Impact of whole grains on the gut microbiota: the next frontier for oats?

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(Submitted 7 October 2013 – Final revision received 18 March 2014 – Accepted 6 May 2014)

Abstract
The gut microbiota plays important roles in proper gut function and can contribute to or help prevent disease. Whole grains, including oats, constitute important sources of nutrients for the gut microbiota and contribute to a healthy gut microbiome. In particular, whole grains provide NSP and resistant starch, unsaturated TAG and complex lipids, and phenolics. The composition of these constituents is unique in oats compared with other whole grains. Therefore, oats may contribute distinctive effects on gut health relative to other grains. Studies designed to determine these effects may uncover new human-health benefits of oat consumption.

Key words: Bacteria; Prebiotic; Health; SCFA

The role that human colonic bacteria, or the gut microbiota, plays in health and disease is an area of research with intense current interest that is fuelled by provocative reports suggesting that the gut microbiota plays a role in many diseases that plague the modern society, including obesity, diabetes and colorectal cancer.[1] Diet plays an important, albeit incompletely understood, role in maintaining healthy gut–microbiota interactions.[2] While a wealth of research has focused on prebiotics and isolated dietary fibres and their contribution to gut health,[3] little research has been conducted on how dietary fibres and other constituents from whole-food matrices affect the gut microbiota.

Whole grains, for instance, are rich sources of dietary fibres and other bioactive compounds[4,5] that may modulate the gut microbiota and thereby impact on consumer health.[6,7] In particular, oats may contribute specialised influences on the gut microbiota in comparison with other grains. Although most cereals contain very little soluble dietary fibre, oats contain high levels of soluble fibre in the form of mixed linkage (1→3),(1→4)-β-D-glucan (hereafter, β-glucan).[8] Oats also contain the highest lipid content among the major grains together with potential bioactives[9,10]. This article discusses the effects of whole grains on gut health and then highlights some of the unique aspects of oats that may contribute to enhanced gut health.

Influence of whole grains on the gut microbiota

Although the principal non-digestible components in whole grains are cross-linked arabinoxylan and cellulose (see online supplementary Table S1) – substrates that are generally considered poor for gut microbial fermentation – whole grains have the potential to play an important role in maintaining a healthy gut microbiota. Two human trials have suggested a bifidogenic effect from the consumption of whole-grain cereals.[6,7] Some strains of Bifidobacterium have been reported in the literature as markers of a healthy gut microbiota.[3] Other studies have shown increases in butyrate-producing bacteria, including Roseburia, Eubacterium rectale and the Clostridium leptum group (which includes Faecalibacterium prausnitzii).[11,12] Butyrate is an important metabolite of gut microbial fermentation of carbohydrates for its contribution to host colonic epithelial cell energy, anti-inflammatory properties and anti-cancer effects.[13] Whole grains have been shown to decrease protein fermentation by the gut microbiota[14]. Protein fermentation is associated with undesirable fermentation metabolites and detrimental effects on the host.[15] Whole grains may also increase the diversity of the microbiota[12], a potential benefit considering that reduced diversity is associated with obesity and disease.[16,17] Notably, consumption of many purified dietary fibres has not been shown to increase diversity.[18,19]

The beneficial effects of whole grains on health are likely to be a combined result of many components within the grain rather than one specific component[5]. Three components of whole grains that are likely to impact the gut microbiota with trophic effects on the host are discussed later.

Dietary fibre

The insoluble, NSP in cereals have long been recognised for their faecal bulking properties and reduction in gastrointestinal

Abbreviation: RS, resistant starch.

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transit time\(^{(20)}\). These effects may be particularly important for older adults, who typically consume less dietary fibre and have reduced gastric motility\(^{(21)}\). However, because of their poor utilisation by colonic bacteria, the impact of NSP on the gut microbiota is often overlooked. The poorly fermentable, dietary fibres in whole grains contribute to reduced distal colonic pH and higher faecal butyrate concentrations\(^{(22,23)}\). This is likely because the poor fermentation of the NSP allows it to persist into the distal colon and provide some carbohydrate substrate for gut bacterial metabolism in this region, a characteristic not attributable to most soluble and highly fermentable dietary fibres. Such conditions are consistent with reduced inflammation and carcinoma development\(^{(13,24)}\).

