ATRANTIL®
(Ah-tran-teal)

TRAINING MANUAL

NON GMO Project VERIFIED nongmoproject.org

GLUTEN FREE

GOOD MANUFACTURING PRACTICE CERTIFICATION GMP QUALITY

USA

NSF CERTIFIED SPORT

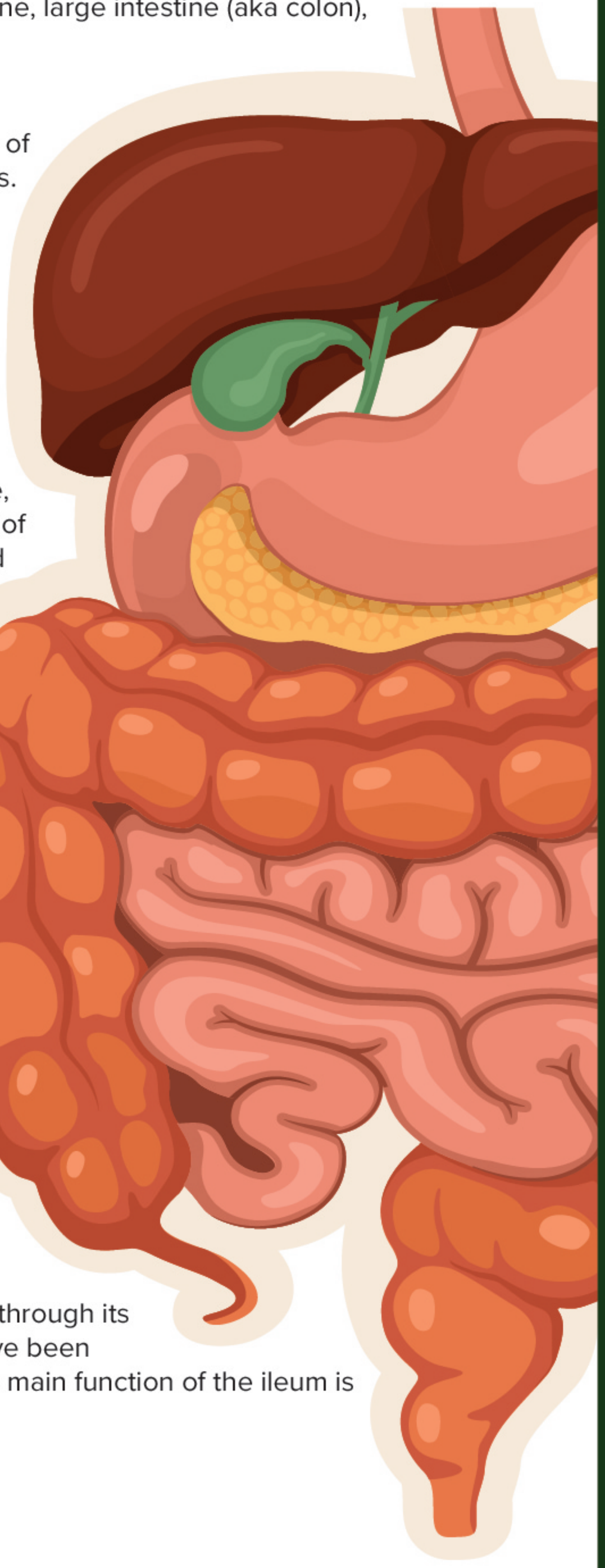
TOPICS DISCUSSED

1. GI Tract Anatomy
2. GI Problems & Diseases
3. Atrantil (Product History and Use)
4. Methane & Hydrogen Sulfide Problems
5. Polyphenols as a Therapy
6. Atrantil PRO
7. Atrantil Clinical Trial Links
8. Gluten Exposure Protection
9. Common Competitors

GASTROINTESTINAL TRACT

The gastrointestinal tract, also called digestive tract or alimentary canal, pathway by which food enters the body and solid wastes are expelled. The gastrointestinal tract includes the mouth, pharynx, esophagus, stomach, duodenum, small intestine, large intestine (aka colon), and anus.

For the purposes of understanding where Atrantil and Atrantil PRO have activity, be familiar with the locations of the duodenum, small intestine, large intestine, and anus.



