

Carol Rees Parrish, MS, RDN, Series Editor

## FODMAPS Everywhere and Not a Thing to Eat!



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**FODMAP is an acronym for fermentable oligosaccharides, disaccharides, monosaccharides and polyols. Dietary restriction of FODMAPs helps patients with the irritable bowel syndrome. Registered dietitians are essential for the education of patients in initial FODMAP restriction, structured re-introduction and final implementation of a personalized diet. Further areas of research include the adverse effects of FODMAP restriction on the microbiome, the effects of long-term FODMAP restriction on nutrition and intestinal health and the possible use of low FODMAP diets in other disease states.**

### INTRODUCTION

**F**ODMAP is an acronym that stands for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. These are all fermentable short-chain carbohydrates of 3-10 sugars and are commonly found in many everyday foods (Table 1). These are carbohydrates that are poorly absorbed and osmotically active in the small intestine, drawing water into the lumen and fermented by bacteria in the colon producing gas. Dietary restriction of FODMAPs improves symptoms of diarrhea, abdominal pain, distention and bloating in patients with irritable bowel syndrome. A comprehensive review of this subject has recently been published.<sup>1</sup>

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### Carbohydrates and Their Absorption

Simple sugars are monosaccharides (glucose, fructose and galactose) and disaccharides (sucrose, lactose, maltose) that are present in milk, fruits, and vegetables that add varying degrees of sweetness to food. Disaccharides consist of two monosaccharides chemically joined together. The important disaccharides are sucrose (table sugar), lactose (milk sugar) and maltose (a product of starch digestion). Sugar alcohols are derivatives of monosaccharides. As with other sugars they taste sweet and are a source of energy, but they provide the same degree of sweetness as sugar with fewer calories and are therefore used as low-calorie sweeteners. They are absorbed more slowly than monosaccharides. Polysaccharides are long chains of monosaccharides. The way the monosaccharides are linked makes them absorbable (starch) or non-absorbable (fiber). Plants store energy as starch, which is a complex carbohydrate made of long chains of monosaccharides. Glycogen is also called

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animal starch and is used to store energy in humans and other animals. Most glycogen in slaughtered animals deteriorates within 24 hours. Pancreatic amylase breaks starch into smaller units of maltose.

### FODMAP Absorption

Most carbohydrate digestion and absorption takes place in the small intestine. All carbohydrates must be broken down into monosaccharides for absorption. A sodium-dependent transporter moves the monosaccharides glucose and galactose into the enterocyte.

### Monosaccharides

Fructose is a monosaccharide, which is absorbed in the presence of glucose. Fructose is transported primarily by either GLUT-2 or GLUT-5 carrier proteins across the intestinal epithelium. The GLUT-5 transporter is specific to only fructose, but the GLUT-2 transporter relies on glucose to facilitate passage of fructose.<sup>2</sup> Clinical studies have shown that a fructose:glucose ratio of 1:1 is ideal for absorption for fructose; higher proportions of fructose are malabsorbed.<sup>3</sup> Approximately half the U.S. population cannot absorb and tolerate > 25 grams of fructose, yet the fructose content of many diets regularly exceeds 50 grams (an amount that 100% of humans cannot absorb), primarily due to

the ingestion of sweetened beverages (most often with high fructose corn syrup)<sup>4,5</sup> (Table 2).

### Oligosaccharides

Oligosaccharides are carbohydrates, which are made up of 3-10 simple sugars, composed mainly of fructans and galacto-oligosaccharides (GOS). A fructan is a polymer of fructose molecules. Fructans with a short chain length are known as fructo-oligosaccharides. They are poorly absorbed because the human body does not possess the enzyme to break them apart.

### Disaccharides

Disaccharides such as lactose are variably absorbed because lactase, the enzyme needed to digest this sugar is genetically determined and absent in some populations (68% of the world's population is lactase nonpersistent).<sup>6</sup>

### Polyols

The last group consists of polyols, which are sugar alcohols that add the taste and texture of sugar with approximately half the number of calories. They are slowly absorbed by passive diffusion. Polyols are sugar alcohols found naturally in some fruits and vegetables (Table 3). They are also widely manufactured and used as artificial sweeteners. Absorption of sugar alcohols is dose dependent and

