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The Relationship between Resistant Starch and Glycemic Control: A Review on Current Evidence and Possible Mechanisms

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List of abbreviations used: RS, resistant starch; RDS, readily digestible starch; HAM-RS2, high-amylose maize type-2 resistant starch; AUC, area under curve; FFA, free fatty acid; PYY, peptide YY; GLP-1, glucagon-like peptide-1; GPR, G-protein coupled receptors

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Abstract

Good glycemic control, which is vital for patients with type 2 diabetes, could be achieved via dietary intervention. Resistant starch (RS) is a type of carbohydrate that largely resists digestion in the small intestine. Instead, it is fermented by the gut microbiota that resides in the large intestine into short-chain fatty acids (SCFAs), which are found to have beneficial effects on human glucose metabolism. This review first provides an overview of the classification of different types of RS, as well as the fermentation process of RS by the gut microbiota. The effects of RS consumption that contribute to glycemic control were then discussed with reference to animal and human studies. Although beneficial effects of RS consumption were observed, results from animal and human studies were inconclusive regarding the mechanisms behind. Additional research effort is necessary in order to have a better understanding of the effects of habitual RS consumption on glycemic control.

Keywords:

Resistant starch, blood glucose, insulin resistance, adiposity

Introduction

According to the World Health Organization (WHO), chronic high blood glucose is the third largest reason for premature mortality [1]. It was estimated that in the year of 2015, one in every 11 adults around the world had diabetes and 12% of the global health expenditure was spent on treating diabetes [2]. Maintaining glycemic control has been established as the primary treatment goal for diabetes and pre-diabetes, as it can reduce the chance of complication and mortality [2]. Lifestyle interventions, including dietary changes, has long been suggested as the primary treatment to enable patients to manage their blood glucose level [3].

Blood glucose level is directly affected by the intake of readily digestible carbohydrates, such as sucrose and starch, which is the polymer formed by glucose molecules linked together by alpha-1,4 and alpha-1,6 glycosidic bonds. Starch is mostly digestible in the human gastrointestinal tract, except resistant starch (RS), which are special forms of starch able to resist digestion in the stomach and small intestine [4]. Instead, it reaches the large intestine mainly undigested and is fermented by the bacteria that reside there. Research has shown that RS consumption positively affects blood glucose metabolism in human [5, 6]. With the recent emergence of human and animal trials regarding the breakdown of indigestible carbohydrate by the gut microbiota, our understanding of the effect of RS consumption on blood glucose control has been greatly enhanced. This review provides an update on the evidence and the mechanisms involved.

Classification of Resistant Starch

Englyst et al. [4] classified different types of RS into four main categories, depending on the cause of resistance to digestion. One new form of resistant starch was discovered later on and became the fifth type of RS, resulting in the new classification as shown in **Table 1**. RS1 refers to starch molecules that are contained in an indigestible outer layer, such as cell wall and protein matrix. RS2 refers to starch molecules with type B or C polymorph. Molecules in these structures are less susceptible to enzyme hydrolysis [7]. RS3 refers to starch molecules that have undergone retrogradation i.e. the realignment of starch molecules upon cooling after gelatinization. Retrograded starch molecules have a higher gelatinization temperature, and these molecules are unable to fit into the substrate binding site of amylase [8]. RS4 are starch molecules that have undergone chemical modifications, such as the addition of cross-linkages or chemical derivatives. These modifications include limiting the ability of the starch molecule to swell during heating, or changing the structure of the molecule such that it can no longer fit into the binding site of the digestive enzymes [9]. It was found that the reaction parameters of RS4, such as the availability of reactant and reaction temperature, could be modified to control the ability of the molecules produced to resist digestion [10]. RS5 refers to the complex that consists of a fatty acid molecule and an amylose chain, which are straight chains of glucose molecules linked together by alpha-1, 4 glycosidic bonds. The complexes then aggregated to form a superstructure, which were found to be resistant to enzymatic hydrolysis [11, 12].. **Figure 1** illustrates the structures of

different types of RS.

Fermentation of Resistant Starch by Gut Bacteria

The fermentation of RS in the large intestine is a stepwise process, involving different bacteria. The outer protective layer (if there is any) is first degraded, then the starch polymers are broken down into oligosaccharides and the glycolytic processes follow, with short-chain fatty acids (SCFAs) being the major end products.

Studies have shown that the ability of bacteria to adhere to the resistant starch molecules is an important first step for fermentation, and it was found that this process involves multiple binding proteins. For example, the starch-utilization gene (*sus*) cluster, that was identified in the genome of the bacteria *Bacteriodes thetaiotaomicron*, coded for a variety of proteins which were responsible for the transportation of carbohydrate molecules into the periplasm of the bacterial cell and the breakdown of the molecule [13]. Cellulosome is another complex which was found to be involved in the digestion of cellulose, the protective layer which prevents the digestion of starch in RS1. In this complex, different protein components were found to be responsible for attaching cellulose molecules to the bacterial cell surface, as well as for the subsequent breakdown of them [14]. Multiple strains of gut bacteria have been found to utilize this mechanism in starch degradation [14]. In addition, starch binding of some gram-positive bacteria was found to be accomplished via cell-bound α-amylase [5]. After the adhesion

of bacterial cells to the starch molecules, enzymes were responsible in cleaving different bonds within the molecules, such as α-amylase and α-glucosidase for cleaving α-1,4 linkages, and type 1 pullulanase for cleaving α-1,6 linkages [5, 15].