DUODENUM

In humans, the duodenum is a hollow jointed tube about 25–40 centimeters (10–15 inches) long connecting the stomach and is the first section of the small intestine. It begins with the duodenal bulb and ends at the suspensory muscle of duodenum.

The duodenum breaks down food in the small intestine, using enzymes. The duodenum also regulates the rate of emptying of the stomach using hormones. Secretin and cholecystokinin are released from cells in the duodenal epithelium in response to acidic and fatty contents present when the pylorus opens and emits gastric chyme into the duodenum for further digestion. These triggers the liver and gallbladder to release bile, as well as the pancreas to release bicarbonate and digestive enzymes such as trypsin, lipase, and amylase.

SMALL INTESTINE/SMALL BOWEL

The small intestine or small bowel is where most of the absorption of nutrients from food takes place. It lies between the stomach and large intestine (aka Large Bowel or Colon) and receives bile and pancreatic juice through the pancreatic duct to aid in digestion. The small intestine is about 5.5 meters (18 feet).

The small intestine has three distinct regions – the duodenum, jejunum, and ileum. The duodenum is the shortest. The jejunum is specialized for the absorption through its lining by enterocytes: small nutrient particles which have been previously digested by enzymes in the duodenum. The main function of the ileum is to absorb vitamin B12, bile salts.

The small bowel is specifically suited to absorb fats and fat-soluble vitamins (A, D, E, & K). The small bowel ALSO is not designed to have bacteria colonize. In other words, bacteria should always be in transit through the small bowel. (Hint, this is where problems begin.)

The general function of the small intestine is the absorption of the food we eat. During and after a meal, the intestine normally shows very irregular or unsynchronized contractions.

The contractions move the food content back and forth and mix it with the digestive enzymes that are secreted into the intestine. However, these contractions are not entirely unsynchronized; they move the contents of the intestine slowly toward the large intestine.

Typically, it takes around 90-120 minutes for the first part of a meal we have eaten to reach the large bowel, and the last portion of the meal may not reach the large intestine for five hours. This pattern of motility is called the “fed (or eating) pattern.”

Between meals, the intestine shows cycles of activity that repeat about every 90-120 minutes. The cycle consists, in order, of:

A short period of no contractions (Phase I)
A long period of unsynchronized contractions that appear similar to the fed pattern (Phase II)
A burst of strong, regular contractions that move down the intestine in a peristaltic fashion (Phase III).
Phase III represents a continuation of the “housekeeper waves” that start in the stomach. Its function is to sweep undigested food particles and bacteria out of the small intestine and into the large intestine. This should ideally function to keep all of the bacteria in transit.

Discrete clustered contractions are brief bursts of contractions (each burst lasts only a few seconds) which are synchronized (peristaltic). They occur mostly in the upper small intestine and fade out before moving too far down-stream. They occur in most people at infrequent intervals, but in people with irritable bowel syndrome (IBS) they may be associated with abdominal pain.

The second type of contraction is the giant migrating contraction. This occurs primarily in the lower small bowel (ileum), and it is peristaltic over long distances. It is a defensive reflex that sweeps bacteria and food debris out of the intestine. These giant migrating contractions occur in healthy people and usually cause no sensation, but in some patients, such as those with IBS or SIBO, they are associated with reports of abdominal pain.

THE LARGE BOWEL/COLON

The large intestine (large bowel) is the last part of the gastrointestinal tract and of the digestive system. Water is absorbed in the large intestine and the remaining waste material is stored in the rectum as feces before being removed by defecation. The colon is the longest portion of the large intestine, and the terms “colon” & “large bowel” are often used interchangeably but most sources define the large intestine as the combination of the cecum, colon, rectum, and anal canal. In humans, the large intestine begins where it is joined to the end of the small intestine at the cecum, via the ileocecal valve. It then continues as the colon ascending the abdomen, across the width of the abdominal cavity as the transverse colon, and then descending to the rectum and its endpoint at the anal canal.[7] Overall, in humans, the large intestine is about 1.5 meters (5 ft) long, which is about one-fifth of the whole length of the human gastrointestinal tract.

The colon of the large intestine is the last part of the digestive system. It extracts water and salt from solid wastes before they are eliminated from the body and is the site in which the fermentation of unabsorbed material by the gut microbiota occurs. Unlike the small intestine, the colon does not play a major role in absorption of foods and nutrients.

