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The fermentation of polydextrose in the large intestine and its beneficial effects

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REVIEW ARTICLE

Abstract

Polydextrose is a randomly bonded glucose polymer with a highly branched and complex structure. It resists digestion in the upper gastrointestinal tract and is partially fermented in the large intestine by the colonic microbes. Due to its complex structure, a plethora of microbes is required for the catabolism of polydextrose and this process occurs slowly. This gradual fermentation of polydextrose gives rise to moderate amounts of fermentation products, such as short chain fatty acids and gas. The production of these metabolites continues in the distal part of the colon, which is usually considered to be depleted of saccharolytic fermentation substrates. The fermentation of polydextrose modifies the composition of the microbiota in the colon, and has been shown to impact appetite and satiety in humans and improve the gastrointestinal function. The purpose of this short review is to summarise the *in vitro*, *in vivo* and human studies investigating the fermentation properties of polydextrose in the large intestine.

Keywords: polydextrose, fibre, sustained fermentation, colon, prebiotic

1. Introduction

Polydextrose (PDX) is a highly branched, randomly bonded glucose polymer with an average degree of polymerisation (DP) of 12, ranging from DP 2 to 120. The molecule contains all possible combinations of α- and β-linked 1→2, 1→3, 1→4 and 1→6 glycosidic linkages, though the 1→6 (both α and β) predominates (Lahtinen *et al.*, 2010). Due to its complex structure, PDX is not hydrolysed by mammalian digestive enzymes in the small intestine. In the large intestine, its fermentation is gradual and incomplete. It modifies the composition of the colonic microbiota and results in the production of short chain fatty acids (SCFA) and gas. PDX has been acknowledged as a soluble fibre mediating beneficial effects on gut health, postprandial glycaemia and satiety (Tiihonen *et al.*, 2011). Its prebiotic properties have also been investigated. A prebiotic is a non-viable food component that confers a health benefit on the host, associated with selective modulation of the microbiota composition and/or activity (Pineiro *et al.* 2008).

This review summarises the data obtained from various *in vitro*, *in vivo* and human intervention studies addressing the fermentation of PDX in the large intestine and the effects deriving from this sustained fermentation. Classical microbiological and *in vitro* cell cultures have been used as well as multi-stage dynamic colonic fermentation models, i.e. human colon simulators. In these simulators, the colonic fermentation of substrates at different stages of the colon can be studied using anaerobic, connected glass vessels with varying environmental conditions (flow rate, pH) that simulate the conditions in the human colon. These systems work continuously or semi-continuously. Animal studies have also been used to investigate possible mechanisms of action of PDX in a living system facilitating the study of the effects of PDX at various stages of the colon. The effects seen in the *in vitro* and *in vivo* animal models have to large extent been reproduced in human intervention trials, thus validating the models and permitting the connection of these effects to possible health benefits.

2. Fermentation of polydextrose

Fermentation of PDX in the large intestine has been investigated in several *in vitro* studies and it is evident, presumably due to the complex structure of the molecule, that a consortium of microbes is needed to degrade this polymer. This was demonstrated in simple pure culture

studies with single microbes where PDX was hardly fermentable (Mäkeläinen *et al.*, 2010b), whereas in batch and colonic fermentation simulations utilising complex microbiota PDX was slowly degraded by the microbes, and fermentation products could be measured from the fermentation fluids (Probert *et al.*, 2004; Wang and Gibson, 1993). In colon simulator studies (Mäkeläinen *et al.*, 2007), a gradual disappearance of PDX from simulated digesta has been shown (Figure 1), demonstrating its slow fermentation extending from proximal to distal parts of the modelled colon (Mäkeläinen *et al.*, 2007, 2010a; Mäkivuokko *et al.*, 2005). This finding is in agreement with animal and human studies. In a feeding trial with pigs, PDX was observed to gradually disappear from the digesta obtained from different parts of the intestines, being still measurable in the contents of distal colon (Fava *et al.*, 2007). Similarly, in a human intervention trial, PDX was detected in faecal samples after consumption (Costabile *et al.*, 2011). Thus, the sustained fermentation of PDX that has been demonstrated in laboratory and animal experiments is in agreement with human clinical data, and it is evident that PDX is also available for fermentation in the distal part of the colon. The relevance of this is discussed in the following sections.

Although all subjects excrete PDX in their faeces, substantial subject-to-subject variation has been observed (Costabile *et al.*, 2011) suggesting that different gut microbiota exhibit different abilities to degrade PDX. The fermentation of the molecule has also been investigated in more detail. An *in vitro* trial with simulated colon fermentation showed that the non-branched molecules became more abundant, while the relative proportion of branched molecules decreased as the fermentation of PDX progressed. Also, the relative abundance of α-1,6 pyranose glucose molecules decreased. This indicates that the degradation of PDX is not a random process, but that intestinal microbes have a preference for branched PDX components and certain glycosidic linkages when fermenting the complex molecule (Lahtinen *et al.*, 2010). The data regarding PDX fermentation are summarised in Table 1.

