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Review article

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The gut microbiome and dietary fibres: implications in obesity, cardiometabolic diseases and cancer

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Abstract

Dietary fibres constitute a heterogeneous class of nutrients that are key in the prevention of various chronic diseases. Most dietary fibres are fermented by the gut microbiome and may, thereby, modulate the gut microbial ecology and metabolism, impacting human health. Dietary fibres may influence the occurrence of specific bacterial taxa, with this effect varying between individuals. The effect of dietary fibres on microbial diversity is a matter of debate. Most intervention studies with dietary fibres in the context of obesity and related metabolic disorders reveal the need for an accurate assessment of the microbiome to better understand the variable response to dietary fibres. Epidemiological studies confirm that a high dietary fibre intake is strongly associated with a reduced occurrence of many types of cancer. However, there is a need to determine the impact of intervention with specific dietary fibres on cancer risk, therapy efficacy and toxicity, as well as in cancer cachexia. In this Review, we summarize the mechanisms by which the gut microbiome can mediate the physiological benefits of dietary fibres in the contexts of obesity, cardiometabolic diseases and cancer, their incidence being clearly linked to low dietary fibre intake.

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Introduction

Dietary fibres are compounds present in the edible part of plant products (for example, root and leaf vegetables, tubers, fruits and cereals) that resist digestion by intestinal and pancreatic enzymes, and have a role in the prevention of chronic diseases in humans[1,2] (Box 1). Dietary fibres are a heterogeneous class of molecules, with various chemical structures and a variable degree of polymerization[1,2]. From a chemical point of view, they can be classified into resistant carbohydrates and non-starch (poly)saccharides. Their solubility in water or ethanol, viscosity and capacity to be fermented by the gut microbiome can be used as criteria for their classification. The fact that dietary fibres can be soluble or non-soluble does not necessarily preclude their biological properties. For example, the often-used simplification that soluble dietary fibres are equivalent to fermentable dietary fibres does not always apply, as some insoluble fibres, such as certain resistant starches, can also be fermented.

Technological progress has allowed the isolation and purification of dietary fibres from plants, as well as the synthesis and modification of non-digestible oligosaccharides or polysaccharides. This expands the panel of dietary fibres that can be either incorporated into food products for nutritional or technological properties, or taken as food supplements. There is a distinction between intrinsic fibres in natural food sources and dietary fibres that are purified or synthesized to be used as food ingredients or supplements[3]. In whole foods, dietary fibres are often integrated into a three-dimensional cell wall matrix that embeds other nutrients (digestible carbohydrates, lipids and micronutrients) and phytochemicals (polyphenols, phytosterols and phytoestrogens). This co-localization can influence the digestion and the bioavailability of the bioactive compounds and nutrients associated with dietary fibres in the plant matrix. Dietary fibres affect transit time, water availability and trapping of nutrients within the stool matrix, which may lead to microbial modulation[4].

Dietary processing such as milling, grinding and cooking can drastically alter the small intestinal digestibility of carbohydrates, some of them, thus, becoming available for further fermentation by gut microorganisms. For example, one interesting study has shown that this effect may promote gut microbial contribution to host energy status[5]. Different contents, types and structures of resistant starches have been produced by controlling cooking conditions. Those procedures impact the gut microbiota and the subsequent effects on human health, from correlation implications to causal mechanisms[6]. The difference of processing can largely determine the effects of rice resistant starch on gut microbiota composition and microbial metabolite production[6].

Having an adequate intake of dietary fibres is a common dietary recommendation worldwide[2]. However, official dietary guidelines show some discrepancies regarding the quantity of dietary fibres required for health maintenance[2,7,8]. Although adequate intakes of dietary fibres differ upon age, 25–30 g daily is widely recommended for adults. Only a small proportion of the global population meets these recommendations[8]. In North America and Europe, grain-based foods followed by vegetables, potatoes and fruits are the predominant contributors to dietary fibres, with little contribution from legumes, nuts and seeds.

Recommended dietary fibre intakes were mostly established to maintain normal laxation and cardiovascular health. However,

Box 1 | Dietary fibres: the evolution of a concept

The heterogeneity of sources, chemical structures, and physicochemical and biological properties of dietary fibres, as well as the evolution of analytical techniques, led to discrepancies in their classification worldwide and across decades. Below is a timeline of the evolution of the concepts and definitions. For a detailed overview of dietary fibres, please refer to refs. 1,2.

- 1953: the first time the term 'dietary fibre' is announced, referring to non-digestible material in faeces. By its definition, dietary fibre encompasses a mixture of lignin, cellulose and hemicellulose, which are non-starch polysaccharides[157].
- Later on, epidemiological studies in Africa reveal that the lack of dietary fibre in the diet increases the risk of apparently unconnected diseases such as diabetes and cancer in Western countries[158].
- 1970s: dietary fibre is defined as "the skeletal remains of plant cells that are resistant to hydrolysis by the enzymes of man"[159]. After the 1970s, a caloric value of 1.5–2 kcal g^{-1} was attributed to fermentable dietary fibre, reflecting the metabolic contribution of short-chain fatty acids.
- 1980s: the standardization of dietary fibre analysis allows their inclusion in the food composition tables. Dietary fibres are classified into 'soluble' and 'insoluble'[160,161].

Progress in the field of surgery, specifically with the development of ileostomy (a procedure that creates an opening in the abdomen through which the end of the small intestine is brought to the surface of the abdomen), reveals that the types of compounds resisting digestion in the upper gastrointestinal tract are more numerous than previously thought: resistant starch or oligosaccharides correspond to the 'physiological' definition of dietary fibre, based on their resistance to digestion by human enzymes.

- 1990s: the first definition of prebiotics, referring to non-digestible carbohydrates that can be (selectively) fermented by the gut microbiota, thereby impacting health[162].
- 2008: the Association of Official Analytical Chemists (AOAC) develops different methodologies to analyse dietary fibres by considering the variety of dietary fibre components; the United Nations's Codex Alimentarius brokered an international agreement on a definition of dietary fibre that included non-starch polysaccharides, resistant starch and non-digestible oligosaccharides. Not all countries agree on the definition and sources of dietary fibre (for instance, crustaceans are considered a source of dietary fibre in Japan only).
- 2010s: the definition of prebiotic extends to all components that interact with the gut microbiota. These include (readily) fermentable dietary fibre and complex dietary fibre containing phenolic and other phytochemicals, which have a relevant effect on health[163,164].
- 2020s: debate on the exclusion of fermentable oligosaccharides, disaccharides, monosaccharides and polyols, including non-digestible oligosaccharides found in vegetables, in the management of inflammatory bowel disorders.

