, 15 female) aged 18–65 y. Participants were instructed to consume one of 7 treatments on a single occasion, with no washout periods between treatments.	At $t = 30$ min, breads made with high-amylose wheat (wholewheat or refined) had significantly lower peak glucose levels than those made with low-amylose wheat (wholewheat or refined) ($P < 0.05$). Three-hour iAUC glucose was significantly lower for the breads made with high-amylose wheat (wholewheat or refined) than for those made with low-amylose wheat ($P < 0.001$). There were no significant differences at any time for plasma insulin, but the 3-h iAUC insulin was significantly lower for breads made with high-amylose wheat than for those made with low-amylose wheat ($P < 0.01$).
Bodinham et al (2013) ⁵⁰	The intervention was 48 g RS from high-amylose corn starch. The control was 32 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	30 healthy males (aged 24–26 y). Participants visited the clinic to consume a breakfast and lunch meal with or without the intervention on 2 occasions, at least 1 wk apart.	Over the 7-h postprandial period, there were no differences between the RS and control group for plasma glucose or insulin. The RS group had significantly lower iAUC insulin for $t = 180$ – 300 min than the control ($P = 0.034$), but not for $t = 0$ – 180 min.
Granfeldt et al (1995) ⁵¹	The intervention tested 16 g or 25 g RS from high-amylose corn flour. The control was 2 g RS from common corn flour. The high-amylose corn flour dose was adjusted to match the control dose for available CHO.	9 healthy participants (4 male, 5 female) aged 28–40 y. Participants visited the clinic on 3 occasions to consume a breakfast meal made with or without the intervention, at least 1 wk apart.	Consumption of both RS doses (16 g, 25 g) resulted in a significant decrease in PP glucose compared to the control at $t = 0$ – 70 min ($P < 0.05$) and a significant decrease in PP insulin compared to the control at $t = 0$ – 45 min ($P < 0.05$). iAUC glucose and iAUC insulin (0–95 min, 0–120 min) were significantly lower for the two RS doses (16 g, 25 g) than for the control ($P < 0.05$, $P < 0.05$).
Higgins et al (2004) ⁵²	The intervention tested 2.5 g, 5 g, or 10 g RS from high-amylose cornstarch. The control was 0 g RS. Meals were formulated to match the control for total CHO.	12 healthy participants (7 male, 5 female) aged 28–45 y. Participants visited the clinic on 4 occasions to consume a meal with varying doses of RS, with a 4-wk washout period.	There were no significant differences in PP glucose, PP insulin, 6-h iAUC glucose, or 6-h iAUC insulin between the doses of RS.

(continued)

Table 2 Continued

Reference	Study characteristics	Participants	Results
Hospers et al (1994) ⁵³	The intervention tested 13 g or 14 g amylose from high-amylose corn starch. The control was 8 g or 9 g of amylose. Meals were formulated to match the control for total CHO.	16 healthy males aged 28–53 y. Participants visited the clinic twice a week for 2 weeks to consume the test and control meals.	At t = 30 min and 60 min, the 13-g or 14-g dose of amylose had significantly lower PP glucose than the 8-g or 9-g amylose dose ($P < 0.03$, $P < 0.034$); however, there were no significant differences in overall plasma glucose responses. At t = 60 min, 120 min, and 180 min, the 13-g or 14-g dose of amylose had significantly lower PP insulin than the 8-g or 9-g amylose dose ($P < 0.01$, $P < 0.001$, $P < 0.001$).
Keogh et al (2007) ⁵⁴	The intervention was 22.5 g fiber from high-amylose barley flour. The control was 11 g fiber from common wheat flour. Meals were not formulated to match the control for total or available CHO.	14 healthy females aged 20–37 y. Participants consumed breakfast and lunch meals made with or without the intervention on 1 occasion, separated by a 7-d washout period.	There were no significant differences in glucose or insulin levels upon arrival to the clinic (6 hours post breakfast treatment) between the high-amylose barley group and control group. After consuming the test lunch, 3-h iAUC glucose and 3-h iAUC insulin were significantly lower for the high-amylose barley group than for the control ($P = 0.05$, $P < 0.02$). PP insulin was significantly lower for the high-amylose barley group than for the control at t = 60 min and 120 min ($P < 0.05$).
King et al (2008) ⁵⁵	The intervention was 31 g fiber from high-amylose barley flour. The control was a 50-g glucose drink or 6 g fiber from common barley flour. Meals were not formulated to match the control for total or available CHO.	29 healthy participants (12 male, 17 female) aged 34–71 y. Participants consumed 3 test breakfast meals on 3 occasions after a 7-d washout period.	PP glucose was significantly lower at t = 30 min for the high-amylose barley cereal than for the glucose drink and common barley cereal ($P < 0.001$, $P < 0.001$). Three-hour iAUC insulin was significantly lower for the cereal made with high-amylose barley than for the cereal made with common barley ($P = 0.023$).
Li et al (2010) ⁵⁶	The intervention was 8 g RS from high-amylose rice. The control was 1 g RS from common rice. Meals were formulated to match the control for total CHO.	16 healthy participants (9 male, 7 female) aged 23–26 y. Participants consumed 3 test meals on 3 occasions after a 7-d washout period.	At t = 30 min, both rice meals had significantly lower peak glucose values than the glucose drink ($P < 0.05$) and the high-amylose rice meal had a significantly lower peak glucose than the common rice meal ($P < 0.05$). Also, 90-min, 120-min, and 240-min iAUC glucose was significantly lower for the high-amylose rice meal than for the common rice meal ($P < 0.05$, $P < 0.05$, $P < 0.05$). At t = 45 min, 60 min, 90 min, and 120 min, both rice meals had significantly lower plasma insulin concentrations than the glucose drink ($P < 0.05$) and the high-amylose rice meal had significantly lower plasma insulin levels than the common rice meal ($P < 0.05$). Also, 90-min, 120-min, and 240-min iAUC insulin was significantly lower for the high-amylose rice than for the common rice meal ($P < 0.05$, $P < 0.05$, $P < 0.05$).

