The benefits of dietary fiber on inflammatory bowel disease may be related to the fermentative production of butyrate in the colon, which appears to decrease the inflammatory response. The benefits of dietary fiber against colon cancer may be related to both fermentative and non-fermentative processes, although poorly fermentable fibers appear more influential. Dietary fiber fermentation profiles are important in determining optimal fibers for colonic health, and may be a function of structure, processing conditions, and other food components. A greater understanding of the relationships between fermentation rate and dietary fiber structure would allow for development of dietary fibers for optimum colonic health.

Key words: butyrate, Crohn’s disease, microbiota, short chain fatty-acids, ulcerative colitis

INTRODUCTION

Originally, the benefits of dietary fiber were thought to be limited to providing fecal bulk and laxation. Today, it is recognized that dietary fiber plays a role in numerous physiological functions, as well as in the prevention and treatment of certain diseases.

The discovery of these roles of dietary fiber in human health prompted the Food and Nutrition Board (FNB) of the Institute of Medicine (IOM) to include recommendations for dietary fiber in the new Dietary Reference Intakes (DRIs). Adequate intake for dietary fiber was set at 38 and 25 g/d (14 g/1000 kcal) for adult men and women, respectively. This recommendation was based on the minimum amount of fiber required to have a positive impact on health and disease. Current data suggest that an adequate amount of daily dietary fiber reduces the risk of coronary heart disease, prevents constipation and diverticular disease, provides energy for colonic bacteria, provides satiety, and attenuates blood glucose and lipid levels. In the United States, 25 g of dietary fiber daily has been used when calculating percent Daily Value (% DV) for nutrition labels based on a 2000 kcal/d diet, as outlined by the Nutrition Labeling and Education Act. These values are slightly lower (~3 g/1000 kcal) than the DRIs.

Studies have shown that the average diet in the United States falls substantially short of these recommendations. For example, in the Continuing Survey of Food Intakes by Individuals (1994–1996, 1998), mean intakes of dietary fiber were 18.4 and 13.7 g/d, respectively, for men and women (not including pregnant or lactating) aged 31 to 50 years. Indeed, less than 5% of respondents consumed at least the recommended amount of fiber described above. The consequences of consuming a diet low in fiber cannot be ignored. Low-fiber diets have been associated with heart disease, type 2 diabetes, inflammatory bowel disease (IBD), and certain types of cancer. This article will focus on IBD and colon cancer.

IBD includes both ulcerative colitis and Crohn’s disease, and is characterized by a chronic inflammation of the gut with a waxing and waning course. The incidence of IBD has increased steadily in some areas of the world over the past 40 years. This may be due to changes in dietary habits, particularly the consumption of diets low in fiber content in recent years. Further studies are needed to determine whether there is any direct correlation between dietary fiber and incidence (disease pattern and course) of IBD.

Colon cancer is a consequence of a series of genetic mutations that result in the transformation of a normal
epithelial cell into a cancerous cell.\textsuperscript{12} According to the Annual Report to the Nation on the Status of Cancer,\textsuperscript{14} colon cancer is the third most common type of cancer in both incidence and mortality. The authors of that report concluded that the long-term goals of cancer research should be focused, in part, on ways to prevent the onset of cancer. One effective means of achieving this goal is to identify the factors responsible for the initiation of mutagenesis and carcinogenesis. Dietary factors such as dietary fiber may cause or contribute to (in susceptible subjects) genetic mutation (mutagenesis). These factors can also influence the effects of genetic mutation on epithelial cells, thus modifying the rate and extent of epithelial cell transformation into cancerous cells.

The purposes of this review are to discuss the role of dietary fiber as it relates to IBD and colon cancer, and to explore how this knowledge may be applied to the development of fibers that target the prevention and/or treatment of these diseases.

**PHYSIOLOGICAL ROLES OF DIETARY FIBER**

The benefits of dietary fiber on human health can be divided into two categories: non-fermentative and fermentative (Table 1). Non-fermentative effects are due to the dietary fiber itself. For example, many dietary fibers can bind bile acids and increase their excretion in the feces.\textsuperscript{15} This interrupts normal enterohepatic circulation, thus increasing the amount of cholesterol the body must devote to bile acid production. This can lower serum cholesterol levels in a manner analogous to bile acid sequestrant drugs, such as cholestyramine or colestipol. This is one mechanism whereby dietary fiber may exhibit a protective role against cardiovascular disease.\textsuperscript{4}