**Table 1. Short-Chain Carbohydrate Subtypes and Sources**

F	Fermentable	
O	<b>Oligosaccharides</b>	Fructans: wheat, onions, garlic, inulin, chicory root, pistachios, cashews, teas- chamomile/chai Galacto-oligosaccharides: beans, lentils, green peas, soy beans/milk
D	<b>Disaccharides</b>	Lactose: milk, yogurt, ice cream, cottage cheese, ricotta cheese
M	<b>Monosaccharides</b>	Fructose (in excess of glucose): high fructose corn syrup, honey, apples, pears, watermelon, mango, asparagus, artichoke, rum
A	<b>And</b>	
P	<b>Polyols</b>	Mannitol: cauliflower, mushrooms Sorbitol: blackberries, avocado, prunes Xylitol, maltitol, isomalt - candy, gum, mints sweetened with sugar-alcohols Medications: beware of cough syrups, liquid non-steroidals and any suspensions, elixirs, etc.

Table 2. Fructose Content of Foods

Fruit	Serving Size	Fructose (Grams)	Fructose in Excess of Glucose (Grams)
Strawberries	½ cup sliced	2.03	0.37
Cantaloupe	1 cup diced	2.92	0.52
Orange	1 fruit	3.15	0.39
Blueberries	½ cup	3.68	0.07
Watermelon	1 cup diced	5.11	2.71
Banana	1 medium	5.72	Glucose > Fructose
Orange Juice	1 cup	6.05	0.4
Mango	1 cup pieces	7.72	4.4
Dates	1 date	7.67	Glucose>fructose
Apple	1 medium	10.74	6.32
Pear	1 medium	11.43	6.8
Apple Juice	1 cup	14.2	7.68
Sweet Cherries	100g	6.2	0.2
Grapes	100g	7.6	0

Table 3. Sorbitol Content of Some Foods

Item	Serving Size	Sorbitol (grams)
Apple	1 fruit	0.5
Apricot	1 fruit	0.9
Blackberries	10 berries	2.1
Nectarine	1 fruit	0.9
Pear	1 fruit	3.8
Prunes	¼ cup	9.6
Sugar-free gum	1 piece	1-2 grams
Sugar-free candy	4 pieces	15 grams

influenced by the molecular size of the individual polyol. Sorbitol intolerance is a common problem in healthy individuals and can cause bloating and abdominal distress.<sup>7</sup> These symptoms tend to occur with intakes of just 10-20 grams/day; greater amounts of up to 50 grams can have a laxative type effect.<sup>8</sup> Sorbitol, mannitol and xylitol are examples of sugar alcohols used as sweeteners. For example, sorbitol is often used in chewing gum, breath mints, candy and many liquid medications such as cough

syrops, analgesics, etc. and is an important source of symptoms in some patients. Many commonly used medications contain sorbitol<sup>9</sup> (Table 4).

## Physiological Effects of FODMAPs

### *Small Intestine Water Volume*

FODMAPs are osmotically active and draw water into the lumen of the small bowel. Using subjects with an ileostomy, a two-fold increase in ileostomy fluid output was demonstrated with the oral administration of fructose and sorbitol.<sup>10,11</sup> The increase in intestinal volume results in distention of the small intestine and can cause pain in patients with visceral hypersensitivity.<sup>12</sup> A scintigraphic study has demonstrated that ingestion of an oral fructose-sorbitol solution reduces transit time from the mouth to the cecum in healthy individuals, without altering gastric emptying; thereby demonstrating increased motility of the small intestine.<sup>13</sup> An increase in motility in the small intestine contributes to symptoms of diarrhea.

### *Colonic Gas Production*

Colonic bacteria ferment poorly absorbed

**Table 4. Medications that Contain Sorbitol<sup>9</sup>**

- Acetaminophen Children's (chewable)
- Acetaminophen, Dextromethorphan Hydrobromide and Phenylephrine Hydrochloride
- Carbamazepine (Chewable)
- Clonazepam (dispersible)
- Diphenhydramine Hydrochloride
- Docusate Calcium
- Docusate Sodium
- DOK docusate sodium
- Isentress (Chewable)
- Lansoprazole suspension
- Mytab Gas
- Naproxen Sodium
- Nifedipine
- Night Time Cold & Flu acetaminophen / dextromethorphan hydrobromide / doxylamine succinate
- Ondansetron Hydrochloride (Orally Disintegrating)
- Robitussin Peak Cold Nighttime Cold + Flu acetaminophen dextromethorphan hydrobromide / doxylamine succinate
- Simethicone
- TL-Care DHA Prenatal Multivitamins with Folic Acid and Docusate
- Tums Extra Strength 750 (Sugar Free Orange) calcium carbonate
- Tums Kids (Cherry Blast) calcium carbonate
- Vicks DayQuil Cold & Flu acetaminophen dextromethorphan hydrobromide / phenylephrine hydrochloride
- Ondansetron Hydrochloride (Orally Disintegrating)
- Simethicone
- Tums Extra Strength (Sugar Free Orange)
- Tums Kids (Cherry Blast)