The main products of RS fermentation are SCFAs, which include acetate, propionate and butyrate [16, 17]. It was found that SCFA production mainly happens in the cecum and proximal colon, where the pH was found to be the lowest [18]. The SCFAs produced were mainly absorbed by colonocytes or metabolized by other gut bacteria, with only 5-10% of the SCFAs excreted with feces [19].

Effects of Resistant Starch Consumption leading to Improved Glycemic Control

RS consumption has been shown to improve glycemic control in both animal and human studies, yet the mechanisms behind remain poorly understood. Several possible mechanisms are discussed below, as outlined in **Figure 2**.

Reduction in Glycemic Load

The rate of digestion of RS-containing food in the small intestine is much lower when compared with food containing only readily digestible starch (RDS). As a result, consumption of such food leads to a sustained and lower level of glucose release [20]. This effect is reflected by the glycemic index (GI), a ranking system which organizes different food items according to the change of glycemic response

upon food consumption [21]. Upon inducing retrogradation in the test foods, researchers observed a decrease in starch digestibility of the treated food when compared with the untreated food [22]. They also observed a slower rise in blood glucose level in human subjects upon consuming the treated food, when compared with those consuming the untreated food [22, 23].

It should be noted that the beneficial effects on postprandial glucose metabolism upon RS consumption were observed only when RS replaced RDS, but not when RS was added to RDS (the concept was shown in **figure 3**). In a study conducted by MacNeil *et al.* [24] different test foods were produced by mixing normal wheat flour and RS2-containing flour at different ratios and were consumed by subjects with type 2 diabetes. The researchers observed lower incremental area under curves (AUC) and lower peak levels of postprandial glucose and insulin in subjects who consumed the RS2-containing test food, which had the same amount of carbohydrate with the control food. This difference was notobserved in subjects who consumed the other type of test food, which was made by adding RS2 directly to a portion of control food. Similar findings were seen in a study conducted by Luhovyy *et al.* [25] whose team replaced the wheat flour by RS2-containing flour when producing the test food, so that the total amount of carbohydrate was the same between the treatment food and the control food. Also, they observed a dose-dependent effect of RS content on postprandial glucose level, such that consuming a higher dose of RS led to a lower AUC of postprandial glucose curve. On the other hand, in studies where RS was added as an extra portion to the test foods, the results on postprandial glucose and

insulin levels were mixed i.e. both positive and negative results were observed [26-28]. The reason behind this was that the postprandial glucose level was directly affected by the portion of available carbohydrate, thus adding RS alone without decreasing the available carbohydrate content of the food may not efficiently decrease postprandial glucose levels [24]. This view was supported by the European Food Safety Authority (ESFA), which recommended the replacement of digestible carbohydrate by RS rather than addition for improvement to be observed in postprandial glycemic control [29].

Improved Glycemic Response of the Subsequent Meal

RS consumption may also diminish the glycemic response of the subsequent meal when compared with consuming RDS only (**figure 4**). MacNeil *et al.* [24] found that the consumption of RS2-containing food led to a lower rise in glucose and insulin after the consumption of a subsequent standard meal three hours later when compared with consuming RDS only. The researchers attributed the improved response to the increased insulin secretion, which was found to be in line with the variation of the level of glucose-dependent insulinotropic polypeptide (GIP). However it was previously shown that this improved postprandial glycemic response after the second meal was not due to the acute insulin secretion. Instead, an increase in postprandial glycogen storage, which was caused by a suppressed free fatty acid (FFA) level in the circulation, was proposed to be the real cause [30]. In contrast, Luhovyy *et al.* [25] found a higher postprandial AUC of glucose upon consuming the second meal in the treatment group who consumed RS-containing cookies two hours before. They argued that the release of glucose

159 from the previous meal was still ongoing when consuming the second meal, thus leading to the
160 elevated postprandial glucose level. Although the fact that the second meal being provided *ad libitum*
161 affected the results, this view was possible as the digestion time of RS could last for up to seven hours
162 [20]. More studies are needed to investigate the second meal effect of RS consumption, with the
163 nutrition profile of the second meal standardized for a valid comparison.
164
165 **Improvements in Muscular and Hepatic Glucose Handling**
166 The SCFA produced upon the fermentation of RS by the gut microbiota have profound effects on
167 glucose homeostasis in liver and muscle tissues. G-protein coupled receptors (GPR) 41 and 43, which
168 are SCFA receptors, have been found on both muscle and liver cell membranes Activation of GPR
169 41/43 by SCFAs has been found to lead to an increase in glucose uptake and glycogen storage at
170 muscle tissues [18].
171
172 Unfortunately, studies investigating the effect of RS consumption and the impact of glucose
173 homeostasis in muscle tissues were scarce. Robertson *et al.* [31] fed an extra 30g of RS2 on top of an
174 RDS portion to a group of healthy subjects, while the other group had only the RDS portion in their
175 diet, for 12 weeks. Their postprandial glucose clearance in the muscle was measured by analyzing the
176 arterialized venous blood collected at the contralateral forearm. The researchers found that subjects
177 who consumed RS had improved in muscle glucose clearance and insulin sensitivity, as well as a

concomitant increase in SCFA uptake at muscle, when compared with patients consuming only RDS. Nonetheless, the AUCs of glucose levels upon receiving meal challenges were not different between the two groups. On the other hand, Bodinham *et al.* [32] fed an additional 40g of RS2 to subjects with type 2 diabetes (T2DM) when compared with the control group. They observed a higher glucose uptake in the muscles in the RS group, although this was not statistically significant. However, they found that the plasma level of propionate and acetate in the RS-consuming subjects were lower. They argued that the lower plasma level of SCFAs could be the result of an increased uptake by the peripheral tissues, which was observed in a previous study [31]. In contrast to the previous study, they observed lower postprandial glucose AUCs for the RS group, when compared with the group without RS consumption. Owing to the inconclusive results, more studies are needed to further establish the role of SCFA in affecting the glucose handling of muscle, as well as the impact of such changes towards the overall glucose homeostasis.