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Physiological Response</th>
<th>Physiological Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-fermentative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased fecal bulk</td>
<td>Increased fecal output</td>
<td>Dilution of carcinogens and other toxins in the colon</td>
</tr>
<tr>
<td>Decreased colonic transit time</td>
<td>Increased frequency of defecation</td>
<td>Decreased contact time of carcinogens and toxins with colonic epithelium</td>
</tr>
<tr>
<td>Carcinogen binding</td>
<td>Excretion of carcinogens in the feces</td>
<td>Decreased contact time of carcinogens and toxins with colonic epithelium</td>
</tr>
<tr>
<td>Bile salt binding</td>
<td>• Decreased resorption of bile salts</td>
<td>• Increased requirement for cholesterol and decrease in blood cholesterol</td>
</tr>
<tr>
<td></td>
<td>• Decreased conversion of primary bile acids to secondary bile acids</td>
<td>• Decreased levels of secondary bile acids (co-carcinogens) in the colon</td>
</tr>
<tr>
<td>Increased digesta viscosity</td>
<td>Decreased rate of glucose absorption in the small intestine</td>
<td>Decreased postprandial blood glucose response</td>
</tr>
<tr>
<td><strong>Fermentative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Production of short-chain fatty acids</td>
<td>Decreased colonic pH</td>
<td>• Decreased growth of harmful bacteria in the colon</td>
</tr>
<tr>
<td></td>
<td>• Decreased activity of glucuronidase, glycosidase, and 7α-hydroxylase (involved in bile acid metabolism)</td>
<td>• Decreased inflammatory response</td>
</tr>
<tr>
<td></td>
<td>• Increased mineral absorption</td>
<td>• Decrease pro-inflammatory cytokine secretion (decreased inflammatory response)</td>
</tr>
<tr>
<td>Production of butyrate</td>
<td>• Decreased production of pro-inflammatory cytokines</td>
<td>• Decrease inducible nitric oxide synthase activity (decreased inflammatory response)</td>
</tr>
<tr>
<td></td>
<td>• Inhibition of nuclear factor-κB activation</td>
<td>• Decrease expression of vascular cell adhesion molecule-1 and intracellular cell adhesion molecule-1 (decreased inflammatory response)</td>
</tr>
<tr>
<td></td>
<td>• Enhanced production of peroxisome proliferator-activated receptors</td>
<td>• Decreased inflammatory response</td>
</tr>
</tbody>
</table>
Some benefits of dietary fiber appear to be unrelated to the fiber itself, arising from metabolic products of fermentation. When dietary fiber reaches the colon, it can be fermented to different degrees by colonic bacteria, the microbiota. These bacteria produce enzymes that are capable of breaking down glycosidic and other chemical bonds that are not digested in the upper portion of the gastrointestinal (GI) tract. The products of fermentation are short-chain fatty acids (SCFA), mainly acetate, propionate, and butyrate; gases; and other metabolites (lactate, pyruvate, ethanol, etc.), all of which have physiological functions (Table 1). Thus, dietary fibers can influence intestinal physiology and pathology through both their direct (non-fermentative) and indirect (their metabolic products, fermentative) effects on epithelial cells; therefore, the effect of fiber on colonic diseases depends on the type of fiber (solubility, fermentability) and patient characteristics (microbiota).

COLON DISORDERS

Inflammatory Bowel Disease

The benefits of dietary fiber on IBD appear to be related to the production of butyrate from the metabolism of SCFA by bacteria in the colon. These SCFA are an important energy source for colonicocytes. SCFA also exert trophic effects on the colon, stimulate water and electrolyte absorption, and increase colonic blood flow. SCFA and/or dietary fiber may also be important in the maintenance of the integrity of colonic barrier function.17,18

Of the SCFA produced during fermentation, butyrate has received considerable attention due to its possible influence on the inflammatory response. In a normal physiological state, nuclear factor κB (NF-κB) is bound to an inhibitory binding protein, inhibitory κB (IkB), and is inactive in the cytoplasm. During pathological states, NF-κB is activated by degradation of IkB. Once activated, NF-κB translocates from the cytoplasm to the nucleus of the cell and mediates the expression of various pro-inflammatory cytokines, initiating the inflammatory cascade.19,20 In vitro studies have revealed that butyrate suppresses the immune response by inhibiting NF-κB activation, and patients treated with butyrate enemas have shown decreased inflammation related to a reduction in the number of macrophages positive for NF-κB.22

Although most research surrounding dietary fiber and IBD has focused on ulcerative colitis, the mechanism of butyrate-induced suppression of NF-κB activation is likely to play an important role in the alleviation of Crohn’s disease as well.23