(continued)

Table 2 Continued

Reference	Study characteristics	Participants	Results
Luhovyy et al (2014) ⁵⁷	The intervention tested 11.1 g or 22.2 g RS from high-amylose wholegrain corn flour. The control was 1 g RS from refined wheat flour. Meals were formulated to match the control in calories.	30 healthy males aged 22–23 y. Participants underwent testing on 3 consecutive occasions. Participants consumed a test cookie, and 2 h later were given an ad-libitum pizza meal.	At t = 30 min, the high-dose RS group had significantly lower peak glucose concentrations than the control ($P < 0.05$). Posttreatment (0–120 min) iAUC glucose was significantly lower for both RS groups than for the control ($P < 0.0001$) and was significantly lower for the high-dose RS group than for the low-dose RS group ($P < 0.0001$). Post-second-meal (120–200 min) iAUC glucose was significantly lower for both RS groups than for the control ($P < 0.0001$). Cumulative iAUC glucose (0–200 min) was significantly lower for the high-dose RS group than for the low-dose RS group and control ($P = 0.0007$).
MacNeil et al (2013) ⁵⁸	The control was 1 g RS from refined wheat flour. Three treatments (B, C, and D) were formulated with high-amylose cornstarch to deliver equal amounts of total CHO and available CHO as control. B: 21 g RS with same total CHO, less available CHO compared to control. C: 33 g RS with more total CHO, but equal available CHO as control. D: 21 g RS with more total CHO, but equal available CHO as control.	7 type 2 diabetics (5 male, 2 female) aged 50–66 y. Participants consumed 4 test meals on 4 separate occasions, each separated by a 1-wk washout period. They consumed the test meal for breakfast, and 3 h later were given a standard lunch meal.	Three-hour (0–180 min) iAUC glucose was significantly lower for treatment B than for treatments C and D ($P < 0.05$, $P < 0.05$). Three-hour (0–180 min) iAUC insulin was significantly lower for treatment B than for the control and treatment C ($P < 0.05$). At t = 60 min, 90 min, and 120 min, treatment B had significantly lower PP glucose than the control and treatments C and D ($P < 0.05$). At t = 90 min and 120 min, treatment B had significantly lower PP insulin than the control and treatments C and D ($P < 0.05$). There were no differences in second-meal (180–300 min) iAUC glucose between the 4 treatments, but the second-meal (180–300 min) iAUC insulin for treatment C was significantly higher than for the control ($P < 0.05$).
Maziarz et al (2017) ⁵⁹	The intervention was 30 g RS from high-amylose corn starch. The control was 20 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	Healthy, overweight participants aged 27–35 y who received RS treatment (2 males, 9 females) or no RS treatment (6 females, 1 male). Participants consumed their respective treatment daily for 6 wk.	There were no significant differences in PP glucose or PP insulin between the treatment and control group after 6 wk. However, there was a significant within-group decrease in 2-h iAUC glucose after 6 wk ($P = 0.028$) within the RS group.
Noakes et al (1996) ⁶⁰	The intervention was 17 g RS for females, 24 g RS for males, from high-amylose cornstarch. The control was foods made with wheat, rice, and/or low-amylose starch. Diets were formulated to contain equal amounts of total CHO.	23 (13 male, 10 female) overweight individuals aged 44–64 y with high plasma triglycerides and/or mild hypertension. Participants underwent a 12-wk trial with 3 phases of different dietary interventions, each lasting 4 wk. There was no washout period between the treatments. At the end of the treatments, participants underwent an MTT using food products from the intervention.	At t = 45 min, PP glucose was significantly lower for the high-amylose diet than for the low-amylose diet ($P < 0.03$). At t = 75 min, PP insulin was significantly lower for the high-amylose diet than for the low-amylose diet ($P < 0.001$). There were no significant differences between the low-amylose and high-amylose diet for iAUC glucose (105 min), but the iAUC insulin (105 min) was significantly lower for the high-amylose diet than for the low-amylose diet ($P < 0.01$).

