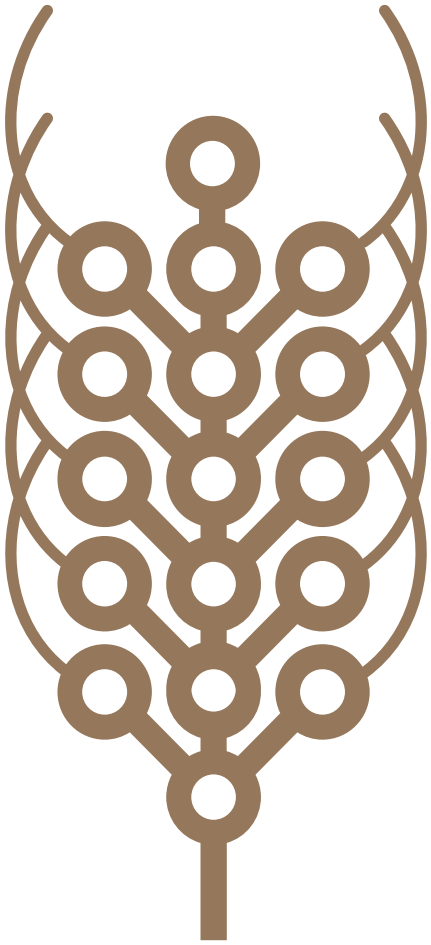
APPLIED NUTRITION SCIENCE

BARLEY+

RESISTANT STARCH AND PREBIOTIC FIBER FOR GUT HEALTH AND THE MICROBIOTA



freedom FOODS
Making food better

Barley+ is produced using the unique, non-genetically engineered BARLEYmax™ whole grain

The Barley+ Muesli and Muesli Bar product range contains the whole grain BARLEYmax™ as its key ingredient. BARLEYmax™ is a new, non-genetically engineered, hull-less whole grain barley cultivar, developed by Australia's prestigious research institution, the CSIRO. Due to its exceptional nutrition density and potential to positively influence human health, the CSIRO has a long-held interest in barley. BARLEYmax™ emerged from research stemming back to the 1990s, when amongst a collection of new non-genetically engineered barley grains, BARLEYmax™ was identified as a superior cultivar, due to its high levels of dietary fiber including resistant starch-like fiber (for its prebiotic activity), soluble fiber (incl. beta-glucan in high amounts) and insoluble fiber (cellulose, lignin) compared with other conventionally consumed whole grains (Figure 1)[1-3].

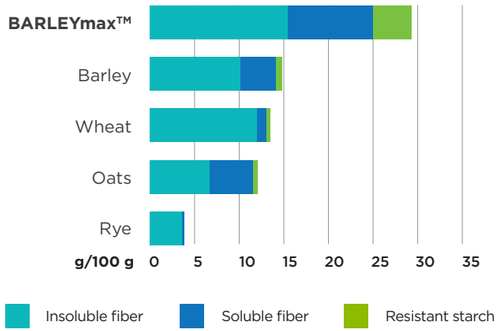


Figure 1: Resistant starch, soluble and insoluble fiber levels in BARLEYmax™ compared to other common whole grains [1].

Americans do not meet recommended intakes of fiber and whole grains

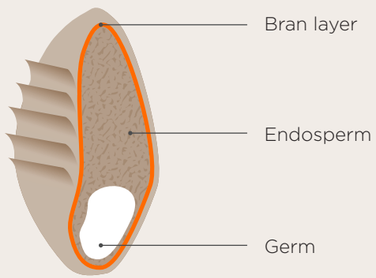
Dietary fiber is found at high levels in whole fruit, vegetables and whole grains. While some Americans have increased their dietary fiber intakes in recent years, most Americans continue to consume far too little and increased consumption is recommended[8-10]. Whole grains are an excellent source of fiber.

The 2015-2020 Dietary Guidelines for Americans recommend that Americans consume at least 3 serves of 1 ounce-equivalent whole grains each day at the 2,000-Calorie level, and to limit the intake of refined grains and products made with refined grains[10]. A 1 ounce-equivalent of whole grains is 16 g[10].