Unfortunately, patients with the greatest need for the anti-inflammatory effects of butyrate may be the least able to derive its benefits. Studies have reported lower butyrate concentrations in colons of patients with ulcerative colitis compared with healthy individuals.24 In addition, researchers have found impaired butyrate oxidation and utilization by colonicocytes obtained from patients with ulcerative colitis.25

Since SCFA are believed to be a major nutrient source for the colon, it is reasonable to assume that the loss of this nutrient source may be detrimental to colonicocyte viability. This concept was first demonstrated in patients who developed inflammation in the rectal remnant after surgical diversion of the fecal stream (diversion colitis).26 Four patients with diversion colitis responded to treatment with irrigation of the rectal remnant with an SCFA enema for 2 to 3 weeks. Because of the endoscopic and histological similarities between diversion colitis and ulcerative colitis, Scheppach et al.27 treated 10 patients with active left-sided ulcerative colitis with butyrate enemas for 2 weeks and found a 90% endoscopic and a 70% histologic improvement. This is similar to therapy with topical 5-aminosalicylate treatment (enema) and superior to therapy with topical steroid enemas. The authors felt that by delivering a concentrated amount of butyrate to the inflamed mucosa, the impaired butyrate metabolism previously noted in the colonic mucosa of patients with ulcerative colitis could be overcome, with resultant improvement in the inflammatory condition.27

Not all studies evaluating the efficacy of SCFA enemas in distal colitis have shown efficacy. In a large, multicenter, randomized, controlled trial, Bruer et al.28 failed to demonstrate significant improvement in patients with distal ulcerative colitis given twice daily SCFA enemas for a period of 6 weeks. The authors pointed out that the patients randomized to SCFA therapy demonstrated positive trends in every component of their clinical and histologic activity scores, and speculated that lack of compliance with and retention of the enemas may have negatively impacted the results. A subgroup analysis suggested that patients with a shorter duration of disease might benefit most from this therapy.28

Considering the evidence that butyrate is an important factor in regulating inflammation, a carbohydrate oral delivery that is metabolized by gut microbiota to butyrate might help alleviate colonic inflammation. Kaunachi et al.29 evaluated the effect of germinated barley foodstuff (GBF) on clinical symptoms and mucosal injury in a dextran sodium sulfate-induced rat model of colitis. GBF more effectively prevented bloody diarrhea and mucosal damage compared with control rats and those receiving sulfasalazine. Higher levels of butyrate were also found in the cecal contents of rats receiving GBF, and the authors speculated that this SCFA may be
instrumental in guarding against the dextran sodium sulfate-induced damage.\(^{29}\) In a pilot, open-labeled (non-placebo), uncontrolled study,\(^{30}\) the beneficial effects of GBF were evaluated in 10 patients with ulcerative colitis. Most patients had left-sided disease, and their disease activity was considered mild to moderate but refractory to conventional therapy. Anti-inflammatory medication was continued while adding 30 g of GBF daily for 4 weeks. The authors were able to demonstrate a significant clinical and endoscopic improvement in this small cohort of patients that was independent of the extent of disease. The authors reported that patients experienced an exacerbation of the disease 4 weeks after stopping GBF in spite of continuation of standard ulcerative colitis drugs.\(^{30}\) In another study,\(^{31}\) the efficacy of GBF in the treatment of mild to moderate ulcerative colitis was evaluated in a multicenter, randomized, open-labeled, controlled, clinical trial. Eighteen patients were randomized into a GBF group, who received GBF plus their standard anti-inflammatory therapy, or a standard therapy group, who only received their regular anti-inflammatory therapy. There was a significant decrease in the disease activity index at 4 weeks in the GBF group compared with the group receiving standard therapy. These authors suggested the possible contribution of butyrate to this improvement, but also cited a prebiotic effect of GBF leading to a “favorable change in [microbiota]” and further reported a significant water-holding capacity of GBF, which may moderate diarrhea.\(^{31}\)