3. Fermentability of polydextrose by the gut microbiota

Effects on microbiota composition

As discussed above, PDX is partially fermented by the gut microbiota in the colon, and this fermentation affects the numbers of different microbial groups in the colon. The human gut microbiota is dominated by three phyla of microbes, i.e. *Firmicutes, Actinobacteria* and *Bacteroidetes* (Lay *et al.*, 2005). In a recent study by Hooda *et al.* (2012), a high-throughput pyrosequencing analysis revealed that PDX consumption resulted in significant shifts in the microbiota composition of healthy adult males. Various microbes in the *Firmicutes* phylum were affected, where the abundance of e.g. *Faecalibacterium*, *Clostridiaceae*, *Akkermansia* and *Dialister* genera was greater and the abundance of e.g. *Ruminococcus*, *Eubacterium* and *Coprococcus* genera was lower after PDX consumption, as opposed to no supplemental fibre as a control. The abundance of the phylum *Actinobacteria* was significantly decreased, including *Bifidobacterium* and *Coriobacterium* genera. When looking into the abundance of single species of microbes, the abundance of *Faecalibacterium prausnitzii*, known for its ant-inflammatory properties, and *Clostridium leptum* was greater after PDX supplementation, but the levels of *Bifidobacterium, Eubacterium rectale*

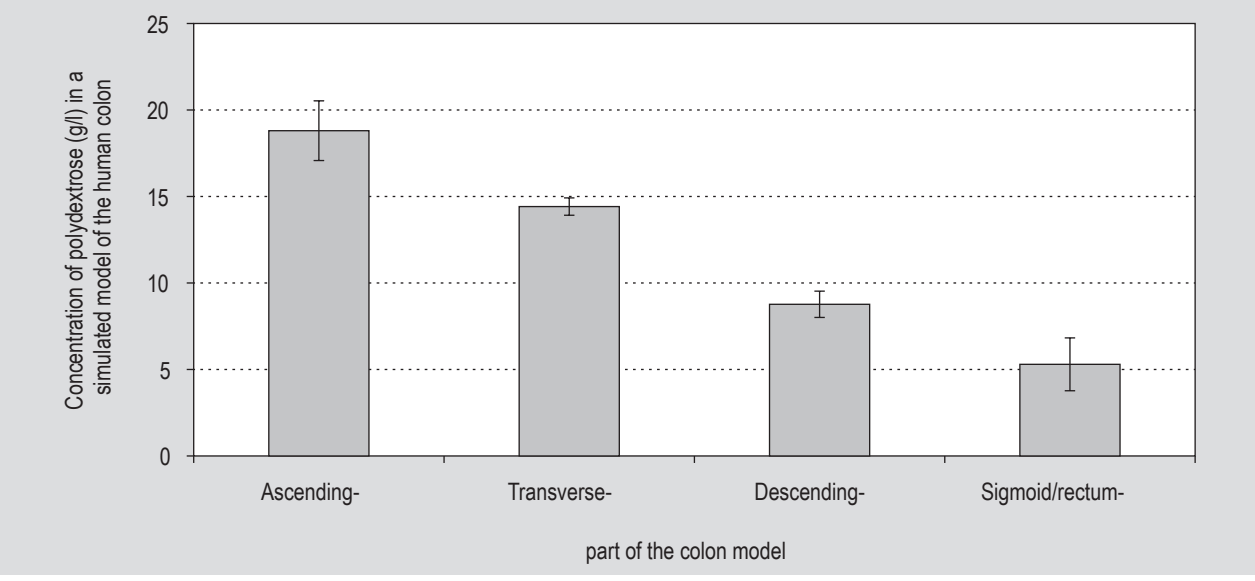

Figure 1. Gradual disappearance of polydextrose from the faecal slurry in a simulated model of the human large intestine (Enteromix model). Data are expressed as mean values ± standard deviation. Figure modified from Mäkeläinen *et al.* (2007).

Table 1. Fermentation of polydextrose (PDX) in different *in vitro*, *in vivo* and human clinical trials.

Reference	Study type	Amount of polydextrose	Results	Conclusions
Mäkeläinen *et al*., 2010a	pure culture	1% concentration	Only minor growth of single microbes was observed when PDX was the sole carbohydrate source.	Single microbes were not able to degrade PDX.
Mäkivuokko *et al*., 2005	colon simulator	0.5, 1, 1.5% concentration	PDX degradation proceeded from proximal part to distal part of the model; the amount of degraded PDX was dependent on the concentration added.	PDX was gradually fermented by gut microbiota and available for degradation in the distal part of the colon model.
Mäkeläinen *et al.,* 2007	colon simulator	2% concentration	PDX levels decreased gradually from the proximal to the distal part of the colon model. Part of the fed PDX was still present in the distal part.	Gut microbiota degraded PDX slowly and part of the fed material remained intact throughout the colon model.
Lahtinen *et al.,* 2010	colon simulator	2 or 3% concentration	Gut microbes had a preference for branched PDX molecules and 1,6 pyranose linkages.	Degradation of PDX in the gut was not a random process; PDX was degraded slowly and sustainably.
Fava *et al.,* 2007	animal study	30 g/day	The amount of PDX decreased in digesta taken from the distal small intestine, caecum, proximal colon, middle colon and distal colon.	PDX was gradually fermented in the pig gut and still present in the distal colon.
Costabile *et al.,* 2012	human intervention	8 g/day	PDX was recovered (on average 0.8 g) from faecal samples after a two-week intervention period	Sustained fermentation of PDX also occurred in humans and part of the fed PDX was still present in the distal colon

and *Ruminococcus* species decreased. In another human intervention trial, Costabile *et al*. (2012) also saw increased numbers of *C. leptum* group members, but the levels of *F. prausnitzii* and *Bifidobacterium* remained unchanged. The changes observed in the microbiota composition are summarised in Table 2.

