Fiber in Our Diet and Its Role in Health and Disease

12

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Abstract

Lifestyle and dietary habits directly influence the health of an individual constraining to understand the role of different types of diet components. Recently, dietary fibers are being studied comprehensively to understand its role in prevention of heart diseases, obesity, diabetes, cancer, etc. Dietary fibers provide nutrition to the gut microbiota directly and to intestinal epithelial cells indirectly via its fermentation products mainly short-chain fatty acids (SCFAs). Dietary fiber consumption alters gut microbiota, and its fermentation product mainly short-chain fatty acids modulates disease condition by maintaining energy homeostasis and immune response. Dietary fibers reduce serum LDL cholesterol and blood pressure preventing heart diseases. Dietary fiber consumption also helps in reducing BMI via inducing satiety signals and provides bulking effect. SCFAs act on different tissues via GPCR receptors and modulate disease condition. In case of obesity and diabetes, SCFA improves insulin secretion and glucose homeostasis via gut-brain axis.

Keywords

Dietary fibers · SCFA · Type 2 diabetes · GPCR · Gut microbiota · Metabolism.

12.1 Introduction

Lifestyle and dietary habits directly influence the health of an individual constraining to understand the role of different types of diet components. Recently, dietary fibers are being studied comprehensively to understand its role in prevention of

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heart diseases, obesity, diabetes, cancer, etc. Plant non-starch polysaccharides like cellulose, hemicellulose, pactin, β-glucan, and fibers contained in wheat bran, oats, etc. are the examples of dietary fibers. Dietary fibers can be defined as plant carbohydrates and lignins which cannot be digested and absorbed in small intestine by the conventional digestive enzymes [31]. Dietary fibers provide nutrition to the gut microbiota directly and to intestinal epithelial cells indirectly via its fermentation products mainly short-chain fatty acids (SCFAs). The beneficial effects of dietary fibers can be explained as they protect mucus membrane of host from being degraded by the microbiota. In case of fiber deficiency, the microbiota degrades the colonic mucus layer and thus providing access to the pathogenic bacteria for infecting the host [9]. The SCFAs regulate metabolic as well as immune response of an individual by maintaining energy and immune homeostasis, respectively.

12.2 Types of Dietary Fibers

Dietary fibers can be defined as plant polysaccharides, lignin, or oligosaccharides such as resistant starch and inulin that cannot be digested by the human digestive enzymes [31]. Undigested or partially digested dietary fibers are fermented by the gut microbiota in small intestine or colon. On the basis of solubility, dietary fibers can be classified as soluble and insoluble dietary fibers. Fruits and vegetables are rich source of soluble dietary fibers (pectin, inulin, etc.), while wheat bran, oats, and barley have more amount of insoluble dietary fibers (cellulose, hemicellulose, etc.). Almost all high-fiber-containing foods provide rich source of soluble and insoluble fibers to some extent [21].

Soluble dietary fibers such as viscous or fermentable fibers like β-glucan and pectin have very important role in insulin-mediated glucose homeostasis in diabetic individuals. While soluble fibers are fermented in colon and their fermentation products have the beneficial effects, insoluble fibers like wheat bran provide bulking effect and partially fermented in colon. Daily consumption of guar gum, pectin, β-glucan, and hydroxypropyl methylcellulose reduced serum LDL cholesterol and thus prevents atherosclerosis and cardiovascular diseases. Psyllium husk is the most important component of fiber-supplemented products that lowers blood pressure, cholesterol, sugar, and risk of heart diseases [2]. Guar gum and other soluble fibers reduce gastric acid production and prevent duodenal ulcer disease [32].