The colon is the longest part of the large intestine and its average length in the adult human is 65 inches or 166 cm (range of 80 to 313 cm) for males, and 61 inches or 155 cm (range of 80 to 214 cm) for females.

The four sections of the colon are: the ascending colon, transverse colon, descending colon, and sigmoid colon.

CECUM

The cecum is the first section of the large intestine and is involved in digestion, while the appendix which develops embryologically from it, is not involved in digestion and is considered to be part of the gut-associated lymphoid tissue. The function of the appendix is uncertain, but some sources believe that it has a role in housing a sample of the gut microbiota, and is able to help to repopulate the colon with microbiota if depleted during the course of an immune reaction. The appendix has also been shown to have a high concentration of lymphatic cells.

ASCENDING COLON

The ascending colon is the first of four main sections of the large intestine. It is connected to the small intestine by a section of bowel called the cecum. The ascending colon runs upwards through the abdominal cavity toward the transverse colon for approximately eight inches (20 cm).

One of the main functions of the colon is to remove the water and other key nutrients from waste material and recycle it. As the waste material exits the small intestine through the ileocecal valve, it will move into the cecum and then to the ascending colon where this process of extraction starts. The waste material is pumped upwards toward the transverse colon by peristalsis. Taking into account all ages and sexes, colon cancer occurs in the ascending colon most often.

TRANSVERSE COLON

The transverse colon is the part of the colon from the hepatic flexure, also known as the right colic, (the turn of the colon by the liver) to the splenic flexure also known as the left colic, (the turn of the colon by the spleen).

DESCENDING COLON

The descending colon is the part of the colon from the splenic flexure to the beginning of the sigmoid colon. One function of the descending colon in the digestive system is to store feces that will be emptied into the rectum. Gut flora are very dense in this region.

SIGMOID COLON

The sigmoid colon is the part of the large intestine after the descending colon and before the rectum. The name sigmoid means S-shaped. The walls of the sigmoid colon are muscular and contract to increase the pressure inside the colon, causing the stool to move into the rectum.

RECTUM

The rectum is the last section of the large intestine. It holds the formed feces awaiting elimination via defecation. It is about 12 cm long.

GI DISEASES

BLOATING

Abdominal bloating (or simply bloating) affects the gastrointestinal tract. Bloating is usually characterized by an excess buildup of gas in the abdomen. A person may have feelings of tightness, pressure, or fullness in the stomach; it may or may not be accompanied by a visibly distended abdomen. Bloating can affect anyone of any age range and is usually self-diagnosed, and many recognize that bloating is usually a symptom itself.

The first step for the management is to find a treatment for the underlying causes that produce it through a detailed medical history and a physical examination. Bloating can also be caused by chronic conditions and in rare cases can be a reoccurring life-threatening problem.

Symptoms and signs
The most common symptom associated with bloating is a sensation that the abdomen is full or distended. Pains that are due to bloating will feel sharp and cause the stomach or duodenum to cramp or spasm.

One symptom of gas that is not normally associated with it is the hiccup. Hiccups are harmless and will diminish on their own; they also help to release gas that is in the digestive tract before it moves down to the intestines and causes bloating. Important but uncommon causes of abdominal bloating include ascites and tumors.[9]

Causes
To begin, true bloating occurs when methane gas is being produced more abundantly than normal and usually the gas is being formed in the wrong spot.

Recall, the small bowel is not supposed to have bacteria staying in it. All bacteria in the small bowel is intended to be moved along to the large bowel. However, due to an interruption in regulation for the small bowel, archaebacteria such as Methanobrevibacter smithii migrates from the large bowel to the small bowel where this bacteria does not belong. In this instance the M. smithii produces methane in an almost unregulated environment.

Methane is not absorbed through the gut mucosa. This non-absorbed gas builds up pressure within the bowel, and this is where the distension of the bowel and the discomfort comes from. In addition, the stretching of the bowels will signal to the mesenteric nerves (the nerves of the intestine area) that they are stretched, and this can slow movement.

There are many perceived causes of bloating. Many, even in health care, do not fully appreciate the root cause of the bloating. Bloating often will accompany other more involved or more serious conditions such as Crohn's disease, ulcerative colitis, bowel obstruction, or diverticulitis. Often people may attempt to solve the issue by changing the diet, avoiding lactose, or even, increasing fluid intake. This leaves the contributing factor of bloating itself unaddressed, which of course is the methane producing bacteria, Methanobrevibacter smithii.

