INTRODUCTION

The main role of our diet is to provide sufficient macro- and micronutrients to satisfy our needs for energy, growth, and development. During the past decades, the concept of “functional foods” has emerged, implying that some foods or its components are biologically active and can regulate various body functions, thereby being beneficial to health and reducing the risk of several diseases. Dietary fibre, an essential part of the human diet, consists of many substances of plant origin that are not digested in the human upper gastrointestinal tract, including polysaccharides such as cereal β-glucans, arabinofuranosyl cellulose and cellulose. Starch is not a part of dietary fibre, because it is hydrolysed by enzymes and absorbed in the small intestine. Dietary fibre regulates the rate of nutrient digestion and absorption, serves as a substrate for the gastrointestinal microflora of the gut and promotes laxation. The fibre affects gastrointestinal function through properties including viscosity, water holding capacity, bulk, fermentability and binding of bile acids (Schneemann, 1987). An important feature of fibre is to reduce the rate of absorption of nutrients. One effect of fibre is conversion of carbohydrate components into a slow release form that requires less insulin and also increases the elimination of bile acids. Fibre also alters the colonic short-chain fatty acid profiles (Jenkins et al., 2001). Oats (Avena sativa) are cereals rich in dietary fibres, antioxidants, proteins and unsaturated fat, which makes them interesting as functional food ingredients (Sangwan et al., 2014). As the most common component of oats to be searched and studied are β-glucans. Therefore our literature review will be focused on oat β-glucan and its impact on the gastrointestinal tract. We searched for articles in the PubMed database describing studies with oat-based products and gastrointestinal tract. The search was limited to full-text English
language articles, including review articles and meta-analyses. The studies were carried out mostly in humans, but some of the studies conducted in vitro and animals also included. Additional articles were identified by searching titles of references in relevant articles obtained from a database search.

**OAT β-GLUCAN. MOLECULAR STRUCTURE**

Oat consists of germ, endosperm and bran, which is rich in valuable nutrients. In comparison to other cereals, oat contains more total proteins, carbohydrate (may reach up to 75–80%), fat, non-starch fibre, as well as unique antioxidants (one of them — avenanthramides), vitamins, and minerals (Brand et al., 1996; Peterson et al., 1997). One of the most often studied components of oats is β-glucan ((1→3),(1→4)-β-D-glucan) — a type of soluble dietary fibre, which is located throughout the starch endosperm, but with the highest concentration in bran (Fig. 1). It contributes 3.6–5.1% of dry weight of the oat whole grain (Hampshire, 2004). Many studies have shown the beneficial health effects of oat β-glucan as a soluble dietary fibre. Until now, most of the relevant studies have been conducted in the cardiovascular and diabetology field. Consuming oats lowers the level of blood cholesterol and attenuates postprandial glucose response. A new meta-analysis published in the American Journal of Clinical Nutrition in 2014 shows that daily consumption of at least 3 g of oat β-glucan can lower the risk of coronary heart disease (FDA, 1997). The evidence presented indicates that the cholesterol-lowering effect of oat beta-glucan may depend on the increased viscosity in the small intestine, which reduces reabsorption of bile acids, increases the synthesis of bile acids from cholesterol, and reduces circulating (LDL) cholesterol concentrations.

Oat β-glucan has a capacity to form highly viscous solutions. The hypocholesterolemic effect of β-glucan was related to the elevation of intestinal viscosity caused by β-glucan. Viscosity in the small intestine is determined by the concentration, molecular weight (MW) and solubility of oat beta-glucan (Wood et al., 1991). This is supported by a recent randomised clinical trial (RCT) that showed a reduced cholesterol lowering efficacy of oat β-glucan with low MW (210 kDa) compared to high MW (>2000 kDa) or medium MW (530 kDa) oat β-glucan (Wolever et al., 2010). Oats also reduce the glucose and insulin responses. From molecular point of view, oat β-glucan is a linear polysaccharide that consists only of β-D-glucopyranosyl units (Fig. 2). These units are joined by either (1→3)- or (1→4)-β-D-linkages, hence the name mixed-linkage (13),(14)-β-D-β-glucan. The distribution of the individual (13)-, (14)-linkages is not random, nor is it regular. The (14)-β-links occur mostly in groups of two or three and are separated by a single (1→3)-link, as first reported by Parrish et al. in 1960 and later on by others (Reese et al., 1962). The building blocks, 1,3-linked cellotriosyl and 1,3,4-triols contain over 90% of the molecule (Wood et al., 1994). The (1→3)-link prevents close packing of the molecule and makes the molecule partly soluble in water, unlike cellulose, which is built entirely of β-(1→4)-linked D-glucosyl units and is capable of close packing to crystalline structures. To summarise, cellulose is a (1→4)-β-D-glucan, where the β-glucoside bond makes the cellulose indigestable and insoluble. The mixed linked (1→3),(1→4)-β-D-glucan is composed of β(1→4)-linked glucose units with a single β(1→3)-linked glucose every two or three units. It is the (1→3) linkages that make β-glucans soluble (Johansson, 2006). 20% of oat and 46% of barley β-glucan is insoluble (Aaman et al., 1987).