(continued)

Reference	Study characteristics	Participants	Results
Regina et al (2006) ⁶¹	The intervention was 9 g RS from high-amylose wheat flour. The control was 8 g fiber from wheat bran and low-amylose wheat. Meals were not formulated to match the control for total or available CHO.	6 Sprague-Dawley rats in the control group; 6 Sprague-Dawley rats in the treatment group. Rats were fed treatment or control diets for 13 d.	The rats consuming diets rich in high-amylose wheat had significantly higher pools of acetate ($P < 0.01$), propionate ($P < 0.02$), butyrate ($P < 0.05$), and total short-chain fatty acid ($P < 0.01$) than those consuming the low-amylose wheat diet, but there were no differences in short-chain fatty acid concentrations between the two groups. The rats consuming diets rich in high-amylose wheat had significantly lower colonic pH than those consuming the low-amylose wheat ($P < 0.05$).
Zafar (2018) ⁶²	Three treatments using high-amylose cornstarch were studied: 75 g glucose, 37.5 g amylose/37.5 g glucose, 75 g amylose. The control was artificially sweetened water. Meals were formulated to contain equal amounts of total CHO.	15 healthy females aged 17–25 y for Experiment 1 and Experiment 2. Participants consumed a beverage containing a placebo or various doses of RS on 4 separate occasions, each separated by a 1-wk washout period. The participants were also served lunch 2 h (Experiment 1) or 4 h (Experiment 2) after consuming the test beverage.	In Experiment 1, the 75-g amylose beverage elicited a significantly lower PP glucose response throughout the 2-h testing period ($P < 0.05$) and a significantly lower 2-h iAUC glucose ($P < 0.05$) than the 0-g and 38-g dose of amylose. In Experiment 2, the 75-g amylose beverage elicited a significantly lower PP glucose response throughout the first 2 h of the testing period ($P < 0.05$), but not the second 2 h, than the 0-g and 38-g dose of amylose. The 75-g amylose beverage had a significantly lower 4-h iAUC glucose ($P < 0.05$) than the 0-g and 38-g dose of amylose.
Zhu et al (2012) ³⁹	The intervention was a rice starch slurry with 15% RS from high-amylose rice starch (exact dose not provided). The control was a rice starch slurry with 0% RS from common rice starch. Meals were not formulated to match the control for total or available CHO.	6 Male Zucker diabetic fatty rats. The animals were fed a slurry of high-amylose rice starch or common rice starch suspended in water.	At $t = 30$ min, 60 min, and 90 min, the rats that consumed the high-amylose rice slurry had significantly lower plasma glucose levels than the control rats (p value not provided).

Abbreviations: CHO, carbohydrate; iAUC, incremental area under the curve; MTT, meal tolerance test; PP, postprandial; RDS, rapidly digestible starch; RS, resistant starch.

$P < 0.05$, $P < 0.05$).⁵⁶ In addition, plasma insulin levels were significantly lower at 45, 60, 90, and 120 minutes for the high-amylose rice meals than for the wild-type rice meals ($P < 0.05$).⁵⁶

Five further studies explored the effect of resistant starch supplementation from high-amylose grains on postprandial metabolites with no adjustments for total carbohydrate, available carbohydrate, or other nutrients that may have affected the digestion and absorption of food products. Two of these studies used high-amylose wheat as the intervention, but the fact that 1 study was performed on animals and the other study has not been published in a peer-reviewed journal means that only limited scientific conclusions can be drawn from these sources. Regina et al found that rats fed diets containing high-amylose wheat flour had a significantly lower colon pH ($P < 0.05$) and significantly higher pools of acetate ($P < 0.01$), propionate ($P < 0.02$), butyrate ($P < 0.05$), and total short-chain fatty acids ($P < 0.01$) than the rats fed common wheat flour.⁶¹ It has been suggested that short-chain fatty acids play a role in glucose and insulin homeostasis, and thus more research is needed to understand whether the fermentation of high-amylose wheat exerts these potential effects in humans. Belobrajdic et al found that healthy adults who consumed breads made with high-amylose wheat flour had significantly lower peak glucose levels ($P < 0.05$), 3-hour iAUC glucose ($P < 0.001$), and 3-hour iAUC insulin ($P < 0.01$) than those who consumed breads made with common wheat flour.⁴⁹ One particular study focused on the effect of high-amylose rice on postprandial metabolism, but the study was conducted on animals and lacked statistical analysis; thus, only limited scientific conclusions could be drawn. The publication reported that diabetic rats fed high-amylose rice starch had significantly lower plasma glucose levels at 30, 60, and 90 minutes than diabetic rats fed wild-type rice (P value not provided), which suggests that high-amylose rice may play a role in improving acute glucose and insulin responses, but more research involving humans is needed.³⁹ Another 2 studies looked at the effect of high-amylose barley flour on postprandial glucose and insulin responses. In a study conducted by Keogh et al, participants consumed breakfast and lunch meals made with or without high-amylose barley flour and the results showed that there was a significantly lower 3-hour iAUC glucose and 3-hour iAUC insulin ($P = 0.05$, $P < 0.02$) for the high-amylose barley group than for the control.⁵⁴ In addition, King et al found that 3-hour iAUC insulin was significantly lower when subjects consumed a cereal made from high-amylose barley compared to the control cereal ($P = 0.023$), and that peak postprandial glucose was significantly lower at 30 minutes with the