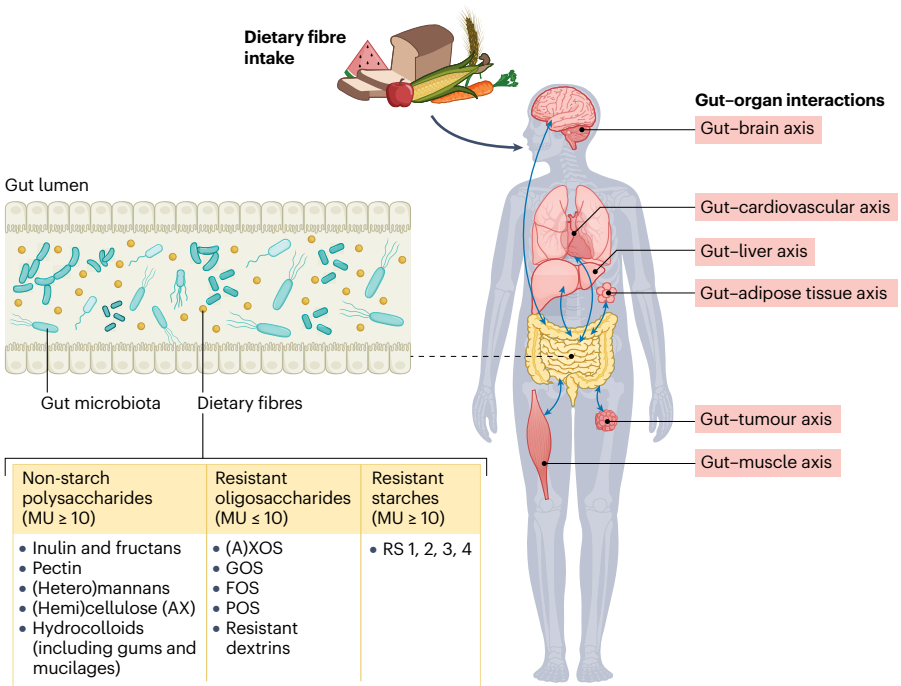


Fig. 1 | Dietary fibres at the cross-section of the interactions between the gut and other organs. Dietary fibres can be classified into non-starch polysaccharides, resistant starches and resistant oligosaccharides. Fibres can impact various physiological axes. Authorized health claims related to dietary fibre intake in the European Union are as follows: reduces intestinal transit time; reduces blood cholesterol or dietary and biliary cholesterol absorption; contributes to maintaining normal blood cholesterol levels; contributes to an increase in faecal bulk; contributes to maintaining normal bowel function; contributes to maintaining regular laxation; contributes to weight loss in an energy-restricted diet; contributes to reduction in postprandial glycaemic response; contributes to reducing the risk of cardiovascular disease and type 2 diabetes; contributes to reducing the risk of some types of cancer (colorectal)[2,155]. AX, arabinoxylans; (A)XOS, (arabino) xylo-oligosaccharides; FOS, fructo-oligosaccharides; GOS, galacto-oligosaccharides; MU, monomeric units; POS, pecto-oligosaccharides.

emerging evidence suggests that their potential benefits extend well beyond these outcomes, including their impact on the gut microbiome (Fig. 1). In this Review, we describe how dietary fibres interplay with human physiology and gut microbial ecology. Our understanding of how dietary fibres impact microbiome–host interactions helps define their contribution to healthy eating[9]. Epidemiological studies have demonstrated that dietary fibres are protective in a variety of chronic diseases that have been linked to the gut microbiota[10]. Therefore, we explore the role of microbiome–dietary fibre interaction in the context of the most crippling, costly and fatal chronic non-communicable diseases worldwide, namely obesity, cardiometabolic disorders and cancer[11].

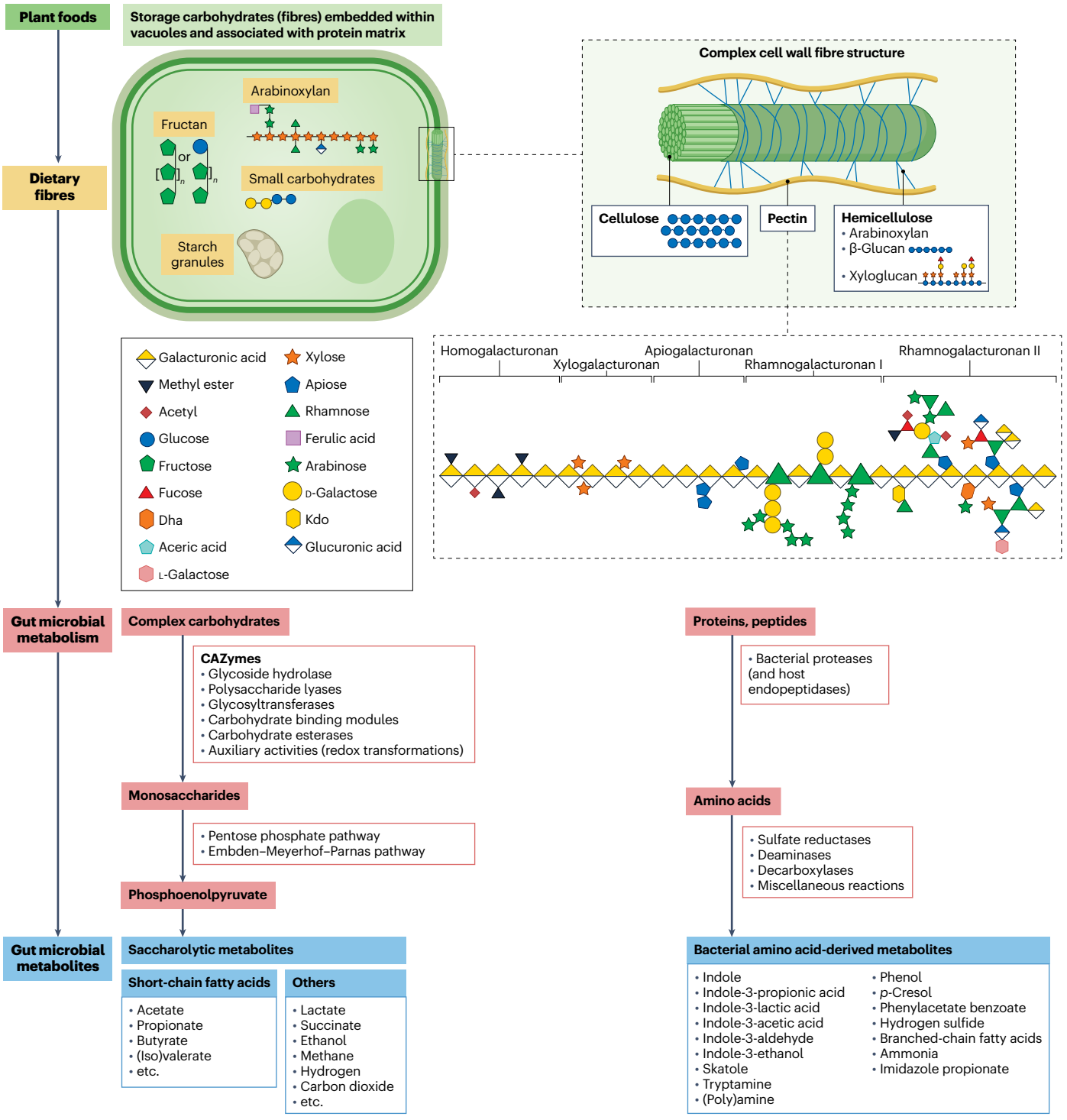
Interaction between dietary fibres and the gut microbiome

The ability of dietary fibres to be fermented by bacteria has a crucial role in their capacity to modulate the gut microbiome. The metabolism of non-digestible carbohydrates is performed by bacteria expressing carbohydrate-active enzymes (CAZymes), which include glycoside hydrolase, glycosyltransferase, carbohydrate esterase and polysaccharide lyase families[12,13] (Fig. 2). A wide range of activities allows the degradation of the complex mixtures of dietary fibres that are present in plant products. 'Simple' dietary fibres composed of mostly one monomer, such as fructan, will require the activity of one or two CAZyme families, whereas more complex dietary fibres, such as pectin, require at least seven CAZymes families. The products issued from dietary fibre degradation by CAZymes — consisting of either five-carbon or six-carbon monosaccharides — are taken up by the bacteria owing to transporter systems for glycan utilization, for example, the polysaccharide utilization loci. In bacterial cells, the monosaccharides are catabolized into pyruvate either via the pentose phosphate (five-carbon) pathway or via the Embden–Meyerhof–Parnas (six-carbon) pathway[14]. Pyruvate and phosphoenolpyruvate are the precursors of short-chain fatty acids (SCFAs). Importantly, the profile of SCFAs depends on dietary fibre fermentation by different bacterial genera and species, as well as on the bacterial metabolism of amino acids derived from proteins[15].

Effects of dietary fibres on gut microbial ecology and functionality

Dietary fibres may influence gut microbial diversity and the presence of specific taxa, with this effect varying substantially between individuals. In addition, microbial functions can also be modified by dietary fibres, leading to changes in the profile of specific metabolites involved in host physiology. The National Centre for Biotechnology Information (NCBI) has recently modified the name of some bacteria in accordance with the recent inclusion of rank 'phylum' in the International Code of Nomenclature for Prokaryotes (ICNP); to be in accordance with most cited references, we have kept the name of the bacteria as they appeared in their original publication.