carbohydrates that reach the colon resulting in the production of methane and hydrogen. Breath testing shows an increase in hydrogen and methane gas production with high FODMAP diets.<sup>14</sup> An increase in colonic gas leads to bloating and distention, and in patients with intestinal hypersensitivity, causes pain. Oligosaccharides have shown a greater fermentative effect than other FODMAPs and MRI studies show greater colonic distension with inulin (a plant polysaccharide) compared to fructose (a monosaccharide).<sup>15</sup>

### ***Visceral Hypersensitivity***

Fermentation results in the production of short chain fatty acids (SCFAs) in the colon. SCFAs consist of acetate, propionate, and butyrate and serve as a fuel source for colonocytes. They also play a role in lipid, glucose, and cholesterol metabolism and are important for intestinal health.<sup>16</sup> High FODMAP diets increase serum levels of lipopolysaccharides leading to gut permeability, intestinal inflammation, and visceral hypersensitivity.<sup>17</sup> This increases the likelihood of developing pain with intestinal distention.

### ***Gut Microbiome***

Oligosaccharides are known for their prebiotic effect on the body. A restriction of these carbohydrates with a low FODMAP diet has been shown to reduce levels of luminal bifidobacter, which has been well established in contributing positive health benefits including improved immune function.<sup>14,18</sup> A 3-4 week duration of FODMAP restriction resulted in 6-fold reduction in bifidobacteria (a desirable bacterial species in the microbiome) compared to controls.<sup>19</sup> Another recent study also showed a change in the bacterial content of the intestinal microbiome after short-term administration of a low FODMAP diet.<sup>20</sup> Co-administration of a probiotic while on a low FODMAP diet restored concentrations of bifidobacter along with providing symptom relief.<sup>21</sup>

### ***Effect of Low FODMAP Diets on the Metabolome***

Foods result in the generation of small-molecule chemicals in the body that have physiological effects. These chemicals are called the food-induced metabolome. Low FODMAP diets have

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an effect on the metabolome. Three active food-induced chemicals (histamine, p-hydroxybenzoic acid, and azelaic acid) were studied in an experimental intervention using a high FODMAP and a low FODMAP diet. Histamine, a measure of immune activation, was decreased 8-fold on the low FODMAP diet.<sup>22</sup> Histamine may have a role in IBS as histamine levels have been shown to be elevated in these patients.<sup>23</sup>

### Use in Gastrointestinal Disorders

#### ***Irritable Bowel Syndrome (IBS)***

A meta-analysis of short-term studies on low FODMAP diets in IBS found 6 randomized controlled trials and 16 non-randomized trials demonstrating substantial improvements in IBS symptoms with a low FODMAP diet.<sup>24</sup> A more recent meta-analysis found seven randomized controlled trials comparing a low FODMAP diet

with control interventions. A low FODMAP diet was associated with reduced global symptoms compared with control interventions, but the quality of the data was low.<sup>25</sup>

#### ***Inflammatory Bowel Disease (IBD)***

Functional gastrointestinal symptoms are present in a proportion of patients with inflammatory bowel disease. Functional symptoms are more likely in patients with Crohn’s disease compared to patients with ulcerative colitis perhaps due to disease location.<sup>26</sup> There is some evidence to support use of a low FODMAP diet in patients with IBD in whom the inflammatory bowel disease is controlled, but symptoms persist. Improvements were seen in stool consistency and frequency along with decreased severity of abdominal pain, bloating, and flatulence.<sup>27</sup>

#### ***Celiac Disease on a Gluten Free Diet (GFD)***

Life-long adherence to a gluten-free diet is the

**Table 5. Low FODMAP Diet**

Phase		Duration
1. Elimination	Avoidance of all high FODMAP foods	2-6 weeks
2. Reintroduction	Structured challenges of individual FODMAPs	6-8 weeks
3. Maintenance	Personalized FODMAP diet	Long term for symptom relief

