The role of polydextrose in body weight control and glucose regulation

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Purpose of review
The purpose of this review was to highlight recent research developments on effects of the dietary fibre polydextrose (PDX) on appetite, satiety and energy intake and glucose metabolism. For this purpose, clinically relevant human studies were reviewed and putative mechanisms and pathways were discussed.

Recent findings
A number of acute human intervention studies provide strong indications for an energy and glucose metabolism-regulating role of PDX. These effects might be mediated via a reduced gastro-intestinal transit reducing glycaemia and insulinemia after PDX ingestion and the potential of PDX as soluble dietary fibre to alter the intestinal microbial composition, which might lead to changes in signalling in both peripheral and central pathways involved in energy metabolism and glucose homeostasis.

Summary
In acute studies, PDX seems to have an inhibiting effect on energy intake and satiety and to reduce glycaemic and insulinemic response through effect on gastro-intestinal transit time and macronutrient absorption as well as through effects of the microbial products such as short-chain fatty acids on energy and substrate metabolism. In particular, well controlled human intervention studies are required to confirm these effects in the long term. Overall, supplement PDX to the daily diet may be a promising approach for the management and treatment of obesity and associated metabolic disorders.

Keywords
energy intake, glucose metabolism, gut microbiota, intestinal transit time, polydextrose, short-chain fatty acids

INTRODUCTION

Dietary fibres are nondigestible food ingredients that include oligosaccharides, lignin, nonstarch polysaccharides and analogous polysaccharides, which may have beneficial metabolic health effects, thereby resulting in a reduced risk for the development of obesity and type 2 diabetes mellitus (T2DM) [1]. Evidence is growing that an increased dietary fibre content in our daily diet may prevent weight gain and disturbances in glucose and lipid metabolism [2]. Several mechanisms may explain the positive health effects. First, the ability of dietary fibres to physically modify nutrient absorption may affect glycaemic and insulinemic responses, which may, in the longer term, be related to T2DM development [3], and second, a dietary fibre induced shift in the gut microbial composition, which might alter the host's energy and substrate metabolism through local improvement of mucosal health in the gut, and/or by altering systemic biochemistry and/or signalling functions [1].

Dietary fibres can be classified by solubility, fermentation ability by colonic microbes and viscosity. The randomly polymerized branch-chained glucose polymer polydextrose (PDX) is nonviscous and completely soluble in water and cannot be hydrolyzed by digestive enzymes, passing intact into the colon, in which it is partly fermented by the local microbiota. Studies have shown that PDX can act as prebiotic and may beneficially modify the colonic microbial composition, which may have pronounced consequences for host lipid and glucose metabolism. These effects might be at least partly mediated through microbial metabolites

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KEY POINTS

- A relatively high number of short-term human intervention studies indicated beneficial effects of PDX on appetite, satiety and energy intake and glucose control.
- PDX may affect body weight and glucose control by a decrease in gastrointestinal passage time, resulting in a delayed nutrient absorption and prolonged feeling of satiety.
- PDX may beneficially alter the colonic microbial composition, which may improve the host's energy and glucose metabolism.
- The nonviscous soluble dietary fibre PDX is partly fermented by the colonic microbiota into SCFA.
- These SCFA may be strongly involved in the beneficial effects, by the production of anorexic hormones, through effects on central appetite regulation and an improved inflammatory state.

including short-chain fatty acids (SCFA) [4–6]. PDX may also affect body weight and glucose control by a decrease in intestinal passage time, resulting in prolonged feelings of satiety and a slower nutrient uptake, which might result in decreased postprandial glucose and insulin responses [7▪].

This review aims to provide an overview of available human studies indicating beneficial effects of PDX on body weight control, insulin sensitivity and glucose metabolism, and subsequently putative mechanisms will be discussed in detail.

COMPARATIVE EFFECTS OF POLYDEXTROSE ON ENERGY INTAKE, INSULIN SENSITIVITY AND GLUCOSE METABOLISM

Recent human studies

Obesity develops under conditions of a positive energy balance. Any factor lowering energy intake or increasing energy expenditure would result in a negative energy homeostasis, and thus prevent the development of obesity and obesity-related cardiometabolic disorders such as T2DM.