Overall, the changes in the observed composition of the microbiota following PDX intervention vary greatly from study to study, perhaps due to the different methods used (classical plating method, quantitative PCR/fluorescence *in situ* hybridisation or high-throughput sequencing) and due to different subject populations. *In vitro* studies and earlier human interventions have mainly focused on assessing the effects of PDX fermentation on a few specific species and genera, such as *Bifidobacterium, Lactobacillus, Bacteroides* and *Clostridium*, which are traditionally considered to be important members of the microbiota (Fuller and Gibson, 1997). However, as our knowledge of the composition of the microbiota is improving, the traditional division into solely 'beneficial' (bifidobacteria and lactobacilli) and 'harmful' (clostridia and *Bacteroides*) components is problematic. For instance, the beneficial and selective prebiotic effects could be mediated through increased numbers or activities of butyrate-producing microbes, such as *E. rectale/Roseburia* species and *F. prausnitzii* belonging to clostridial clusters IV and XIVa (Louis and Flint, 2009). Decreased levels of these microbes in the gut have been recently linked to inflammatory bowel diseases (Sokol *et al.*, 2008; Takaishi *et al.*, 2008), and their faecal levels strongly correlate with faecal butyrate concentrations. The numbers of these microbes are modifiable with dietary carbohydrates and fibre (Benus *et al.*, 2010; Duncan *et al.*, 2007) and according to a recent study by Hooda *et al.* (2012), their numbers also respond favourably to a PDX-supplemented diet.

Fermentation products

The fermentation of non-digestible carbohydrates in the colon leads to production of SCFA (acetate, propionate and butyrate) and gases (hydrogen, methane and carbon dioxide). The production of various fermentation metabolites is dependent on the composition of the colonic microbiota. Prebiotic carbohydrates as well as other types of carbohydrates, e.g. polyols and plant-derived gums and fibres, may cause extensive gas production after consumption and lead to undesired side-effects, such as distension and bloating of the stomach and loose

Table 2. Effects of polydextrose on gut microbiota composition.

	Hooda *et al.* (2012)[1,2]	Costabile *et al.* (2012)[1,3]
Phylum *Firmicutes*		
Faecalibacterium	↑	-
Ruminococcus	↓	-
Eubacterium	↓	x (*Eubacterium rectale/Clostridum coccoides* group)
Clostridiaceaea	↑	↑ (Clostridial cluster I and II)
Clostridium	↑	-
Akkermansia	↑	-
Dorea	↓	-
Dialister	↑	-
Coprococcus	↓	-
Lactobacillus	x	↓ (*Lactobacillus/Enterococcus* spp.)
Phylum *Actinobacteria*		
Bifidobacterium	↓	x
Coriobacterium	↓	-
Phylum *Bacteroides*		
Bacteroides	x	x
Species/strains		
Faecalibacterium prausnitzii	↑	x
Clostridium leptum	↑	↑
Ruminococcus spp.	↓	-
Ruminococcus intestinalis	-	↑
Eubacterium rectale	↓	-
Eubacterium hallii	↓	-
Bifidobacterium spp.	↓	x

[1] ↑ = significantly increased numbers (P<0.05); ↓ = significantly decreased numbers (P<0.05); x = no change; - = not tested in this trial.
[2] Determined by 16S rRNA gene pyrosequencing.
[3] Determined by fluorescence *in situ* hybridisation and quantitative PCR.

stools (Flood *et al.*, 2004). The gas production of PDX has been compared *in vitro* to other carbohydrates, and it was seen that the more rapidly fermented short chain oligosaccharides resulted in more rapid production and accumulation of gas than the substrates with greater degrees of polymerisation, such as PDX. Also, the total amount of gas produced from PDX was substantially less; this was mainly due to less production of H_2 (Hernot *et al.*, 2009). This effect owes most likely to the slow degradation of the PDX molecule. Furthermore, short chain oligosaccharides blended with PDX had a lower gas production rate as well as a reduced rate of SCFA production compared to short chain oligosaccharides fermented alone (Vester Boler *et al.*, 2009), although neutral effects were also reported (Ghoddusi *et al.*, 2007). In humans, PDX has been reported to be well tolerated upon consumption (Boler *et al.*, 2011; Costabile *et al.*, 2011), even in large single doses of up to 50 g or daily consumption of 90 g (Flood *et al.*, 2004). The high tolerability is most likely due to the slow fermentation rate of the complex molecule and, thus, less and slower gas production.