cereal made from high-amylose barley than with the control cereal ($P < 0.001$).⁵⁵

Overall, the data compiled from short-term and long-term studies that examined the effects of resistant starch type 2 from high-amylose cereal grains on end points relating to acute glucose and insulin response show positive results only when digestible carbohydrates are replaced with resistant starch in food products. The majority of the studies analyzed showed improvements in postprandial metabolite production and utilization, but these studies were not matched for available carbohydrate and thus the lowering of postprandial glucose and/or insulin may be partially explained by a decrease in available carbohydrate delivered to the small intestine. Studies that tested equal doses of available carbohydrate in the test and control interventions showed that resistant starch had no effect on postprandial glucose and/or insulin response. This suggests that resistant starch does not participate in any mechanisms that slow the digestion of food and thus the release of glucose into the bloodstream, but it can effectively replace digestible carbohydrates in food products, which will yield a lower acute glucose and insulin response.

Resistant starch and its effect on long term markers of glucose and insulin response

A number of longer-term studies have also been conducted to measure end points related to long-term glucose and insulin control. The findings are summarized in [Table 3](#).^{21,63–75}

[Table 3](#) describes the analyzed studies that observed the effects of resistant starch on long-term glucose and insulin response. [Table 3](#) includes details on the resistant starch dose, control dose, participant characteristics, study characteristics, and the comprehensive results reported by the respective authors.

Ten studies looked at how resistant starch supplementation from high-amylose cornstarch affected long-term glucose and insulin control when the resistant starch dose was adjusted to match the control for available carbohydrate. Four of these studies showed no significant improvements in markers of long-term glucose and insulin control when participants consumed resistant starch.^{63,64,71,73} The remaining 6 studies yielded mixed results. Johnston et al found that in healthy adults who consumed resistant starch daily for 12 weeks, no significant changes were observed in insulin resistance (as measured by the degree of insulin sensitivity, HOMA%S, and level of beta-cell function, HOMA%B), but insulin sensitivity as measured by the euglycemic-hyperinsulinemic clamp did improve compared to the control ($P = 0.023$).⁶⁹ Subjects with type 2

Table 3 Characteristics of studies investigating long-term markers of glucose and insulin response