In addition, since SCFAs have been shown to positively affect the glucose homeostasis of liver [18], it is possible for such benefits to also be conferred by RS consumption. Unfortunately to date there was no human study that looked at this effect, and animal studies were scarce in this regard. Polakof *et al.* [33] fed a batch of rats with a high-fat diet and replaced the carbohydrate portion of the test diet with RS2 for some of the rats. They found that in rats which consumed both the high-fat diet and RS, hepatic insulin sensitivity was improved, and the liver inflammation statuses were alleviated. This

improvements were not observed in rats consuming a high-fat diet without RS replacement. Furthermore, the activities of hepatic enzymes involved in glycolysis (e.g. glucokinase and pyruvate kinase) were found to be reduced by consuming the high-fat diet, yet this was partially restored by RS consumption [33]. Given the central role of liver in maintaining blood glucose level and glucose homeostasis in human [34], the effect of RS consumption on hepatic glucose handling warrants further investigation. More trials are needed to confirm the relationship between RS consumption and hepatic glucose metabolism on human.

Increase Insulin Sensitivity by Reducing Adiposity

Overweight and obesity have long been referred to as a risk factor for insulin resistance and T2DM. The prolonged excess in energy intake leads to ectopic fat storage, i.e. fat deposits around internal organs in the abdominal area. This condition was found to inducelocal and systemic insulin resistance via the induction of abnormal inflammation pathways [18, 35]. Moreover, the hypertrophic growth (i.e. expansion in size) of adipocytes, which also results from a prolonged oversupply of energy, is related to the development of insulin resistance as well [36, 37]. This is due to the stress induced by the rapidly expanded adipose tissues as they are inadequately vascularized. As a consequence, the inflammatory pathways in those stressed adipocytes become activated, and the secretion of pro-inflammatory cytokines increases, thus interfering with insulin signaling pathways [38]. RS consumption has been associated with a lower mass of adipose tissues and the suppression of inflammatory pathways (**figure**

5).

Animal studies were able to demonstrate the beneficial effects of RS consumption on fat metabolism and glucose and insulin tolerance. For instance, Harazaki *et al.* [39] fed obese rats with a diet with 55% (w/w) high-amylose maize type-2 RS (HAM-RS2) for four weeks and observed improvements in insulin sensitivity, when compared with rats fed the control diet (55% cornstarch instead of HAM-RS2). They also found that the size of the mesenteric adipocytes in RS2-fed rats was smaller than those fed the control diet. In addition, the mRNA levels of molecules related to the inflammation of adipose tissues were found to be lower in RS-fed rats. Apart from that, Polakof *et al.* [33] conducted a 9-week feeding trial on three groups of Wistar rats: one group was fed a low-fat diet (5% fat), one consumed the high-fat diet (30.4% fat), and the other group consumed the high-fat diet with HAM-RS2 replacing the carbohydrates (41.6% w/w). They found that the group which consumed the high-fat diet showed the greatest glucose excursion and insulin secretion, while both measurements for the RS group were similar to the low-fat diet group. Moreover, genes coding for important proteins involved in fatty oxidation (e.g. *PPAR1*) were down-regulated, and those coding for proteins involved in lipogenesis (e.g. *SREBP-1c*) were up-regulated in the high-fat diet group when compared with the low-fat diet group. These elevated expressions were not shown in the RS group. Results from these studies showed that RS consumption lowered the abdominal fat mass, alleviated the inflammatory status and improved the insulin resistance caused by the consumption of a high-fat diet.

Meanwhile, results from human studies have been inconclusive, such that the improvements in glucose metabolism did not always occur with improvements in adipose tissue weight or release of pro-inflammatory cytokines. The trial by Robertson *et al.* [31] showed positive results: they observed improvements in insulin sensitivity using euglycemic-hyperinsulinemic clamp(s) in a group of subjects adding 30g RS2 into their diet every day for 12 weeks, over those who did not incorporate RS into their diet. They also found that the postprandial output of triacylglycerol (TAG) from adipose tissues and the rate of action of hormone-sensitive lipase decreased in the treatment group. Yet in some studies, changes in anthropometric measurements and adipose tissue content were not detected [28, 40, 41], and the release of pro-inflammatory cytokines were found to be similar between treatment group and control group [32, 40, 41]. For example, in the feeding trial conducted by Maki *et al.* [41], participants (overweight adults) received different treatments: consuming only RDS, an extra 15g or extra 30g/day of HAM-RS2 (~60% RS2) in a randomized crossover manner. At the end of the study, no difference in body weight and waist circumference was observed. Moreover, improvement in insulin sensitivity was only observed in male subjects, while no difference in fasting levels of pro-inflammatory cytokines was observed between treatment conditions. In another 12-week feeding trial conducted by Johnston *et al.* [28] on insulin resistant adults, one group consumed an extra 40g of HAM-RS2 while the other group consumed only RDS. It turned out that the body weight and fat storage on all body locations measured were not significantly different between the two groups. Also, no variation was seen in fasting levels of

inflammatory factors (e.g. IL-6 and hsCRP). However, the insulin sensitivity was improved for the group consuming HAM-RS2. The results from human studies may imply that the relationship between improvement in adiposity and the improved insulin sensitivity is more indirect than it is previously assumed.