12.3 Health Benefits of Dietary Fibers

The dietary fiber offers health benefits related to metabolic regulation, energy homeostasis, and immune regulation. Dietary fibers aid in maintaining good health and combat various diseases like obesity, diabetes, dyslipidemia, hypertension, colon cancer, etc. The beneficial effects of dietary fibers are due to its viscous nature improving satiety and control body weight gain. Dietary fibers inhibit the absorption of cholesterol and fat and prevent bile acid recycling in the liver. The bile acid formation in the liver utilizes cholesterol and thus lowers blood cholesterol [2]. Dietary fiber intake has inverse correlation with risk of cardiovascular disease and coronary heart disease [18]. Reduced levels of C-reactive protein (CRP), the inflammatory marker, have been observed in high-fat diet consuming rats following fiber ingestion. Dietary fibers maintain glucose and energy homeostasis via hypothalamic regulation in the brain by modulating neuropeptides affecting gluconeogenesis in the brain and intestine [6].

Soluble fibers pectin and guar but not bran have been shown to exert hypocholesterolemic effects in human. It has been reported in animal studies that diet-induced rise in cholesterol and atherosclerosis is inhibited by dietary fibers. Animal experiments suggest that some components of the complex mixture of substances called fibers could reduce cholesterol levels to a modest extent and inhibit atherosclerosis induced by diet. In man the data center on the effects of fiber on plasma cholesterol levels and some fibers such as pectin or guar exert significant hypocholesterolemic effects, whereas others, such as bran, do not. Oats and barley mediated reduction in total, and LDL cholesterol is due to the presence of soluble fiber, β-glucan, in it. Daily intake of 3 g oat β-glucan for 13 years has been shown to significantly reduce total and LDL cholesterol in hypercholesterolemic or normocholesterolemic individuals [24]. It has been shown that oats and buckwheat consumption is associated with decrease in body mass index (BMI), serum triglyceride, LDL cholesterol, total cholesterol, HDL cholesterol, and blood pressure. Daily intake of 9–30 g guar gum, 12–24 g pectin, 5 g β-glucan, and 5 g hydroxypropyl methylcellulose in nondiabetic individuals has been reported to reduce LDL cholesterol by 10.6%, 13%, 11.1%, and 8.5%, respectively. Blood LDL cholesterol-lowering efficiency of dietary fibers has been shown to reduce risk of cardiovascular diseases and coronary heart disease. Dietary fibers such as β-glucan from processed oats and barley foods also lower post-prandial blood glucose in healthy as well as diabetic subjects [34].

The dietary fibers delay gastric emptying and increase satiating hormones that create sense of fullness. High-fiber consumption is associated with incretin gut hormone secretion from intestinal L cells regulating insulin secretion and glucose homeostasis [1]. A high intake of dietary fiber was associated with a reduced risk of pancreatic cancer [19]. High-fiber diet containing low levels of red meat and alcohol has been reported to minimize risk of colorectal cancer. The beneficial effects of these three components might be because of gut microbiota alteration and their metabolites affecting balance between health and disease like colorectal cancer [35].

12.4 Dietary Fibers and Gut Microbiota

Gut microbiota is well known for its pivotal role in maintaining gut immune homeostasis via regulation of inflammation. Gut microbiota alteration has also been shown to induce obesity and insulin resistance via modulation of gut permeability, systemic inflammation, and energy metabolism. Dietary fiber has been shown to increase the abundance of *Bacteroidetes* while decrease the abundance of *Firmicutes* with elevated levels of propionate in plasma [6]. The gut microbiota-mediated alterations are thought to be due to its fermentation products, i.e., short-chain fatty acids (SCFAs), derived from dietary fibers.

One of the mechanisms by which dietary fibers prevent disease risk has been reported by Mahesh et al. In gnotobiotic mice colonized with fully sequenced human gut microbiota, the dietary fiber-deprived diet consumption leads to degradation of host colonic mucus membrane. In such condition, the gut microbiota utilizes mucus glycoproteins as nutrient source and degrades mucus barrier providing access to mucosal pathogen *Citrobacter rodentium* leading to colitis. Thus, dietary fibers have prominent role in diet-mediated gut microbiota shift and preventing intestinal permeability-mediated pathogenic invasion [9]. Gut microbiota alteration using spectrum-specific antibiotics lowers LPS levels in circulation and reduces GPCR expression as well as pro-inflammatory cytokines [28, 29].