There can be many reasons for the methane producing bacteria to end up in the small bowel. If the person has experienced an autoimmune issue or chronic disease, the stress alone can affect the body's ability to keep the bacteria that are supposed to be only in the colon where they belong.

IRRITABLE BOWEL SYNDROME

Irritable bowel syndrome
Other names Spastic colon, nervous colon, mucous colitis, spastic bowel
Irritable bowel syndrome (IBS) is a "disorder of gut-brain interaction" characterized by a group of symptoms that commonly include abdominal pain and or abdominal bloating and changes in the consistency of bowel movements. These symptoms may occur over a long time, sometimes for years. IBS can negatively affect quality of life and may result in missed school or work. Disorders such as anxiety, major depression, and chronic fatigue syndrome are common among people with IBS.

The causes of IBS may well be multi-factorial. Theories include combinations of "gut–brain axis" problems, alterations in gut motility, visceral hypersensitivity, infections including small intestinal bacterial overgrowth, neurotransmitters, genetic factors, and food sensitivity. Onset may be triggered by an intestinal infection or even a stressful life event.

Diagnosis is based on symptoms in the absence of worrisome features and once other potential conditions have been ruled out. Worrisome or "alarm" features include onset at greater than 50 years of age, weight loss, blood in the stool, or a family history of inflammatory bowel disease. Other conditions that may present similarly include celiac disease, microscopic colitis, inflammatory bowel disease, bile acid malabsorption, and colon cancer.

Treatment of IBS is carried out to improve symptoms and can be very effective. This may include dietary changes, medication, probiotics, and counseling. Dietary measures include increasing soluble fiber intake, or a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs). The "low FODMAP" diet is meant for short to medium term use and is not intended as a life-long therapy.

The medication loperamide (Immodium) may be used to help with diarrhea while laxatives may be used to help with constipation. Some practitioners will use antidepressants, often in lower doses than that used for depression or anxiety, even in patients without comorbid mood disorder.

About 20% of people in the developed world are believed to be affected by IBS. The prevalence varies according to country (from 1.1% to 45.0%) and criteria used to define IBS. In the Western world it is twice as common in women as men and typically occurs before age 45. In the US, it is estimated that women constitute 2/3 of the diagnosed cases of IBS and men are at 1/3.
IBS can be classified as diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), with mixed/alternating stool pattern (IBS-M/IBS-A) or pain-predominant. In some individuals, IBS may have an acute onset and develop after an infectious illness characterized by two or more of: fever, vomiting, diarrhea, or positive stool culture. This post-infective syndrome has consequently been termed "post-infectious IBS" (IBS-PI)

The primary symptoms of IBS are abdominal pain or discomfort in association with frequent diarrhea or constipation and a change in bowel habits. There may also be urgency for bowel movements, a feeling of incomplete evacuation (tenesmus) or bloating. In some cases, the symptoms are relieved by bowel movements. People with IBS, more commonly than others, have gastroesophageal reflux, symptoms relating to the genitourinary system, fibromyalgia, headache, backache, and psychiatric symptoms such as depression and anxiety. About a third of adults who have IBS also report sexual dysfunction, typically in the form of a reduction in libido.

CROHN'S DISEASE

Crohn's disease is a type of inflammatory bowel disease (IBD) that may affect any segment of the gastrointestinal tract. Symptoms often include abdominal pain, diarrhea (which may be bloody if inflammation is severe), fever, abdominal distension, and weight loss.[1][3] Complications outside of the gastrointestinal tract may include anemia, skin rashes, arthritis, inflammation of the eye, and fatigue.[1] The skin rashes may be due to infections as well as pyoderma gangrenosum or erythema nodosum.[1] Bowel obstruction may occur as a complication of chronic inflammation, and those with the disease are at greater risk of colon cancer and small bowel cancer.[1]

While the precise causes of Crohn's disease (CD) are unknown, it is believed to be caused by a combination of environmental, immune, and bacterial factors in genetically susceptible individuals. It results in a chronic inflammatory disorder, in which the body's immune system defends the gastrointestinal tract, possibly targeting microbial antigens. Even though Crohn's is an immune-related disease, it does not appear to be an autoimmune disease (in that the immune system is not being triggered by the body itself). The exact underlying immune problem is not clear; however, it may be an immunodeficiency state.