Several explanations were provided for the inconsistent results in terms of the changes in adiposity and insulin sensitivity upon consuming RS. Some argued that this is because the treatment dosage used in animal studies were too high for human consumption (up to 50% w/w), thus hindering the translation of results into human studies [28]. Also in mice studies since RS were fed shortly after the mice were born, adipose tissue remodeling and a lower ectopic fat storage could take place with growth. On the other hand, adipose tissues in human were already *in situ* at the beginning of the studies, thus the changes in adiposity may be less visible [28]. It is also worth to note that while some studies included the level of free fatty acid (FFA) in circulation as a study outcome, it has been argued that high FFA levels *per se* do not lead to insulin resistance [38]. It has been found that in obese individuals, hyperinsulinemia may be a mechanism to suppress FFA release, while the release of FFA decreased with the expansion in the mass of adipose tissues [42]. Alternative hypotheses for the impaired insulin sensitivity in the context of overweight or obesity, such as the abnormal adipose fat storage and the dysfunction in the release of adipokines and cytokines, have been proposed [42].

Effects on Gut Hormone Release

Another possible mechanism where RS consumption may impact on blood glucose control is via the induction of gut hormone release, mainly glucagon-like peptide-1 (GLP-1) and peptide YY (PYY). GLP-1, secreted by intestinal L-cells, is a type of incretin hormone able to stimulate insulin secretion and inhibit glucagon secretion [43]. GLP-1 is also related to pancreatic beta-cell proliferation and the enhancement of peripheral insulin sensitivity [43]. PYY, which has been found to be expressed both in the GI tract and in the pancreas, is initially found to inhibit appetite thus lowering energy intake [44]. Nonetheless, in recent studies it has also been found to exhibit paracrine and exocrine effects on pancreatic islet cells, leading to enhanced insulin secretion [44]. The releases of both hormones are triggered by the presence of nutrients in the intestinal lumen, which is detected by membrane-bound transporters found on enterocytes along the intestinal lining [45]. In recent studies, SCFA receptors were found to be present in the distal gut and were associated with enhanced GLP-1 and PYY secretion [18] (**figure 5**).

In animal studies, both increase [46-48] and decrease [49] in serum level of GLP-1 and PYY had been found when comparing between animals consuming diets with RS and those with digestible cornstarch as a control, while the effect on blood glucose homeostasis and insulin sensitivity varied. For example, Zhou *et al.* [46] fed healthy rats with either RS2 (30% of diet) or normal cornstarch for 10 days and found that the serum levels of GLP-1 and PYY in the RS group were elevated throughout the day of

292 data collection when compared with the group consuming cornstarch as a control. In the same study, a
293 separate group of rats received the same dietary treatments, followed by streptozocin injections in order
294 to induce diabetes. The RS group showed improved glucose tolerance when compared with the
295 cornstarch group. In contrast, da Silva *et al.* [49] showed that after feeding pigs with retrograded starch
296 (RS3, 35% of diet) for 14 days, the postprandial level of GLP-1 decreased while that of PYY did not
297 change, when compared with pigs fed the similar amount of readily digestible cornstarch. Nonetheless,
298 they found a lower postprandial insulin and glucose response in the RS group. They argued that the
299 lowered bioavailability of nutrients in the food, as a result of RS replacing the readily-digestible
300 carbohydrates, caused a diminished release of gut hormones [49]. This view was supported by another
301 RS consumption study carried out on pigs [16]. In that study when comparing the pigs that were fed an
302 RS diet (RS2, 11.3% w/w) for six days with those that were fed a low fibre diet (0.7% diet) for the
303 same period of time, they found improvements on postprandial blood glucose and insulin level, despite
304 no difference in GLP-1 level between treatment groups [16].
305
306 The mixed results of animal studies may partly be due to the physiological differences between the
307 animal models and the different types and doses of the RS used. Nonetheless, the inconsistent results
308 between RS consumption and the effect of GLP-1 and PYY may imply a more complicated association
309 between gut hormone release stimulated by RS consumption and glucose homeostasis. The
310 mechanisms in how RS consumption changes the release of gut hormones, as well as its subsequent

311 metabolic effects on animal models warrant further investigation.

312

313 Findings from acute feeding studies on human have been inconsistent. In a study run by Bodinham *et al.*
314 [27] a group of healthy adults was fed a test meal with 48g of RS2, while the other group consumed
315 cornstarch instead of RS2 in the meal. The level of postprandial GLP-1 in the RS group is lower than
316 those who consumed the control meal, yet the level of postprandial glucose and insulin did not differ
317 between treatments. In another study, Klosterbuer *et al.* [26] showed that healthy subjects who
318 consumed a standard breakfast with 25g RS3 added had a lower postprandial GLP-1 level, as well as a
319 lower postprandial glucose and insulin level when compared with subjects consuming only the standard
320 breakfast. Edwards *et al.* [50] provided two dishes for two groups of ileostomy patients, one being a
321 wheat porridge made of coarse durum wheat flour (test meal) and the other made with fine durum
322 wheat flour (control meal, the test meal had 33% lower digestible starch content than the control meal).
323 They found that patients consuming the test meal had a lower postprandial glucose level and a lower
324 GLP-1 and PYY level when compared with patients consuming the control meal, although that was not
325 statistically significant. They argued that the lowered digestibility of the test meal decreased the amount
326 of available nutrients, thereby reducing the release of GLP-1 and PYY [50]. However as SCFAs
327 resulted from fermentation by the gut microbiota have also been linked to gut hormone release [18], it
328 is possible that gut hormones produced in this pathway compensated for the suppressed secretion of gut
329 hormones due to a lower bioavailability of nutrients.