In addition to the principal NSP in whole grains, they also contain water-extractable arabinoxylan and mixed-linkage β-glucan (see online supplementary Table S1). The extent of fermentation and the types of bacteria that are favoured with these polymers depend on solubility, monosaccharide composition, presence of non-carbohydrate moieties, molecular weight and glycosidic linkages\(^{(25,26)}\). Viscosity was reported to affect the types of bacterial groups that are enriched with β-glucan\(^{(27)}\), although because the viscous property of β-glucan is rapidly lost upon contact with gut bacteria\(^{(28)}\) it is likely that these differences were due to molecular weight rather than viscosity. Fermentation of isolated water-extractable arabinoxylan and β-glucan by human intestinal bacteria \textit{in vitro} is generally associated with an enrichment in propionate production compared with other dietary fibres\(^{(25,29–34)}\). Important propionate producers in the gut microbiota are members of clostridial cluster IX and \textit{Bacteroides} \(^{(35)}\). Neither one of these polysaccharides is particularly bifidogenic, although bifidogenicity increases when partially hydrolysed\(^{(25,36)}\).

Whole grains also contain widely varying quantities of resistant starch (RS), depending on the types of grain used and product and processing conditions\(^{(37)}\). RS has received considerable attention in recent years for its influence on the gut microbiota and subsequent impacts on the host\(^{(180)}\). Even though the exact content type of RS in most whole-grain foods is fairly modest (typically 1–3\%)\(^{(37)}\), this may still have a positive impact on health. For instance, in subjects who consumed whole-wheat or wheat-bran cereals, a bifidogenic effect was only observed in the whole-wheat cereal\(^{(6)}\). The difference between the two cereals was mainly the starch content. This suggests that the prebiotic effect of the whole-grain cereals could have been at least partially a result of RS fermentation, as RS has shown prebiotic properties\(^{(180)}\). Furthermore, RS is also particularly butyrogenic, and in an \textit{in vitro} trial, Costabile \textit{et al.} \(^{(6)}\) found greater butyrate production when the whole-grain wheat cereal was fermented with faecal bacteria compared with the wheat-bran cereal.

Finally, whole grains contain about 0.1–1\% α-galactosyl derivatives of sucrose (mainly raffinose and stachyose) and 0.3–4\% β-fructosyl derivatives of sucrose (referred to as fructan; see online supplementary Table S1). These carbohydrates are generally located in the outer portions of the grain, with raffinose and stachyose concentrated in the germ\(^{(5)}\). Although their content in grain products is fairly low compared with some other plants, the prevalence of grain-based foods in the diet makes them an important dietary source of these carbohydrates\(^{(38)}\). Raffinose and stachyose are rapidly fermentable and bifidogenic\(^{(5)}\). These carbohydrates also possess several health benefits\(^{(39)}\). When consumed as isolated ingredients, they can cause bloating, flatulence and, at very high intakes, diarrhoea\(^{(40)}\); however, these high intakes are not likely to be achieved through whole-grain consumption. The fructans in whole grains contain an average degree of polymerisation of four to six with few oligomers containing more than nine degrees of polymerisation\(^{(40)}\). Furthermore, fructans in whole grains contain branched structures with both (2 → 1) and (2 → 6) β-fructosyl linkages\(^{(41)}\). No studies have isolated fructans from any whole grain and determined its fermentation properties; however, short-chain fructan oligomers are generally rapidly fermented by gut bacteria and highly bifidogenic\(^{(5)}\). Several reviews have demonstrated the positive impact that fructans impart on human health\(^{(42,43)}\).

**Lipids**

Evidence in mice has suggested that diets high in fat in the form of bulk lipids (predominantly TAG) have a detrimental effect on the gut microbiota and host metabolic parameters\(^{(44)}\). In particular, diets high in saturated fats have been shown to decrease proportions of beneficial bacteria\(^{(45)}\) and decrease microbial diversity\(^{(46)}\). de Wit \textit{et al.}\(^{(46)}\) suggested that saturated fats were especially detrimental to the gut microbiota because they persisted into the distal small intestine where they exhibited an antimicrobial effect (and consequently reduced diversity). Whole grains are comparatively low in fat, and the fat that they do contain is highly unsaturated.

Whole-grain lipids themselves may also more directly affect the gut microbiota with subsequent influences on health. For instance, hamsters fed diets supplemented with up to 5\% wholegrain sorghum lipids showed significantly increased Bifidobacteria and decreased Coriobacteriaceae in the faeces\(^{(47)}\). Bifidobacteria concentration was positively correlated with plasma HDL-concentration, while Coriobacteriaceae were positively correlated with non-HDL-cholesterol and cholesterol absorption. In another study\(^{(48)}\), rice bran oil incorporated into the diets of mice increased bile acids in the faeces with accompanying positive correlations with the family Lactobacillales (which contains lactic acid bacteria). Martínez \textit{et al.}\(^{(49)}\) theorised that this was due to the sterol esters in the lipid extract (about 10\%). When hamsters were fed purified steryl esters, cholesterol absorption decreased, which led to an increase in the cholesterol pool in the gut and a decrease in Coriobacteriaceae and Erysipelotrichaceae. These two families have shown positive correlations with the deleterious host lipid parameters\(^{(37,50)}\). Whole grains are rich sources of plant sterol esters in comparison with other foods\(^{(51)}\). In addition, other lipid components of grains, for example the policosanols, may also affect the gut microbiota, although this remains to be determined.