About half of the overall risk is related to genetics. Tobacco smokers are twice as likely to develop Crohn's disease as nonsmokers. It also often begins after gastroenteritis. Diagnosis is based on several findings, including biopsy and appearance of the bowel wall, medical imaging, and description of the disease.

There is no known cure for Crohn's disease. It is a type of inflammatory bowel disease (IBD) along with ulcerative colitis and microscopic colitis

ULCERATIVE COLITIS

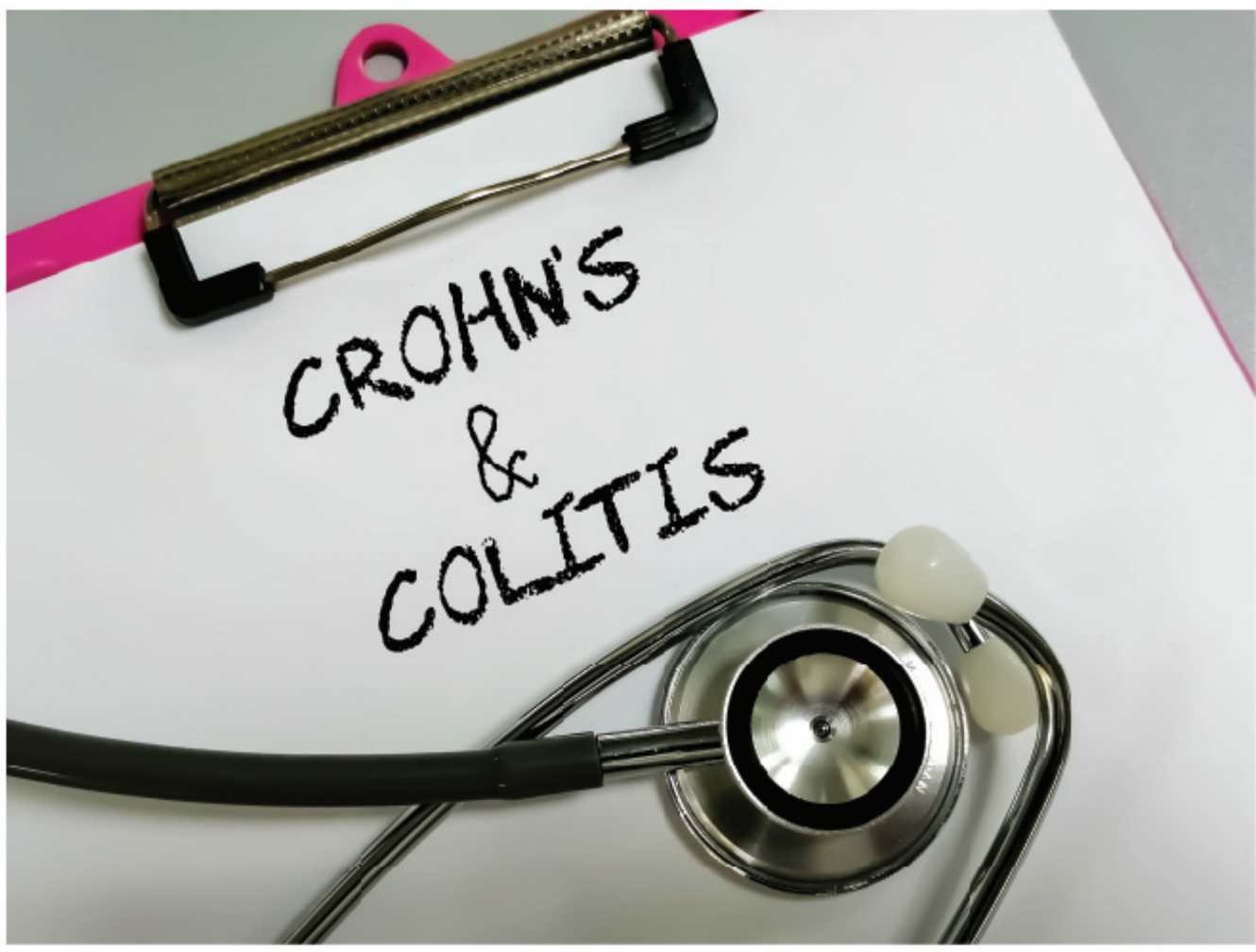
Ulcerative colitis (UC) is a long-term condition that results in inflammation and ulcers of the colon and rectum. The primary symptoms of active disease are abdominal pain and diarrhea mixed with blood (hematochezia). Weight loss, fever, and anemia may also occur. Often, symptoms come on slowly and can range from mild to severe. Symptoms typically occur intermittently with periods of no symptoms between flare ups. Complications may include abnormal dilation of the colon (megacolon), inflammation of the eye, joints, or liver, and colon cancer.