**Table 6. FODMAP Resources**

Resource	Link	Comment
<b>Monash University Mobile App</b>	Apple and Android app stores	Links to an extensive database of FODMAP containing foods
<b>A little bit yummy</b>	<a href="https://alittlebitummy.com">https://alittlebitummy.com</a>	Meal plans and recipes
<b>Casa de Sante</b>	<a href="http://Casadesante.com">Casadesante.com</a>	Low FODMAP foods, recipes, dookboksetc.
<b>FODY foods</b>	<a href="https://www.fodyfoods.com/blogs/news">https://www.fodyfoods.com/blogs/news</a>	Blog, convenience foods
<b>Books</b>	The Complete Low-FODMAP Diet: A Revolutionary Plan for Managing IBS and Other Digestive Disorders by Sue Shepherd, PhD and Peter Gibson, MD  The Low-FODMAP Diet Step by Step: A Personalized Plan to Relieve the Symptoms of IBS and Other Digestive Disorders by Kate Scarlata	Book stores



only current treatment for patients with celiac disease. Despite strict adherence to a gluten-free diet, symptoms are reported by 47% of patients with celiac disease.<sup>28</sup> A randomized, controlled trial of patients with celiac disease on a gluten free, low FODMAP diet showed significant improvement in functional gastrointestinal symptoms and psychological health scores.<sup>29</sup>

### **Non-Celiac Gluten Sensitivity**

Non-celiac gluten sensitivity is characterized by symptom improvement after gluten withdrawal in the absence of celiac disease. Wheat is a very important source of fructans in the U.S. diet. A recent study aimed to evaluate the effects of gluten and fructans on the genesis of symptoms in patients with non-celiac gluten sensitivity. In a double-blind trial, patients with non-celiac gluten sensitivity and IBS were given a low FODMAP diet for 2 weeks followed by a high-gluten, low-gluten and a control period of whey protein.<sup>30</sup> Symptoms improved on the low FODMAP diet, but worsened equally when gluten or whey protein was added to the diet suggesting that the cause of food sensitivity may be multi-factorial. Skodje et al. studied subjects who did not have celiac disease, but were on a self-imposed gluten-free diet.<sup>30</sup> These individuals were administered diets containing gluten, fructans or placebo concealed in muesli bars for 7 days. After a wash-out period, the subjects were re-randomized until all three diets were administered

to all subjects. Symptoms of bloating and overall symptoms of IBS worsened during fructan administration, but the effect of gluten containing diets was similar to placebo. This trial suggests that fructans may have a role in the development of symptoms and therefore a low FODMAP diet could help these patients. Another recent study evaluated the effect of a low FODMAP compared to a gluten-free diet on clinical symptoms, psychological well being, intestinal inflammation and integrity, and stool microbiota in subjects with non-celiac gluten sensitivity. Both the low FODMAP diet and the gluten free diet resulted in a significant improvement in symptoms in patients with non-celiac gluten sensitivity. There was a decrease in duodenal intraepithelial lymphocytes and mucin-producing Goblet cells after administration of a gluten free diet. Significant changes were seen in the stool microbiota composition in patients with non-celiac gluten sensitivity and controls. This study suggests that symptom generation may be multi-factorial in patients with non-celiac gluten sensitivity.<sup>31</sup>

### **Low FODMAP Diet Implementation**

A practical guide to implement the FODMAP diet in clinical practice has recently been published and this subject is only briefly covered here.<sup>32</sup>

### **Elimination**

The elimination phase is the first of three phases

**Table 7. FODMAP Reintroduction**

<b>Challenge Week</b>	<b>Examples of Test Foods</b>
<b>1. Lactose</b>	½ cup of milk or ¾ cup plain yogurt (without sweeteners or other high FODMAP ingredients)
<b>2. Fructose</b>	1 tablespoon of honey or ½ mango
<b>3. Polyols- sorbitol</b>	⅔ cup blackberries or ¼ avocado
<b>4. Polyols- mannitol</b>	⅓ cup cauliflower or ¾ cup sweet potato
<b>5. Fructans – wheat</b>	1 cup cooked pasta or 2 slices whole wheat bread
<b>6. Fructans- onion</b>	1 tablespoon diced onion
<b>7. Fructans- garlic</b>	1 clove of garlic
<b>8. Galacto-oligosaccharides</b>	½ cup of black beans, kidney beans, or thawed peas 15-25 almonds

of the low FODMAP diet (Table 5). It is during this time that patients restrict all high FODMAP foods from the diet for 2-6 weeks. The goal during this phase is to determine if there is sensitivity to FODMAPs because not all patients will elicit a response. A biomarker may be helpful to identify patients who would benefit from a low FODMAP diet. In one study, measurement of volatile organic compounds in stool predicted with 97% accuracy whether an IBS patient responded to a low FODMAP diet.<sup>33</sup> Further validation of this biomarker is needed. A number of resources are listed in Table 6 and can help patients through this phase.