Clinical trials have shown that other dietary fiber supplements can play a role in the treatment of IBD. Hallert et al.\(^{32}\) administered either psyllium husks or placebo for 4 months to patients with ulcerative colitis in remission. During the treatment, GI symptoms including abdominal pain, diarrhea, loose stools, urgency, bloating, incomplete evacuation, mucus, and constipation were recorded via questionnaire. Both treatments resulted in improvement of symptoms compared with baseline; however, 69% of those in the psyllium group reported fewer symptoms compared with 24% in the placebo group.\(^{32}\) In a related study,\(^{33}\) 102 patients with ulcerative colitis in remission were randomized to receive mesalazine alone, psyllium seeds alone, or a combination of mesalazine and psyllium seeds. The primary end point was maintenance of remission for 12 months. The authors found increased fecal butyrate concentrations in the patients given the fiber seeds, and found no significant differences between the three groups for maintenance of remission. This means that psyllium was as effective as mesalazine, although there was a significant drop-out rate in this study: approximately one-third of the patients in each group.\(^{33}\) A similar trial was undertaken to evaluate the effects of oat bran in patients with quiescent ulcerative colitis.\(^{34}\) The authors’ primary aim was to increase the levels of SCFA in the stools of these patients. Stool butyrate concentrations were significantly increased after both 4 and 14 weeks; however, there was no relapse of the underlying colitis in either the supplemented or the control group. There were more nonspecific GI complaints in the supplemented group that were believed to be due to the fiber supplement, but these improved by the end of the study.\(^{34}\)

Current research regarding the effects of dietary fiber and butyrate production on the inflammation of ulcerative colitis is promising but not definitive. Conflicting results may be due, at least in part, to our limited understanding of the effects of fibers on intestinal epithelial function, the intestinal immune system, and intestinal microbiota. In addition, fermentation reactions, even in healthy individuals, are not constant throughout the colon (Table 2). Butyrate levels decline as carbohydrates are metabolized, and the production of phenolic compounds, branched chain fatty acids, and ammonia is increased.\(^{35}\) Finally, the microbiota in many patients with IBD may be abnormal (dysbiosis), and thus the final products of fiber metabolism may differ from those in healthy subjects. Therefore, it appears that reproducible delivery of beneficial fermentable dietary fiber to the site of inflammation, depending on the disease type and disease extent, requires specific fibers designed to target a specific region of the colon. This “designer” fiber

| Table 2. Conditions in the Right (Proximal) and Left (Distal) Colon\(^35\) |
|---------------------------------------------|-----------------|-----------------|
|                                     | Right | Left      |
| Fermentation rate                      | High  | Low      |
| Fermentable carbohydrates               | High  | Low      |
| SCFA                                    | High  | Low      |
| \(H_2\)                                 | High  | Low      |
| Methane                                 | Low   | High*    |
| Ammonia                                 | Low   | High     |
| Total phenolic compounds                | Low   | High†    |
| Specific phenolic compounds             | Higher in phenolic acids | Higher in phenol and \(p\)-cresol |
| pH‡                                     | Lower | Higher   |
| Metabolites                             | Higher in electron sink metabolites (lactic, pyruvate, ethanol) | Higher in branched-chain fatty acids§ |

* In methanogenic individuals.
† From breakdown of aromatic amino acids.
‡ Can affect enzyme activity and growth of microorganisms.
§ From breakdown of branched-chain amino acids.
SCFA, short-chain fatty acids.
concept, which may include one or a mixture of fibers, should: 1) have positive effects on microbiota to produce the protective, healing, and anti-inflammatory products of fiber (prebiotic effects); 2) deliver the fiber to the site of inflammation for local fermentation; and 3) limit the rate of putrefactive (undesirable) reactions. For example, psyllium seeds and oat bran are unique sources of fiber because they contain high amounts of both soluble and insoluble fiber. A combination of both soluble and insoluble fibers may supply a constant level of butyrate and other potential anti-inflammatory, healing products along the entire length of the colon. Specific combinations of rapidly and poorly fermentable fibers may therefore be of most benefit in the treatment of IBD. Further studies are needed to better understand the interaction between different fibers and the intestinal epithelium and microbiota to design the optimal fiber or combination of fibers to test in clinical trials.

**Colon Cancer**

An increased intake of dietary fiber has been associated with a decreased risk of colon cancer in a number of meta-analyses. The strongest evidence for this comes from case-controlled studies comparing various dietary fiber intakes with colorectal cancer incidence. These studies have repeatedly demonstrated a protective effect against colorectal cancer in subjects with a high fiber intake. Cause-and-effect relationships have been harder to establish due to part in confounding factors and the length of time needed to establish such a relationship. Indeed, in a recent study, dietary fiber intake was inversely associated with risk for colorectal cancer; however, after accounting for other dietary risk factors, high dietary fiber intake was not associated with a reduced risk of colorectal cancer. As noted by Baron, the complexity of dietary fibers, for example, soluble and insoluble, should be considered in epidemiological studies. Intervenational studies using secondary end points, either biochemical or histological, have been undertaken, and supportive results have been conflicting. Nevertheless, epidemiologic data coupled with the biologic plausibility provide substantiation for the protective effects of dietary fiber. In general, it is estimated that an intake of 30 g of dietary fiber per day is associated with a 50% reduction in risk of colon cancer, and insoluble cereal fibers seem to be more effective than soluble fibers.