Dietary fibres and gut microbial α-diversity. The α-diversity of the gut microbiota refers to the richness (number of taxonomically distinct microorganisms) and evenness (relative abundance of microorganisms) of its composition. Several studies reveal inverse associations between α-diversity and disease states[16]. Although fermentable dietary fibres can establish niches in the gut, there are controversies about the fact that diversity (in particular, richness) can be increased through dietary fibre intake in humans. A study has reported that higher microbiota richness was associated with higher microbiota stability upon increased dietary fibre intake[17]. Most intervention studies with fibre supplements do not record an increase in α-diversity, and in some cases, they even report a decrease[18–22]. The latter finding can be caused by changes in community evenness (through blooms of



microorganisms) or through the loss of bacterial species[20,23]. There is no evidence that the decrease in α-diversity linked to dietary fibre intake precludes potentially harmful effects. Coherently, a systematic review and meta-analysis has concluded that a dietary fibre intervention had no effect on the diversity of the gut microbiota, but it increased the abundance of specific bacteria (*Bifidobacterium* and *Lactobacillus* species) and faecal butyrate concentration in healthy adults[16].

Effects of dietary fibres on specific bacterial taxa. Dietary fibre supplements with discrete chemical structures can be used to modify the composition of the gut microbiota. We illustrate below that the influence of dietary fibre intake on the composition of the gut microbiota cannot be generalized to all dietary fibres, and merely depends on the physicochemical characteristics of the fibres. For example, the microbial shifts induced by resistant starches with crystalline

Fig. 2 | Structure of dietary fibres and their metabolism by the gut microbiota. Dietary fibres either form a complex 3D structure that constitutes the backbone of plant cells, or are encapsulated as storage carbohydrates with various other nutrients such as lipids, proteins and polyphenols in the plant vacuole[3]. The fibres present in the plant cell wall are constituted by cellulose that forms fibrils stabilized by hemicellulose and further strengthened by pectin[156]. Storage carbohydrates such as fructans, arabinoxylans and starch granules are embedded in a protein matrix. The cells of some fruits and vegetables contain also vacuoles mainly filled with small carbohydrates, water and other nutrients. Complex carbohydrates and proteins of plant cells are fermented by the microbial communities present in the gut, leading to the production of saccharolytic and proteolytic metabolites. Some of these metabolites include short-chain fatty acids (SCFAs) such as acetate, propionate and butyrate, bacterial amino acid-derived metabolites such as indoles, phenols and *p*-cresol, and other metabolites such as lactate, ethanol and methane. The figure highlights the major metabolic pathways, such as carbohydrate-active enzymes (CAZymes)[13] involved in complex carbohydrate metabolism, the pentose phosphate pathway and the Embden–Meyerhof–Parnas pathway involved in the metabolism of monosaccharides to phosphoenolpyruvate, and bacterial proteases and other enzymes that metabolize proteins and peptides into bacterial amino acid-derived metabolites. The figure also illustrates the intermediates involved in the production of microbial-derived metabolites such as SCFAs, branched-chain fatty acids, gases (hydrogen, methane, carbon dioxide, hydrogen sulfide) and indolic compounds[15]. Dha, 3-deoxy-D-lyxo-heptopyran-2-ularic acid; Kdo, 3-deoxy-D-manno-oct-2-ulosonic acid.

structures, namely, an increase in *Eubacterium rectale*, *Ruminococcus bromii* and related *Ruminococcus* species, are almost completely distinct from those induced by cross-linked type 4 resistant starches (RS4), which increase the abundance of *Parabacteroides distasonis*[24,25]. Both types of resistant starches induce *Bifidobacterium adolescentis*, although the response is highly individualized. Arabinoxylans specifically promote the growth of *Bifidobacterium longum*. Intervention studies versus placebo with purified inulin-type fructans have also shown a substantial increase in bifidobacteria, occurring in most individuals[18,21,26,27]. Specific bifidobacteria (*B. longum, Bifidobacterium pseudocatenulatum* and *B. adolescentis*) are increased by fructan intake in volunteers with obesity, whereas other species are not modified (*Bifidobacterium animalis* and *Bifidobacterium breve*)[28]. Interestingly, human gut microbiomes enriched in both *B. longum* and *B. adolescentis* are associated with gut microbiome diversity and a higher abundance of butyrate-producing bacteria and are more prevalent in healthy individuals[29]. Galacto-oligosaccharides also enhanced several species of bifidobacteria in faecal samples[30]. The specificity in the response to dietary fibres can go down to the genus, species and even sub-species level[31–33]. Complex dietary fibres can also induce specific responses. For example, complex corn arabinoxylan is highly specific for *B. longum* and *Prevotella copri*, whereas arabino-oligosaccharides promote several species of *Bifidobacterium* and *Prevotella*, as well as other genera such as *Eubacterium* and *Roseburia*, being thus less specific[34]. This type of observation led some authors to postulate that the complexity of dietary fibres may drive the specificity of their effect on gut bacterial species.

Microbial ecological responses to dietary fibres. Although there can be substantial impact of dietary fibres on specific bacterial populations, the responses can also be highly individualized. This can be assessed by evaluating intra-subject β-diversity indexes, which reflect individuality (that is, species diversity among habitats, sites and samples at different time points). For example, less than 50% of individuals showed an increase in bifidobacteria upon interventions with arabinoxylan, galacto-oligosaccharides or resistant starches[24,25,30,35]. Our understanding of the elements driving the individualized host responses to dietary fibres is still rudimentary. The initial composition of the gut microbiome, host behavioural characteristics (physical exercise, stress and so on) or exposure to xenobiotics — including drug treatment — could all be implicated in the differential modulation of the gut microbiome composition upon dietary fibre interventions[36]. Whereas the response of *P. copri* to arabinoxylans is mainly determined by the presence of the species, which is rare in industrialized societies, the response of *B. longum* is not primarily linked to the presence of its own species[35].

Microorganisms often utilize dietary fibres in ecological guilds. To understand the targeted response to dietary fibres and predict the outcome, responses are often differentiated into primary and secondary ones[37,38]. Primary responses are determined by the genetic capacity of microorganisms to utilize the discrete fibre structure. These primary responses are often highly specific. Following this primary response, secondary responses can occur, involving other bacteria that can be either promoted or inhibited. In the gut lumen, some bacterial metabolites issued from the fermentation of dietary fibres are used as substrates by specific gut bacteria participating in cross-feeding. For example, lactate can be used as an energy substrate by some bacteria, which metabolize lactate into other SCFAs such as butyrate. This contributes to promoting bacteria that are dependent on SCFAs as substrates. Some microbial metabolites, such as propionate, are bacteriostatic or lead to a decrease in pH (Fig. 3). The resulting reduction in pH can lead to a drop of *Bacteroides* species upon dietary fibre exposure such as galacto-oligosaccharides[30] and resistant starches[25], despite the fact that the bacteria are able to utilize the substrate. Reduction of *Bacteroides* spp. owing to low pH is well established through work on dietary fibres using in vitro systems, in which the pH can be strictly adjusted[39]. The effects of secondary responses on the microbiota, especially if they are inhibitory, are much less specific than the selective enrichments caused by fibres, and probably much harder to predict using metagenomic and machine learning approaches, because they are driven by complex ecological interactions[25]. A study has shown that the precise modulations of the gut microbiome at the species level through different RS4 types are linked to directed shifts in the output of either propionate or butyrate. Although these specific effects on microbiome composition and function have not yet been proved as drivers of clinical outcomes, they open the possibility of precise modulation of the metabolic output of the gut microbiota for the development of targeted therapeutics and medical foods.