Similarly, studies about long-term RS consumption and its effect on GLP-1 release and glucose level on human yielded inconsistent results. Robertson *et al.* [31] found no effect upon including RS in meals for 12 weeks on GLP-1 level, yet improvement in glucose clearance and insulin sensitivity was observed. Another 12-week study ran by Bodinham *et al.* [32] on subjects with type 2 diabetes found that subjects receiving the treatment food had elevated fasting GLP-1 level but lowered GLP-1 level after a meal, while a smaller postprandial glycemic variation was also observed.

In light of the inconsistent findings from acute feeding studies, it has been proposed that a longer study duration is needed for a better exhibition of the beneficial effects of RS consumption and to determine the effective dose [27, 28, 51]. Since the human gut microflora takes time to adapt to the continuous addition of RS in diet [52], the mixed results may not be truly reflecting the effects of RS consumption. Long term consumption studies would hopefully be able to add on to the body of evidence regarding the effect of RS consumption towards gut hormone secretion, as well as the subsequent effects on human glucose homeostasis.

Conclusion

The beneficial effects of RS consumption on glycemic control have been widely observed in animal and human studies, yet the mechanisms behind were still poorly understood. Several mechanisms

behind the impact that RS consumption might have on glycemic control were assessed in this review, yet the evidence was inconclusive – some effects of RS consumption were being shown only in animal studies but not in human studies. Several reasons could be possible, including the difficulty in controlling the baseline parameters in human subjects, such as adiposity and gut microbiota profile, as well as the fact that the amount of RS used in animal studies may not be suitable or effective for human consumption. Nonetheless, it should be noted that glucose level is influenced by several factors at the same time, including absorption, clearance, and release from internal organs, thus carefully planned studies with suitable controls are vital for reliable and valid results. Additional research efforts are required to further establish the mechanisms behind the beneficial effects of RS consumption towards glycemic control.

Conflict of Interest

The authors have no conflict of interest to declare.

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519 Figure legends

520 Figure 1 – different types of RS. (a) the structure of RS1: the starch molecules were encapsulated by a
521 physical barrier; (b) B-polymorph of starch molecules. The helical amylose chains, as depicted by
522 circles, are closely and orderly aligned, enabling the structure to resist enzyme degradation; (c) the
523 process of retrogradation, thereby forming RS3; (d) cross-linkages in RS4 and (e) starch molecules
524 linked by a new functional group, e.g. acetyl group or phosphate group, forming another type of RS4;
525 (f) the structure of RS5. The complex is formed by an amylose chain wrapping around a fatty acid
526 molecule. Multiple complexes aggregate into forming a superstructure, which is resistant to enzyme
527 degradation.

528 Figure 2 – concept map of the effects of RS consumption. RS, resistant starch; CHO, carbohydrate;
529 SCFAs, short chain fatty acids; PYY, peptide YY; GLP-1, glucagon-like peptide-1

530

531 Figure 3 – the difference in effects between (a) consuming RDS only, (b) replacing RDS with RS,
532 keeping the same amount of total carbohydrate as control, and (c) addition of RS as an extra portion to
533 RDS. RS, resistant starch; RDS, readily digestible starch.

534

535 Figure 4 – inclusion of RS in the first meal leads to a lower rise of postprandial glucose after
536 consuming a standardized second meal. RDS, readily digestible starch; RS, resistant starch.