Most Americans do not meet these recommended intakes, with average intakes of whole grains falling far below the recommended levels across all age-sex groups (Figure 2), and average intakes of refined grains well above recommended limits for most age-sex groups (Figure 2). *This means Americans are missing out on health benefits derived from the different fiber types combined that are naturally present in whole grains*.

One 63 g serving of Barley+ Muesli adds around 2 ounce-equivalent of whole grains to a daily intake and so Barley+ can help Americans meet their recommended intakes of whole grains.

Barley kernel



Adequate consumption of whole grains is a well-accepted dietary pattern associated with reduced risk of chronic disease[4-5]. The benefits come from whole grain foods but not refined grains[6], which emphasizes the importance of consuming whole grains like BARLEYmax™. The accepted US definition for whole grains is that they contain all 3 key parts of the kernel: 1) the bran; 2) the germ; and 3) the endosperm. Whole grains used as ingredients in food products may be labeled as whole grains only if they contain the same proportions of bran, germ and endosperm in the final grain ingredient as in the original grain[7]. Refined grains typically lose at least part of their whole grain integrity and consequently, part of their nutrition value.

Average US whole and refined grain intakes versus recommended daily intakes*

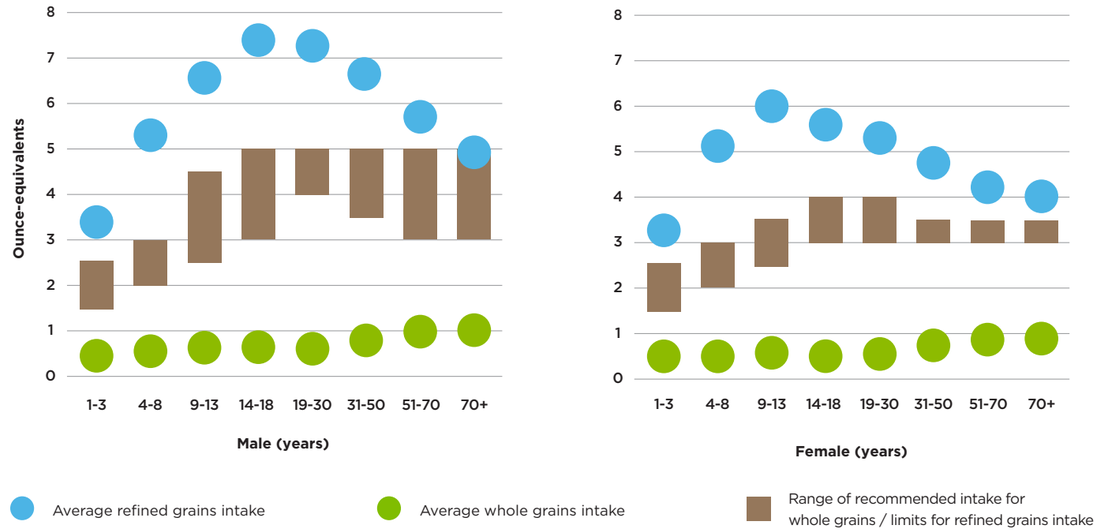


Figure 2: Average whole and refined grain intakes in ounce-equivalents per day by age-sex groups, compared to ranges of recommended daily intake for whole grains and limits for refined grains. The brown vertical bars on this graph represent one half of the total grain recommendations for each age-sex group, and therefore indicate recommendations for the minimum amounts to consume of whole grains or maximum amounts of refined grains. To meet recommendations, whole grain intake should be within or above the brown bars and refined grain intake within or below the bars. Graphs adapted from reference [10].

*NOTE: Recommended daily intake of whole grains is to be at least half of total grain consumption.

Defining prebiotic dietary fiber, its effects on gastrointestinal microbiota and probiotic ingredients

Dietary prebiotics are defined as *"selectively fermented ingredients that result in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health"* [11, 12]. Examples of foods rich in dietary prebiotic fiber include Barley+, legumes and lentils, Jerusalem artichokes, onions, garlic, leek and asparagus[13]. Dietary prebiotics essentially provide substrate for the gut microbiota and subsequently can change the composition and activity of resident gut microbiota[13, 14].