Several human studies strongly implicate that PDX could be a useful food supplement to beneficially affect body weight control and glucose homeostasis. These trials focused on the acute or short-term effects of PDX. Hull *et al.* [8] found a decreased feeling of hunger and a decreased energy intake when yoghurt-based drinks containing 12.5 g PDX were consumed 90 min before an ad-libitum lunch and dinner. In line, another acute study by Ranawana *et al.* [9] showed that the consumption of a smoothie (containing 12 g of PDX) 60 min prior to lunch significantly reduced energy intake. Moreover, a dose-dependent decrease in energy intake was reported by Astbury *et al.* [10], when 6.25, 12.5 and 25 g PDX were added to a liquid preload and consumed 90 min before an ad-libitum lunch. Konings *et al.* [7▪] found a pronounced decrease in feeling of hunger, as determined by visual analogue scales, and an increase in whole-body fat oxidation, as well as a reduced postprandial peak glucose and insulin response when 30% of the daily carbohydrate intake was replaced by PDX at breakfast and lunch. In addition, Olli *et al.* [11▪] showed that the supplementation of 15 g PDX to a high-fat meal reduced feelings of hunger, which was accompanied by increased plasma concentrations of the satiety-stimulating incretin glucagon-like peptide-1 (GLP-1).

To the author's knowledge, only two human longer-term human intervention studies on PDX effects on energy homeostasis are published. An interesting study by Astbury *et al.* [12▪▪] showed a reduced total daily energy intake during experimental and free-living conditions when PDX and whey protein were incorporated in snack bars as compared with isoenergetic control snack bars three times a day for 14 days. Interestingly, the PDX group showed reduced glucose and ghrelin concentrations and increased GLP-1 and peptide tyrosine–tyrosine (PYY) responses. In another study by Costabile *et al.* [5], patients consumed 8 g PDX in powder form for 21 days. The PDX group showed reduced consumption of snacks and increased intestinal butyrate-producing microbes, which have been associated in several studies with improved insulin sensitivity and prevention of T2DM [13–15]. A detailed overview of these human intervention studies can be found in Table 1.

The above data provide indications that PDX may beneficially affect body weight control and glucose homeostasis through effects on satiety, substrate oxidation and glycaemic and insulinemic responses. However, so far experiments were only performed in acute settings or during a relatively short intervention period (14 and 21 days), whilst long-term effects of PDX on body weight control and glucose metabolism are missing. This clearly indicates the need to perform well controlled longer-term human intervention studies. In the following section, putative mechanisms involved in these hypophagic and glucose-regulating effects of PDX will be discussed.

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Table 1. Recent human intervention studies investigating the effects of polydextrose on appetite, satiety, energy intake and glucose homeostasis

Subjects	Study design	Dose	Results	Author
31 lean, healthy adults	21-day, randomized, double-blind, placebo-controlled crossover	8 g/day PDX powder	PDX reduced the snack consumption and increased butyrate producing intestinal bacteria content	Costabile *et al.* [5]
44 lean, healthy adults	Acute, randomized, single-blinded, placebo-controlled, cross-over design	Yogurt-based drinks containing different amounts of PDX (0, 6.25 and 12.5g)	PDX consumed 90 min before ad-libitum lunch and ad-libitum dinner decreased the feelings of hunger. The highest PDX dose decreased energy intake at lunch	Hull *et al.* [8]
26 healthy males	Acute, repeated-measures randomized, single-blind, placebo-controlled cross-over design	400-g fruit smoothie containing 12 g (3%) of PDX	PDX dose 60 min before ad-libitum lunch resulted in a lower energy intake at lunch	Ranawana *et al.* [9]
21 lean, healthy adults	Acute, randomized within-patient, placebo-controlled and cross-over design	837 kJ liquid preload containing 0, 6.25, 12.5 and 25 g PDX	PDX dose 90 min before ad-libitum lunch decreased the energy intake in a dose-dependent manner	Astbury *et al.* [10]
18 overweight adults	Single-blind, randomized cross-over study	30% of the available carbohydrates with PDX at breakfast and lunch	Replacement of carbohydrates with PDX increased fat oxidation and decreased postprandial peak glucose and insulin responses and decreased appetite ratings	Konings *et al.* [7▪]
10 lean men	14-day, randomized, double-blind, placebo-controlled and crossover design	PDX and whey protein mixed snackbar (PPX) or an isoenergetic control snack bar as a midmorning, between-meal snack	The total daily energy intake was lower when PPX snacks were consumed during experimental days, and during the free-living part of the intervention. PPX decreased glucose and ghrelin and increased GLP-1 and PYY responses	Astbury *et al.* [12▪▪]
18 nondiabetic, obese adults	Acute, multicenter, randomized, double-blind, placebo-controlled and cross-over design	high-fat meal (4293 kJ, 36% from fat) with or without PDX (15 g)	PDX supplementation increased plasma GLP-1 levels. PDX reduced feeling of hunger and increased satiety during the postmeal period	Olli *et al.* [11▪]

GLP-1, glucagon-like peptide 1; PDX, polydextrose; PYY, peptide tyrosine tyrosine.

