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Review

Cereal β-glucan: a promising prebiotic polysaccharide and its impact on the gut health

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Summary Recently, polysaccharides dietary fibres have emerged as promised functional and nutraceutical food ingredients due to their several health boosting properties. Cereal β-glucan is a water-soluble, prebiotic and bioactive polysaccharide dietary fibre that has a tendency to play a significant role in health regulation. β-glucans from cereal sources have a number of unique functional properties, that is higher solubility, viscosity and tendency to completely be fermented by gut microbiota. These functional characteristics show promising positive effects on human health, such as cancer prevention, anti-inflammatory activity, skin protection, antioxidant, immune modulation and reduction of glycaemia and serum cholesterol. The present review primarily focuses on the prophylactic and therapeutic role of cereal β-glucans on gut health in terms of its barrier permeability, modulation of gut microbiota, the intestinal immune system and intestinal inflammation, colon cancer protection and short-chain fatty acids production. Cereal β-glucans principally perform different biological actions through specific cytokines and hormones regulation.

Keywords Cereal β-glucans, dietary fibre, gut health, gut microbiota, prebiotic, short-chain fatty acids.

Introduction

In recent few years, nutrition in terms of a balanced diet emerged as one of the main regulators of human health, particularly in the management of complex metabolic syndrome (Gong *et al.*, 2018). Metabolic syndrome is a group of metabolic disorder diseases such as obesity, diabetes mellitus type 2, dyslipidaemia, hyperglycaemia and hypertension that is significantly increasing in the western world (Rebello *et al.*, 2014). Gut microbiota can play an unprecedented role in the management of various metabolic disorders by intestinal maturation, improving immune response, cracking nutrients from diet over the digestion of complex polysaccharides and gut protection from enteric pathogens (Barko *et al.*, 2018; Cerqueira *et al.*, 2020). Indeed, the human gut microbial community composition and homeostasis have an intense and intimate linkage to human physiological functions and health (Clemente *et al.*, 2012). The human gut microbiota is mainly supported by non-digestible food components (Tamura *et al.*, 2017). Dietary fibre and plant polyphenols are the leading food constituents metabolised by the bacteria (Jalil *et al.*, 2019). Recently, dietary interposition has appeared as an impressive strategy to modulate the gut microbiota to upgrade the host health (Vieira *et al.*, 2016). Among the food components, cereal dietary fibre is one of the principal constituents with prebiotic characteristics that act as substrate for gut microorganisms to provide a health benefit (Carlson *et al.*, 2017). Human digestive enzymes do not hydrolyse dietary fibre, but gut microbes act upon it producing vitamins, short-chain fatty acids (SCFAs) and other metabolites. These metabolites can both become a substratum for other microbes or be addressed to the host's bloodstream, influencing the metabolic control, gene expression, cell proliferation, apoptosis, chemotaxis and differentiation of cells (Ursell *et al.*, 2012; Den Besten *et al.*, 2013). Several studies have demonstrated that the increasing of SCFAs levels is positively related to enhanced insulin sensitivity, weight control management and reduction of inflammation, all factors able to minimise the risk of developing metabolic diseases (Myhrstad *et al.*, 2020).

Recent studies have indicated cereal β-glucans as well-recognised bioactive carbohydrates with manifold functions and recommended as potential prebiotics. In

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fact, cereal β-glucans undergoes complete fermentation that facilitates gut microbiota due to their prebiotic activity (Lam *et al*., 2018). Cereal β-glucans have promising prophylactic and therapeutic properties such as anticancer, antidiabetic, immune-modulatory, anti-inflammatory and skin protectors (Clemente *et al*., 2012; Shen *et al*., 2016; Jayachandran *et al*., 2018).

Cereal β-glucan belongs to the soluble fibre group, which is of important physiological significance because its consumption is directly linked to the reduction of both cholesterol and postprandial glucose concentrations (Atanasov *et al*., 2020). Moreover, blood glucose and cholesterol regulation health claims of cereal β-glucan have been recognised by European Food Safety Authority (EFSA) and U.S. Food and Drug Administration (FDA) in 2011 (Henrion *et al*., 2019). Cereal β-glucan has the ability to make the intestinal lumen highly viscous; this slows down gastric emptying, and reduces the absorption of glucose, food lipids and bile acids (Havrlentova & Kraic, 2006).

As cereal β-glucan has promising prophylactic and therapeutic potential to inhibit various metabolic disorders through improving the gut health, this article presents a comprehensive review of impact of cereal β-glucans on the intestinal environment and mechanism of action to exert its health beneficial effects.