In contrast, **probiotics** are defined as *"live microorganisms which when administered in adequate amounts, confer a health benefit on the host"*[15].

Probiotics are essentially living microorganisms already present in fermented foods such as yogurt, kefir, miso, sauerkraut or kimchi, or as ingredients *added* to functional foods and dietary supplements. However, many probiotic commercial products contain bacteria species (bifidobacteria and lactobacilli), which are dominant species in milk-fed infants, but are relatively minor species in adults[14, 16]. It has been suggested that for effective use of probiotics, particular strains or species should target specific conditions[14].

The favorable influence of good dietary prebiotic intake on gut microbiota may be a better route to a healthier gut profile in some people. This may be especially relevant when specific probiotics are used in individual condition management.

Gastrointestinal microbiota, diet and disease

The gastrointestinal tract is inhabited by vast and diverse populations of microorganisms, with the largest and most important found in the colon[12, 17]. Over one trillion bacteria contribute to the make up of the human gut microbiota, and play a fundamental role in the wellbeing of the host[17-19]. The constituents of the microbiota have been shown to interact with one another and with the host immune system in ways that influence the development of disease[17, 20-22]. For instance, changes in the intestinal microbiota can disrupt normal intestinal function[20], irritable bowel disease pathogenesis is linked to the gastrointestinal microbiota[17, 23] and some[24, 25] but not all[26] studies show that obesity is associated with an imbalance in normal gut microbiota. The importance of the link between dietary intake, colonic microorganism metabolism and human health is becoming increasingly well recognized[14, 21, 27] and may at least partly explain the relationship between the protective effects of specific dietary fiber types and serious chronic diseases, including colorectal cancer[18, 28, 29].

Gut microbiota: typical bacteria profile

The bacterial composition of the gut microbiota varies considerably between healthy individuals, depending on their diet and other environmental factors[17]. However, it has been shown that bacteria of the bacteroidetes and firmicutes phyla typically dominate the gut bacteria communities[17, 30]. Further, it is suggested that the microbiota profile of most adults can be classified into one of three 'types' or enterotypes, based on their particular dominant genera and their ratios to one another[17, 26]. Enterotype 1 is dominated by the bacteroides genera; enterotype 2 is dominated by the prevotella genera; and enterotype 3 is dominated by the ruminococcus genera[17, 26]. **Interestingly, these broad gut microbiota enterotype patterns are largely determined by diet**[17, 27].

Resistant starch prebiotic activity

In humans, one of the major functions of the large bowel microbiota is to produce short chain fatty acids (SCFA), which supply energy to the intestinal cells of the host. Intake of fermentable prebiotic fiber can alter microbiota profiles and increase specific bacteria numbers in the large bowel by providing substrate to gut bacteria or by increasing SCFA supply to other gut microbes and intestinal cells[31-33]. Insufficient SCFA supply limits substrate availability and is understood to influence poor gut health[34]. **Resistant starch specifically has been shown in human and animal models to modify gut microbiota[35-39], and to promote beneficial effects on large bowel function in healthy adults[39].** As expected, the type and magnitude of response to resistant starch is highly variable between individuals, is reversible and is tightly associated with resistant starch intake[39]. Recently, resistant starch has also been shown to improve insulin sensitivity independently of the gut microbiota in rodents, highlighting that resistant starch may also exert health effects via other metabolic pathways, such as alterations in the bile acid cycle[40]. Other well documented prebiotic effects in humans stem from fructans and fructooligosaccharides[41-43], which make up ~10% of BARLEYmax™ whole grains.

BARLEYmax™ prebiotic activity and a healthier gut microbiota

BARLEYmax™ and so Barley+ is a rich source of various prebiotic dietary nutrients, including resistant starch, fructans and fructooligosaccharides. It is the bacteria-generated SCFA metabolic end products of dietary nutrient fermentation that contribute significantly to human health[32, 44]. Butyrate, propionate and acetate are the bacteria-generated SCFAs of principal importance to colonic health[14, 29, 44] (Figure: 3).