The structure and properties of oat β-glucan vary between species and varieties of oats, and are also affected by the growing and storage conditions and processing of oat grain. In addition, the extraction and analysis methods may also contribute to the variations in the structure, molecular weight (Wang et al., 2014).

![Fig. 1. Location of β-glucan in oat grain (www.oatsandhealth.org).](image1)

![Fig. 2. Molecular structure of oat β-glucan.](image2)
OATS AS PREBIOTICS, ITS INFLUENCE ON INTESTINAL MICROFLORA

In humans, intestinal microbiota plays an important role in the maintenance of host health by providing energy, nutrients, and immunological protection. The composition of the intestinal microbiota plays a significant role in human immunology, nutrition, and pathological processes (Zoetendal et al., 2004). Describing the complexity and ecology of the intestinal microbiota is important for defining its effects on overall human health. Human intestinal microbiota undergoes maturation from birth to adulthood and is further altered with ageing. The major bacterial groups are Clostridium leptum, Clostridium cocoides, Bacteroidetes and Escherichia coli. In healthy adults, 80% of the identified fecal microbiota can be classified into three dominant phyla: Bacteroidetes, Firmicutes and Actinobacteria. In general terms, the Firmicutes to Bacteroidetes ratio is regarded to be of significant relevance in human gut microbiota composition. Although the intestinal microbiota is relatively stable throughout adult life, recent studies indicated that modifications occur in the composition in elderly individuals. For example, a reduction in the numbers of Bifidobacteria and Bacteroides has been observed, accompanied also by a decrease of Lactobacilli. The major functions attributed to the microbiota present in the gut begin to manifest at the end of the second year of life and comprise: i) nutrients absorption and food fermentation; ii) stimulation of fest at the end of the second year of life and comprise: i) nutrient determining the metabolic activity and growth of human microflora. In a study from Romania and Italy, oat bran extract added to milk selectively promoted the number

of probiotic bacteria (Lactobacillus rhamnosus, Lactobacillus paracasei, and also their combination SYNBIO) in milk and maintained overall microbial counts over a 28-day storage period with respect to controls (whole milk without substrates). Therefore, a new symbiotic product (combination of prebiotics and probiotics) was developed. The probiotic strains were recovered from fecal samples from 40 volunteers fed for 4-week period (Coman et al., 2013). Oats have been shown to increase the proportion of short chain fatty acid (SCFA) butyrate, which has regulatory functions in cell proliferation and differentiation. β-glucan, however, leads mainly to the production of another SCFA — propionate, which is suggested as one of the mechanisms for the cholesterol lowering effects of oats and other β-glucan-containing products (Wolever et al., 1991). Similar results were obtained in a study in Greece (Mantzouridou et al., 2013). A study in the United Kingdom (Kedia et al., 2009) showed that oat bran fraction added to human fecal cultures decreased culturable anaerobes and clostridia and promoted increase in bifidobacteria and lactobacilli populations.