Reference	Study characteristics	Participants	Results
Al-Mana and Robertson (2018) ⁶³	The intervention was 48 g RS from high-amylose cornstarch. The control was 32 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	10 overweight, insulin-resistant, males aged 18–32 y. Participants consumed breakfast and lunch meals made with either the intervention or the control on 2 separate days, at least 1 wk apart.	Treatment by time interactions showed the consumption of RS resulted in a significant decrease in PP glucose ($P = 0.004$), but there was no significant treatment effect of RS compared with the control. Compared to placebo, no significant differences were found for PP insulin, HOMA-IR, or PP insulin sensitivity for RS consumption.
Bodinham et al (2010) ⁶⁴	The intervention was 48 g RS from high-amylose cornstarch. The control was 32 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	20 healthy males, aged 19–31 y. Participants visited the clinic to consume a breakfast and lunch meal with or without the intervention on 2 occasions, at least 1 wk apart.	Over the 7-h postprandial period, there were no differences between the RS and control group for HOMA% ₅ , HOMA%B, or PP insulin sensitivity, but there was a significantly lower insulin response with the RS group than with the placebo ($P = 0.029$).
Bodinham et al (2012) ⁶⁵	The intervention was 40 g RS from high-amylose cornstarch. The control was 27 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	12 overweight subjects (8 male, 4 female) aged 33–41 y with insulin resistance. Participants consumed the test or placebo daily for 4 wk, separated by a 4-wk washout period. At the end of each phase, participants arrived at the clinic for a FSVGTT.	At wk 4, fasting glucose concentrations were significantly lower for the RS group than for the placebo ($P = 0.049$), but there were no significant differences between the groups for fasting insulin. There were no significant differences in PP glucose between the RS and control group, but there was a significant increase in PP insulin in the RS group, compared to the control ($P = 0.009$). The RS group had significantly higher first-phase insulin secretions than the control group ($P = 0.009$), but there were no differences in insulin sensitivity.
Bodinham et al (2014) ⁶⁶	The intervention was 40 g RS from high-amylose cornstarch. The control was 27 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	17 type 2 diabetics (12 male, 5 female) aged 52–58 y. Participants consumed test or placebo daily for 12 wk, separated by a 12-wk washout period. At the end of each intervention phase, participants arrived at the clinic for a euglycemic-hyperinsulinemic clamp test and an MTT.	At the end of the 12-wk intervention period, there were no significant differences in fasting glucose, fasting insulin, fasting insulin sensitivity, beta-cell function, or HbA1c between the RS and control group. The euglycemic-hyperinsulinemic clamp test yielded no significant differences between the RS and control group for insulin sensitivity. The MTT showed a significant reduction in 2-h iAUC glucose for the RS group, compared to the control group ($P = 0.036$). The arteriovenous sampling across the forearm revealed that the RS group had a higher glucose uptake than the control group ($P = 0.077$).
Dainty et al (2016) ⁶⁷	The intervention was 25 g RS from high-amylose corn starch. The control was 7 g RS from hard wheat flour. Test and control bagels were formulated to contain similar amounts of total CHO.	24 participants (16 male, 8 female) at risk of type 2 diabetes. Participants replaced a bread-based food normally consumed with a bagel made with the test or placebo treatment daily for 56 d, with a 4-wk washout period. At the beginning (day 1) and end (day 57) of each intervention phase, participants arrived at the clinic for an OGTT.	At the end of the 56-d intervention period, there were no significant differences in fasting glucose between the RS and control group; however, the RS group did have significantly lower fasting insulin ($P = 0.04$). There was no significant difference in postprandial glucose and 3-h iAUC glucose between the RS and control group, but the RS group did have a significantly lower 2-h iAUC insulin and 3-h iAUC insulin than the control group ($P = 0.008$, $P = 0.05$). HOMA-IR and HOMA-%B were significantly lower for the RS group than for the control group at the end of the 56-d intervention period ($P = 0.04$, $P = 0.009$).

(continued)

Table 3 Continued

Reference	Study characteristics	Participants	Results
Gower et al (2016) ⁶⁸	The intervention was 15 g or 30 g RS from high-amylose cornstarch. The control was 12 g RDS. Test and control meals were formulated to contain similar amounts of total CHO.	51 healthy women aged 22–67 y. Participants consumed 2 servings of the test or control product every day for 4 wk, separated by a 4-wk washout period. At the end of each intervention period, subjects reported to the clinic for a FSIVGTT.	Of the 51 women who originally enrolled on the study, only 23 completed all 3 arms. Of these, 14 were classified as IR and 9 were classified as IS. When consuming the 30-g RS/dose, IR women who completed all arms of the study, or at least 1 arm of the study, had significantly higher insulin sensitivity than those in the 15-g RS group ($P < 0.05$, $P < 0.05$). There were no significant differences in insulin sensitivity in the IS women who completed all, or at least 1 arm, of the study. There were also no significant differences in fasting glucose or insulin after consuming either RS dose, compared to the control, for the IR and IS populations.
Johnston et al (2010) ⁶⁹	The intervention was 40 g RS from high-amylose cornstarch. The control was 27 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	20 healthy subjects with insulin resistance (8 female, 12 male) aged 46–54 y. Participants consumed test or placebo daily for 12 wk. On days 1 or 3 before and after the study, participants underwent a euglycemic-hyperinsulinemic clamp test.	There were no differences in fasting insulin sensitivity and beta-cell function (as measured by HOMA) between the control and the RS group, but insulin sensitivity significantly improved following the RS treatment, compared with the control ($P = 0.023$).
Karimi et al (2016) ⁷⁰	The intervention was 10 g RS from high-amylose cornstarch. The control was maltodextrin. Test and control meals were adjusted to deliver similar amounts of total CHO.	56 females with type 2 diabetes aged 32–65 y (28 in control group, 28 in intervention group). Participants were divided into 2 groups and were instructed to consume the RS supplement or placebo every day for 8 wk.	After 8 wk, the RS group had significantly lower HbA1c, fasting insulin, and HOMA-IR ($P < 0.05$, $P < 0.05$, $P < 0.05$). There were no significant differences in fasting glucose between the intervention and control group. There was a within-group decrease in the RS group for fasting plasma glucose and HOMA-IR ($P < 0.05$, $P < 0.05$).
Maki et al (2012) ⁷¹	The intervention was 15 g or 30 g RS from high-amylose cornstarch. The control was 12 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	33 healthy participants (11 male, 22 female) with an elevated waist circumference and aged 45–52 y. Participants were instructed to consume the treatment or control every day for 4 wk, each with a 3-wk washout period. At the end of each treatment period, participants arrived at the clinic and underwent an IVGTT.	In women and men with an elevated waist circumference, there were no differences in fasting plasma glucose, fasting plasma insulin, HOMA-IR, or HOMA-IR. In women with an elevated waist circumference, there were no significant differences in insulin sensitivity with the 3 treatments. In men with an elevated waist circumference, the 15-g and 30-g dose of RS significantly improved insulin sensitivity (S_i) ($P = 0.031$, $P = 0.019$).
Penn-Marshall et al (2010) ⁷²	The intervention was 12 g RS from high-amylose cornstarch. The control was 0 g RS. Test and control meals were not matched for available or total CHO.	17 overweight participants (8 male, 9 female) aged 35–38 y who had a first- or second-degree relative with type 2 diabetes. Participants consumed breads made with or without the intervention daily for 6 wk, with a 2-wk washout period.	There were no significant differences in HbA1c, insulin, HOMA-IR, or HOMA-IR between the RS and control group. Fasting plasma glucose was significantly lower in the control group than in the RS group at the end of the study ($P = 0.018$), and the end of the 2-wk washout period ($P < 0.0001$).
Peterson et al (2018) ⁷³	The intervention was 45 g RS from high-amylose cornstarch. The control was 30 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	Participants were aged 35–75 y and overweight with prediabetes; they received the RS treatment (15 males, 14 females) or control (5 males, 25 females). Participants were instructed to consume their respective treatments daily for 12 wk. They underwent an IVGTT at the beginning and end of the study.	The consumption of RS did not affect fasting glucose, fasting insulin, 3-h iAUC glucose, 3-h iAUC insulin, or insulin sensitivity. There was a significant reduction in HbA1c levels with the consumption of RS ($P = 0.05$); however, this was driven by an increase in HbA1c in the control, not a decrease in HbA1c as a result of RS supplementation.