### **Re-introduction**

The low FODMAP diet is too restrictive for long-term use. Therefore, the next step is to systematically challenge the patient with each FODMAP component. The general principle is to introduce small amounts of one group and gradually increase the dose on day two and three if the food is tolerated. If symptoms develop, the challenge is stopped and a 3-4 day wash out period is started until symptoms resolve. If no symptoms are observed, the next FODMAP challenge begins. This process typically lasts 6-8 weeks. No evidence-based guidance is available at this time, but Table 7 shows our approach to the re-introduction of foods.

### **Maintenance**

The final phase of the diet modification is long-term adherence to a personalized FODMAP plan. The individualized plan is created based on the results of the previous phase. FODMAPs that trigger symptoms are limited, but the others are added back to the diet.

### **FODMAPS and Enteral Feeding**

FODMAPs may have an important role in adverse effects caused by enteral feeding. In a retrospective study of patients with diarrhea caused by enteral feeding in Australia, the FODMAP content of the enteral feeding ranged from 10.6 to 36.5 g/day. A low FODMAP enteral formula was associated with a five-fold reduction in diarrhea rates.<sup>34</sup> A randomized, controlled trial of a low, moderate, and high FODMAP enteral feeding was conducted in Korea. There was a significant reduction in diarrhea

and improvement in nutritional parameters and clinical outcome in patients randomized to the low FODMAP enteral feeding formula.<sup>35</sup> Quantifying FODMAPs in enteral formulas has proved to be difficult because of the interference with in vitro assays of fructans and raffinose caused by the maltodextrin content of the formula.<sup>36</sup> Therefore, there is a no ready source for the FODMAP content of enteral feeding formulations in the United States. However, in symptomatic patients, a trial of FOS, fiber, and inulin free formulas may be beneficial.

### **The Role of a Dietitian**

A low FODMAP diet is restrictive and can be confusing to implement without guidance. Patients benefit from instruction provided by a dietitian who specializes in GI nutrition and is familiar with the low FODMAP diet.<sup>37</sup> A recent survey of over 1,500 gastroenterologists suggested that most felt that dietary intervention was as good, or better, than other available treatments for IBS.<sup>38</sup> The survey also demonstrated that only a small portion of gastroenterologists refer patients to a dietitian with specialized GI training despite the fact that the majority believed that GI trained dietitians would be of benefit to their patients. This may be related to the lack of access to dietitians with specialized training. Resources for low FODMAP diets are becoming more available to the general public and there is a tendency to give the patient a handout and refer them to on-line resources (Table 6). We gave up this approach in our department when patient dissatisfaction and a poor response to dietary intervention lead us to re-evaluate it. All our patients are now instructed by a registered dietitian and are followed until a personalized diet plan is developed. The dietitian may also have a role in monitoring the nutritional status of patients who are on low FODMAP restricted diets for long periods of time.

### **Long-Term Risks and Unanswered Questions**

Dietary intervention carries the risk of being considered “all-natural” and risk-free. Limited data are available on the nutritional consequences of prolonged restriction of FODMAPs in the diet. Changes in the microbiome and in the composition of gut content may have adverse effects on health. For example, short chain fatty acids are decreased

in the colon on low FODMAP diets. Short chain fatty acids are trophic to the colon mucosa and essential for intestinal health.

## CONCLUSION

A low FODMAP diet can be an effective treatment for IBS, but increasing evidence suggests a possible use in symptomatic patients with quiescent inflammatory bowel disease, non-celiac gluten sensitivity, and celiac disease with persistent symptoms on a gluten-free diet and normal celiac serology. In some patients, FODMAPs in enteral feeding formulas can cause bloating and diarrhea in tube-fed patients. Registered dietitians are essential for the education of patients in initial FODMAP restriction, structured re-introduction and final implementation of a personalized diet. Further areas of research include the adverse effects of FODMAP restriction on the microbiome, the effects of long-term FODMAP restriction on nutrition and intestinal health and the possible use of low FODMAP diets in other disease states. ■

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