Gut microbiota-derived metabolites

There is a huge variety of metabolites that can be produced by the gut microbiome. Metabolites such as SCFAs can be primarily issued from dietary fibre fermentation. Branched-chain fatty acids (BCFAs) such as isobutyrate, 2-methylbutyrate and isovalerate can be produced via bacterial fermentation of branched-chain amino acids such as valine, isoleucine and leucine, respectively. Secondary bile acids (BAs) or bacterial amino acid-derived metabolites are not produced upon dietary fibre fermentation, but their profile can be indirectly influenced by

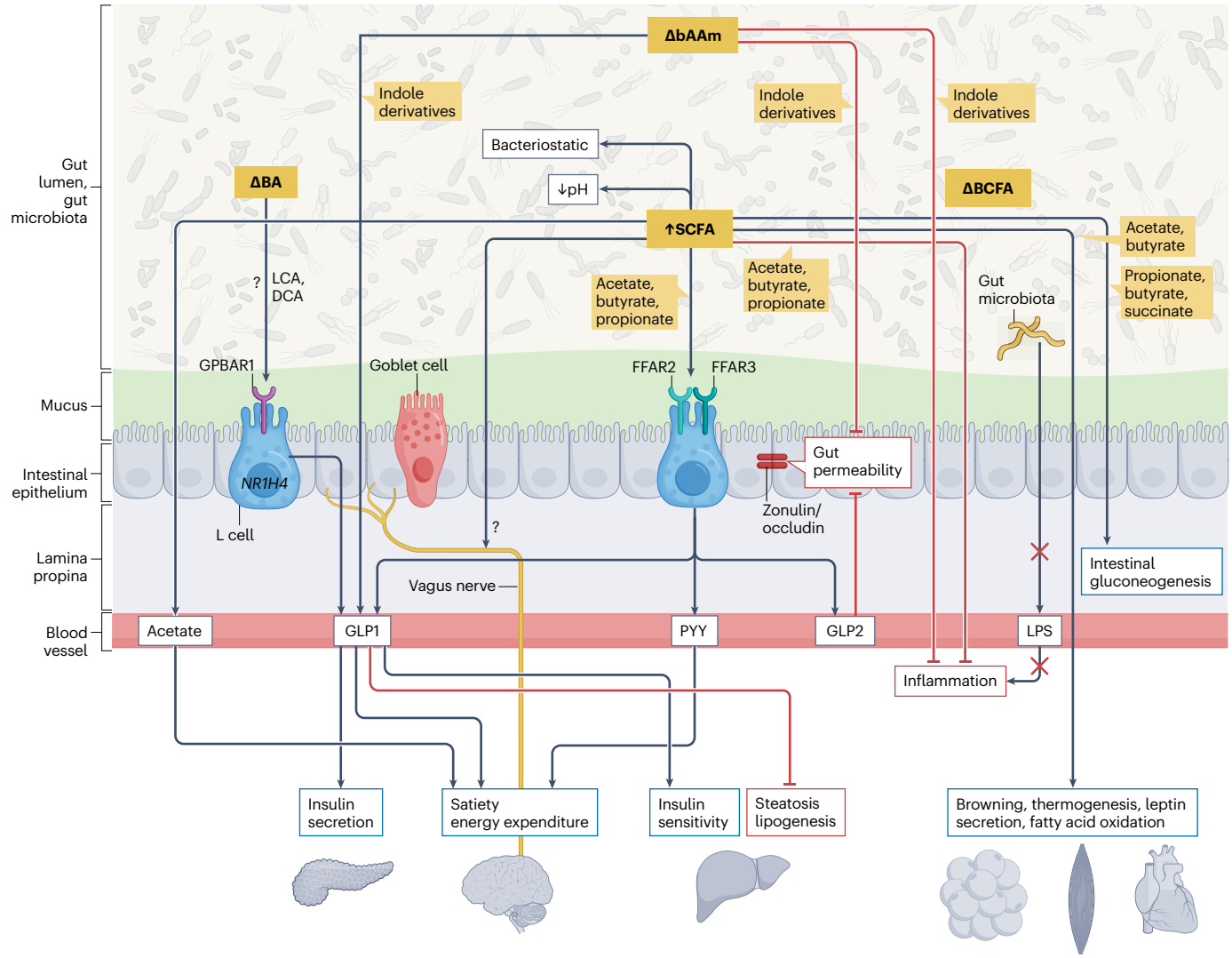


Fig. 3 | Mechanisms by which dietary fibres promote gut microbial-dependent systemic effects. Dietary fibre fermentation by microbial communities occurring in the intestinal lumen can lead to the production of different metabolites such as short-chain fatty acids (SCFAs) and branched-chain fatty acids (BCFAs), which have important effects on host physiology at the systemic level. However, other secondary metabolites that are not produced by the microbial-dependent fermentation of dietary fibres, such as secondary bile acids (BAs) or bacterial amino acid-derived metabolites (bAAm), also contribute to these effects. Some of these metabolites such as SCFA can influence sympathetic activity with consequences on energy metabolism. SCFA can directly reduce hepatic and gut inflammation and could promote vagal afferent neuron stimulation energy homoeostasis[15]. Some SCFAs or BAs activate G protein-coupled receptors such as free fatty acid receptor 2 (FFAR2) and 3 (FFAR3) and G protein-coupled bile acid receptor 1 (GPBAR1) expressed by intestinal epithelial cells (particularly, L cells), leading to the production of gut hormones such as glucagon-like peptide 1 (GLP1) and 2 (GLP2) and peptide YY (PYY). These hormones affect intestinal transit, satiety and glucose homoeostasis or influence gut permeability. The improvement of the gut barrier (notably via improved distribution of the tight junction proteins zonulin and occludin) decreases endotoxaemia (lipopolysaccharide (LPS) translocation shown by arrows with red cross) and systemic inflammation. bAAm can reduce gut inflammation and modulate the epithelial cell barrier. Some SCFAs, such as propionate, are bacteriostatic or lead to a decrease in pH whereas others such as acetate, or bacterial components such as LPS, may also reach the circulation and directly affect peripheral tissue (adipose tissue, liver, brain and muscle) metabolism and function. Blue and red boxes are used to respectively highlight positive and negative metabolic or inflammatory outcomes in the context of cardiometabolic diseases. The mechanisms shown in this figure are mainly based on experimental studies. Links that are not clearly demonstrated are indicated by question marks. DCA, deoxycholic acid; LCA, lithocholic acid.

dietary fibres. This section describes the metabolic effects of these microbial-derived bioactive compounds.

Short-chain fatty acids. Dietary fibres serve as substrates for different microbial communities, resulting in SCFAs and gas production[40]. SCFAs may be used as energy substrates in intestinal cells, but also in peripheral organs, wherein they may have a role as metabolic regulators within host cells[40,41] (Fig. 3). As compared with non-fermentable dietary fibres that provide no calories because they are excreted without biotransformation, the production of SCFAs upon fermentation allows the

recovery of 1.5 to 2 kcal per gram of dietary fibre[42]. Among the molecular processes of metabolic regulation, SCFAs modulate histone acetylation and methylation, bind to G protein-coupled receptors (GPCR), promote the secretion of various hormones (for example, glucagon-like peptide 1 (GLP1) or 2 (GLP2) and peptide YY (PYY)) and neurochemicals (for example, serotonin), and act on vagus nerve signalling. All those mechanisms may contribute to improved insulin sensitivity through their impact on adipose tissue and skeletal muscle, as well as on liver metabolism and function[43]. The action of SCFAs on histone deacetylases and GPCR may also contribute to blunt cancer initiation and progression[44]. The fermentation of dietary fibres into SCFAs often leads to beneficial effects, including interference with the production of potentially harmful metabolites. Indeed, by lowering the pH in the gut through the production of SCFAs, dietary fibre fermentation inhibits proteolytic fermentation and the related production of potentially detrimental end-products, such as phenols, ammonia and amines[45]. It is worth noting that some studies have found detrimental effects of SCFAs on host health. For example, they have been shown to promote neuroinflammation and motor symptoms in a mouse model of Parkinson disease[46].