12.5 Dietary Fibers and Short-Chain Fatty Acids

Our gut microbiota ferments dietary fibers that are incompletely hydrolyzed due to lack of the appropriate enzymes, which results in the production of SCFAs [7]. Although common SCFAs include formic, acetic, propionic, butyric, isobutyric, valeric, isovaleric, and caproic acids, 90–95% of the SCFAs present in the colon are constituted by acetate, propionate, and butyrate. Most SCFAs production occurs in the caecum and proximal colon and utilized as energy sources by intestinal epithelial cells and liver [23]. SCFAs with concentrations of about 60% acetate, 25% propionate, and 15% butyrate are found in the colon. Butyrate oxidation is the major source of energy for colonic epithelial cells. Propionate, entering the portal circle, is primarily utilized in gluconeogenesis in the liver, whereas acetate enters the blood circulation and gets access to different tissues [27]. SCFAs are rapidly transferred from gut to the bloodstream, and the usual concentration in peripheral blood is around 100–150 μM for acetate, 4–5 μM for propionate, and 1–3 μM for butyrate.

SCFAs are recognized by free fatty acid receptors FFAR2 and FFAR3. Acetate and propionate activate Ffar2 more specifically than butyrate, while butyrate and propionate are more specific for Ffar3 than acetate [3]. Both receptors are expressed in a variety of cells, including colonic enteroendocrine L cells, mucosal mast cells, adipose tissue, neutrophils, and monocytes. The intracellular signaling cascade triggers inositol 1,4,5-trisphosphate formation, intracellular [Ca^{+2}] mobilization, activation of extracellular signal-regulated kinase 1/2, and inhibition of intracellular cAMP accumulation. FFAR3 is involved in regulation of leptin production by adipocytes as well as expression and secretion of peptide yy (PYY). FFAR2 seems to be more involved in obesity and insulin resistance via regulation of glucagon like peptide-1 (GLP-1) secretion and modulation of inflammation. FFAR2 activation suppresses insulin signaling and fat accumulation in adipocytes and positively influences metabolism of unincorporated lipids and glucose in other tissues [4].

12.5.1 SCFAs and Metabolism

The SCFAs play vital roles in the pathophysiology of obesity and type 2 diabetes. Butyrate and propionate control blood glucose and body weight by activating gluconeogenesis in intestine via gut-brain neural circuit [6]. Acetate modulates the expression of neuropeptides regulating appetite in hypothalamus via TCA cycle activation [12]. GPR43 has a key role in fat accumulation regulation as indicated by Ffar2-deficient mice being obese on normal diet while Ffar2-overexpressing mice being protected from diet-induced obesity. Ffar2 inhibits Akt phosphorylation and insulin signaling in adipose tissues while promotes fatty acis oxidation in muscles and lowers triglyceride in the liver [16].

The gut microbiota-produced SCFAs regulate PYY secretion from intestinal L cells via Ffar3 as indicated by increased PYY secretion from wild-type germ-free mice after colonization with specific microbes but not from Ffar3 knockout mice [13]. Propionate-induced FFAR3 activation in sympathetic ganglia resulted in increased heart rate and energy expenditure via sympathetic outflow [15]. The SCFAs abrogate insulin resistance by FFAR3 activation in peripheral nerve via gut-brain neural circuit [6].

Propionate regulates body weight and lipid metabolism in adipose tissue and liver in overweight adult individuals [5]. Butyrate upregulates the expression of peroxisome proliferator-activated receptor-gamma coactivator 1α (PGC-1α) and the phosphorylation of adenosine monophosphate-activated kinase (AMPK) in muscle and liver tissues as well as PGC-1α and mitochondrial uncoupling protein-1 (UCP-1) in brown adipose tissues and thus improves fat oxidation and thermogenesis [10]. SCFA maintains the balance between lipid oxidation and lipogenesis via PPARγ regulation in high-fat diet-induced obesity [8]. Butyrate treatment has been shown to increase AMPK activity and accelerated the assembly of tight junctions. Butyrate enhances the intestinal barrier function, at least partly, by increasing expression of some major tight junction proteins and facilitating the assembly of tight junctions [25].