Fermentable dietary fibre is the most important source for formation of SCFA in the large intestine. Beta-glucans, pectin and resistant starch are fermented to 70–100 %, whereas, for example, cellulose is usually not fermented at all. The major SCFAs produced after fermentation of dietary fibres are acetate, propionate and butyrate. Certain colonic bacteria generate energy from these fermentation products. The properties of the microflora and the composition of the substrate (dietary fibre) are important factors both for the total and individual SCFA formed. The SCFAs are physiologically active in different ways. Acetate is readily taken up from the intestine and transported to the liver, where it can serve as a substrate for cholesterol biosynthesis. Butyrate serves as a fuel for epithelial cells and can also regulate cell proliferation and differentiation. Recently, butyrate was suggested to have influence on lipid metabolism by regulation of intestinal fat absorption. Propionate may contribute to hypocholesterolemic action by either inhibiting HMG-CoA reductase or by preventing utilisation of acetate for cholesterol synthesis. A substantial amount of bacteria is present in the ileum, but the vast majority of bacteria exist in the proximal large bowel, where fermentation also takes place. It is in the caecum and ascending colon that the SCFA production reaches its highest concentration in humans. At both the colonic and systemic levels, fermentation and especially SCFA production play an integral role. Colonic epithelial cells preferentially use butyrate as an energy source, even when competing substrates such as glucose and glutamine are available. Butyrate is considered a key nutrient determining the metabolic activity and growth of colonocytes and may function as a primary protective factor against colonic disorders, although data on this topic are conflicting (Andersson, 2009). SCFAs are water-soluble and are absorbed into the blood stream. The brain, muscles, and tissues metabolise acetate systemically, whereas propionate is cleared by the liver and may lower the hepatic production of cholesterol by interfering with its synthesis.
Transport to and further metabolism of SCFAs in the liver, muscle, or other peripheral tissues is thought to contribute about 7–8% of host daily energy requirements (Cummings et al., 1991). Fermentation and SCFA production also inhibit the growth of pathogenic organisms by reducing luminal and fecal pH. Low pH reduces peptide degradation and the resultant formation of toxic compounds, such as ammonia, amines, and phenolic compounds, and decreases the activity of undesirable bacterial enzymes (Thorton, 1981; Smith et al., 1996). The gastrointestinal microbiota plays important roles in health and disease, but the diversity of the microbiota is poorly defined and yet far from completely characterised. In another study from Ireland and UK, although β-glucans displayed no apparent prebiotic potential, it significantly modulated the microbial communities and the resulting SCFA (51 : 32 : 17; acetate : propionate : butyrate) profile. Acetate was the most prevalent SCFA in all treatments; accounting for 44% of the SCFA produced with the β-glucan treatments; 67.3% in the no treatment control, and 63.3% with inulin, at 48 h. However, fermentation of β-glucan resulted in higher total amounts and proportions of propionate; ranging from 30% with 150-kDa oat β-glucan treatment, to 37.1% with 172-kDa barley-glucan, at 48 h. This study revealed that the main group of human faecal microbial communities involved in β-glucan fermentation was the C. histolyticum group, and to a lesser extent Clostridia cluster IX and the Bacteroides–Prevotella and Atopobium groups (Hughes et al., 2008).

β-GLUCANS AND IRRITABLE BOWEL SYNDROME (IBS)

One of the most common gastrointestinal diseases of the world is IBS, affecting 8–22% and accounting for 20–50% of referrals to gastroenterology clinics. It is characterised by abdominal pain, excessive flatus, variable bowel habit and abdominal bloating for which there is no evidence of detectable organic disease (Madden et al., 2002). Although the pathogenesis is still not fully understood, one of the popular theories is altered gastrointestinal microflora, as some bacteria are more prone to gas production than others. In a study, 60 IBS patients were randomised in two groups: for a period of four weeks one group received rose-hip drink containing Lactobacillus plantarum and oat flour, and the other group were given plain rose-hip drink. The results of the study showed that patients receiving Lactobacillus plantarum and oat flour drink had decreased pain and flatulence compared with the placebo group. Therefore, probiotic therapy with oat fibre (as prebiotics) could be one of the treatment options in patients with IBS. Although fibre content of the test solution was minimal and it is unlikely that the fibre content could have had any effect, this type of probiotic therapy warrants further study in IBS patients (Nobaek et al., 2000). In a study from Italy, 50 patients with IBS received pills made from beta-glucans and inositol (Biointol™) for four weeks. Patients who were treated with Biointol significantly decreased abdominal bloating, flatulence and abdominal pain, with a slightly increasing urgency of bowel movements, compared with the placebo group (Ciaci, 2011). Other studies showed similar decrease of gastrointestinal symptoms after probiotic therapy, but without oat-based product addition (Guyonnet et al., 2007; Kajander et al., 2008). These studies stressed the possible role of altered gastrointestinal microflora in pathogenesis of IBS as well as role of prebiotics, including oat β-glucans and probiotics in the treatment of IBS.