Although the relationship between colon cancer risk and dietary fiber intake is still somewhat controversial, a number of mechanisms whereby dietary fiber protects against colon cancer have been proposed. Non-fermentative mechanisms that support these properties include: dilution of carcinogens through increased fecal bulk, decreased carcino-gen-colon contact time due to reduced transit time, decreased availability of carcinogens due to carcino-gen-fiber binding interactions, and increased excretion of bile acids (limiting their conversion to harmful secondary bile acids) through binding to dietary fiber (Table 1). Fermentative mechanisms responsible for the protective effect of dietary fiber against colon cancer have focused on butyrate. In vitro studies have shown that butyrate reduces oxidative damage to DNA, induces apoptosis in DNA-damaged cells, inhibits tumor cell growth, and increases the activity of detoxifying enzymes. Butyrate and other SCFA can decrease the activity of co-carcinogenic enzymes such as glucuronidases, glycosidases, and 7α-hydroxylases.

In contrast, some studies have failed to find a beneficial effect of butyrate on colon cancer. For example, the incidence of colon cancer was higher in rats whose water was spiked with 1% butyrate than in the control group. In another study, diets containing wheat bran or oat bran (6 g/100 g) were fed to rats. Those that were fed oat bran had greater concentrations of SCFA and butyrate in the feces than rats receiving wheat bran, but also a higher incidence of azoxymethane-induced cancer lesions.

Despite conflicting results of the influence of butyrate on colon cancer, it appears that slowly or poorly fermentable fibers are more beneficial. These fibers have the ability to reduce transit time, bind bile acids, and other toxins, and may supply some degree of fermentable substrate in the distal colon, thereby increasing butyrate in a region chronically low in butyrate under normal circumstances and possibly limiting the production of ammonia and phenolic compounds. This is significant considering that most colon cancer lesions occur in the distal colon. On the other hand, a mixture of fibers with differing effects on intestinal immune reaction, colon epithelial cell biology, and microbiota may be even more beneficial than a slowly or poorly fermentable fiber alone. As mentioned previously, a better understanding of fiber characteristics and fiber metabolism, as well as a detailed study on the interactions between fibers, the microbiota, and colon cell biology (e.g., cell growth, apoptosis, cell proliferation) are needed to design such a dietary fiber.

**DETERMINATION OF FERMENTATION RATE**

The above sections suggest that fermentation rate and total butyrate production play integral roles in the benefits of dietary fiber on colonic health. Therefore, in the development of dietary fibers that have been optimized for the prevention and alleviation of colonic diseases, it is necessary to determine what structural and physical characteristics are responsible for changes in fermentation pattern. Unfortunately, the physical inac-
cessibility of the colon to analysis has made this difficult. In vivo measurements of dietary fiber fermentation have been reviewed. These methods are summarized in Table 3, and in vitro methods are summarized in Table 4. As indicated, each of these methods has disadvantages that make clear relationships between fermentation pattern and fiber type difficult to determine. New methods that are more reproducible and better models of the human colon would be invaluable.

**FACTORS THAT INFLUENCE FERMENTATION RATE**

While extrinsic factors such as non-fiber components and the microbiota undoubtedly have some effect on the fermentation rate of dietary fiber, the focus of this section is on the fiber itself. Structure, both chemical and physical, processing conditions, and combinations of dietary fibers have great potential to influence dietary fiber fermentation properties.

### Chemical and Physical Structure

Many of the physiological benefits of fiber have been related to its structure. For example, arabinoxylans are a specific type of dietary fiber from cereal grains that may be cross-linked through oxidative dimerization of ferulic acid moieties that are esterified to the arabinoxylan polymer. The effect of cross-linking on fermentation rate of arabinoxylans was examined by Hopkins et al. Ferulic acid cross-links were synthesized in arabinoxylans by incubation with horseradish peroxidase.