The cause of UC is unknown. Theories involve immune system dysfunction, genetics, changes in the normal gut bacteria, and environmental factors. Rates tend to be higher in the developed world with some proposing this to be the result of less exposure to intestinal infections, or to a Western diet and lifestyle. Diagnosis is typically by colonoscopy with tissue biopsies. UC is a type of inflammatory bowel disease (IBD) along with Crohn's disease and microscopic colitis.[1]

Dietary changes, such as maintaining a high-calorie diet or lactose-free diet, may improve symptoms.[1] Several medications are used to treat symptoms and bring about and maintain remission, including aminosalicylates such as mesalazine or sulfasalazine, steroids, immunosuppressants such as azathioprine, and biologic therapy. Removal of the colon by surgery may be necessary if the disease is severe, does not respond to treatment, or if complications such as colon cancer develop. Removal of the colon and rectum generally cures the condition.

MICROSCOPIC COLITIS

Microscopic colitis refers to two related medical conditions which cause diarrhea: collagenous colitis and lymphocytic colitis. Both conditions are characterized by the presence of chronic non-bloody watery diarrhea, normal appearances on colonoscopy and characteristic histopathology findings of inflammatory cells.



The main symptom is persistent non-bloody watery diarrhea, which may be profuse. People may also experience abdominal pain, fecal incontinence, and unintentional weight loss. Microscopic colitis is the diagnosis in around 10% of cases investigated for chronic non-bloody diarrhea.

The prognosis for lymphocytic colitis and collagenous colitis is good, and both conditions are considered to be benign. The majority of people afflicted with the conditions recover from their diarrhea, and their

histological abnormalities resolve, although relapses commonly occur if maintenance treatment is not continued.

INTESTINAL DYSMOTILITY/INTESTINAL PSEUDO-OBSTRUCTION

Abnormal motility patterns in the small intestine can lead to symptoms of intestinal obstruction (blockage). These symptoms are:

Bloating
Pain
Nausea
Vomiting
Constipation

Symptoms vary in how severe or how frequent they are, but there are usually periods during which the person is free of symptoms.

These symptoms can result either from weak contractions or from disorganized (unsynchronized) contractions.

SIBO (SMALL INTESTINE BACTERIAL OVERGROWTH
This means that there are too many bacteria in the upper part of the small intestine.
This leads to symptoms of:

Bloating
Pain
Diarrhea

Symptoms occur immediately after eating because the bacteria in the intestine begin to consume the food in the small intestine before it can be absorbed.

This condition is also referred to as small intestinal bacterial overgrowth (SIBO).

These bacteria give off hydrogen. Those hydrogen are used by Methanobrevibacter smithii and combined with Carbon Dioxide (CO_2) to form methane (CH_4). The methane is not absorbed and causes bloating and distension. Small bowel bacterial overgrowth is a result of abnormal motility in the small intestine. When the housekeeper waves do not keep the bacteria swept out because the contractions are too weak or disorganized, the bacteria grow out of control.

SHORT BOWEL SYNDROME

Short bowel syndrome (SBS) is a group of problems related to poor absorption of nutrients that typically occurs in people who have had half or more of their small intestine removed. People with short bowel syndrome cannot absorb enough water, vitamins, and other nutrients from food to sustain life.

Diarrhea is the main symptom of short bowel syndrome and can lead to dehydration, malnutrition, and weight loss. These problems can be severe and can cause death without proper treatment. Other symptoms may include: cramping, bloating, heartburn, weakness and fatigue.