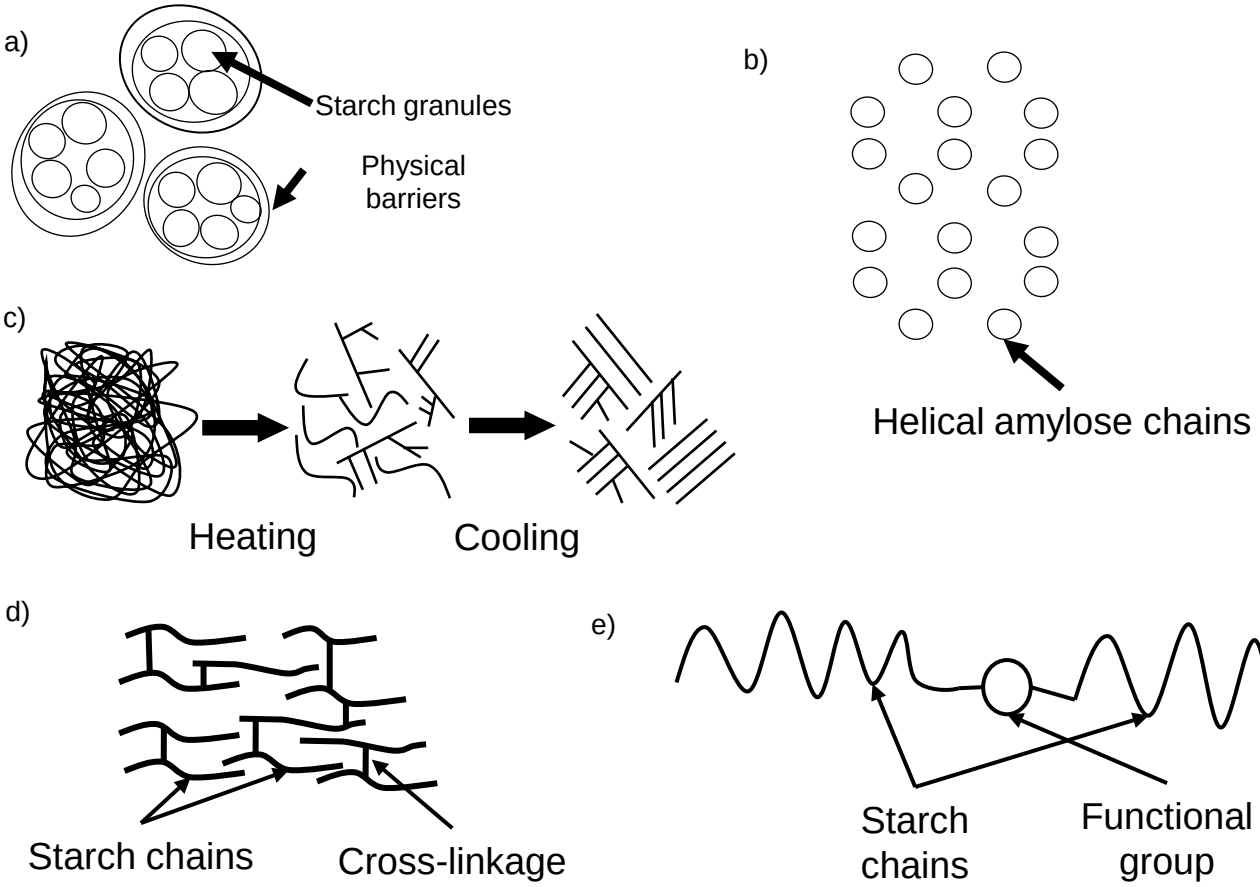
537

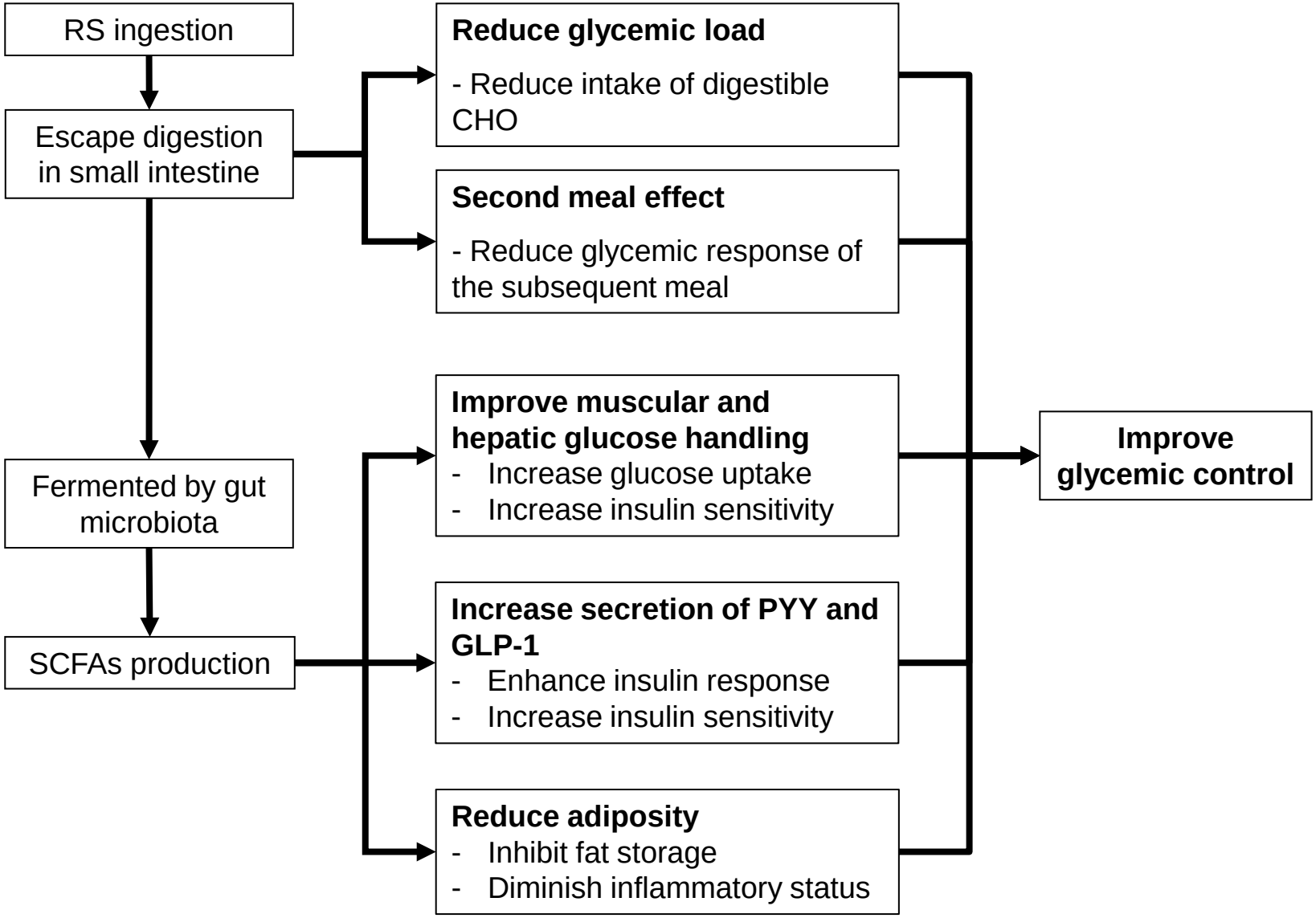
Figure 5 – the benefits conferred by RS consumption via SCFA production. Broken lines depicts progression, while solid lines depicts enhancement and inhibition. RS, resistant starch; SCFA, short-chain fatty acid; PYY, peptide YY, GLP-1, glucagon-like peptide-1, GPR, G-protein coupled receptors.