Butyrate is the preferred substrate for the cells in the colon and importantly, butyrate appears to promote a normal phenotype in these colon cells[32].

Fermentation of prebiotic nutrients

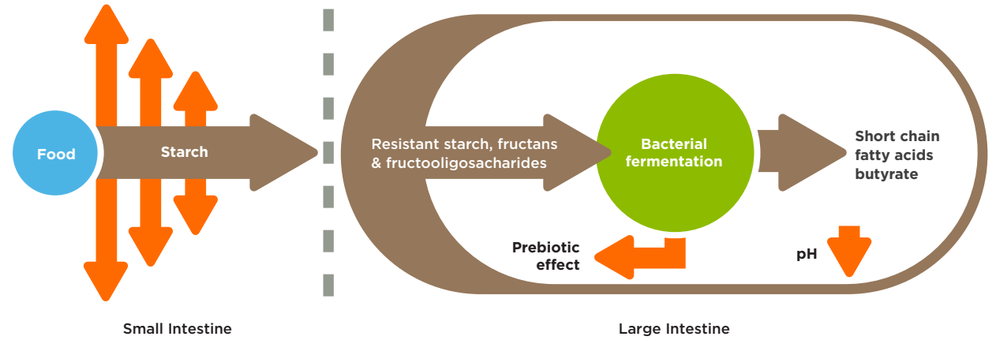


Figure 3: Fermentation of dietary prebiotic resistant starch and fructooligosacharides and butyrate production in the large bowel. Lower pH values (and raised SCFA) are believed to prevent the overgrowth of pH-sensitive pathogenic bacteria[32]. Figure adapted from reference[32].

Resistant starch is the major substrate for colonic butyrate production[29, 39]. Fermentation of BARLEYmax™ resistant starch and prebiotic fiber has been shown to favor the production of the butyrate SCFA in the colon[45, 46]. It has been suggested that butyrate has the strongest protective effect against colorectal cancer[29]. To this end, some experts suggest that the higher colorectal cancer rates observed in developed nations relative to lower risk populations may be attributable to insufficient consumption of resistant starch and other more fermentable fiber types, while populations at lower risk consume higher levels of resistant starch via whole grain intakes and cooking practices [28, 44].

Importantly, it appears that observations of beneficial prebiotic properties of resistant starch to dietary modulation of colorectal cancer risk may be maximized with the combined consumption of insoluble fiber[47]. Consuming insoluble fiber and resistant starch together pushes the fermentation of resistant starch further distally in the colon, which subsequently improves conditions in distal colonic regions where tumors most commonly occur[47]. BARLEYmax™ has high levels of both resistant starch and insoluble fiber, compared with other conventionally consumed whole grains.

While further human clinical studies are needed to elucidate the exact effects of resistant starch and prebiotic dietary fiber on gut microbiota shifts and consequent specific benefits, the following is well established:

- BARLEYmax™ is a non-genetically engineered whole grain barley cultivar developed by Australia's CSIRO and contains more resistant starch, soluble fiber and insoluble fiber in the one whole grain versus other commercial grains;
- Adequate consumption of whole grains is a well-accepted dietary pattern associated with reduced risk of chronic disease[4, 5];
- BARLEYmax™ and Barley+ provide a rich source of resistant starch and other fermentable nutrients with prebiotic effects;
- Dietary prebiotics result in specific changes in the composition and/or activity of the gastrointestinal microbiota and confer benefit(s) upon host health[11, 12];
- Resistant starch and fermentable dietary nutrients can modify gut microbiota [35-38] and promote beneficial effects on large bowel function in healthy adults[39];
- Fermentation of BARLEYmax™ resistant starch and prebiotic fiber has been shown to favor the production of the butyrate SCFA in the colon[45, 46]; butyrate is the preferred fuel for colon cells.

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