Amino acid-derived metabolites. Bacterial amino acid-derived metabolites, such as imidazole–propionate, phenylacetate, benzoate, *p*-cresol and phenol, have been shown to exhibit deleterious effects on host metabolism. Individuals with obesity have exhibited increased urinary *p*-cresol and phenol, which decreased upon weight loss[47]. A low level of microbial gene richness was also linked to a higher microbial production of phenylacetic acid that drives hepatic steatosis[48]. By contrast, the production of indole may contribute to the secretion of GLP1 by intestinal enteroendocrine cells and may have a beneficial impact on epithelial cell barrier properties, as well as on liver inflammation associated with obesity[49–51]. The fermentation of proteins and amino acids leads to the production of hydrogen sulfide, ammonia and *p*-cresol, which may contribute to the development of colorectal cancer[52]. In fact, these metabolites may affect the oxidative metabolism of colonocytes and ATP production. They can also lead to an increase in reactive oxygen species, cause DNA damage and alter the cell cycle, ultimately decreasing colonocyte proliferation. Human studies have shown that dietary fibre intake may impact the occurrence of certain harmful metabolites. For instance, the consumption of resistant maltodextrin for 24 weeks reduced the levels of some opportunistic virulent metabolites, such as imidazole propionate and trimethylamine, in individuals with haemoglobin A1c (HbA1c) levels higher than 6%, which initially presented elevated amount of those metabolites[53]. Another study has found that middle-aged and older individuals with high adherence to a Mediterranean diet presented greater faecal concentrations of benzoic and 3-hydroxyphenylacetic acids, which positively correlated with the intake of the main classes and subclasses of polyphenols and fibres and higher levels of beneficial *Clostridium* cluster XVIa and *Faecalibacterium prausnitzii*[54]. These results demonstrate a link between the Mediterranean dietary pattern, the bioactive compounds of the diet, and the faecal metabolic phenolic profile.

BCFAs are markers for bacterial protein fermentation, but little is known about their potential effects on human health[55,56]. A recent systematic review has revealed a beneficial association of BCFAs with cardiometabolic disorders in humans: statistically significant inverse associations were shown between serum BCFAs and adipose tissue, insulin resistance, triglycerides, skeletal muscle insulin resistance and/or body mass. However, a randomized feeding trial has reported no significant differences in concentrations of BCFAs in stool or body mass index among participants with obesity who were assigned to fruit–vegetable or whole-grain diet groups compared with a refined-grain control group[57]. A very recent study has found an association between high BCFA levels and improved glucose homoeostasis in a cohort of 219 non-Hispanic white participants and 126 African American participants[58]. A negative correlation was found between the consumption of dietary insoluble fibre and faecal levels of BCFAs in the adult population[59]. Furthermore, in vitro studies suggest that specific dietary fibres may reduce the production of BCFAs and harmful *p*-cresol, with this effect being dependent on the characteristics of the gut microbiome and dietary pattern of donors[60]. Consistently, a double-blinded, randomized, crossover study in healthy adults has shown that supplementation with fructan moderately decreased the total concentration of BCFAs in faeces[61].

Bile acids. BAs are a class of structurally diverse molecules issued from cholesterol metabolism[62]. Primary BAs are produced by hydroxylation from cholesterol, which is catalysed by cholesterol 7 α-hydroxylase (CYP7A1) in the classic pathway or oxysterol 7 α-hydroxylase (CYP7B1) in the alternative pathway. BAs are then conjugated in the liver, released in the gut, wherein they are modified by the gut microbiota into secondary BAs, and reconjugated in the liver. Multiple BAs-responsive membrane and nuclear receptors have been identified to explain the mechanisms by which BAs coordinate signal transduction in various cell types and tissues (Fig. 3). These receptors include the nuclear receptor subfamily 1 group H member 4 (NR1H4, also known as nuclear receptor farnesoid X receptor (FXR)) and the G protein-coupled bile acid receptor 1 (GPBAR1, also known as Takeda G protein-coupled receptor 5 (TGR5)). GPBAR1 signalling is particularly affected by the microbiome. Conjugated versus unconjugated primary BAs and primary versus secondary BAs exert divergent effects by acting on NR1H4 or GPBAR1 in organs implicated in the enterohepatic system[62]. The secondary BAs, lithocholic acid and deoxycholic acid, and their conjugated forms are potent GPBAR1 activators. Over the past two decades, BA mimetics targeting NR1H4 and GPBAR1, or both, have proved efficacious in alleviating chronic metabolic and inflammatory disorders, including obesity.

Although findings from human studies are inconsistent, intake of dietary fibres, notably those acting as BA sequestrants, has been associated with improved cardiovascular risk[63]. For example, highly specific effects on faecal secondary BAs (that is, reductions in deoxycholic acid, isolithocholic acid, taurolithocholic acid, taurodeoxycholic acid and glycodeoxycholic acid) have been detected after 6 weeks of supplementation with cellulose, whereas arabinoxylans did not reduce BA concentrations relative to baseline[23].

Dietary fibres may also provide bioactive compounds by influencing the availability of other nutrients. Although this has been mostly shown in animal models, dietary fibres such as inulin-type fructans, for example, may decrease fatty acid absorption and sugar digestion and increase gluten digestibility, thereby changing the sources of substrates for the gut microbiome in the colon[64–66].

In conclusion, many metabolites produced by the gut microbiota and whose production is influenced by the intake of dietary fibres impact host metabolism through the interaction with nuclear and membrane receptors or by altering energy metabolism.

Dietary fibres, the gut microbiota and chronic diseases

According to the WHO, obesity and cancer represent the greatest public health challenges of the twenty-first century. Obesity is a risk factor for

two of the world's leading causes of death, including cardiovascular risk and diabetes (WHO fact sheet for obesity and overweight), but also various types of cancer (WHO fact sheet for cancer). The Global Burden of Disease study enounces that cardiovascular diseases and cancers caused 19.4 million (29%) and 9.8 million (15%) deaths (considering both sexes, all ages) in 2021, respectively (Institute for Health Metrics and Evaluation). Around one-third of cancer cases in Western countries are attributed to preventable factors such as high body mass index, low fruit and vegetable intake, tobacco use, alcohol consumption and lack of physical activity (WHO fact sheet for cancer).

Gut microbiome analyses have revealed specific features of the gut microbiome in cohorts of patients with obesity or cancer[67,68]. Despite controversies raised by discrepancies between small cohort studies[69], meta-analyses confirm that specific genera (*Odoribacter*, *Oscillospira*, *Akkermansia*, *Alistipes* and *Bacteroides*) were depleted in obesity[70]. A reduction in SCFA producers (several *Alistipes* species, *Odoribacter splanchnicus* and so on) and depletion of bacterial promoters of gut barrier integrity (*Akkermansia muciniphila* and *B. longum*) also characterized the gut microbiome of individuals with obesity[71].

The gut microbiome of patients with cancer also differs from that of healthy individuals. This has been mostly established in patients with colorectal cancer, who curiously present reproducibly higher microbiome richness than healthy patients, an effect related to the expansion of species derived from the oral cavity, such as *Fusobacterium nucleatum*, *Solobacterium moorei*, *Parvimonas micra* and *Pseudostreptococcus stomatis*[72]. Large pan-cancer cohort analyses remain scarce and often include patients undergoing treatment, thereby making it difficult to distinguish the impact of cancer from the impact of treatment[68]. A study has performed shotgun metagenomic-based analysis of faecal material collected from over 1,900 individuals with cancer across eight different malignancies of varying stages, most under treatment, and compared the data with those obtained in more than 5,500 healthy individuals[73]. This analysis has revealed a reduced abundance of 25 taxa (for example, *P. copri*, *Eubacterium hallii*, *E. rectale*, *Anaerostipes hadrus*, *B. adolescentis*) and an increased abundance of bacterial species such as *Clostridium bolteae* and *Butyrimonas virosa* across five or six out of eight types of cancer compared with individuals without cancer.

Diet and lifestyle explain around 20% of the microbial structural variations in humans[74]. This highlights the potential for dietary strategies in the management of non-communicable diseases through gut microbiota modulation, particularly obesity and cancer[74–77]. There is strong evidence that dietary fibre is a key dietary component in this context. A study has analysed existing high-quality data (135 million person-years of data) and found that individuals who consume high amounts of dietary fibres experienced a decrease of 15–30% in the incidence of cardiometabolic diseases such as coronary heart disease, stroke and type 2 diabetes, as well as colorectal cancer, and overall mortality, compared with those who consume low amounts of dietary fibres. The authors of this study concluded that the minimum intake of dietary fibres in adults should be of 25–29 g per day, with additional benefits linked to further increase in dietary fibre intake[78]. In the following sections, we will explore how dietary fibres can impact gut microbial modulation in relation to obesity and cardiometabolic risk, as well as its effects on cancer risk and management.