544 Table 1. Classification of RS and examples [4, 9, 53]

Classification	**Description**	**Example**
RS1	Physically inaccessible starch	Whole grains
RS2	Starch with B- or C-polymorph	Uncooked potato, high-amylose maize (HAM) starch
RS3	Retrograded starch	Cooked and cooled potato starch
RS4	Chemically modified starch	Cross-linked starch in thickeners
RS5	Amylose-lipid complex	Palmitic acid-amylose complex

545

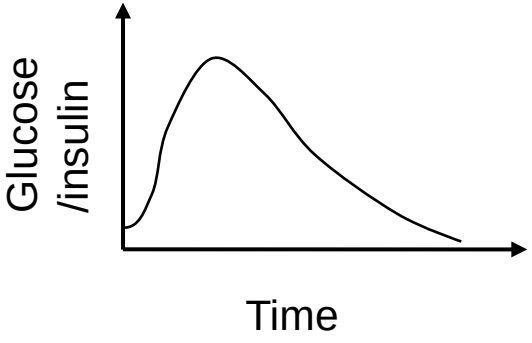

a)
Starch granules
Physical barriers
b)
Helical amylose chains
c)
Heating
Cooling
d)
Starch chains
Cross-linkage
e)
Starch chains
Functional group
f)
Fatty acid molecule
Helical amylose chain


RS ingestion
Escape digestion in small intestine
Fermented by gut microbiota
SCFAs production
Reduce glycemic load
- Reduce intake of digestible CHO
Second meal effect
- Reduce glycemic response of the subsequent meal
Improve muscular and hepatic glucose handling
- Increase glucose uptake
- Increase insulin sensitivity
Increase secretion of PYY and GLP-1
- Enhance insulin response
- Increase insulin sensitivity
Reduce adiposity
- Inhibit fat storage
- Diminish inflammatory status
Improve glycemic control

a)

RDS

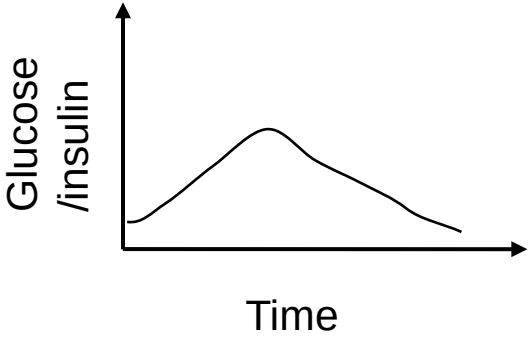
Control



b)

RDS | **RS**

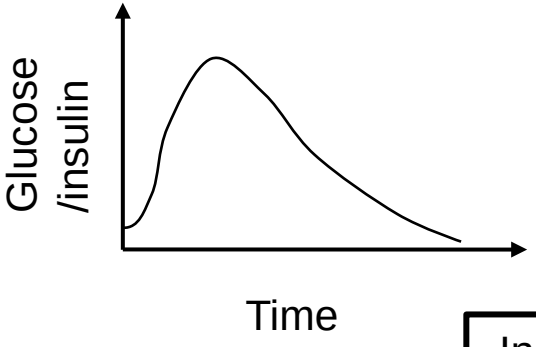
Part of RDS replaced by RS



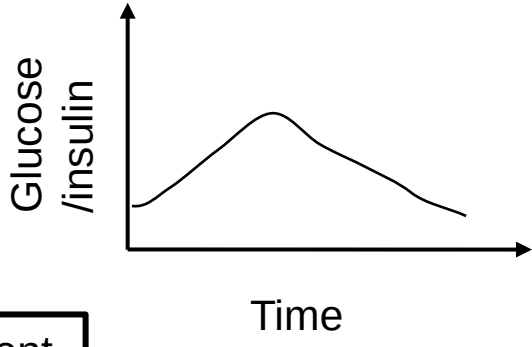
c)