Pancreatic beta cell mass and function are damaged in case of inflammation, insulin resistance, and stress which can be protected by SCFA-mediated secretion of GLP-1 [27]. SCFAs have been reported to increase incretin levels when orally administered in mice. Butyrate induces GLP-1, GIP, and PYY secretion along with increased concentrations of insulin and amylin via stimulating pancreatic beta cells. Propionate administration also showed elevated levels of GIP, insulin, and amylin without affecting GLP-1 and PYY. Butyrate and propionate exert its beneficial effect on body weight and GIP stimulation via FFAR3 [17]. GLP-1 improves insulin resistance via enhanced secretion of insulin and suppression of glucagon secretion by activation of GLP-1 receptor which also plays role in beta cell proliferation via activation of PKB and PDX1 and apoptosis inhibition [11, 26]. Thus, SCFAs improve pancreatic insulin secretion and maintain lowered blood glucose levels.

12.5.2 SCFAs and Immune Regulation

Among SCFAs, butyrate has been shown to prove the best anti-inflammatory molecule as it can affect immune cell adhesion, migration, and cytokine expression and induces T cell energy to prevent antigen-mediated obesity-associated inflammation [22]. In obese mice, butyrate also enhances the immune homeostasis maintaining T regulatory cells (T reg cells) which inhibit effector T cells [22]. Saemann et al. showed that, in *Staphylococcus aureus*-infected PBMC-derived monocytes, butyrate inhibited IL-2 and IFN-γ while upregulated IL-4- and IL-10-mediated T regulatory cells [30]. SCFAs inhibit inflammatory TNFα release by LPS induction in human blood-derived neutrophils, and they also inhibit NFkB activation in human colon adenocarcinoma cell line [33].

SCFAs, particularly propionic acid and butyric acid, have anti-inflammatory effects via downregulation of pro-inflammatory cytokines TNF-α, IL-1β, and IL-6 [20]. SCFA receptor FFAR2 influences the differentiation and activation of monocyte- and neutrophil-mediated inflammation. SCFA-mediated activation of FFAR2 was shown to trigger recruitment of circulating leukocytes to the inflammatory site via activation of intracellular signaling pathways including MAPK, protein kinase C (PKC), and phospholipase C (PLC) [36]. Butyrate has been shown to downregulate TNF-α-mediated expression of adhesion molecule VCAM-1 which prevents leucocyte migration [22]. Propionate and butyrate but not acetate inhibit inflammatory cytokine release, NFkB pathway, and immune-related gene expression in vitro [33]. SCFA, mainly butyrate, has been shown to induce IL-10-mediated T regulatory cell function and suppression of inflammation. SCFA-mediated HDAC inhibition leads to mTOR pathway activation and IL-10 production [14].

12.6 Conclusion

High-fiber consumption improves health, prevents disease development, and helps cure various diseases. The dietary fiber offers health benefits related to metabolic regulation, energy homeostasis, and immune regulation. Dietary fibers aid in maintaining good health and combat various diseases like obesity, diabetes, dyslipidemia, hypertension, colon cancer, etc. (Fig. 12.1). Increasing the intake of high-fiber foods or fiber supplements lowers blood pressure, improves blood glucose homeostasis for diabetic individuals, improves serum lipoprotein, and reduces weight gain. Inulin and certain soluble fibers have been reported to enhance immune function in humans. Dietary fibers prevent mucus membrane digestion as well as maintain intestinal membrane integrity preventing pathogen invasion and disease development.