Chemical structure of cereal β-glucan

Cereal β-glucan is a soluble dietary fibre, largely found in the cell walls of the endosperm and aleurone layer of oat and barley grains. However, other cereals such as rye and wheat contain lower concentration of β-glucan (Havrlentova & Kraic, 2006). The structure consists of D-glucose residues bound with mixed linkage β-(1 → 3, 1 → 4), which differentiate its structure from that of cellulose and enable the water solubility of the polymer. This is essential for the ability of β-glucan to generate viscosity in aqueous solutions (Du *et al*., 2019). Structurally, cereal β-glucan is a linear homo polysaccharide of D-glucopyranose arranged as cellulosic blocks of β-(1 → 4)-linked glucose units, linked by single β-(1 → 3) linkages (Fig. 1) (Du *et al*., 2019). The biological functionality of β-glucans depends upon primary structure, molecular weight, polymer charge, degree of branching, solubility and viscosity (Atanasov *et al*., 2020). The cereal β-glucans are predominantly linear and unbranched polysaccharides. In food industry, most of the processing operations cause some degree of damage to the cereal β-glucan structure, which results in the decrease of β-glucans molecular weight and loss of viscosity. Fermentation, baking and frying are typical processes that can lead to the degradation of β-glucans and, therefore, the deriving products contain moderately or extensively degraded β-glucans (Henrion *et al*., 2019). In addition, food processing, especially those at high temperatures, may generate the oxidation of hydroxyl groups of the glucose monomers in β-glucans, leading to the formation of carbonyl or carboxyl groups or even to ring opening. However, oxidation can improve the cereal β-glucan's physical and health boosting properties (Marasca *et al*., 2020).

Technological and nutraceutical value of cereal β-glucan

In recent years, functional and nutraceutical foods are the core focus in food research due to their vast prophylactic and therapeutic potential against various ailments. Cereal β-glucans are one of the highly favourable food ingredients, due to their many technological and health supporting properties (Jayachandran *et al*., 2018). In the food industry, cereal β-glucans are largely used in the preparation of beverages, sauces, soups and other foodstuffs due to their stabilising, thickening, emulsification and gelation properties. Baking industry utilised cereal β-glucan in the preparation of bread and cakes to enhance their physical properties and increase the quantity and volume of bread loafs (Zhu *et al*., 2016). Mosele *et al*. (2018) highlighted the

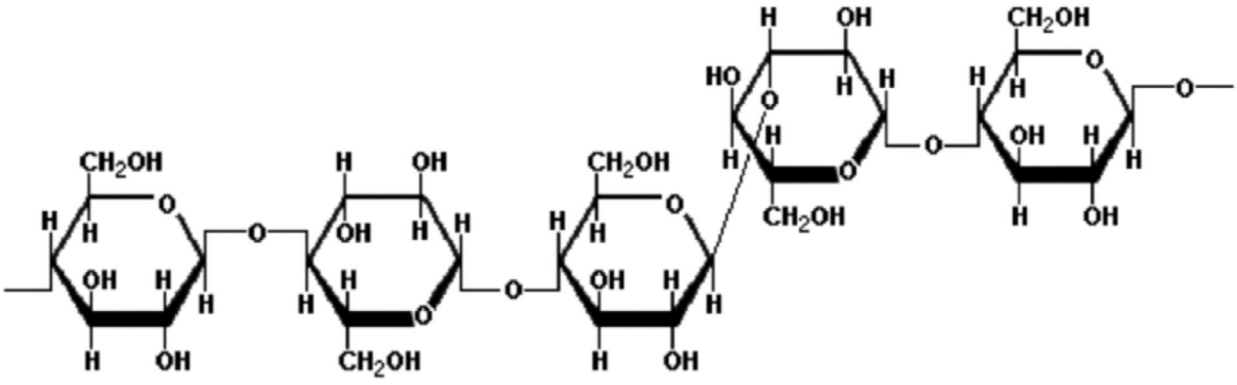

Figure 1 Basic structure of β-glucans in cereals combined with glycosidic linkage β-(1 → 3) and β-(1 → 4).