In line with gas production, the rate of SCFA production from PDX is also more moderate than from short chain oligosaccharides, such as fructo- and galacto-oligosaccharides (Hernot *et al.*, 2009; Mäkeläinen *et al.*, 2010a). *In vitro* studies have demonstrated that PDX fermentation leads to increased concentration of all three SCFA commonly found in the intestine (Mäkeläinen *et al.*, 2007, 2010a; Probert *et al.*, 2004). *In vitro* methods enable accurate analyses of the microbial metabolites formed, as the fermentation end-products accumulate in the growth media in batch and simulator experiments. In animal and human trials, the fermentation products are quickly absorbed and/or utilised by the colonocytes or other cells in the body, thus the concentrations measured in faecal samples do not describe the total production rate. However, in animals it is also possible to collect the contents of the intestine, which gives a better view of PDX fermentation in a physiological situation. In contrast to *in vitro* studies, fermentation of PDX reduced the concentrations of all SCFA in the colon of pigs (Fava *et al.*, 2007). Concomitantly, increased levels of acetate and lactate measured from blood

samples suggest an improved absorption rate from the gastrointestinal tract rather than a reduced production by the microbes. Similar results have been reported in human dietary interventions; PDX has a neutral or even decreasing effect on the faecal SCFA concentrations (Boler *et al.*, 2011; Costabile *et al.*, 2011; Hengst *et al.*, 2008). As the faecal levels of acetate have been inversely correlated with the acetate absorption rate from the human distal colon (Vogt and Wolever, 2003), it may also be that the serum levels of these fermentation metabolites are increased in humans as in pigs, although no data on blood levels currently exist.

The levels of metabolites derived from protein fermentation are reduced in the presence of PDX. It has been shown in human interventions (Boler *et al.*, 2011; Jie *et al.*, 2000) as well as in animals (Fava *et al.*, 2007; Peuranen *et al.*, 2004) and *in vitro* (Mäkeläinen *et al.*, 2007, 2010a) that the levels of proteolytic fermentation metabolites, such as branched chain fatty acids, faecal ammonia, phenol compounds, indole and cresole, decrease in association with PDX. This effect is sustained into the distal part of the colon and is presumably due to the partial fermentation of PDX over protein. The production of various fermentation metabolites from PDX is summarised in Table 3.

4. Beneficial effects of polydextrose consumption

Slow and gradual fermentation of PDX has been documented in various studies and the beneficial effects of PDX are mediated either through the metabolites produced and/or altered microbiota composition. Enhanced production of SCFA after PDX consumption was shown to improve the absorption of minerals from the colon. Calcium and magnesium absorption were enhanced in a postmenopausal rodent model (Legette *et al.*, 2012), and increased bone calcium content had also been observed (Weaver 2010). PDX has also been shown to improve iron absorption in rats (Santos *et al.* 2010). Other beneficial effects are thought to be mediated by increased SCFA levels in the gastrointestinal tract and beyond. These effects include relief of constipation, growth inhibition of pathogenic microorganisms, and impact on cholesterol biosynthesis in the liver (Topping and Clifton, 2001; Wong *et al.*, 2006). Indeed, PDX has been reported to shorten gastrointestinal transit time in constipated (Hengst *et al.*, 2008) and healthy subjects (Timm *et al.,* 2013) and soften the stools of healthy humans (Costabile *et al.,* 2012). Butyrate is considered to be a particularly beneficial SCFA, as it provides nutrition for colonocytes, enhancing the integrity of the colonic mucosa. It also promotes appropriate cell differentiation (Hamer *et al.*, 2008). Conversely, acetate acts more systemically, influencing fatty acid and cholesterol synthesis in the liver, whilst propionate may impact satiety by participating in the regulation of gastrointestinal-derived hormones (Hosseini *et al.*, 2011). PDX has been shown to induce short-term satiety and suppress energy intake in humans (King *et al.*, 2005; Ranawana *et al.*, 2012) in a dose-dependent manner (Astbury *et al.,* 2013). These effects can derive and be mediated by the increased concentrations of various SCFA from sustained PDX fermentation. For example, satiety and energy intake can be affected through free fatty acid receptors expressed on enterocytes, which in turn modulate the release of gut hormones, such as glucagon-like peptide-1, controlling insulin release and appetite in the central nervous system (Tolhurst *et al.*, 2012).