The fermentation product of dietary fibers, SCFAs, is thought to be the major factor providing beneficial effects of dietary fibers. Butyrate and propionate regulate insulin secretion and glucose homeostasis via incretin production. SCFAs further increase pancreatic β cell mass and insulin secretion as well as reduce glucagon

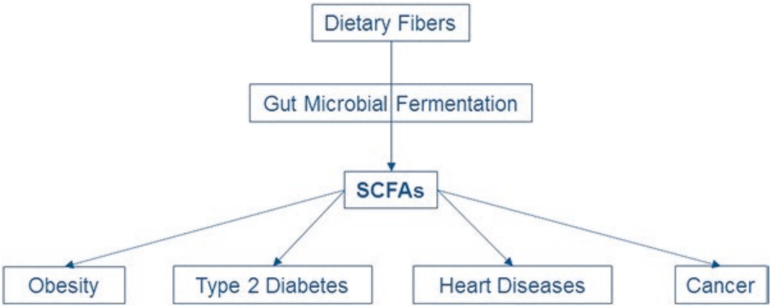

Fig. 12.1 Role of dietary fiber in health. Dietary fiber fermentation products, i.e., SCFAs, have a role in prevention of obesity, diabetes, heart diseases, cancer, etc.

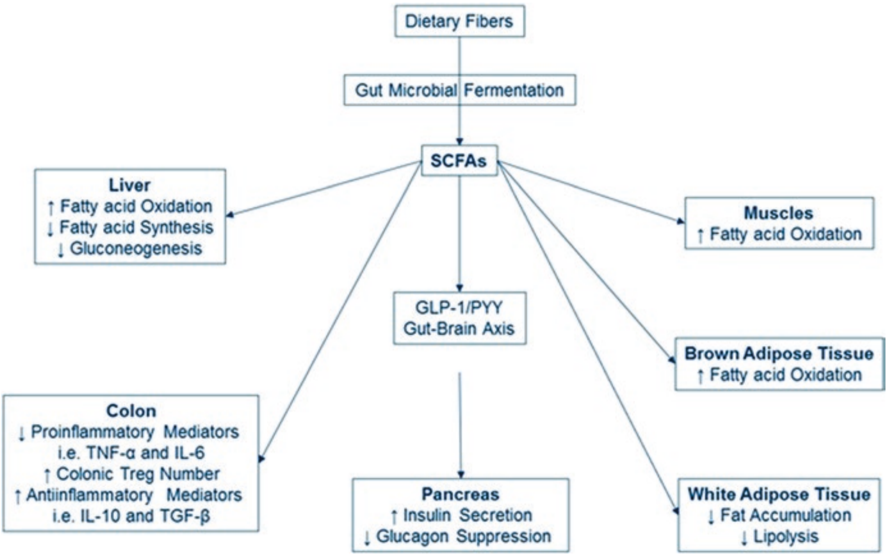

Fig. 12.2 Metabolism of action of dietary fiber. SCFAs modulate fat metabolism leading to reduced serum free fatty acid by inhibiting adipose tissue lipolysis as well as reduced fat accumulation by improving fat oxidation in the liver, muscles, and brown adipose tissue. SCFA-mediated HDAC inhibition leads to suppression of inflammation (TNF-α, IL-6), induction of colonic T regulatory cells and secretion of anti-inflammatory IL-10 and TGF-β. SCFAs also improve insulin secretion and inhibit glucagon suppression via gut-brain axis

secretion and thus regulate glucose metabolism. Butyrate enhances fatty acid oxidation in the liver, muscles, and adipose tissues. SCFAs, especially butyrate, seem to exert broad anti-inflammatory activities via downregulation of pro-inflammatory cytokines TNF-α, IL-1β, and IL-6. SCFA-mediated HDAC inhibition leads to mTOR pathway activation and IL-10 production that induce T regulatory cells and suppress inflammation (Fig. 12.2).

Thus, high-fiber-containing foods and supplements are recommended to be consumed daily for health benefits and prevention of metabolic as well as inflammatory diseases.

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