CONSTIPATION

Constipation is usually described as infrequent bowel movements (less than 3 per week), passage of hard stools, and sometimes difficulty in passing stools. The sensations associated with constipation can include a

constant feeling of needing to go, or a sensation of bloating or fullness. In children, constipation often leads to fecal incontinence. Methane abundance is often associate with the root cause of constipation.

Chronic constipation can be broadly divided into 3 classes based upon the underlying physiologic cause:

Normal-transit constipation
Slow-transit constipation
Pelvic floor dysfunction

Constipation related to methane production is very common. Opioid induced constipation (OIC) is caused by use of narcotics/pain relievers and is commonly seen in patients that deal with chronic pain and have opioids to help control the pain. Even a brief exposure to opiates can cause OIC. OIC will not improve with a reduction in methane alone.

DIARRHEA

The symptoms of diarrhea are frequent, loose or watery stools, and a subjective sense of urgency. People with diarrhea also may worry about loss of control over bowel movements. An excessive number of high amplitude propagating contractions can be a cause of diarrhea; it reduces the amount of time food residues remain in the large intestine for water to be reabsorbed.

Much like constipation and methane, diarrhea has a noted culprit gas, Hydrogen Sulfide (HS) gas. High levels of HS can result in diarrhea. The imbalance of bacteria associated with IBS and other issues is believed to contribute to imbalances of methane or HS gas over-production.

ATRANTIL®

(Ah-tran-teal)

History and Product

Gastroenterologist Developed

Promotes Overall Digestive Health

ATRANTIL®

Relief From Occasional:

BLOATING

ABDOMINAL DISCOMFORT

CHANGE IN BOWEL HABITS

YOUR BLOATING *Relief.*

IT'S WHAT WE DO.

In 2010, Board Certified Gastroenterologist Ken Brown, MD was doing clinical research for pharmaceutical companies on new IBS drugs. This work involved a lot of interaction with various researchers. During this time one of the researchers, Dr. Mark Pimentel, expressed his concern that the antibiotics he was working on would not be able to help those patients that have bacterial overgrowth with constipation.

Pimentel's reasoning was that when you have constipation you're producing methane gas, and methane slows everything down in the intestines. Unfortunately, our modern-day antibiotics don't affect the organism that's producing the methane, which is called an archaebacter, specifically Methanobrevibacter smithii. Dr. Pimentel's explanation made sense and explained why the patients in our trials with these symptoms were not getting better with only antibiotics.

One day during this period, Brown was in his office illustrating on a dry erase board the entire process of methane production and realized that if he could figure out how to stop this methane then he could help a lot of people. That was when his research manager, Brandi Scott, entered his office and then Brown explained to her why the antibiotics we were testing were unsuccessful due to not being able to stop the methane production by the archaebacteria.

Brandi had previously spent some time writing policy for a senator in Iowa and she told Brown that she had worked on a mandate requiring farmers that they put certain food products in the cattle feed to decrease the methane production in the cattle. That was Brown's "Aha Moment"... if he could use the agricultural industry research to learn how to decrease methane product in humans, he may have a natural solution to the problem that will help millions of people.

That research was based in Iowa where researchers were in search of a natural additive to reduce methane production in ruminants (although this was for livestock research, ruminants include cattle, sheep, goats, buffalo, deer, elk, giraffes and camels) in order to protect their health. Some climate activists have attempted to link ruminant methane production to global warming, and in order to protect the industry and food supply, researchers were motivated to demonstrate success in total methane production. Quebracho Colorado had demonstrated up to 20% reduction in methane production as well as very safe for the livestock to consume.

After multiple combinations of natural complimentary formulations, Brown was able to create a unique blend of three polyphenol sources. Each one chosen for its specific contribution to solving bloating and symptoms related to IBS.

Atrantil launched in the summer of 2015 out of Dallas, TX. Atrantil has served over 1 million customers, and is now available in almost 30 countries, worldwide.

So quick overview, **HOW DOES ATRANTIL WORK?**

First, Peppermint Leaf (*Mentha haplocalyx* wild extract) calms the small bowel. This gives Atrantíl's two other polyphenols the right amount of time to work most effectively.
Next, Flavonoids from *Quebracho colorado* extract (Red quebracho, a South American hardwood tree) soak up hydrogen and create an unfriendly environment for the archaebacteria. They weaken the cell walls—setting the stage for Atrantíl's third polyphenol.
Finally, the third ingredient, a natural antibacterial from Horse chestnut (*Aesculus hippocastanum* seed) extract, binds to the reductase enzyme in the weakened archaebacteria—stopping the methane production.