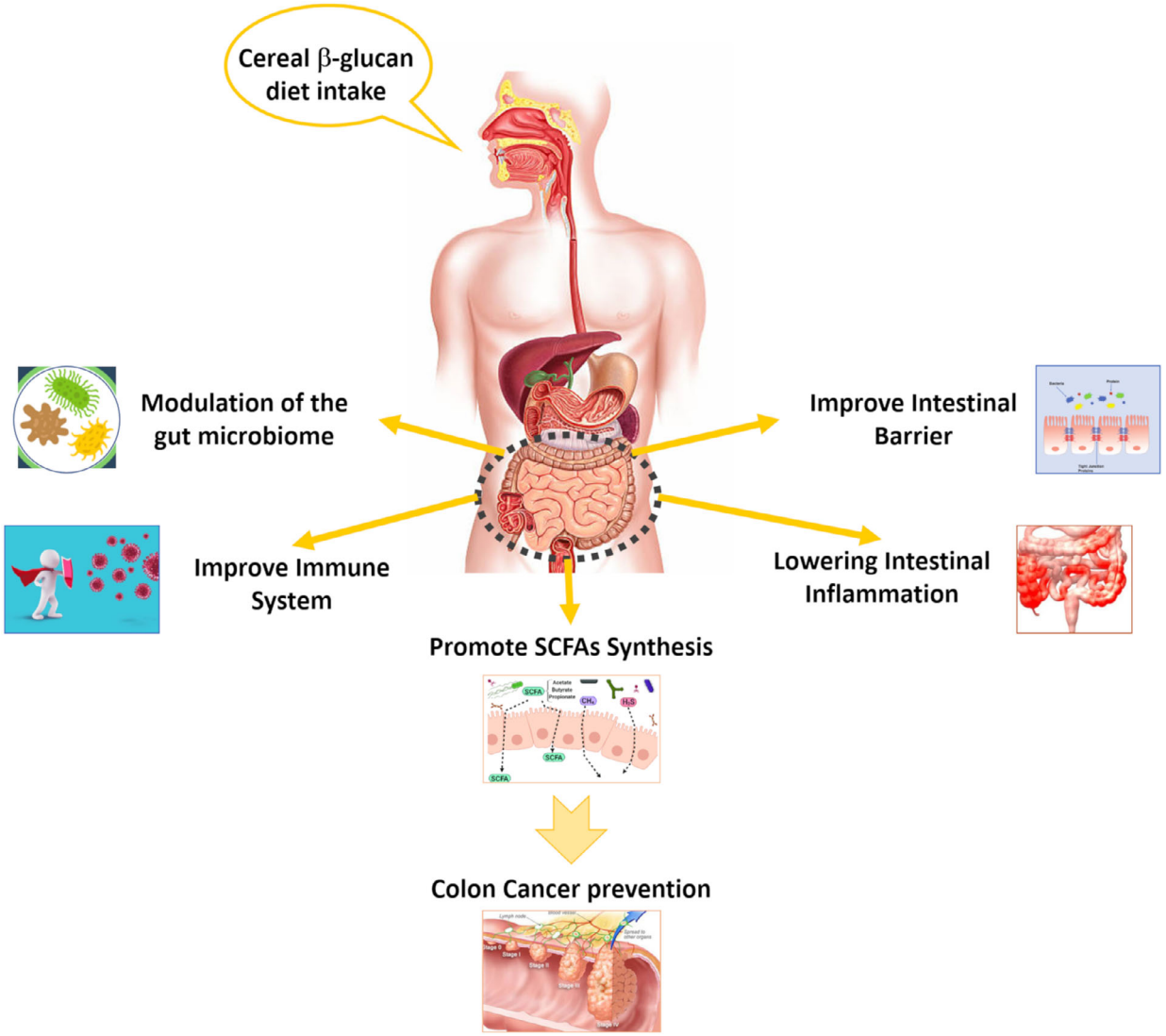

Figure 2 Effect of cereal β-glucan on gut health. [Colour figure can be viewed at wileyonlinelibrary.com]

protective effect of barley β-glucans at the lower level of colon through *in vitro* digestion of barley-based crackers, cookies and fresh pasta. Addition of β-glucans in the low-fat ice creams and yogurts improved their texture and rheological properties (Jayachandran *et al.*, 2018). The cholesterol-lowering effect of cereal β-glucans is well documented (Henrion *et al.*, 2019). Oat β-glucan's cholesterol-lowering mechanism is mainly based on SCFA (propionate) production through gut microbiota (Joyce *et al.*, 2019). The gut microbiota metabolises the fibres and gives the host the SCFA. The increase in the propionate-to-acetic acid ratio (main substratum for biosynthesis of cholesterol) results in decreased biosynthesis of cholesterols (Theuwissen & Mensink, 2008). Besides, β-glucans derived from cereals are helpful in promoting skin health, as cereal β-glucans can strengthen the skin owing to their antioxidant, anti-wrinkle, anti-ultraviolet, wound healing and moisturising properties (Du *et al.*, 2014).

Effect of cereal β-glucans on Gut health

Human gut is considered as second brain and vital in the proper body functions. Cereal β-glucan may significantly boost the work efficiency of different parts of the human gut through producing various biological compounds. Several authors have studied the beneficial effects of β-glucans from cereals on human gut (Fig. 2). Table 1 summarises the main effects discussed in the most recent studies.

Table 1 Main beneficial effects of cereal β-glucan as reported by the most recent studies