Epidemiological studies have long suggested an inverse association between fibre intake and a range of colonic and systemic illnesses, such as certain cancers and cardiovascular disease (Divisi *et al.*, 2006). Fermentation of fibre into SCFA, especially butyrate, has been speculated to be behind the protective mechanisms (Hamer *et al.*, 2008), but also the decreased production of other types of metabolites may contribute to the effect. Diseases of the colon manifest themselves predominantly in the distal part of the colon. The increased proteolytic fermentation taking place when carbohydrate substrates are depleted may result in the production of harmful substrates in the distal part of the colon, which are implicated in disease progression. In humans, the genotoxicity of faecal water on colonocytes was decreased after PDX consumption, implying that PDX fermentation led to desirable changes in the composition of the lumen contents and, therefore, might decrease the risk of disease development (Costabile *et al.*, 2011). Cell culture studies further suggest that the fermentation products deriving from PDX may partly mediate their protective activities through modulation of gene expression of the colonocytes. The expression of colorectal cancer markers, such as the COX-2 gene, can be suppressed by PDX fermentation metabolites (Mäkivuokko *et al.*, 2005). Using a metagenomic approach, PDX fermentation has been shown to modify the expression of genes in colon cancer cells that are related to cell cycle, apoptosis and energy metabolism (Putaala *et al.*, 2011). In animal trials, PDX tended to decrease the expression of mucosal COX-2 in pigs (Fava *et al.*, 2007). Furthermore, diets with PDX as soluble fibre have been shown to increase urinary excretion of polychlorinated biphenyls (environmental carcinogens) compared to diets with water-insoluble fibre in rats (Kimura *et al.*, 2004). These effects of PDX on the metabolite concentrations may contribute to the health of the colon, especially in the distal part. It should be reiterated that the composition of the gut microbiota impacts the composition of metabolites that are produced from the fermentation of carbohydrates. Nevertheless, the changes in the numbers of specific microbes in the colon is not a health benefit as such, but should be connected to a beneficial shift in a biomarker of a disease and, therefore, it is difficult to conclude yet whether PDX possesses 'true prebiotic properties' in addition to its fibre properties.

Table 3. Fermentation metabolites produced from polydextrose (PDX).

Reference; study type; amount of polydextrose	Results[1]	Conclusions
Gas production		
Hernot *et al.,* 2009; batch fermentation; 0.1% concentration	At all measurement points, PDX fermentation produced the least total gas and H_2 of all the tested carbohydrates.	PDX fermentation was slower than that of short chain oligosaccharides.
Vester Boler *et al.,* 2009; batch fermentation; 0.1% concentration	PDX produced the lowest volume of gas of all tested carbohydrates. Blending of PDX with short chain oligosaccharides (FOS, GOS) reduced the rate and amount of gas formation in batch cultures.	Mixing of long and short chain oligosaccharides attenuated gas production.
Ghoddusi *et al.,* 2007; batch fermentation; 0.1% concentration	Low amounts of gas were generated from PDX during the first 8 h, but higher amounts after 32 h. Mixing PDX with short chain oligosaccharide did not lower the amount of gas produced.	Slow gas production indicated a slow fermentation rate of PDX .
SCFA production		
Hernot *et al.,* 2009; batch fermentation; 0.1% concentration	Acetate, propionate and butyrate were produced from PDX, but no lactate was formed. The concentration of SCFA was significantly lower than that from short chain oligosaccharides.	Slower fermentation rate and longer time to attain maximal production rate caused fewer SCFA produced from PDX.
Mäkeläinen *et al.,* 2010b; colon simulator; 2% concentration	Concentrations of all SCFA were significantly increased in the middle and distal part of the colon model. GOS increased acetate and butyrate levels already in the proximal part of the model.	Slower fermentation of PDX resulted in less and slower production of SCFA.
Probert *et al.,* 2004; colon simulator; 1% concentration	PDX increased the production of all SCFA in all stages of the simulator, acetate being most pronounced.	PDX stimulated bacterial metabolism, as judged by the increased levels of SCFA.
Fava *et al.,* 2007; animal study; 30 g/day	PDX reduced the levels of all SCFA in the small and large intestines of pigs. Increased levels in blood were measured.	Decrease of SCFA in the lumen might indicate increased absorption, as measured from blood samples.
Costabile *et al.,* 2012; human intervention; 8 g/day	No significant changes were observed in the faecal levels of SCFA after PDX or placebo treatments	PDX consumption did not increase faecal SCFA levels
Boler *et al.,* 2011; human intervention; 21 g/day	Faecal acetate, propionate and butyrate concentrations were lower after PDX consumption compared to control (no fibre).	PDX consumption decreased faecal SCFA concentrations. SCFA were not measured from blood.
Hengst *et al.,* 2009; human intervention; 8 g/day	Faecal levels of SCFA remained constant over the whole study period.	PDX had no effect on faecal SCFA concentration.
Proteolytic metabolites		
Mäkeläinen *et al.,* 2010a; colon simulator; 2% concentration	PDX decreased the levels of branched chain fatty acids in the colon model.	PDX fermentation decreased the production of proteolytic metabolites in the colon model.
Peuranen *et al.,* 2004; animal study; 2% in feed	PDX ingestion reduced the production of BCFA and few biogenic amines in rat caecum.	PDX fermentation decreased the production of proteolytic metabolites in rats.
Kimura *et al.,* 2004; animal study; 10% in feed	In rats, PDX increased the urinary excretion of polychlorinated biphenyls compared with water insoluble fibre.	PDX increased the excretion of environmental carcinogens from rats.
Boler *et al.,* 2011; human intervention; 21 g/day	Faecal ammonia, 4-methylphenyl, indole and branched chain fatty acids were decreased after PDX consumption.	All measured protein fermentation metabolites were decreased after PDX fermentation.
Hengst *et al.,* 2009; human intervention; 8 g/day	Branched chain fatty acid levels decreased in faeces after PDX consumption. A significant decrease of cholesterol degradation products was measured as well as a decreased faecal excretion of bile acids.	PDX consumption decreased putrefactive protein fermentation and changed bile acid and sterol excretion.