Obesity and cardiometabolic diseases

A healthy eating pattern (diets high in fruits, vegetables and whole grains; low-fat and non-fat dairy and lean protein; low in saturated fat, *trans*-fat, sodium and added sugars) is an important contributor to adequate weight maintenance lifelong and helps decrease the risk of development of obesity-linked metabolic disorders[79]. The adherence to a Mediterranean diet, characterized by vegetable fibre-rich food, is associated with a reduced risk of non-communicable diseases such as cardiovascular diseases and obesity[80].

A recent systematic review with meta-analysis of 22 randomized controlled trials has highlighted that taking isolated soluble dietary fibre supplements can help reduce body weight, with a significant decrease in body mass index, waist circumference, fasting blood insulin and insulin resistance (determined through HOMA-IR (homeostatic model assessment of insulin resistance)) in people with overweight or obesity[81].

The mechanism allowing dietary fibres to modulate weight loss is not fully understood[7,82] (Fig. 3). A study has suggested that dietary fibres may decrease energy intake[83], but the satiating effect of dietary fibres upon ad libitum test meals remains inconclusive[84–86]. The effect of dietary fibres on the release of peptides such as GLP1, PYY or ghrelin, which regulate appetite and glucose metabolism, has been mostly shown in intervention studies with relatively high doses of purified dietary fibres. Although many intervention studies have evaluated the impact of dietary fibres on obesity and related metabolic disorders, only a few have examined the link with changes in the gut microbiome. In Supplementary Table 1, we summarize published data on placebo-controlled studies describing dietary fibre interventions (food-based versus isolated fibre supplements) in individuals with overweight or obesity; these studies have considered both microbiome analysis and health outcomes (specifically, obesity and cardiometabolic disorders). In Supplementary Table 1, we list clinical studies, the different interventions and placebo used, the doses of dietary fibre, and the duration of the studies, as well as the effect of other factors such as gender, exercise and gut microbial enterotype on health outcomes.

In terms of changes in the gut microbiome upon dietary fibre intervention, almost half of the studies have reported an increase in bifidobacteria (or actinobacteria) in all interventions with inulin-type dietary fibre, as well as with other types of fibre (galacto-oligosaccharides, arabinoxylans, whole-grain diet, Mediterranean-like diet and the addition of beans). Several studies have shown a decrease in *Bacteroides* spp. upon dietary fibre intervention. However, there are some debates regarding changes in the level of SCFAs, which can either increase or decrease. In some studies, although the biological effect of dietary fibre intervention compared with placebo was not statistically significant, the authors reported interesting correlations (not implying causality) between biological outcomes and gut microbiome characteristics (see Supplementary Table 1). One of the studies has found that specific bacteria promoted by inulin-type fructan supplementation in individuals with obesity, along with specific bacterial-related metabolites (phosphatidylcholine, lactate, hippurate), inversely correlated with serum lipopolysaccharide levels, despite a lack of significant effect on body weight[26]. The pre-intervention levels of *Anaerostipes*, *Akkermansia* and *Butyricicoccus* species influenced the reduction in body mass index in response to inulin[87]. Importantly, changes in *Bifidobacterium*, *Dialister* and *Catenibacterium* genera owing to inulin were only significant when participants exercised more[88]. Factors such as the initial composition of the gut microbiome, drug treatments or physical activity levels explain the variable responses in body weight reduction by inulin[21,87,88]. This interesting interaction between dietary fibre intake, physical exercise and gut microbiota composition warrants further study, as the mechanisms of such interactions are not fully understood.

Regarding biological outcomes, consumption of dietary fibres was associated with positive health effects related to metabolic and inflammatory improvements, rather than effects on body weight or fat mass. A few studies have also reported an effect of dietary fibres on satiety[23,89]. Arabinoxylans improved lipid and glucose metabolism in healthy individuals and in individuals with metabolic syndrome and type 2 diabetes, supporting a health claim made by the European Food Safety Authority for such purified viscous dietary fibres when used as supplements[49,90].

The mechanisms behind the effect of dietary fibres on obesity and related metabolic diseases often involve the production of bioactive metabolites, such as SCFAs. Circulating, rather than faecal, SCFAs are related to insulin sensitivity and GLP1 concentrations in humans[91]. Despite abundant evidence from animal data, support of human data is required for the implementation of evidence-based gut-derived SCFA interventions to combat obesity and obesity-associated metabolic disorders[92]. A study has compared the bioavailability of two different SCFA-enriched triglycerides (butyrate and hexanoate esterified with long-chain fatty acids or solely butyrate and hexanoate) and investigated whether they reach the circulation and affect postprandial metabolism in men with overweight and/or obesity[93]. Although postprandial circulating butyrate and hexanoate levels increased after administration of the liquid high-fat mixed meal containing SCFA-enriched triglycerides, the study has found no effects on hydrogen breath, appetite, gastrointestinal complaints, or concentrations of circulating GLP1, free fatty acids, glucose, triglycerides, insulin and cytokines.

Two recent randomized crossover studies have tested fibre mixtures in lean and prediabetic men with overweight or obesity, and have described changes in SCFA production[94]. In one of the trials, prediabetic men who received supplements combining inulin and resistant starches showed increased plasma acetate levels compared with men receiving inulin or maltodextrin alone. The mixture of both dietary fibres increased energy expenditure and carbohydrate oxidation and decreased postprandial glucose concentrations compared with maltodextrin while increasing markers of dietary fibre fermentation. In the other trial, β-glucan and resistant starch supplements increased plasma butyrate in prediabetic individuals compared with maltodextrin but did not affect other fermentation or metabolic markers. The change in faecal microbiome induced by dietary fibres was variable between individuals and more pronounced with the fibre mixture containing inulin compared with the β-glucan mixture.

Overall, the reported findings reinforce the need for an accurate assessment of the gut microbiome (activity and composition) to evaluate the interindividual response to dietary fibres in the context of obesity and related metabolic disorders. Microbiome changes per se, if not causally linked to clinical benefit, could hardly be proposed as a useful biomarker. Even if SCFAs are often cited as the modulators of appetite and metabolism, new metabolomic data will surely reveal other microbial-related regulators of body weight and food-related behaviour.

Cancer

A high dietary fibre intake has been repeatedly associated with lower cancer incidence[1,78,95]. This association has been consistently reported in colorectal cancer[78,96] and breast cancer[97] with a low to moderate degree of evidence. Meta-analyses have also reported the association between high dietary fibre intake and low cancer incidence in pancreatic[98], bladder[99], ovarian[100] and endometrial[101] cancers. Glioma stands out as an exception to this pattern: a combined prospective study including 1,262,104 participants followed for 15.4 million person-years did not find a negative association between higher dietary fibre intake and increased glioma risk[102]. These recent reports further reinforce the scientific relevance of the health claim made by the Food and Drug Administration (FDA) in 1993, which states that "diets low in fat and high in fibre-containing grain products, fruits, and vegetables are associated with a reduced risk of some types of cancer"[103].

The health benefits attributed to higher dietary fibre intake are often proposed to be shared by most types of fibres[1]. However, considering that dietary fibres differentially impact the gut microbiota and that the microbiota partially mediates the beneficial effect of dietary fibres on host physiology, it is questionable that all fibres would be equivalent in their ability to prevent or delay cancer. Different fibres are characterized by variable BA-binding capacity and fermentability and related SCFA profile[23,25]. There is ongoing debate about the potential role of some dietary fibres in cancer. Even though many preclinical studies have reported an antitumoural effect of inulin-type fructans[44,104–106], a few papers have indicated a pro-tumorigenic effect in susceptible mice[107,108]. In the large cohort of adults from the NutriNet-Santé study, a significant positive association was found between intake of fermentable oligosaccharides, disaccharides, monosaccharides and polyols – including resistant oligosaccharides – and the risk of cancer development[109]. These aspects support the notion that not all fibres are equivalently associated with cancer risk.