Cereal β-Glucan impact on Gut Health	Health Benefits	References
Modulation of Gut microbiota	Significant increase in the *Bifidobacteria* spp	Mitsou *et al.* (2010)
	↑ *Roseburia hominis*, *Ruminococcus* ssp, *Clostridiaceae* spp. ↓ *Fusobacteria* and *Firmicutes*	De Angelis *et al.* (2015)
	↑ *Bifidobacterium* spp. and *Akkermansia municiphila*	Velikonja *et al.* (2019)
	↑ *Bacteroidetes* and ↓ *Firmicutes*	Wang *et al.* (2016)
	↑ *Bifidobacterium* ↓ *Bacteroides/Prevotella* and *Lactobacillus*	Mikkelsen *et al.* (2017)
	↑ *Prevotella* and *Roseburia*	Fehlbaum *et al.* (2018).
	↑ *Clostridium*, and *Butyricoccus*, ↓ *Bacteroides*, *Lactobacillus*, *Oscillospira*, and *Ruminococcus*	Zhu *et al.* (2020)
Boosting short-chain fatty acid (SCFA) synthesis	No change in SCFAs Levels	Valeur *et al.* (2016)
	↑ Acetate, Propionate and Butyrate production, ↑ 1.4 ~ 3.4-fold caecal and colonic lactate	Hong *et al.* (2016)
	↑ Butyrate concentration	Nie *et al.* (2017)
	↑ Propionate production (4.76 μmol mL^{-1})	Carlson *et al.* (2017)
	↑ SCFAs Levels in stool	Thandapilly *et al.* (2018)
	↑ SCFAs Levels in colon	Chen *et al.* (2019)
	↑ Concentrations of acetate and n-butyrate, ↑ Total SCFAs	Aoe *et al.* (2019)
	↑ Concentrations of SCFAs (especially, Butyrate)	Miyamoto *et al.* (2018)
Improve the gut permeability flux	100 nm latex beads reduction in intestinal permeability.	Mackie *et al.* (2016)
	↑ Plasma concentration of GLP-2 (Intestinal barrier Biomarker)	Nilsson *et al.* (2015)
	No change in GLP-2 level	Nilsson *et al.* (2016)
	No effect on intestinal permeability	Skouroliakou *et al.* (2016).
Reduction in intestinal inflammation	↑ Pro-inflammatory markers	Therkelsen *et al.* (2016)
	↓ Inflammatory markers, improved the cytokine and chemokine signalling pathways	Żyła *et al.* (2019)
	Low molar mass β-glucan reduced the colon inflammation	Kopiasz *et al.* (2020)
Colon cancer protection	↑ Apoptosis of tumour cells	Shen *et al.* (2016).
	↓ LT97 cells (colon adenoma cells), ↑ caspase-3 activity (6.3 times)	Schlörmann *et al.* (2020)
	↑ Phagocytosis and IL-2 secretion	Vetvicka & Vetvickova (2020)
Cereal β-glucan as immunomodulator	↑ Chemokine production and expression of adhesion molecules	Ramakers *et al.* (2007)
	↓ IL-12 production in colon,	Wilczak *et al.* (2015).
	↑ THP-1 macrophages	Arena *et al.* (2016)
	↓ pro-inflammatory cytokines (IL-6, IL-8, IL-1β).	
	Yeast β-glucan has higher immunomodulatory effect than oat β-glucan	Chaiyasut *et al.* (2018)

Modulation of gut microbiota

The commensal bacteria in the gastrointestinal tract (GIT) perform multiple functions from tissues formation to breaking down indigestible carbohydrates, immune system development, vitamins synthesis, inhibit the colonisation of pathogens and barrier function of the intestine (Clemente *et al.*, 2012; Jayachandran *et al.*, 2018; Atanasov *et al.*, 2020). Any change in the gut microbiota composition and diversity may cause dysbiosis that leads to several metabolic disorders (Carding *et al.*, 2015). However, complex dietary fibre, particularly β-glucan from oat and barley, supported the growth of both *Lactobacilli* and *Bifidobacteria* spp. that may helpful in to retard dysbiosis. In an *in vivo* study, 52 healthy volunteers were subjected to 0.75 g of barley β-glucan per day for 30 days. There was significant increase in the count of *Bifidobacteria* spp (Mitsou *et al.*, 2010). Similarly, in another clinical study administration of β-glucan-rich durum wheat flour and whole-grain barley pasta increased the levels of *Roseburia hominis*, *Ruminococcus* ssp and *Clostridiaceae* spp. Additionally, Fusobacteria and Firmicutes population was lowered (De Angelis *et al.*, 2015). Fortification of yoghurt with β-glucans of barley and oats resulted in an increase in the growth and viability of *Bifidobacterium animalis ssp. lactis* (Vasiljevic *et al.*, 2007).

A double-blind, placebo-controlled RCT was conducted with 43 high-risk or diagnosed individuals with metabolic syndrome. The participants consumed bread containing 6g of barley β-glucans or bread without β-glucans during a four-week intervention time. Supplementation of β-glucans resulted in the change