---

**Table 3. In vivo Methods for Measuring Fermentation Pattern of Dietary Fiber**

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breath hydrogen</td>
<td>Hydrogen gas emitted after a meal containing dietary fiber is measured</td>
<td>• Does not measure SCFA directly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Some oligosaccharides decrease gas production</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Some individuals do not produce hydrogen</td>
</tr>
<tr>
<td>Blood acetate level</td>
<td>Subject is fed the dietary fiber source and blood acetate and propionate levels are measured</td>
<td>• Heart and liver buffer blood acetate above 0.25 µM and release acetate below this level</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Only quantifies acetate</td>
</tr>
<tr>
<td>Stable isotopes</td>
<td>Subject is fed the dietary fiber source and given an intravenous infusion of ^13^C-labeled acetate; the labeled acetate is subtracted from the total acetate to quantify in vivo acetate production</td>
<td>Only quantifies acetate</td>
</tr>
<tr>
<td>Dialysis sacs</td>
<td>Encapsulated dialysis sacs are ingested along with the dietary fiber source, the sac is recovered, and the contents are quantified</td>
<td>• Continuous sampling is not possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The relationship between transit and SCFA is not clear</td>
</tr>
<tr>
<td>Fecal SCFA</td>
<td>Subject is fed the dietary fiber source and SCFA are quantified in the feces</td>
<td>• Relationship between fecal SCFA concentration and in vivo production is unknown</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No measurement of SCFA production rate</td>
</tr>
<tr>
<td>Euthanized animal</td>
<td>Animals are fed the dietary fiber source and then euthanized and colonic contents are analyzed</td>
<td>Animals have different colonic conditions from humans</td>
</tr>
<tr>
<td>Surgically modified animal</td>
<td>Animals (e.g., cannulated) are fed the dietary fiber source and colonic conditions are observed in different regions</td>
<td>Modification of the colon may change conditions</td>
</tr>
</tbody>
</table>

* For detailed methodology, see example references. SCFA, Short-chain fatty acids.
and hydrogen peroxide. The fermentation patterns of cross-linked arabinoxylan and non-cross-linked arabinoxylans were then compared by in vitro fermentation with human fecal flora. Arabinoxylans and cross-linked arabinoxylans produced similar molar ratios of SCFA, but arabinoxylan was fermented more rapidly.\(^6\) Therefore, specific, controlled cross-linking of arabinoxylans may allow for the production of fibers with defined and predictable fermentative properties.

Pectin, another type of fiber commonly associated with fruits and vegetables, is a galacturonic acid polymer with varying degrees of methyl esters. Dongowski et al.\(^5\) studied the effects of degree of methylation on pectin fermentation. Conventional and germ-free rats were fed diets containing 6.5% citrus pectin with 34.5%, 70.8%, and 92.6% methylation for 20 days. Following the test period, the rats were sacrificed and the ileum, cecum, and colon weighed and analyzed for SCFA and galacturonans. A portion of the intestinal contents was also assayed for in vitro fermentation using rat fecal microbiota. They found that a low degree of methylation was associated with high butyrate and total SCFA production, while high methylation produced lower levels of SCFA. Additionally, low methoxyl pectin was rapidly fermented in the ileum and cecum, while high methoxyl pectin was more slowly fermented.\(^5\)

Annison et al.\(^7\) examined the effects of feeding acetylated, propionylated, or butyrylated starches to rats on SCFA concentrations in the proximal and distal colon. They found that esterification of starch with acetate, propionate, or butyrate led to an increase in total SCFA in both the proximal and distal colon, with the greatest increase corresponding to the SCFA that had been esterified to the starch. They concluded that the increase in total SCFA levels was because esterification produced a starch that resisted digestion in the small intestine, thus providing more fermentable substrate. The disproportionately large increase in the SCFA that was esterified to the starch was due to release by bacterial esterases after passage through the upper GI tract.\(^7\)

Salvador et al.\(^7\) studied the relationship between the disappearance of monosaccharides and the production of individual SCFA during in vitro fermentation of five different fibers with human fecal inoculum. They found that the associations between the dietary fiber sugars (e.g., glycosidic linkages, molecular packing, etc.) were the major factors in determining fermentability; however, uronic acids were generally acetogenic, whereas glucose was propionogenic and xylose was butyrogenic.\(^7\) This is inconsistent with results from a number of studies showing that resistant starch, which is composed entirely of glucose, is highly butyrogenic.\(^7\) One explanation for this may be that inocula from certain individuals consistently produce more propionate than butyrate.\(^5\)