[1] BCFA = branched chain fatty acids; SCFA = short chain fatty acids; GOS = galacto-oligosaccharides; FOS = fructo-oligosaccharides.

Table 4. Summary of human intervention trials showing benefits of polydextrose (PDX) consumption.

Reference	Amount of polydextrose	Conclusions
Costabile *et al.,* 2012	8 g/day	PDX reduced genotoxicity of faecal water and improved bowel habits and stool consistency. Intervention also reduced the tendency of snacking of subjects.
Hengst *et al.,* 2009	8 g/day	PDX shortened orofaecal transit time and improved stool consistency in subjects suffering from constipation.
Timm *et al.,* 2009	20 g/day	PDX improved stool consistency and resulted in mild laxative effect in healthy subjects with only mild or none gastrointestinal tolerance issues.
Hull *et al.,* 2012	0, 6.25, and 12.5 g/test day	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, which was not compensated for at dinner. Thus, PDX might aid in increasing satiety and decreasing energy intake in short-term
Konings *et al.,* 2013	30% of carbohydrates of breakfast and lunch	Replacement of carbohydrates with PDX increased fat oxidation and pronounced suppressive effects on appetite ratings, which might affect body weight control over a long period of time
Ranawana *et al.,* 2013	12 g	PDX dose 60 min before *ad libitum* lunch resulted in a significantly lower energy intake at lunch. PDX may be a good fortificant for reducing short-term food intake
Astbury *et al.,* 2013	0, 6.25, 12.5, and 25 g	PDX dose 90 min before *ad libitum* lunch decreased the energy intake in a dose-dependent manner

5. Conclusions

The sustained and slow fermentation of PDX has been demonstrated *in vitro*, *in vivo* and in human dietary intervention trials. In the gastrointestinal tract, PDX acts as soluble fibre. It escapes digestion in the small intestine and is available for fermentation in the large intestine. In the colon, PDX is gradually fermented by the colonic microbes into SCFA and minor amounts of gas. The increased amounts of SCFA in the more distal part of the colon may mediate the beneficial effects connected with PDX consumption, such as increased satiety, absorption of minerals from the colon and improved gastrointestinal function, e.g. relief of constipation and softer stools in humans. The slow and sustained fermentation most likely explain the good tolerance of PDX observed in human intervention studies. It also ensures that PDX is present in the distal part of the colon, where it decreases proteolytic fermentation that would otherwise take place once saccharolytic substrates are depleted. PDX fermentation leads to changes in the composition of the colonic microbiota, However, the reported changes varied greatly between different studies (*in vitro*, *in vivo* and human trials), and their implications are not totally clear yet. In the most recent human clinical trial using modern molecular techniques, microbial groups considered to possess anti-inflammatory properties were enhanced.

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References

Astbury, N.M., Taylor, M.A. and Macdonald, I.A., 2013. Polydextrose results in a dose-dependent reduction in *ad libitum* energy intake at a subsequent test meal. British Journal of Nutrition 110: 934-942.

Benus, R.F., Van der Werf, T.S., Welling, G.W., Judd, P.A., Taylor, M.A., Harmsen, H.J. and Whelan, K., 2010. Association between *Faecalibacterium prausnitzii* and dietary fibre in colonic fermentation in healthy human subjects. British Journal of Nutrition 104: 693-700.

Boler, B.M., Serao, M.C., Bauer, L.L., Staeger, M.A., Boileau, T.W., Swanson, K.S. and Fahey Jr., G.C., 2011. Digestive physiological outcomes related to polydextrose and soluble maize fibre consumption by healthy adult men. British Journal of Nutrition 106: 1864-1871.

Costabile, A., Fava, F., Röytiö, H., Forssten, S.D., Olli, K., Klievink, J., Rowland, I.R., Ouwehand, A.C., Rastall, R.A., Gibson, G.R. and Walton, G.E., 2012. Impact of polydextrose on the faecal microbiota: a double-blind, crossover, placebo-controlled feeding study in healthy human subjects. British Journal of Nutrition 108: 471-481.

Divisi, D., Di Tommaso, S., Salvemini, S., Garramone, M. and Crisci, R., 2006. Diet and cancer. Acta Biomedica 77: 118-123.

Duncan, S.H., Belenguer, A., Holtrop, G., Johnstone, A.M., Flint, H.J. and Lobley, G.E., 2007. Reduced dietary intake of carbohydrates by obese subjects results in decreased concentrations of butyrate and butyrate-producing bacteria in feces. Applied and Environmental Microbiology 73: 1073-1078.

Fava, F., Mäkivuokko, H., Siljander-Rasi, H., Putaala, H., Tiihonen, K., Stowell, J., Tuohy, K., Gibson, G.R. and Rautonen, N., 2007. Effect of polydextrose on intestinal microbes and immune functions in pigs. British Journal of Nutrition 98: 123-133.

Flood, M.T., Auerbach, M.H. and Craig, S.A., 2004. A review of the clinical toleration studies of polydextrose in food. Food and Chemical Toxicology 42: 1531-1542.