of the SCFA production, the composition of gut microbiota, lowering the diversity and richness of the microbial populations. Three participants exhibited a considerable increase in gram-negative bacteria from the genus *Prevotella*. The pre-intervention gut microbiota composition presented abundance of *Bifidobacterium* spp. and *Akkermansia municiphila* in cholesterol-responsive group (Velikonja *et al*., 2019). Mikkelsen *et al*. (2017) supplemented hypercholesteraemic rats with four different diets, that is cellulose (control), purified barley low (LMW, 100 or 150 kDa) and medium (MMW, 530 kDa) molecular weight β-glucan and glucagel (75% β-glucan) for four weeks. All the β-glucan diets enhanced the caecal production of SCFAs compared to the control diet. The glucagel and LMW β-glucan diets roused the population of *Bifidobacterium* in the caecum, while the MMW β-glucan diet decreased the population of both *Bacteroides*/*Prevotella* and *Lactobacillus* in the caecum compared to the control diet. In another *in vivo* comparative study, in which fifty rats were fed with oat β-glucan, oat resistant starch and whole oat foods, all the three products changed the gut microbiota composition with increased genus *Clostridium* and *Butyricoccus*, but decreased genus *Bacteroides*, *Lactobacillus*, *Oscillospira* and *Ruminococcus* (Zhu *et al*., 2020). Wang *et al*. (2016) conducted an *in vivo* RCT in which 30 individuals consumed a breakfast containing 3 g of high molecular weight barley β-glucan (HMW), 3 g or 5 g of LMW barley β-glucan, or wheat and rice for 5 weeks. The results indicated that 3 g/days of HMW β-glucan intake at the phylum level increased *Bacteroidetes* and decreased *Firmicutes* populations compared to control, while, at the genus level, increased *Bacteroides* and *Prevotella*. However, diets containing 5 g and 3 g of LMW β-glucan did not alter the gut microbiota composition. An *in vitro* fermentation screening platform was inoculated with six healthy adult faecal microbiota and exposed to inulin, alpha- and beta-linked galactooligosaccharides, xylo-oligosaccharides from corn cobs and high-fibre sugar cane and β-glucan from oats. β-glucan exhibited significant effects on the microbial composition and metabolism compared to the other fibres. β-glucan enhanced the growth of *Prevotella* and *Roseburia* with a parallel rise in the propionate production (Fehlbaum *et al*., 2018).

Boosting short-chain fatty acid (SCFA) synthesis

Fermentation of β-glucans by microbes in the lower part of the small intestine and in the colon results in the production of SCFAs (Thandapilly *et al*., 2018) which have various positive effects on GIT and human health (Den Besten *et al*., 2013). More specifically, SCFAs are involved in the reduction of gut pH and luminal oxygen levels, improve water and ions absorption, strengthen tight junction proteins and modify villi height: crypt depth *ratio*, enhance innate and adaptive immunity, increase energy availability to the mucosa cells and increase mucus thickening (Adebowale *et al*., 2019) (Fig. 3). Cereal β-glucan can be 100% and more quickly fermented than other dietary fibres due its chemical structure. The major products of the β-glucan fermentation are acetate, propionate and butyrate (Drzikova *et al*., 2005). However, in the colon, fermentation of undigested carbohydrates also results in the formation of lactic acid (a non-SCFA), but *Eubacterium hallii* is able to inhibit the colon accumulation of lactic acid (Flint *et al*., 2015). Dong *et al*. (2017) mentioned that the fermentation profile of β-glucans depends upon the molecular weight. As low molecular weight of oat β-glucans produce a higher total SCFA concentration and *vice versa*, butyrate is the colon's key source of energy for the epithelial cells and has a high anticarcinogenic potential. Furthermore, it is stated that butyrate may also have an anti-inflammatory effect in intestinal cells along with improving intestinal barrier flux. Nie *et al*. (2017) mentioned that consumption of oat β-glucan for 4 weeks significantly increased the faecal butyrate concentration in ulcerative colitis patients. In another study, barley β-glucan administration in 30 volunteers with mild hypercholesterolaemia resulted in a significant increase in SCFA levels in stool samples (Thandapilly *et al*., 2018). Chen *et al*. (2019) demonstrated the effect of barley β-glucan through mouse *in vivo* model. Barley β-glucan treatment improved the colon length and the concentration of SCFAs in mice colon and caecum sections. However, oatmeal porridge feeding in 10 subjects for one week showed no significant change in microbial fermentation evaluated by determination of total SCFA concentration (Valeur *et al*., 2016).

Miyamoto *et al*. (2018) conducted an *in vivo* study in which 4-week-old mice were subjected to a high fat diet with 20% barley flour containing 2% β-glucan. Additionally, mice were fed either with 5% cellulose or 5% barley β-glucan for 12 weeks. This resulted in changing the gut microbiota and increasing SCFAs (especially, butyrate) thus decreasing the food intake and improving insulin sensitivity. Aoe *et al*. (2019) found that the barley line BM, that is combination of three fermentable fibres (fructan, β-glucan and resistant starch), not only improved the microbiota in caecal and distal colonic digesta but also increased the SCFAs production as compared to β-glucan barley line BG. In this *in vivo* study, rats were supplemented with BG and BM for four weeks. The concentrations of acetate and n-butyrate in caecal digesta were considerably higher in both BM and BG groups, while the concentration of total SCFAs in caecal digesta was significantly higher in the BM than that of the BG group. Carlson *et al*. (2017) compared the fermentability