Amrein et al.\(^6\) fermented wheat bran aleurone with human fecal flora and found that glucose, presumably from residual starch, was utilized most rapidly, followed by xylose and then arabinose. This same fermentation order was demonstrated in water-soluble, alkali-soluble, and insoluble rye bran fractions.\(^7\) Hopkins et al.\(^6\) found that the rate of fermentation of a crude arabinoxylan preparation from an unidentified source with human fecal flora was xylose > arabinose > glucose. During in vitro fermentation of ileal effluents

### Table 4. In vitro Methods for Measuring Fermentation Patterns of Dietary Fiber*  

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
<th>Limitations</th>
</tr>
</thead>
</table>
| Enzymatic digestion/ fecal flora fermentation | Fiber source is "digested" with a mixture of proteolytic and amylolytic enzymes, and the residue incubated anaerobically with fecal inocula | • A closed, static system is not a good model of the dynamic system of the colon  
• There is no separation between the proximal and distal colon simulated  
• Metabolic products accumulate rather than being used, as in the colon |
| In vivo digestion/ fecal flora fermentation | Animals are surgically cannulated at the ileum or cecum and fed the fiber source, effluents are collected and incubated anaerobically with fecal inocula | Same as above |

* For detailed methodology, see example references.\(^6\)
collected from cannulated pigs after rye bran arabinoxylan digestion, the rate of fermentation was arabinose > xylose > glucose. In beet fiber fermentation using ileal effluents from pigs fermented with pig fecal flora, galacturonic acids were degraded the fastest, followed by arabinose and then glucose. It is possible that cellulose, which is poorly fermented, may have been the source of glucose in these studies, which would explain why it was fermented so poorly. These results suggest that fermentation products and rate are more likely a function of linkages between monosaccharides, rather than the actual monosaccharide composition.

Gulfi et al. investigated the influence of degree of polymerization on pectin fermentation with human fecal flora and found that fermentation rate was not dependent on degree of polymerization. As mentioned above, the only aspect that did influence fermentation rate was degree of methylation.

With regard to physical structure, Amrein et al. compared the fermentation rates of native and isolated fibers. The investigators used two separation steps to obtain arabinoxylans of increasing purity from wheat bran. Purified arabinoxylans were then fermented with human fecal flora and compared with crude wheat bran. Arabinoxylans of increasing purity degraded more rapidly, with a correspondingly higher production of SCFA. This indicates that purification of a fiber can increase fermentation rate and SCFA production.

Goni et al. studied the in vitro fermentation rates of three types of resistant starches: native, retrograded, and retrograded/boiled. Similar amounts of SCFA were produced from all substrates, except fermentability was delayed slightly in the retrograded starches. This suggests that fermentation rate may be dependent on the type and amount of crystallinity.

Particle size also plays a role in dietary fiber fermentation. Hovey et al. fed diets containing ground or whole legumes to 12 healthy adults in a study with a randomized crossover design. Consumption of intact legumes resulted in greater fecal bulk and greater SCFA concentrations in the stool. This suggests that ingestion of intact seeds may delay fermentation of dietary fiber. Interestingly, legume seeds recovered from passed stool samples were intact, but the interior was eroded and coated with bacteria. This suggests that the outer portion of the seed may have acted as a barrier to digestive enzymes, essentially encapsulating the starch, thus allowing more starch to reach the colon for fermentation.

**Processing**

Processing of dietary fiber includes a broad array of treatments, including extrusion, enzyme and chemical treatments, and milling. These steps are often imposed to increase the dietary fiber functionality for use in common foods. While these steps do increase functionality, they may also alter fermentation rate.

Extrusion cooking causes gelatinization and disruption of starch granules due to the high temperature and moisture, increasing the accessibility of α-amylase to starch. Thus, extrusion may also increase the susceptibility of dietary fiber to fermentative enzymes. Dust et al. studied the effects of increasing the intensity of extrusion on in vitro fermentation of different dietary fiber sources. They tested a variety of products, including barley grits, cornmeal, oat bran, soybean flour, soybean hulls, and wheat bran, and found that for some products, such as barley grits, soybean hulls, and soybean flour, SCFA production using pig fecal inocula decreased with increasing severity of extrusion, while the reverse was true for the other products tested. They concluded that extrusion changed the fermentation pattern of fiber, but that the change was unique to each fiber source.