β-GLUCANS AND INFLAMMATORY BOWEL DISEASE (IBD)

IBD are two related chronic inflammatory disorders characterised by acute flares followed by remission: ulcerative colitis (UC) and Crohn’s disease (CD). UC affects the inner lining of the colon, which becomes inflamed and develops ulcers. UC generally involves the distal part of the colon, but may progress proximally to pancolitis. CD tends to involve the entire bowel wall and commonly affects the terminal ileum and parts of the colon, but may affect any part of the gastrointestinal tract. A major complication of CD, affecting many CD patients is the formation of fistulas and stenosis (Feldman et al., 2010). Furthermore, UC and CD may be considered systemic disorders, as around 6–47% of IBD patients experience extraintestinal complications. The organs most commonly involved include skin, eyes, joints, biliary tract and lungs (Rothfuss et al., 2006). The incidence of IBD varies considerably worldwide with incidence rates between 0.5–24.5/105 and 0.1–16/105 inhabitants for UC and CD. The highest rates are reported in Northern and Western Europe as well as North America (Lakatos, 2006). The etiology and pathophysiology of both UC and CD is complex. Accumulating evidence suggests that an inappropriate immune response to non-pathogenic microbes of the intestine and other luminal antigens plays a critical role in the initiation and pathogenesis of IBD. The increased IBD incidence over the past decades, particularly in developing countries, suggests that environmental factors are implicated in IBD development, although there is evidence about genetic susceptibility as well (Feldman et al., 2010).

IBD is associated with overexpression of pro-inflammatory cytokines, including TNF-α, interferon (IFN), IL-1 and IL-6. CD and UC have been considered to be Th1- and Th2-driven diseases, respectively, although the picture now appears more complex. Th17 cells, a distinct subset of CD4+ T cells characterised by abundant IL-17 production, are associated with intestinal inflammation and tissue pathology and have attracted considerable attention recently. A cytokine IL-23, is central in promoting Th17 cells. The above mentioned cytokines and their producers may prove to be attractive therapeutic targets (Gálvez, 2014; Maloy et al., 2008). IBD is routinely treated with antibiotics, immunosuppressive and anti-inflammatory drugs. Promising antibody-based therapies that block key cytokines and interfere with T cell activation and migration of inflammatory cells have emerged as potent alternative therapies for IBD. Although these strategies may prove effective, available therapeutics are associated with considerable ad-
verse reactions, including opportunistic infections. Patients with severe IBD, refractory to medical treatment or with neoplastic transformation, require surgery. For selected cases (proctocolectomy in UC and ileocolonic resection in Crohn’s disease), minimally invasive surgery can be the treatment option with speeding recovery, reducing costs and decreasing morbidity (Polle et al., 2007). Surgery continues to have an important role in IBD treatment, as 30–40% of UC patients and 70% of CD patients require surgical intervention at some point. Total colectomy, the only cure for UC, is indicated in approximately 25% of UC patients (Surtin et al., 2012). Notably, as many as 40–60% of IBD patients respond poorly to current standard therapy, indicating a considerable need for new, more effective and safe therapies (Katz, 2007).