**Phenolics**

The majority of the antioxidants in whole grains are bound to dietary fibre components, precluding their absorption in the
upper gastrointestinal tract\(^{(52)}\). However, microbial-derived esterases in the lower gastrointestinal tract can release a portion of these compounds from their dietary fibre conjugates, whereupon they are rapidly metabolised. Ferulic acid, the major phenolic acid in whole grains, for instance, is first hydrogenated at the double bond on the propen-2-0ic acid side chain followed by demethylation of the ring diethy ether. Subsequently, this metabolite, 3,4-dihydroxyphenylpropionic acid, is dehydroxylated to 3-hydroxyphenylpropionic acid and phenylpropionic acid\(^{(53)}\). Dimers and oligomers of ferulic acid are also present in whole grains and metabolised either by direct modification of the functional groups or by deconjugation and metabolism as monomers\(^{(54)}\). These metabolites may impart beneficial biological activity\(^{(55)}\), although there are still many questions regarding the effective dose, bioavailability and pharmacokinetics of these compounds in humans.

While microbial esterases are effective at removing a variable portion of bound phenolics, which depends on many factors\(^{(53)}\), many phenolics are still not biologically available\(^{(56)}\). However, the physical presence of high concentrations of bound phenolic antioxidants in the gastrointestinal tract may itself impart several benefits. While the body contains natural defence mechanisms against free radical oxidation, the lumen of the gastrointestinal tract is not protected to the same extent. Furthermore, under some circumstances, such as during inflammation, neutrophils produce free radicals (e.g. HNO\(_3\)) that can lead to mucosal oxidative stress, peroxidation of membrane lipids and tissue damage\(^{(57,58)}\). The presence of bound antioxidants in the lumen, such as those in whole grains, may protect the intestinal epithelium from free radical damage\(^{(56)}\). This is supported by studies showing that the physical presence of ferulic acid in the lumen of the large intestine, administered via enema, leads to reduced inflammation in inflammatory bowel disease patients\(^{(59)}\).

**What about oats?**

As with other whole grains, in vitro trials on the effects of oats on markers of gut health are sparse (see online supplementary Table S2). There are comparatively more in vitro studies; however, the data are far from comprehensive and in many cases conflicting (see online supplementary Table S3). Nevertheless, as mentioned, oats contain a unique chemical composition compared with other grains. The most prevalent differences are in the dietary-fibre composition, the lipid content and the types of phenolics. Because these three fundamental components are likely to have strong effects on the gut microbiota, as discussed, oats are likely to impact the gut microbiota in unique ways compared with other cereal grains. Studies aimed at elucidating these effects may help researchers further establish the mechanisms behind the health benefits of oats, and help breeders and food companies create oats and oat products that maximise the health benefits derived from this grain.

**Dietary fibre**

The high content of \(\beta\)-glucan is the most unique dietary fibre component in oats. While the viscous property of \(\beta\)-glucan is rapidly diminished once \(\beta\)-glucan is exposed to microbial metabolism in the large bowel\(^{(20)}\), fermentation of \(\beta\)-glucan by some gut microbes may play a role in the effects of whole-grain oats and barley on heart diseases. For instance, as mentioned, fermentation of isolated \(\beta\)-glucan generally enhances the production propionate by the gut microbiota\(^{(25,31,55)}\), and studies suggest that propionate may help reduce serum cholesterol\(^{(60)}\). \(\beta\)-Glucan may also contribute to reduced colonic pH compared with other cereals containing less soluble (and fermentable) dietary fibres\(^{(61)}\).

RS content of oats may be an important contributor to its effects on gut health. Connolly et al\(^{(62)}\) studied the differences in in vitro fermentation properties between thin and thick oat flakes (rolled oats). The thick oat flakes resulted in a significant increase in *Bifidobacterium* during fermentation compared with the baseline; this was not observed in the thin oat flakes. Moreover, the thick oat flakes resulted in 2-5 times more butyrate than the thin oat flakes. The authors suggested that the bifidogenic effect and the enhanced butyrate production in the presence of thick oat flakes were results of higher RS in these samples compared with the thin oat flakes. This was supported by another study where oat flours were subjected to in vitro digestion to remove digestive components before faecal fermentation; however, the residue still contained about 15% starch\(^{(63)}\). The subsequent fermentation resulted in an acetate–propionate–butyrate ratio of about 42:24:35, which is typical of starch-containing preparations\(^{(64)}\). High \(\beta\)-glucan in oat and barley cereals has been shown to reduce starch digestion in the small intestine due to its viscosity\(^{(65)}\). Thus, it is possible that oats and barley products contain higher RS than products from other grains because the starch digestion rate may be sufficiently slow as to allow a greater portion of starch to remain intact and reach the colon\(^{(60)}\).