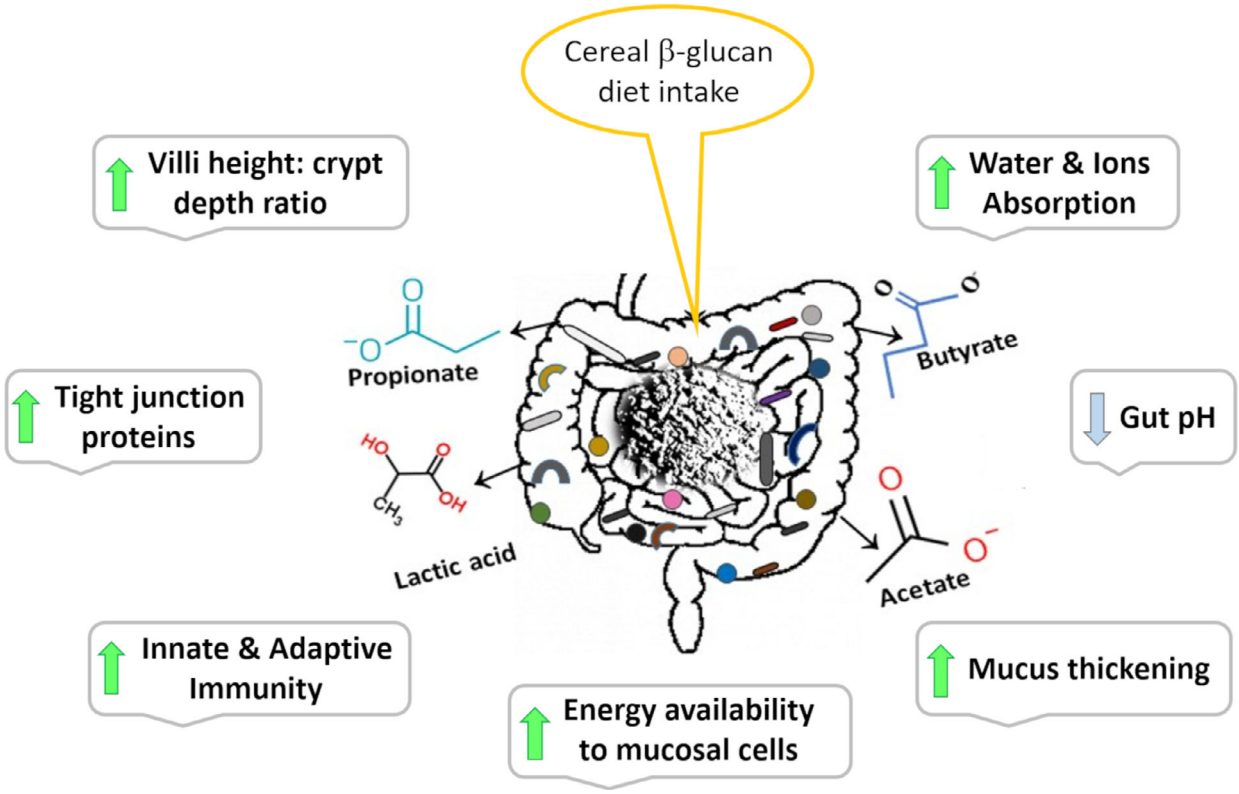

Figure 3 Summary of cereal β-glucan fermentation products in large intestine i.e. SCFAs and their beneficial effects on gut health. [Colour figure can be viewed at wileyonlinelibrary.com]

potential of five fibres, that is pure β-glucan, Oatwell (22% oat β-glucan), xylo-oligosaccharides, whole fibres (dried chicory root containing inulin, pectin, and hemi-celluloses) and pure inulin using an *in vitro* fermentation system measuring changes in faecal microbiota, total gas production and formation of common SCFAs. Oatwell showed the highest production of propionate at 12 h (4.76 μmol mL^{-1}) compared to inulin, whole fibres and xylo-oligosaccharides. Oatwell and pure β-glucan's effect were similar in terms of highest mean propionate production at 24 h. Supplementation of 1% or 5% (w/w) β-glucan diets to rats for 3 weeks induced a notable increase in colonic contents in a dose-dependent manner. 5% β-glucan diets increased the levels of acetate, propionate and butyrate by 1.8, 1.7 and 3.0 times in the caecum and 2.2, 2.9 and 3.1 times than the control group in the colon, respectively. Furthermore, β-glucan diets also substantially improved the levels of caecal and colonic lactate by 1.4 ~ 3.4 times (Hong *et al.*, 2016).

Improve the gut permeability flux

Under anaerobic conditions in colon, excessive consumption of dietary carbohydrates results in pyruvate production, a product of carbohydrates metabolism. This molecule is utilised by gut microbiota that produce acetaldehyde. Acetaldehyde is a toxic metabolite that can increase intestinal permeability (Skouroliakou *et al.*, 2016). Gut barrier functionality is governed by integrity of its intestinal components like intestinal mucosa, intestinal epithelium, microbiome, the Lamina propria and the intestinal immune system (König *et al.*, 2016). The intestinal viscous mucus mainly includes cross-linked mucins, antimicrobial factors (lysozyme, secretory immunoglobulin A and antimicrobial proteins) and trefoil peptides. These trefoil peptides provide an extra physical and chemical shield to protect the intestinal epithelium against pathogenic microorganisms (Wells *et al.*, 2017).