Regarding etiopathology of IBD, which is still under investigation, several studies have reported that IBD is associated with impairment in SCFA production, mainly acetate, propionate, and butyrate. They are produced in the large bowel by anaerobic bacterial fermentation of undigested dietary carbohydrates and fibre polysaccharides, with butyrate being considered as the major fuel source for colonocytes. These SCFAs have been proposed to play a key role in the maintenance of colonic homeostasis. Therefore, it is reasonable to consider therapeutic approaches that increase colonic SCFA production, as can be achieved by administration of dietary fibre to IBD patients, including oats. There is mounting evidence that carboxylic acids (CAs) formed by colonic fermentation of indigestible carbohydrates have positive health effects. In this context, butyric acid and, to some extent, propionic acid have mainly been emphasised. These acids are important energy sources for the colonocytes and may thus improve the condition of the colonocytes and mucosal lesions. Especially butyric acid has been suggested to play a role in the prevention and treatment of colonic diseases, such as ulcerative colitis and colon cancer, and to some extent Crohn’s disease. Carboxylic acids (CAs), especially butyric acid, have been suggested to counteract colonic diseases, such as ulcerative colitis and colon cancer. Unfortunately, there is quite limited documentation of efficacy of dietary fibre in properly designed trials (Galvez, 2005). In the 1990s, a popular study direction was SCFA topical treatment in distal ulcerative colitis, most of which showed positive results (Breuet et al., 1991; Steinhart et al., 1996). Comparing butyrate, which mostly has been investigated, with two other SCFA, namely acetate and propionate, which have less well-documented effect on inflammation, a study in Sweden proved that propionate and butyrate were equipotent, whereas acetate was less effective, but still useful in the treatment of IBD (Tedelind et al., 2007). A study from Italy showed good results with 4 g/day butyrate as enteric coated tablets for 8-week treatment of mild-moderate ileocolonic Crohn’s disease. This therapy was safe and well tolerated and 53% of patients achieved remission (Di Sabatino, 2005).

Most studies on colonic microbiota have focused on faecal material, although increasing evidence suggests that the epithelial surface is also colonised by large and diverse bacterial communities, which are structurally distinct from those that live in gut lumen. These mucosal communities can change markedly in inflammatory conditions, such as inflammatory bowel disease. Importantly, the composition of these mucosal communities in humans can be manipulated through the use of prebiotics (Macfarlane et al., 2004).

**ß-GLUCANS AND COLORECTAL CANCER**

Non-prescriptional use of medicinal herbs among cancer patients has been known around the world. Some chemotherapeutic drugs, like vincristine and taxol, are purified from herbs. ß-glucans are believed to have various immunomodulatory properties. Studies in vitro and in vivo revealed that the immunostimulating activity of ß-glucan depends on structure, molecular weight and number of branches. Based on in vitro studies, ß-glucans act on several immune receptors, including Dectin-1, which is one of better known and studied. There are some limitations of those studies, for example, there are no available ß-glucan control standards with specific molecular weight and branches. Most of the ß-glucans used in research are based on extracts rather purified ß-glucans, and therefore it is not possible to exclude confounding factors. The exact immunological action and signalling pathway are still unclear and have to be further defined (Chan et al., 2009). ß-glucans from various sources possess different characteristics and ß-glucans with additional branching have the highest immunostimulating activity (Freimund et al., 2003). Therefore, until now most studies in oncology have used ß-glucans isolated from yeasts. Searching through PubMed, there are few studies regarding use of oat ß-glucans in prevention or treatment of colorectal cancer. One of them, conducted on 25 healthy subjects in Sweden, suggested that dietary supplementation with oat bran (40 g ß-glucan enriched) per day can serve as an excellent source of carboxyl acids. After 8 and 12 weeks, the fecal concentrations of acetic, propionic and isobutyric acid were higher compared with values at entry. Oat bran may therefore have a preventive potential in regard to colonic diseases (Nilsson et al., 2007). Although the studies until now performed have shown positive results from ß-glucan and its metabolites — CA, on intestinal epithelium, there is one study from Canada, Ontario, with opposite results. The aim of that study was to determine whether ß-glucan from oats can shield intestinal epithelial cells from oxidative cell injury. The study was done on rat small intestine epithelial cells, which were cultured with or without medium viscosity oat ß-glucan at various concentrations and treated with serial diluted H₂O₂. The activity of inflammatory substances (superoxide dismutase activity, expression of TNF-α, activity of caspase-3) was increased by H₂O₂ only under the higher concentration of ß-glucan. Therefore, the study revealed that low levels of ß-glucan do not appear to protect small intestine epithelial cells against H₂O₂ induced oxidative injury, while applica-
tion of higher doses of this soluble fibre promoted oxidative cell injury induced by H$_2$O$_2$. This study expands the current understanding regarding dietary soluble fibre and intestine health and disease, suggesting that oat β-glucan creates a negative challenge to intestinal mucosa cells and may act in synergy with oxidative cell injury induced by reactive oxygen species. However, as this study was conducted on animals, further studies in humans are necessary to prove or reject this unexpected result.

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