(continued)

Table 3 Continued

Reference	Study characteristics	Participants	Results
Robertson et al (2003) ⁷⁴	The intervention was 60 g RS from high-amylose cornstarch. The control was 40 g RDS. Meals were formulated to contain equal amounts of available CHO.	10 healthy participants (4 male, 6 female) aged 23–65 y. Participants consumed a standard diet with a placebo or with an RS treatment for 24 h before attending the clinic for an MTT.	PP glucose and PP insulin were significantly lower at all time points (t = 0–120 min) when the high-RS diet preceded the MTT, compared to the control diet ($P = 0.037$, $P = 0.038$). There was no difference in fasting insulin sensitivity (HOMA-IR) or beta-cell function between the high-RS diet and the control. PP insulin sensitivity was significantly higher in the RS group than in the control group ($P = 0.028$).
Robertson et al (2005) ²¹	The intervention was 30 g RS from high-amylose cornstarch. The control was 20 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	10 healthy participants (4 male, 6 female) aged 24–61 y. Participants supplemented their habitual diet with RS or placebo every day for 4 wk, with a 4-wk washout period between treatments. During the third week of treatment, subjects underwent a euglycemic-hyperinsulinemic clamp test. During the fourth week, subjects underwent an MTT.	There were no differences between the RS group and control group for HOMA%S, HOMA%B, fasting plasma glucose, 5-h IAUC fasting plasma glucose, or fasting plasma insulin levels. The RS group did have a significantly lower 5-h IAUC fasting insulin compared to the control group ($P = 0.024$). Postprandial insulin sensitivity and total glucose uptake by adipose tissue were significantly higher in the RS group than in the control group ($P = 0.05$, $P = 0.007$).
Robertson et al (2012) ⁷⁵	The intervention was 40 g RS from high-amylose cornstarch. The control was 27 g RDS. The high-amylose cornstarch dose was adjusted to match the control dose for available CHO.	15 participants (8 male, 7 female) with insulin resistance and aged 25–70 y. Participants supplemented their habitual diet with RS or placebo every day for 8 wk, with an 8-wk washout period between treatments. At the end of each treatment period, participants underwent a euglycemic-hyperinsulinemic clamp test and an MTT.	There was no difference between the RS group and placebo group for HOMA%B. The RS group displayed significantly lower fasting glucose ($P = 0.017$), fasting insulin ($P = 0.041$), and HOMA-IR ($P = 0.029$) compared to the placebo. The RS group had significantly higher peripheral glucose uptakes after high-dose insulin ($P = 0.031$), compared to the control, during the clamp test. There were no differences in hepatic insulin resistance, but the MTT did show a significant increase in glucose uptake across the forearm in the RS group compared to the placebo ($P < 0.001$).