Various studies have indicated a positive relationship between the cereal β-glucan products and gut barrier function. Mackie *et al.* (2016) conducted a study in which each group of five pigs were fed a standard diet (0.7% cereal β-glucan) and oat bran diet (8.7% oat β-glucan) for 3 days. The collected samples of small intestine mucus and tissue samples were subjected to in vitro digestion to determine β-glucan release, nutrient profile and assessment of mucus permeability. *In vitro* digestion results indicated that 90%

of the β-glucan was released in the proximal small intestine. Intestinal mucus dimensions depicted a 100 nm latex beads reduction in intestinal permeability. Additionally, another *in vivo* intervention study, 20 healthy subjects were administered with a standardised barley seed bread breakfast that contained 6.6 g soluble non-starch polysaccharides per day, for three days. The results showed an increase in plasma concentration of GLP-2, a peptide known as biomarker of intestinal barrier function and involved in the epithelial cell propagation and intestinal growth (Nilsson *et al*., 2015). In contrast, another *in vivo* study on 21 students also fed with barley seed bread, containing 5.0 g soluble non-starch polysaccharides per day, for four days, indicated that there was no significant effect on GLP-2 (Nilsson *et al*., 2016). In double-blind randomised controlled trial (RCT), 23 volunteers were monitored during the daily consumption of barley β-glucan administered as one portion of fortified cake, for one month. The authors mentioned that barley β-glucans did not exert a protective effect in intestinal permeability of healthy adults (Skouroliakou *et al*., 2016).

Reduction in intestinal inflammation

β-glucans from cereals, bacteria yeasts and fungi suppressed the pro-inflammatory markers expression in the colon, ameliorate the colitis clinical symptoms and maintained the gut integrity from epithelial changes, wounds and leucocyte infiltration (Atanasov *et al*., 2020). Butyrate protects tight junction proteins and improves the integrity of the gut barrier. However, an increase in gut barrier permeability may cause intestinal inflammation (Morrison & Preston, 2016). The elimination of macrophage-mediated phagocytosis by soluble β-glucan is linked to a failure in PKC-βII by β-glucan translocation. Oats β-glucan with low molecular weight resulted in a decrease in enteritis groups in rats, primarily due to increased antioxidant defences (Wilczak *et al*., 2015). β-glucans with high molecular weight activate leucocytes directly and modulate the development of pro-inflammatory cytokines and chemokines, while those with low MW activate leucocytes by stimulating nuclear transcription factors (Bai *et al*., 2019). In an *in vivo* RCT, 50 inflammatory bowel disease patients treated with a mushroom β-glucan resulted in satisfactory improvement in pro-inflammatory markers (Therkelsen *et al*., 2016). Kopiasz *et al*. (2020) conducted an *in vivo* study on 150 rats divided into two groups as healthy control and suffering from colitis. The animals fed as three subgroups, with AIN-93M feed without β-glucan (βG−) or with 1% (w/w) of low (βGl+) or high (βGh+) molar mass oat β-glucan for 3, 7 or 21 days. The blood samples analysis showed small changes in lymphocytes count and red blood cells, as well as normalisation of antioxidant activity. Moreover, oat βGl was more effective to reduce the colon inflammation. Moreover, when rats received 1% of βGl or βGh fraction for 21 days, a slight inflammation affecting the colon mucosa and submucosa was observed, with noticeable changes of lymphocytes in the colon tissue, raised cytokines and eicosanoid levels. Overall, βGl reduced the higher levels of the inflammatory markers and improved the cytokine and chemokine signalling pathways (Żyła *et al*., 2019). However, the role of cereal β-glucans in the whole immune system is still unclear (Bai *et al*., 2019).

Colon cancer protection

Colon cancer is more common gut related metabolic disorder in Europe as compared to United States (Kho & Lal, 2018). β-glucans from mushroom source have higher anticancer potential than that of cereals. In colon cancer, butyrate plays a key role as it is a vital SCFA that prevents the colon cancer occurrence (Ma *et al*., 2018). This prophylactic effect could be due to its capability to regenerate the epithelial cells of the intestine (Zhang *et al*., 2010). In an *in vivo* study, oat bran β-glucan dietary supplement was given to 25 healthy volunteers for 8 to 12 weeks. There was a significant increase in the butyrate concentration in faeces thus indicating a potential protection against colon cancer (Nilsson *et al*., 2008). Furthermore, anticancer activity of oat β-glucan has been supported by *in vivo* study of 1, 2-dimethyl hydrazine-induced colon carcinoma in mice. The bile acid content was significantly decreased but the colonic SCFAs content was increased in mice administered with oat β-glucan. Moreover, oat β-glucan considerably enhanced the apoptosis of tumour cells (Shen *et al*., 2016).