Fuller, R. and Gibson, G.R., 1997. Modification of the intestinal microflora using probiotics and prebiotics. Scandinavian Journal of Gastroenterology Suppl. 222: 28-31.

Ghoddusi, H.B., Grandison, M.A., Grandison, A.S. and Tuohy, K.M., 2007. *In vitro* study on gas generation and prebiotic effects of some carbohydrates and their mixtures. Anaerobe 13: 193-199.

Hamer, H.M., Jonkers, D., Venema, K., Vanhoutvin, S., Troost, F.J. and Brummer, R.J., 2008. The role of butyrate on colonic function. Alimentary Pharmacology and Therapy 27: 104-119.

Hengst, C., Ptok, S., Roessler, A., Fechner, A. and Jahreis, G., 2009. Effects of polydextrose supplementation on different faecal parameters in healthy volunteers. International Journal of Food Sciences and Nutrition 60 Suppl. 5: 96-105.

Hernot, D.C., Boileau, T.W., Bauer, L.L., Middelbos, I.S., Murphy, M.R., Swanson, K.S. and Fahey Jr., G.C., 2009. *In vitro* fermentation profiles, gas production rates, and microbiota modulation as affected by certain fructans, galactooligosaccharides, and polydextrose. Journal of Agricultural and Food Chemistry 57: 1354-1361.

Hooda, S., Boler, B.M., Serao, M.C., Brulc, J.M., Staeger, M.A., Boileau, T.W., Dowd, S.E., Fahey Jr., G.C. and Swanson, K.S., 2012. 454-pyrosequencing reveals a shift in fecal microbiota of healthy adult men consuming polydextrose or soluble corn fiber. Journal of Nutrition 142: 1259-1265.

Hosseini, E., Grootaert, C., Verstraete, W. and Van de Wiele, T., 2011. Propionate as a health-promoting microbial metabolite in the human gut. Nutrition Reviews 69: 245-58.

Hull, S., Re, R., Tiihonen, K., Viscione, L. and Wickham, M. 2012. Consuming polydextrose in a mid-morning snack increases acute satiety measurements and reduces subsequent energy intake at lunch in healthy human subjects. Appetite 59: 706-712.

Jie, Z., Bang-Yao, L., Ming-Jie, X., Hai-Wei, L., Zu-Kang, Z., Ting-Song, W. and Craig, S.A., 2000. Studies on the effects of polydextrose intake on physiologic functions in Chinese people. The American Journal of Clinical Nutrition 72: 1503-1509.

Kimura, Y., Nagata, Y. and Buddington, R.K., 2004. Some dietary fibers increase elimination of orally administered polychlorinated biphenyls but not that of retinol in mice. Journal of Nutrition 134: 135-42.

Konings, E., Schoffelen, P.F., Stegen, J. and Blaak, E.E., 2013. Effect of polydextrose and soluble maize fibre on energy metabolism, metabolic profile and appetite control in overweight men and women. British Journal of Nutrition 23: 1-11.

Lahtinen, S.J., Knoblock, K., Drakoularakou, A., Jacob, M., Stowell, J., Gibson, G.R. and Ouwehand, A.C., 2010. Effect of molecule branching and glycosidic linkage on the degradation of polydextrose by gut microbiota. Bioscience, Biotechnology and Biochemistry 74: 2016-2021.

Lay, C., Rigottier-Gois, L., Holmstrøm, K., Rajilic, M., Vaughan, E.E., De Vos, W.M., Collins, M.D., Thiel, R., Namsolleck, P., Blaut, M. and Doré, J., 2005. Colonic microbiota signatures across five northern European countries. Applied and Environmental Microbiology 71: 4153-4155.

Legette, L.L., Lee, W., Martin, B.R., Story, J.A., Campbell, J.K. and Weaver, C.M., 2012. Prebiotics enhance magnesium absorption and inulin-based fibers exert chronic effects on calcium utilization in a postmenopausal rodent model. Journal of Food Science 77: H88-H94.

Louis, P. and Flint, H.J., 2009. Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine. FEMS Microbiology Letters 294: 1-8.

Mäkeläinen, H., Ottman, N., Forssten, S., Saarinen, M., Rautonen, N. and Ouwehand, A.C., 2010. Synbiotic effects of GOS, PDX and *Bifidobacterium lactis* Bi-07 *in vitro.* International Journal of Probiotics and Prebiotics 5: 203-210.

Mäkeläinen, H., Saarinen, M., Stowell, J., Rautonen, N. and Ouwehand, A.C., 2010. Xylo-oligosaccharides and lactitol promote the growth of *Bifidobacterium lactis* and *Lactobacillus* species in pure cultures. Beneficial Microbes 1: 139-148.

Mäkeläinen, H.S., Mäkivuokko, H.A., Salminen, S.J., Rautonen, N.E. and Ouwehand, A.C., 2007. The effects of polydextrose and xylitol on microbial community and activity in a 4-stage colon simulator. Journal of Food Science 72: M153-M159.

Mäkivuokko, H., Nurmi, J., Nurminen, P., Stowell, J. and Rautonen, N., 2005. *In vitro* effects on polydextrose by colonic bacteria and caco-2 cell cyclooxygenase gene expression. Nutrition and Cancer 52: 94-104.