Enzymatic treatments are also employed in the processing of dietary fibers. These treatments often utilize a mixture of cellulases, hemicellulases, and polygalacturonases. For example, carrot and apple pomaces are agricultural waste products that may be a valuable source of fiber in enriched foods. To observe the effects of enzymatic modification of fermentation pattern of these products, carrot and apple pomaces were treated with a series of macerating enzymes. These treatments produced products with varying degrees of fiber breakdown. Though no clear trend was apparent for carrots, increasing levels of enzymatic degradation caused a decrease in the formation of SCFA during fermentation of apple pomace. Aura et al. utilized both extrusion and enzyme treatment to modify rye bran. They compared the fermentation rates of extruded rye bran and the soluble and insoluble fractions of extruded rye bran that had been treated with xylanase. The rate of fermentation in each of the samples was similar, showing a sharp increase in SCFA production between 0 and 8 hours, followed by very little SCFA production between 8 and 24 hours. Xylanase treatment of the soluble fraction of rye bran extrudate produced the most butyrate.

The effects of alkali treatment on fermentation rate have been studied in rye and maize arabinoxylans. Glitso et al. showed that alkali treatment of rye arabinoxylans using pig fecal flora increased fermentation from 0% to 49% over 48 hours. Van Laar et al. treated maize arabinoxylans with 1 M to 4 M potassium hydroxide, and found that mild alkali treatments increased fermentability, whereas more severe alkali treatments decreased it. This may be because mild alkali disrupts some of the hydrogen bonding and ferulate cross-linking that otherwise prevents fermentation, while severe alkali hydrolyzes fermentable polysaccharides. Oxidative treatments
using hydrogen peroxide or sodium chlorite have also been used to remove lignin. These treatments increased fermentability in rye arabinoxylans, but not to the same extent as alkali.87

**Combinations of Fibers**

There is some evidence that ingestion of soluble, highly fermentable fibers in conjunction with insoluble, poorly fermentable fibers can change the fermentation pattern of the fibers. For example, wheat bran contains high levels of insoluble fiber and is poorly fermented, while resistant starch is rapidly fermented in the ileum and cecum. Govers et al.89 hypothesized that a diet containing a combination of wheat bran and resistant starch would exhibit more of a beneficial effect on fermentation than resistant starch alone. Pigs were fed diets containing only resistant starch or wheat bran and resistant starch. The investigators found that without wheat bran, resistant starch was rapidly fermented in the cecum and proximal colon, whereas with wheat bran, there was nearly a 2-fold increase in resistant starch fermentation in the proximal colon and higher butyrate and lower ammonia concentrations in the distal colon.89 Muir et al.61 observed this same effect in humans. Twenty subjects were fed three diets containing wheat bran alone, wheat bran and resistant starch, or neither (control) in a randomized crossover design. Wheat bran in combination with resistant starch resulted in the highest concentrations of butyrate and other SCFA in the feces, suggesting higher butyrate production in the distal colon. Additionally, the diet containing wheat bran and resistant starch increased fecal bulk and frequency of defecation, and decreased transit time, total phenolics, and ammonia in the feces.61

As mentioned previously, Fernandez-Banares et al.33 showed that administration of psyllium seeds to patients with ulcerative colitis exhibited equal effectiveness in preventing a relapse of the disease over a 12-month period compared with mesalamine. Psyllium seeds contain a mixture of soluble and insoluble fibers. The investigators hypothesized that the observed results were due to slow fermentation of fiber in the distal colon, leading to higher butyrate levels.

Henningsson et al.90 studied the effects of consuming a combination of two soluble fibers on fermentation rate in the colon of rats. Rats were fed diets containing a total of 10% indigestible carbohydrate for 13 days. When rats were administered diets containing pectin or guar gum alone, butyrate production was low and took place largely in the cecum. When the two fibers were consumed together, butyrate production doubled and the concentration of butyrate in the distal colon and feces remained high.90 Soluble dietary fibers consumed in combination with starch increase the viscosity of the digesta, resulting in a decrease in the starch digestion rate.8,9 This combination increases starch that reaches the colon and increases SCFA production, but this is mainly restricted to the proximal colon.91

**CONCLUSIONS**

Evidence suggests that dietary fiber plays an important role in the prevention and/or alleviation of IBD and colon cancer. Dietary fiber can be either slowly or rapidly fermentable and, depending on patient needs, both may be beneficial. Further development of specific fibers with clearly defined fermentative properties would be beneficial in the treatment of colonic disorders. These fibers should have positive effects on the microbiota, deliver the fiber to the site of colonic disorders, and limit the rate of undesirable reactions. In the development of these dietary fibers, more detailed knowledge and, in most cases, a more accurate determination of the role of structure, processing, and other food components on fermentation rate and butyrate production of dietary fiber are needed.

**REFERENCES**

8. Cameron-Smith D, Collier GR. Dietary fiber and