Many prospective dietary interventions, including a recommendation for high dietary fibre intake, have been performed in patients at risk of cancer, but no clinical trials have prospectively assessed the impact of specific fibres on cancer occurrence. These dietary interventions, such as the one implemented in the Polyp Prevention Trial in the USA, encouraged the adoption of a high-fibre, high-fruit, high-vegetable and low-fat regimen, in accordance with the scientific evidence supporting the 1993 FDA health claim[110]. The initial assessment of the impact of this intensive counselling revealed no influence on the risk of colorectal adenoma recurrence. However, the level of adherence by participants to this eating pattern was crucial in interpreting the data. For instance, participants who strictly adhered to the three dietary goals at all four annual visits experienced a 35% reduced risk of adenoma recurrence compared with controls[111]. Interventional trials in this area are currently limited to evaluating the impact of dietary fibres on biomarkers of colorectal cancer, mainly in healthy volunteers, which can be assessed in a much shorter time frame than cancer occurrence. For example, consuming butyrylated high-amylose maize starch for 4 weeks prevented the increase in rectal DNA adduct levels induced by a diet rich in cooked red meat in healthy human subjects[112]. Similarly, the administration of konjac glucomannan for 4 weeks reduced faecal water cytotoxicity and DNA-damaging effects in adult volunteers[113]. On the contrary, wheat bran consumption did not improve faecal water cytotoxicity and genotoxicity despite its clear impact on colonic fermentation and gut microbiota composition[114]. Similarly, high-amylose maize starch consumption for 4 weeks did not improve any of the colorectal cancer-related biomarkers[115]. These studies reinforce the conclusion that the impact of dietary fibres on cancer is probably fibre-type dependent.

Several mechanisms may explain the impact of high fibre intake on tumorigenesis in epidemiological studies. Five main mechanisms involving the gut microbiota have been reported (Fig. 4). First, fibre fermentation leads to the production of SCFAs such as butyrate, which have been largely described as antitumoural, in part through the

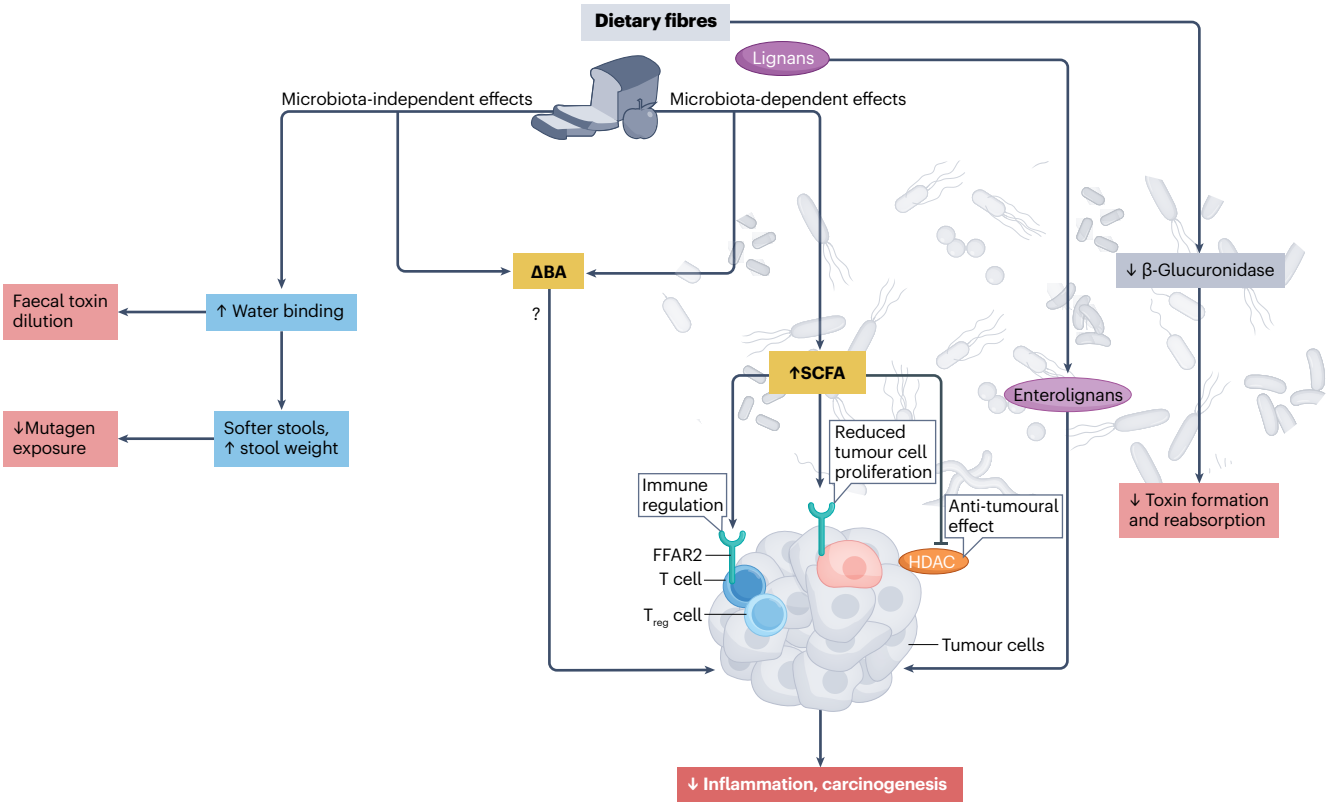


Fig. 4 | Proposed mechanisms explaining the effect of dietary fibres and associated metabolites on cancer. Dietary fibres can decrease the exposure of the host to toxins and mutagens by increasing (↑) water binding and stool weight and can also modulate the pattern of some metabolites, such as bile acids (BAs), in a gut microbiota-independent manner. Short-chain fatty acids (SCFAs) have a vital role in immune regulation by promoting the differentiation of naive T cells into effector cells and regulatory T (T_{reg}) cells and have been largely described as antitumoural through the inhibition of histone deacetylase (HDAC) activity. Some dietary fibres such as inulin-type fructans can reduce tumour cell proliferation, lessen inflammation and increase portal propionate concentration to reduce the proliferation of human cancer cells through activation of free fatty acid receptor 2 (FFAR2)[44]. By reducing the bacterial β-glucuronidase activity, some dietary fibres such as konjac glucomannan may reduce toxin formation and reabsorption[113]. Lignans linked to dietary fibres can be metabolized by bacteria into enterolignans that can influence cellular pathways in cancer cells. BAs, especially secondary ones such as deoxycholic acid, can promote tumour formation. The pattern of BAs can be modulated in both a gut microbiota-dependent and microbiota-independent manner (such as changes in BA absorption owing to viscous soluble dietary fibres). Some of these BAs can induce apoptosis in cancer cells[62]. The mechanisms shown in this figure are mainly based on experimental studies. The link that is not clearly demonstrated is indicated by a question mark.