Peuranen, S., Tiihonen, K., Apajalahti, J., Kettunen, A., Saarinen, M. and Rautonen, N., 2004. Combination of polydextrose and lactitol affects microbial ecosystem and immune responses in rat gastrointestinal tract. British Journal of Nutrition 91: 905-914.

Pineiro, M., Asp, N.G., Reid, G., Macfarlane, S., Morelli, L., Brunser, O. and Tuohy, K., 2008. FAO Technical meeting on prebiotics. Journal of Clinical Gastroenterology 42 Suppl. 3: S156-S159.

Probert, H.M., Apajalahti, J.H., Rautonen, N., Stowell, J. and Gibson, G.R., 2004. Polydextrose, lactitol, and fructo-oligosaccharide fermentation by colonic bacteria in a three-stage continuous culture system. Applied and Environmental Microbiology 70: 4505-4511.

Putaala, H., Mäkivuokko, H., Tiihonen, K. and Rautonen, N., 2011. Simulated colon fiber metabolome regulates genes involved in cell cycle, apoptosis, and energy metabolism in human colon cancer cells. Molecular and Cellular Biochemistry 357: 235-245.

Ranawana, V., Muller, A. and Henry, C.J., 2013. Polydextrose: its impact on short-term food intake and subjective feelings of satiety in males – a randomized controlled cross-over study. European Journal of Nutrition 52: 885-893.

Raninen, K., Lappi, J., Mykkänen, H. and Poutanen, K., 2011. Dietary fiber type reflects physiological functionality: comparison of grain fiber, inulin and polydextrose. Nutrition Reviews 69: 9-21.

Santos, E.F., Tsuboi, K.H., Araújo, M.R., Falconi, M.A., Ouwehand, A.C., Andreollo, N.A., and Miyasaka, C.K., 2010. Ingestion of polydextrose increase the iron absorption in rats submitted to partial gastrectomy. *Acta* Cirurgica Brasileira 25: 518-524.

Sokol, H., Pigneur, B., Watterlot, L., Lakhdari, O., Bermúdez-Humarán, L.G., Gratadoux, J.J., Blugeon, S., Bridonneau, C., Furet, J.P., Corthier, G., Grangette, C., Vasquez, N., Pochart, P., Trugnan, G., Thomas, G., Blottière, H.M., Doré, J., Marteau, P., Seksik, P. and Langella, P., 2008. *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proceedings of the National Academy of Sciences of the USA 105: 16731-16736.

Takaishi, H., Matsuki, T., Nakazawa, A., Takada, T., Kado, S., Asahara, T., Kamada, N., Sakuraba, A., Yajima, T., Higuchi, H., Inoue, N., Ogata, H., Iwao, Y., Nomoto, K., Tanaka, R. and Hibi, T., 2008. Imbalance in intestinal microflora constitution could be involved in the pathogenesis of inflammatory bowel disease. International Journal of Medical Microbiology 298: 463-472.

Tiihonen, K., Röytiö, H., Putaala, H. and Ouwehand, A.C., 2011. Polydextrose functional fibre. Improving digestive health, satiety and beyond. Nutrafoods 10: 23-28.

Timm, D.A., Thomas, W., Boileau, T.W., Williamson-Hughes, P.S. and Slavin, J.L., 2013. Polydextrose and soluble corn fiber increase five-day fecal wet weight in healthy men and women. Journal of Nutrition 143: 473-478.

Tolhurst, G., Heffron, H., Lam, Y.S., Parker, H.E., Habib, A.M., Diakogiannaki, E., Cameron, J., Grosse, J., Reimann, F. and Gribble, F.M., 2012. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. Diabetes 61: 364-371.

Topping, D.L. and Clifton, P.M., 2001. Short-chain fatty acids and human colonic function: roles of resistant starch and non-starch polysaccharides. Physiological Reviews 81: 1031-1064.

Vester Boler, B.M., Hernot, D.C., Boileau, T.W., Bauer, L.L., Middelbos, I.S., Murphy, M.R., Swanson, K.S. and Fahey Jr., G.C., 2009. Carbohydrates blended with polydextrose lower gas production and short-chain fatty acid production in an *in vitro* system. Nutrition Research 29: 631-639.

Vogt, J.A. and Wolever, T.M., 2003. Fecal acetate is inversely related to acetate absorption from the human rectum and distal colon. Journal of Nutrition 133: 3145-3148.

Wang, X. and Gibson, G.R., 1993. Effects of the *in vitro* fermentation of oligofructose and inulin by bacteria growing in the human large intestine. Journal of Applied Bacteriology 75: 373-380.

Weaver, C.M., Martin, B.R., Story, J.A., Hutchinson, I. and Sanders, L. 2010 Novel fibers increase bone calcium content and strength beyond efficiency of large intestine fermentation. Journal of Agricultural and Food Chemistry 58: 8952-8957.

Wong, J.M., De Souza, R., Kendall, C.W., Emam, A. and Jenkins, D.J., 2006. Colonic health: fermentation and short chain fatty acids. Journal of Clinical Gastroenterology 40: 235-243.