Schlörmann *et al*. (2020) analysed the chemo-preventive effect of roasted barley flakes (5.4% β-glucans) through *in vitro* digestion and fermentation to attain fermentation supernatant (FS). SCFAs concentrations were increased in barley FS by 2.5 times with higher butyrate production. The growth of LT97 cells (colon adenoma cells) was substantially reduced by barley FS in a time–dose-dependent manner. Moreover, caspase-3 activity of treated cells was significantly increased up to 6.3 times (Schlörmann *et al*., 2020). Vetvicka & Vetvickova (2020) compared the anticancer, immune-stimulating and anti-infectious potential of five different β-glucans, that is algae, yeast, bacteria, oat and mushroom in 8-week-old mice. The authors compared their effects on the stimulation of phagocytosis of blood cells, on the secretion of IL-2 and on the inhibition of melanoma and breast and lung cancers. Nearly, all the glucans stimulated phagocytosis and IL-2 secretion and reduced cancer growth.

Cereal β-glucan as immunomodulator

β-glucans have promising immunomodulatory potential through activation of macrophages, T helper cells, neutrophils and natural killer cells, promotion of T-cell differentiation and activation of an alternative complement pathway, which affect both cellular and humoral immunity (Mantovani *et al*., 2008). Bermudez-Brito *et al*. (2015) demonstrated that barley β-glucan induced an immunological response in human dendritic cells through reducing the production of IL-8 and increasing the expression of CD83. The immunological response of barley β-glucan to dendritic cells significantly decreased the cytokines IL-12, IL-6 and IL-8 production (Bermudez-Brito *et al*., 2015). An *in vivo* intervention study of diet enriched with oat β-glucan (5 g day^{-1}) in ileostomy patients indicated that incubation of their faecal water with human small intestine and colonic cell improved the immune defence. The increase in the immune defence was mainly due to significant increase in chemokine production and expression of adhesion molecules (Ramakers *et al*., 2007). Arena *et al*. (2016) noted that the use of oats and barley β-glucans for the incubation of human lipopolysaccharides (LPS)-stimulated THP-1 macrophages decreased the expression rate of certain pro-inflammatory cytokines (IL-6, IL-8, IL-1β). These results support the hypothesis that cereals β-glucans exert immunomodulatory properties reducing the pro-inflammatory effect of LPS. In another *in vivo* study, rats were fed with diets supplemented with two oat β-glucan fractions, varying in molecular mass. Oat β-glucan treatment caused a substantial reduction of IL-12 production in colon, whose levels were elevated by LPS treatment (Wilczak *et al*., 2015). Moreover, there was significant decrease in the production of this cytokine levels irrespective of oat β-glucan molecular mass. The authors suggested oat β-glucans have strong anti-inflammatory potential, and it could be proposed for intestinal inflammatory disease patients (Wilczak *et al*., 2015). Chaiyasut *et al*. (2018) compared the immune-modulatory activity of three β-glucan sources, that is yeast, mushroom and oat through an *in vivo* study. Yeast β-glucan stimulated the expression of IL-6, IL-17, IFN-γ, IL-10 and TGF-β more effectively than oat and mushroom ones. Moreover, there was higher antioxidant capacity during yeast-BG supplementation in a dose-dependent manner than oat and mushroom BG.

Conclusion

In recent clinical *in vivo* and *in vitro* studies indicate the promising functional and therapeutic potential of cereal β-glucans against various ailments. Blood cholesterol and postprandial glucose-lowering effects of cereal β-glucans has been already confirmed by the EFSA with health claims. Besides these prophylactic and therapeutic profile, cereal β-glucans consumption has been provided sufficient supportive evidence to demonstrate its positive impacts on the gut health. As gut health is one of the most focus area of research in food these days, clinical studies provides favourable effect of cereal β-glucans on gut microbiota, reducing gut permeability, activation of intestinal immune system, stimulating short-chain fatty acids production and reducing the inflammatory response.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contribution

Mahtab Shoukat: Writing-original draft (lead). **Angela Sorrentino:** Supervision (supporting); Writing-review & editing (supporting).

Ethical approval

Ethics approval was not required for this research.

Peer review

The peer review history for this article is available at https://publons.com/publon/10.1111/ijfs.14971.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

References

*This article is particularly interesting as it describes different biological functions particularly impact of cereal beta glucan on human gut health

**This article highlighted the effects of barley β-glucan through an *in-vivo* study to improve insulin sensitivity by changing the gut microbiota and increasing SCFAs (especially, butyrate) under conventional condition

***This *in-vivo* study briefly explained the effects of soluble and insoluble oat β-glucan on colon carcinogenesis in mice. The results showed that both oat β-glucans promisingly reduced colon cancer through significant reduction of bile acids and enhancement of the colonic short-chain fatty acid content. Moreover, the tumor cells apoptosis was significantly promoted

****In this placebo control *in-vivo* trial, intervention of barley β-glucans decreased the total plasma cholesterol level through significant increase of short chain fatty acids particularly propionic acid. Additionally, considerable changes in gut microbiota were also observed.

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