Abbreviations: CHO, carbohydrate; FSI/GTT, frequently sampled intravenous glucose tolerance test; HbA1c, glycated hemoglobin A1c; HOMA, Homeostasis Model of Assessment; HOMA%B, beta-cell function; HOMA-IR, insulin resistance; HOMA%S, insulin sensitivity; IAUC, incremental area under the curve; IR, insulin resistant; IS, insulin sensitive; MTT, meal tolerance test; OGTT, oral glucose tolerance test; PP, postprandial; RDS, rapidly digestible starch; RS, resistant starch; S_i, insulin sensitivity.

diabetes who consumed 40 g resistant starch daily for 12 weeks showed no improvements in fasting glucose, fasting insulin, insulin resistance (HOMA%S, HOMA%B), glycated hemoglobin (HbA1c), or insulin sensitivity as measured by the euglycemic-hyperinsulinemic clamp, but arteriovenous sampling across the forearm did show higher glucose uptake than the control ($P=0.077$).⁶⁶ A similar study in overweight participants found no significant differences in insulin sensitivity as measured by a FSIVGTT, but there was a significant decrease in fasting glucose for the resistant starch group compared to the control ($P=0.049$).⁶⁵ A short-term study conducted by Robertson et al found that a 60-g dose of resistant starch did not significantly improve insulin resistance (HOMA%S, HOMA%B), but it did increase postprandial insulin sensitivity as measured by an oral glucose tolerance test in healthy participants ($P=0.028$).⁷⁴ In healthy participants who were supplemented with 30 g of resistant starch daily for 4 weeks, there were no differences in insulin resistance (HOMA%S, HOMA%B) or fasting glucose, but there was a significant improvement in postprandial insulin sensitivity as measured by a euglycemic-hyperinsulinemic clamp ($P=0.05$).²¹ Participants with insulin resistance who were supplemented with 40 g of resistant starch daily for 8 weeks had significantly lower fasting glucose ($P=0.017$), fasting insulin ($P=0.041$), and insulin resistance (HOMA-IR; $P=0.029$) than the control subjects.⁷⁵ In addition, there were significant increases in peripheral glucose uptake as measured by a euglycemic-hyperinsulinemic clamp test ($P=0.031$), but no differences in hepatic insulin resistance.⁷⁵

Another four studies explored how resistant starch supplementation from high-amylose cornstarch affected long-term glucose and insulin control when the resistant starch and control interventions were adjusted to contain equal amounts of total carbohydrate. Dainty et al found that there was a significant decrease in insulin resistance as measured by HOMA-IR and HOMA%B when participants at risk for type 2 diabetes consumed bagels made with resistant starch compared to bagels made with no resistant starch every day for 56 days.⁶⁷ While no significant differences were found between the resistant starch group and control group for fasting glucose, there was a significant decrease in fasting insulin ($P=0.04$) for the resistant starch group.⁶⁷ Further, a study conducted by Gower et al examined the effects of consuming crackers and cookies made with either a rapidly digestible starch, or a 15-g or 30-g dose of resistant starch, every day for 12 weeks.⁶⁸ While the study began with 51 participants, only 23 participants completed each arm of the study and there were no significant differences in insulin sensitivity as measured by a FSIVGTT or fasting glucose for these 23 participants

when consuming resistant starch compared to the control.⁶⁸ Insulin-resistant participants who completed all, or at least one arm, of the study had significantly higher insulin sensitivity as measured by a FSIVGTT for the 30-g resistant starch dose than for the 15-g resistant starch dose ($P<0.05$, $P<0.05$).⁶⁸ In female participants with type 2 diabetes, supplementing with resistant starch every day for 8 weeks yielded a significantly lower HbA1c, fasting insulin, and HOMA-IR ($P<0.05$, $P<0.05$, $P<0.05$), but there were no differences in fasting glucose.⁷⁰ In another study, involving overweight individuals who were at risk for developing type 2 diabetes, no improvements were found in insulin resistance or fasting blood glucose after the subjects had consumed 12 g of resistant starch in breads daily for 6 weeks, but this dose of resistant starch may have been too low to elicit any beneficial responses.⁷²