In spite of their similarities in dietary fibre composition, oats and barley seem to induce different effects on the gut microbiota. For example, pigs consuming an oat-based diet showed significantly greater increases in bifidobacteria compared with pigs consuming a barley-based diet\(^{(67)}\). Another study by the same group showed a greater bifidogenic effect on an oat-based diet compared with a wheat-based diet that was supplemented with \(\beta\)-glucan such that the two diets had a similar \(\beta\)-glucan content\(^{(68)}\). The different influences that oats and barley have on the gut microbiota may be due to differences in the structures and molecular weight of \(\beta\)-glucan or other polysaccharides, as well as differences in non-dietary fibre components.

**Lipids**

Although lipid components from whole grains affect the gut microbiota, more research is needed to describe such effects in detail. No studies have demonstrated the effects of isolated oat lipids on the gut microbiota. In the studies cited earlier, plant sterols may affect changes in the gut microbiota with positive impacts on health. Oats contain moderate concentrations of sterols (329–520 mg/kg): lower than wheat and rye (603–715 and 910–1100 mg/kg, respectively), but higher than rice and sorghum (216–401 and 200–350 mg/kg, respectively)\(^{(51,69,70)}\).
Phenolics

While the majority of phenolics in oats are bound ferulic acid, which is similar to other whole grains, oats also contain some unique phenolics including avenacosylates, avenacins and avenanthramides. Avenacosylates are esters of ferulic or caffeic acid with a long-chain wax alcohol (policosanol) and are present in oats at about 50–200 mg ferulic acid equivalents/kg\(^2\). The avenacins are pentacyclic triterpene alcohol glycosides containing esters of aminophenolic or benzoic acid\(^9\). Avenanthramides are conjugates of a phenylpropanoid with anthranilic acid or 5-hydroxy anthranilic acid and are present in oats in widely varying concentrations similar to the avenacosylates\(^9\). It is likely that these compounds are metabolised by the gut microbiota, but this has not been reported in detail\(^7\). Some data suggest that they may function as anti-inflammatory molecules and protect the gut mucosa by modulating NF-κB activation\(^7\).

Conclusions

Whole-grain dietary fibres, despite being poorly fermented in many cases, are the major contributors to distal colonic fermentation\(^2\) which results in a decrease in pH and potentially reduces the risk of some gastrointestinal diseases\(^7\). Furthermore, RS may be a significant contributor to the benefits of whole grains\(^6\) and could be responsible for the bifidogenic effect of whole-grain cereals previously reported\(^6\). Other constituents in whole grains that are often ignored in relation to gut health, namely the lipids and phenolic constituents, may also contribute to gut health\(^4\)\(^5\).

Oats are a unique whole grain that may contribute distinctive effects on the gut microbiota. These effects could be due to the high β-glucan content, the high lipid content or the unique antioxidant profile. β-Glucan fermentation could contribute to the hypcholesterolaemic properties of oats\(^2\). Furthermore, β-glucan may slow the rate of starch digestion and help increase the RS content of oats relative to other grains that are low in β-glucan\(^6\)\(^7\). Oat lipids and antioxidants have not been studied in relation to gut health, but research in other whole grains suggests that they influence the types of bacteria that make up the microbiota and impact on host health\(^4\)\(^7\)\(^8\)\(^9\). The microbiota and gut health are at the intersection of emerging research, particularly when considering the demonstrated and possible health implications of whole grains and dietary fibre that are identified in oats.

Supplementary material

To view supplementary material for this article, please visit http://dx.doi.org/10.1017/S0007114514002244

Acknowledgements

D. J. R. received an honorarium from Quaker Oats Company (a subsidiary of PepsiCo, Inc.) for attending a workshop in May 2012 to discuss the content of the supplement, and University of Nebraska received an unrestricted grant from Quaker Oats Company.

This paper was published as part of a supplement to British Journal of Nutrition, publication of which was supported by an unrestricted educational grant from Quaker Oats Co. (a subsidiary of PepsiCo Inc.). The papers included in this supplement were invited by the Guest Editor and have undergone the standard journal formal review process. They may be cited.

The Guest Editor to this supplement is Roger Clemens. The Guest Editor declares no conflict of interest.

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