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PUTATIVE MECHANISMS OF POLYDEXTROSE INVOLVED IN THE REGULATION OF ENERGY INTAKE, INSULIN SENSITIVITY AND GLUCOSE METABOLISM

Polydextrose decreases the absorption of macronutrients

Previously, the protective effects of soluble dietary fibres have been attributed to the ability to form viscous solutions that prolong gastric emptying, consequently attenuate the absorption of glucose and lipids and induce satiety [16]. The nonviscous soluble PDX misses the physiochemical property of viscous dietary fibres to slow down gastric emptying. Therefore, other mechanisms must be involved in the effects of PDX on energy intake and glucose homeostasis described in the human studies above.

Of note, PDX was shown to shorten gastrointestinal transit time in constipated [17] and healthy patients [18]. The intestinal passage time is an important factor to determine amounts of absorbed nutrients. Decreased transit time might lead to a more gradual nutrient absorption in the proximal intestine and to prolonged feeling of satiety. The delayed nutrient uptake may reduce postprandial glucose and insulin response [7▪,12▪▪]. These reduced glucose and insulin responses might further result in a decreased inhibition of lipolysis, higher circulating fatty acid concentrations and subsequent increased fat oxidation. In turn, an increase in postprandial fat oxidation rate may impact fat storage and satiety and may thereby beneficially affect body weight control in the long term [19]. Furthermore, it may result in decreased ectopic fat accumulation, which is associated with improved insulin sensitivity and glucose metabolism [20]. Reduced postprandial glycaemic and insulinemic responses and a higher fat oxidation were shown in the acute study by Konings *et al.* [7▪]. However, in this study, it remains unclear if these effects are related to the slightly lower energetic value of the PDX diet as compared with the control diet or with the PDX treatment *per se*. Further studies examining the effects of PDX on glucose absorption, substrate and energy utilization are needed.

Polydextrose affects the intestinal microbiota

As described above, when PDX enters the colon, it can be partly fermented by the local microbiota, thus serving as an energy source to promote their growth and survival. Recently, evidence is growing rapidly that the gut microbiota may play an important role in glucose homeostasis, obesity and metabolic syndrome [21]. In a human trial, the bacterial DNA of faecal samples from 20 adult patients was pyrosequenced before and after 21 days of PDX consumption. In this study, the content of well known producers of the SCFA butyrate, such as *Faecalibacterium*, and in particular *Faecalibacterium prausnitzii,* increased in number [4]. Of note, these bacteria are known for their anti-inflammatory property and found to be decreased in T2DM patients as compared with healthy patients in two independent studies [14,15]. However, other bacteria, such as bifidobacteria, which are associated with a lean and metabolically healthy microbiome [22], were decreased after PDX treatment. In line, in the human crossover study by Costabile *et al.* [5], an increase in the *Eubacterium rectale–C.coccoides* group which includes important butyrate-producing microbes, such as *Faecalibacterium prausnitzii* and *Ruminococcus intestinalis*, was found after PDX consumption for 3 weeks. In this study, no effects of the PDX treatment on bifidobacteria were detected. Other human data, on the other hand, indicated that the number of bifidobacteria was increased when PDX was consumed for 3 or 6 weeks [23,24]. This discrepancy could reflect interindividual variances in initial gut microbial composition, but also showed that additional research is needed to claim PDX as a prebiotic. Overall, most evidence is supporting a PDX-induced increase in microbial composition that favours an increased production of SCFA and an improvement in metabolic profile.