inhibition of histone deacetylase activity and the activation of GPCR[44]. A landmark study has used gnotobiotic mouse models colonized with wild type or mutant strains of a butyrate-producing bacterium to demonstrate that dietary fibres do have a potent tumour-suppressive effect, but in a microbiota-dependent and butyrate-dependent manner[116]. Second, BAs, especially secondary ones, can promote tumour formation, as reported by a recent preprint[117]. The pattern of BAs can be modulated by dietary fibres, both through the gut microbiota[118] and independently of the gut microbiota (for example, changes in absorption by viscous soluble dietary fibres)[23,119,120]. In epidemiological studies, multiple circulating BAs have been associated with a higher risk of colorectal cancer. In the Polyp Prevention Trial, baseline circulating BAs were positively associated with adenoma recurrence, and pre-trial dietary fibre intake was inversely associated with total baseline BAs. However, the dietary intervention (a high-fibre, high-fruit, high-vegetable and low-fat regimen) of the study did not modify BA levels[121]. Third, lignans linked to dietary fibres can be metabolized by bacteria into enterolignans (enterolactone and enterodiol). Enterolignans can influence cellular pathways in cancer cells and are associated with reduced colon tumorigenesis in animal models and lower colorectal cancer risk in humans[122]. Interestingly, after receiving a flaxseed lignan supplement for 2 months, individuals with low faecal levels of enterolignans showed reduced anti-inflammatory responses in colonic mucosae biopsies, compared with those with high enterolignans levels[122]. This suggests that the production of enterolignans by the gut microbiota may modulate the outcome of a dietary lignan intervention. Fourth, some dietary fibres can reduce bacterial β-glucuronidase activity, thus decreasing toxin formation and reabsorption, limiting the risk of carcinogenesis[113]. Such an impact on bacterial β-glucuronidase activity may also alleviate the intestinal toxicity of drugs such as irinotecan, thereby fostering the maintenance and efficacy of chemotherapy[123]. Last, dietary fibre intake can promote antitumour immunity. In a mouse model of melanoma, inulin administration reduced tumour growth by promoting a shift towards a tumour microenvironment rich in T cells, which is associated with a more potent antitumour response[106]. Additionally, microbiota-independent mechanisms have also been proposed,

including dilution of faecal toxin content by increasing water binding, decreased transit time and increased stool weights, all of which reduce the exposure of colonocytes to mutagens[113,124].

Whether higher dietary fibre intake after a cancer diagnosis is associated with better survival remains poorly explored in clinical trials. An improved survival may arise from the impact of fibres on cancer progression, cancer treatment efficacy, cancer treatment toxicity and/or cancer-associated dysmetabolism. For instance, consuming dietary fibres may offer benefits during cancer treatment in terms of treatment efficacy and tolerance, considering the impact of fibres on the gut microbiota composition and function and that the gut microbiota has the ability to improve chemotherapy and immunotherapy efficacy and to alleviate drug toxicity[77,125,126].

In terms of treatment efficacy, most of the studies have focused on the impact of dietary fibres on chemotherapy. Inulin and fructo-oligosaccharides consumed in conjunction with 5-fluorouracil reduced tumour development and metastasis and increased overall survival in rat models. Similar effects were observed with various chemotherapeutic agents, including doxorubicin, vincristine, cyclophosphamide, methotrexate and cytarabine[127]. These effects may be mediated by butyrate, which enhances the cytotoxicity of anticancer drugs such as 5-fluorouracil and irinotecan[128]. Irradiation efficacy may also be promoted by dietary fibres: feeding inulin resulted in delayed tumour growth after irradiation in a mouse xenograft model[129]. Regarding immunotherapy, a baseline fibre intake above 20 g per day tended to be associated with better survival and improved response rate in patients with melanoma treated with checkpoint inhibitors[130,131]. These trends are in line with experimental work demonstrating that anti-programmed cell death protein 1 (PD1) therapy was effective at slowing down tumour growth in mice fed with a fibre-rich whole-grain diet but not in mice fed with a low-fibre diet[131], and with a report showing an association between faecal SCFA levels and PD1 inhibitors[132,133]. Conversely, SCFAs appear to limit the efficacy of anti-CTLA4 immune checkpoint inhibitors[134].

Concerning treatment tolerance, co-administration of fructo-oligosaccharides and 5-fluorouracil to rats resulted in the maintenance of intestinal integrity, reduced weight loss and decreased inflammation, suggesting an adjuvant protective effect of this fibre[135,136]. The improvement of doxorubicin side effects by pectin has been attributed to a direct, microbiota-independent inhibition of Toll-like receptor 2 (TLR2)[137,138].

Cancer-associated cachexia or sarcopenia reduces the likelihood of survival in many types of cancer[139]. Cachexia has been defined as a "multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without fat mass loss) that can be partially but not entirely reversed by conventional nutritional support" (ref. 140). Cachexia results from a combination of lower food intake, metabolic changes and inflammation[139,141], and it has also been associated with microbial dysbiosis, gut barrier dysfunction and altered gut bacterial metabolism in preclinical and clinical studies[142–148]. We previously showed that administration of pecto-oligosaccharides reduced anorexia and fat mass loss in cachectic mice[149]. Whether dietary fibres would benefit patients with cancer by modulating their gut microbiota, gut barrier function and inflammation, and associated dysmetabolism remains to be established in human trials.

A high dietary fibre intake, as recommended by the World Cancer Research Fund–American Institute for Cancer Research (WCRF–AICR) may be of help to cancer survivors[124]. In a prospective cohort of 456 individuals who survived colorectal cancer, increasing dietary fibre, fruit and vegetable intake was associated with better physical function and ability to perform daily activities, as well as less fatigue in the first 2 years after the end of treatment[150]. However, adherence to this higher fibre intake recommendation among cancer survivors was low, as shown by a meta-analysis reporting that high fibre intake was one of the recommendations that cancer survivors were least likely to follow[151]. Future studies will have to determine whether the barriers to higher dietary fibre intake in this population are like those faced by the general population.

In summary, although epidemiological studies clearly show that high dietary fibre intake is strongly associated with a reduced occurrence of many cancer types, determining the impact of specific fibres on cancer risk and cancer therapy efficacy, toxicity and cachexia deserves further exploration. To address this knowledge gap, future epidemiological and interventional studies will need to consider the type of dietary fibres, a type of information currently hard to retrieve, and the characteristics of an individual, including the gut microbiome.

Conclusions and perspectives

Dietary fibres are a heterogeneous class of nutrients, and their interaction with the gut microbiome is an undervalued mechanism of their protective role in obesity-related disorders and cancer in humans. The complexity and specificity of interactions between the different types of dietary fibres and the gut microbiome may explain interindividual and interstudy variability in response to dietary fibre interventions. A personalized approach, namely based on gut microbiome assessment, could be elaborated to revise the dietary recommendation in dietary fibres.

The causal role of the gut microbiome in health effects mediated by fermentable dietary fibres is a topic of debate. To determine causal components (taxa, metabolites and so on) within the gut microbiota that are responsible for the physiological effects of dietary fibres, disposing of human intervention trials with strong correlations between the gut microbiome (taxonomic and functional sides) and biological outcomes is the first but not sufficient step[152]. Modern statistical approaches (such as mediation analysis) are needed to infer causality. Complementary gnotobiotic animal studies that recapitulate keystone bacteria prone to interact with dietary fibres, along with experiments comparing the effects of microbial-derived metabolites to placebo, can offer mechanistic evidence of how certain components of the gut microbiome, modulated by dietary fibres, can causally impact host physiology.

The cost and the complexity of microbiome data interpretation can hinder large-scale initiatives in the field, but the policy of open science for database access can help bypass the problem. Another important message of this Review is the need to explore the role of intrinsic edible sources of dietary fibres compared with isolated fibres in microbiome-targeted nutrition. The relevance of dietary fibre variety in managing gut microbial diversity remains debatable, in view of the impact of specific dietary fibres on microbial ecology, which can promote the growth of some genera over others, thereby decreasing α-diversity.

Providing sufficient intake of dietary fibres for good health and 'feeding' the gut microbiome adequately while considering global health are linked challenges. Plant-based food is the main source of dietary fibres and constitutes the major food product for planetary health. Purified dietary fibres also offers opportunities. Some technological developments allow for the use of waste as a source of edible nutrients. Examples are pecto-oligosaccharides produced from

avocado byproducts, lemon peel, orange peel or sugar beet pulp, and arabinoxylans extracted from agricultural and food waste[153,154].

Future research and developments should concentrate on sustainable ways to promote fibre-rich food available for all, to prevent and combat chronic diseases worldwide. Consensual guidelines for food-based qualitative and quantitative dietary fibre intake recommendations should be elaborated, considering the potency of their interaction with the gut microbiome leading to the production of beneficial bioactive compounds in the gut.

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N.M.D. led the work (content, writing and discussion). All authors researched data for the article, contributed to the discussion of the content, and reviewed and/or edited the manuscript before submission.

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The authors declare no competing interests.

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