RDS | **RS**

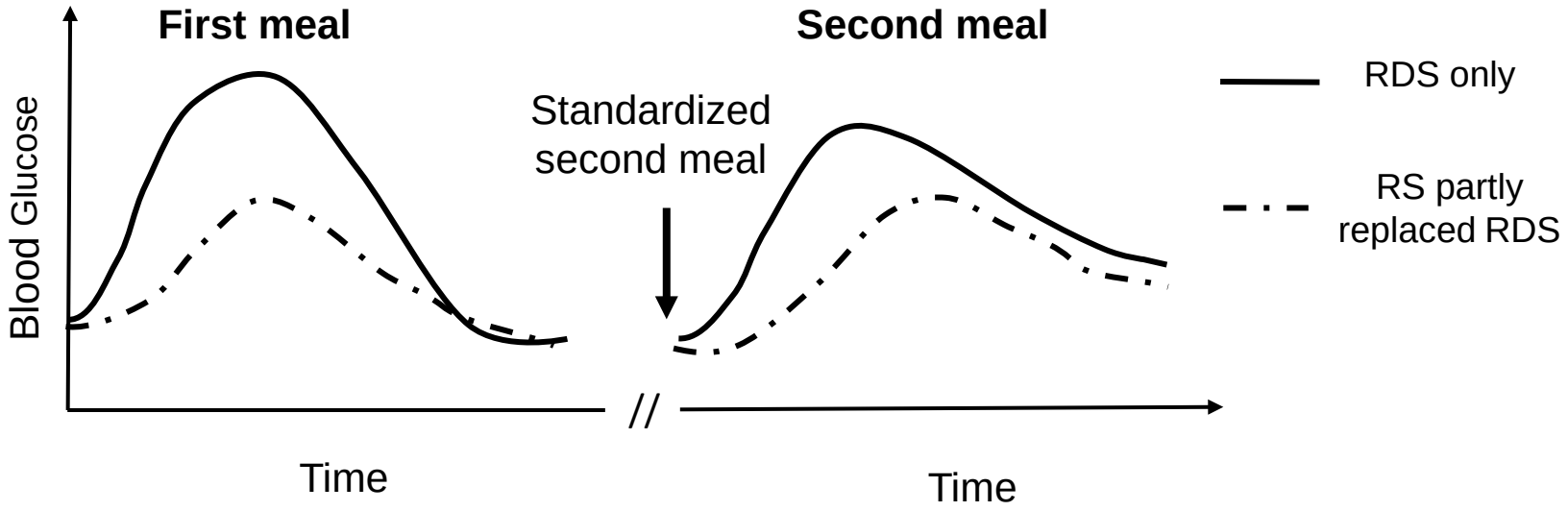
RS added as an extra portion

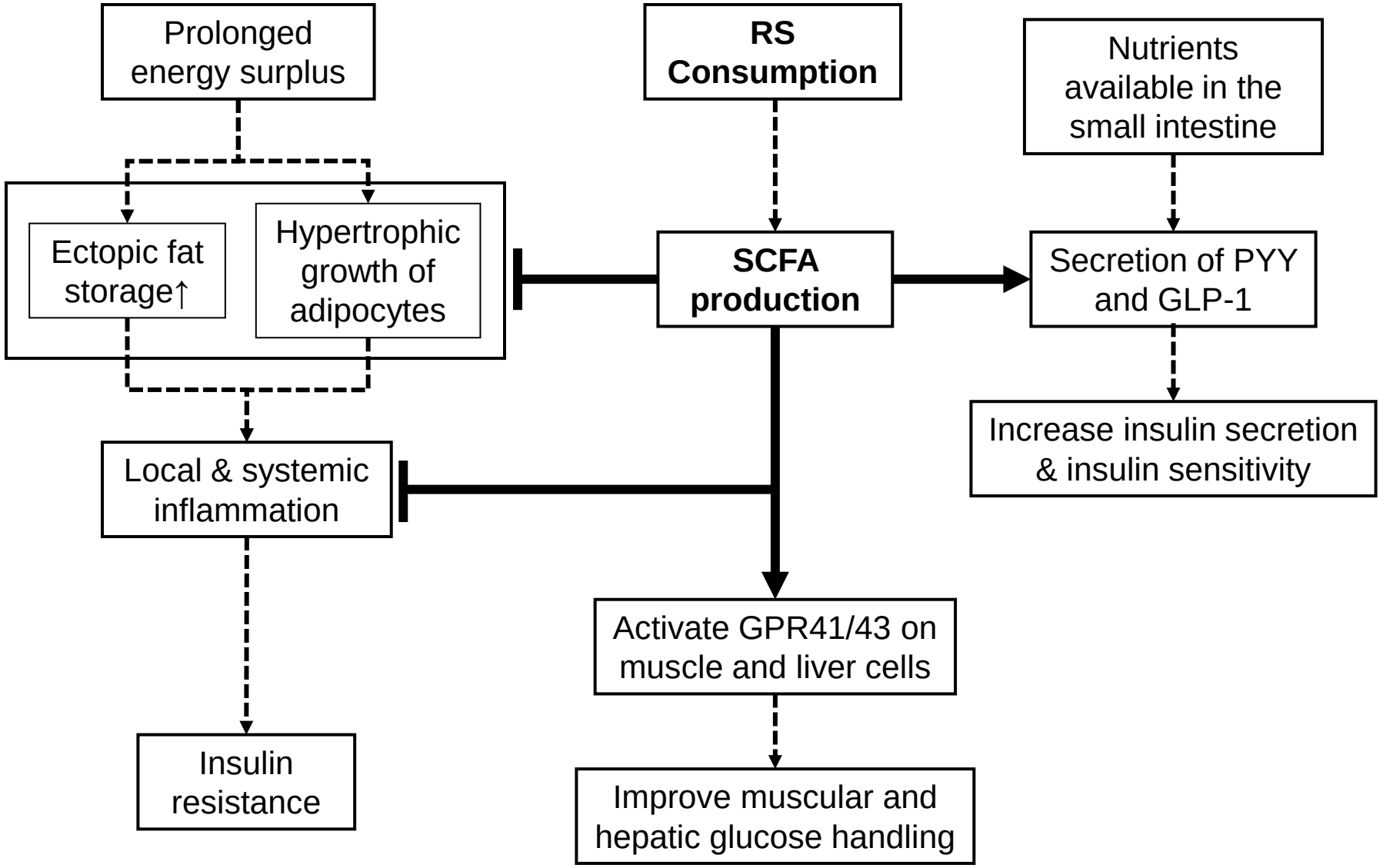


OR



Inconsistent results


First meal
Second meal
Standardized
second meal
RDS only
RS partly
replaced RDS
Blood Glucose
Time
Time


Prolonged energy surplus
RS Consumption
Nutrients available in the small intestine
Ectopic fat storage↑
Hypertrophic growth of adipocytes
SCFA production
Secretion of PYY and GLP-1
Increase insulin secretion & insulin sensitivity
Local & systemic inflammation
Activate GPR41/43 on muscle and liver cells
Insulin resistance
Improve muscular and hepatic glucose handling