The available data from studies assessing the impact of resistant starch from high-amylose grains on improving end points of long-term glucose and insulin control show inconsistent results. While a number of studies with primary end points related to long-term glucose and insulin control yielded significant improvements in acute markers of glucose and insulin response, they failed to show improvements in fasting glucose or insulin sensitivity.^{63,64} All studies, with the exception of one that utilized a low dose of resistant starch,⁷² conducted with test and control interventions containing equal amounts of total carbohydrate revealed improvements in insulin sensitivity and insulin resistance, but these results may have been due to a decrease in available carbohydrate reaching the small intestine and not a function of the presence of resistant starch from high-amylose grains.^{67,68,70} Long-term studies involving test and control interventions incorporating equal amounts of available carbohydrate have revealed mixed results for long-term markers of glucose and insulin control. Some studies showed no effect,^{63,64,71,73} while many others reported improvements in insulin sensitivity^{21,66,69,74,75} and fasting glucose.^{65,75} These inconsistent results between the available data could be due to a number of factors. Not all of the studies utilized the same experimental design, and some studies researched the effects of resistant starch in healthy participants, while others chose participants who were overweight, insulin resistant, and/or had type 2 diabetes. The complex differences in the physiology of these different populations could have elicited different responses to resistant starch consumption. In addition, some studies researched the effects of resistant starch after single-dose supplement use, while other participants received dietary supplementation for up to 12 weeks. The length of time required for resistant starch to make a significant metabolic difference is not well understood

and may vary between different populations. The delivery format of the resistant starch also varied between studies. While most studies provided participants with ready-to-use sachets of resistant starch powders, others provided preprepared foodstuffs such as bagels and breads for the participants to consume. The delivery format of the intervention may not only influence the rate of digestion, and thus the glucose and insulin response, but it may also change the ability of the resistant starch to undergo fermentation in the large intestine. It has been suggested that short-chain fatty acids generated from the fermentation of resistant starch may play a role in insulin sensitivity, and differences in individual fermentation responses may account for the varying results reported.²¹

LIMITATIONS

This literature review has many limitations that may weaken the strength of evidence provided or cast doubt upon the efficacy of the ability of resistant starch type 2 from high-amylose grains to improve glucose and insulin response. One limitation stems from the fact that the technology used to create commercially available high-amylose grains is coveted and not all of the information on their development is publically available. Therefore, technologies may have progressed and the mechanisms to yield high-amylose grains may not be as described in the above review. Additionally, there is limited information on the specific pathways used to create a specific variety of a high-amylose grain. One variety of a high-amylose cereal grain may not have the same genetic profile as another variety of the same high-amylose cereal grain, and thus the association between their physiological effects may not be clear-cut. Authors of clinical research also fail to mention the genetic profile for the variety of grain used in their studies, likely because this information is not publically available.

Limitations in study design also limit the conclusions that can be drawn from this review. While human studies are more physiologically relevant than animal studies, it is more difficult to provide and keep track of all of the foods consumed by human subjects during the long-term intervention studies mentioned in this review. Because of this limitation, it is possible that the results were confounded by other carbohydrate and fiber sources consumed by the subjects during the intervention periods. Some studies utilized a procedure that involved a onetime intervention, while other studies had longer testing durations. Additionally, some study designs required the participants to consume the resistant starch type 2 intervention in a single bolus, while other study designs required the participants to consume their intervention at many points throughout the

day. Another limitation comprises the differences in testing methods for critical parameters explored, such as amylose content, resistant starch content, and total dietary fiber content, as it is known that different methods may elicit different results that can significantly impact the conclusions of this work.

CONCLUSION

There is insufficient evidence to conclude that resistant starch from high-amylose grains can improve measures of glucose and insulin homeostasis, but this should not undermine the significant beneficial effects that have been reported in acute glucose and insulin responses. The majority of American consumers fail to incorporate sufficient fiber in their diet because of a lack of whole grain consumption and a high consumption of foods that contain refined carbohydrates. Government organizations such as the Food and Drug Administration (FDA) are aware of the deleterious fiber gap and have implemented a number of policies surrounding fiber that aim to improve human health. The dietary fiber found inherently in foods such as fruits, vegetables, and non-high-amylose and high-amylose grain flours are classified as “intrinsic and intact” fibers, which are believed to have cumulative health benefits owing to their whole food form.⁷⁶ Isolated and/or synthetic nondigestible carbohydrate sources must have an FDA-approved beneficial physiological effect in order to be classified as a dietary fiber for use in processed foods.⁷⁶ The FDA recently approved a qualified health claim for high-amylose maize starch, stating that “high-amylose maize resistant starch may reduce the risk of type 2 diabetes, although the FDA has concluded that there is limited scientific evidence for this claim.”⁷⁷ The development of high-amylose grains creates an opportunity for the food industry to manufacture products that are high in fiber and enjoyable to consumers. Replacing rapidly digestible carbohydrates that have negative acute metabolic outputs with a palatable fiber source will allow consumers to eat familiar foods without bearing the consequences of spiked glucose and insulin levels, which may benefit their long-term health. Because the current literature shows mixed results, more research is needed to understand the impact of resistant starch from high-amylose grains on insulin resistance and insulin sensitivity.

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