Polydextrose increases the production of short-chain fatty acids

In-vitro fermentation [25] and in-vivo data [26] have shown that microbial PDX fermentation ends up in the production of SCFA, in particular acetate and butyrate. These SCFA might be involved in appetite regulation via the secretion of gut-derived satiety-stimulating hormones PYY and GLP-1 from L-cells in the ileum and colon. In mice, 4-week oral butyrate administration increased plasma GLP-1 and PYY concentrations [27]. Moreover, a study in hyperinsulinemic human females showed that acute rectal infusion of 200 mmol/l sodium acetate enhanced PYY plasma concentrations as compared with saline infusions [28]. PYY is not only an appetite and satiety-regulating hormone [29], but also known to stimulate glucose-induced insulin secretion and insulin sensitivity [30]. Furthermore, the beneficial role of GLP-1 on glucose homeostasis is well determined. It may increase insulin secretion, inhibition of glucagon production and

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increase pancreatic β-cell proliferation and function [31]. Interestingly, as shown above, an increase in plasma levels of these gut hormones after PDX treatment was found in the study by Astbury *et al.* [12▪▪], which was accompanied by a decreased postprandial glucose response.

In addition to the stimulation of the production and secretion of anorectic hormones and glucose-regulating hormones, recently a novel and direct role of SCFA in the regulation of energy intake was discovered. An elegant study in mice using a PET-CT scan methodology has shown that intravenously and colonically administered ^{11}C-acetate crossed the blood–brain barrier, and was taken up by the hypothalamus. Intraperitoneal injection of acetate acutely decreased food intake through appetite suppression accompanied by an increased lactate and gamma-aminobutyric acid production [32]. Therefore, acetate might also be an important central regulator of satiety.

Acetate and butyrate might not only regulate energy intake; they might also increase energy utilization. It has been shown in obese mice that oral administration of sodium butyrate elicits body weight loss, via an increased energy expenditure and fat oxidation [33]. In addition, oral acetate and butyrate administration to high-fat fed mice reduced body weight and improved insulin sensitivity without changing food intake or physical activity [34]. Furthermore, a study [35] showed that butyrate stimulates intestinal gluconeogenesis (IGN) via a gut–brain neural circuit. In wild-type mice, a butyrate-enriched diet improved glucose tolerance, insulin sensitivity and body weight control, whilst these beneficial metabolic effects were completely abolished in mice deficient in IGN [35]. The induction of IGN promotes glucose release in the portal vein, which may lead through a brain-related mechanism to decreased hepatic glucose production and increased satiety and energy expenditure [36].

SCFA may also beneficially affect insulin sensitivity and glucose homeostasis by a reduction of proinflammatory cytokines in the long term. The immune-modulatory effects of SCFA have mainly been demonstrated in in-vitro studies. Acetate and butyrate treatment decreased lipopolysaccharide (LPS)-stimulated tumour necrosis factor-alpha (TNF-α) release from human neutrophils [37]. In line, sodium acetate and sodium butyrate incubation of LPS-stimulated RAW264.7 macrophage-like cells reduced the production of proinflammatory cytokines and LPS-induced nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) activation [38]. Moreover, a human in-vivo crossover study showed that circulating TNF-α concentrations were reduced after acute intravenous sodium acetate (20 mmol in 100 ml sterile water) and rectal sodium acetate (60 mmol in 300 ml water) infusions, when compared with intravenous and rectal saline infusion [28]. So far, no human data are present investigating the effects of PDX on intestinal or circulating inflammatory markers. Nevertheless, PDX enrichment in suckling piglets resulted in increased ileal SCFA concentrations and associated reductions in ileal expression of proinflammatory markers TNFα, interleukin 1-beta (IL-1β) and interleukin 8 (IL-8) [39].

Overall, there are strong indications that the production of SCFA is one of the links between PDX and the decreased satiety and energy intake and improved glucose homeostasis found in the human studies. Nevertheless, more information is required on the direct relation between the PDX-induced putative effects on appetite, satiety, energy intake and glucose metabolism and SCFA production and absorption rates.

CONCLUSION

The relatively high number of acute human intervention studies indicating beneficial effects of PDX on appetite, satiety and energy intake tempt to draw the conclusion that PDX is a potent approach for the prevention and treatment of obesity and comorbidities. However, human long-term data are currently missing and putative mechanisms such as changes in the gut microbiota composition and in SCFA productions have to be studied in more detail. Also, the effects of PDX as a glucose-lowering and insulin-sensitizing agent need further investigations. Well controlled and well phenotyped human intervention studies are required to confirm these effects in the long term. These studies should focus on the impact of changes in glycaemia and insulinemia in the long term and study long-term changes in gut microbiota composition, SCFA production and absorption rates, and gut signalling, induced by microbial products, in relation to metabolic health. These data could provide knowledge, which could be translated into novel strategies for the management and treatment of obesity and related metabolic disorders.

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Conflicts of interest

There are no conflicts of interest.

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