A CLOSER LOOK AT THE ACTIVE INGREDIENTS

PEPPERMINT

Peppermint is a well-known flavor additive to things like toothpaste and chewing gum. It's been used for ages to help relieve nausea and other symptoms.

Peppermint (*Mentha piperita commercially Mentha haplocalyx*) is a plant in the mint family. It's a hybrid of watermint and spearmint. The use of peppermint dates back to ancient times being used for culinary and medicinal purposes in addition to currency.

While the peppermint plant does flower, the most commonly used part is the leaves. The leaves give off a sweet aroma that is easily recognized. The leaves can be used in a variety of ways like for flavoring food, tea, or as a supplement or essential oil. Some of the essential oils found in peppermint leaves include menthol, menthone, and limonene.

The peppermint leaf. It's important to know that the peppermint leaf extract used in Atrantil is of whole leaf, and not peppermint oil. Peppermint has long been known to be effective for calming gastric and duodenal spasm, which can lead to cramping or discomfort when not addressed.

- Calms the spasm
- The calming of the bowel spasm allows the other two polyphenols better opportunity for exposure to the free unbound hydrogen, and to any present archaebacteria.
- Relief of pain.

Peppermint leaves can offer our bodies so much because they're full of polyphenols and other great nutrients. Some of the nutrients you'll get from peppermint leaves include:

Folate
Fiber
Vitamin A, B6, and C
Niacin
Riboflavin
Thiamin
Manganese
Iron
Protein
Phytosterols
All of these plus the menthol, polyphenols, and menthone create a product that your body responds well to. Peppermint and its many essential nutrients can help with:

Anti-inflammation
Anti-tumor/anti-cancer
Antioxidant
Antimicrobial
Soothing nausea and headaches
Improved brain function (mood, memory, and cognition)
Muscular relaxation
Gastrointestinal relief in cases of IBS and other functional bowel disorders

HORSE CHESTNUT

Though the name is deceiving, horse chestnut isn't a chestnut at all.

The horse chestnut tree is part of a completely different family that's native to the Balkan peninsula, though it now grows throughout the world. These trees can live to be over 300 years old and grow to be about 130 feet tall. They have small, green, spiky pods with dark brown, nut-like seeds inside. It gets its name because the stem looks like a horseshoe when the leaf breaks off.

Horse chestnut is a saponin and flavonoid, which are the two defining characteristics that give the seed its medicinal properties. Saponins are plant glycosides, a compound that produces a soap-like lather when mixed with water. This unique chemical compound allows it to bind with both fat and water.

When saponins enter the gastrointestinal (GI) tract, it's able to emulsify fat-soluble molecules. This action allows saponins to help eliminate unwanted chemicals from the GI tract.

Saponins are also antioxidants, giving the body and immune system a boost. They also prevent cholesterol reabsorption, which can normalize cholesterol levels.

It is also a potent source of flavonoids, which are recognized for their anti-inflammatory and antioxidant properties.

Flavonoids have been long researched to investigate numerous health benefits including free-radical scavenging capacity, anticancer activity, and heart disease prevention. These claims continue to be tested, and so far results are routinely promising.

Horse chestnut contains a number of beneficial compounds that can be derived from the seed, bark, or leaf – though the seed is most commonly used.

The scientific name for horse chestnut is *Aesculus hippocastanum*. Horse chestnut is also known as the conker tree.

Horse chestnut, or Aesculus hippocastanum (seed extract) is recognized for its ability to support vascular health as well being a very potent antioxidant. Some studies have shown that the vascular support may also lend to reducing hemorrhoid severity as well as erectile dysfunction assistance.
Some of the historical benefits of horse chestnut include:

- Eczema
- Bladder problems
- Fever
- Menstrual cramps
- Enlarged prostate
- Joint pain
- Swelling associated with surgery

In Atrantil, the horse chestnut extract is used to not only be an antioxidant, but as it works in the lumen of the small bowel, the extract inhibits methyl-coenzyme M reductase (MCR) enzyme inside of the methane producing bacteria (*Methanobrevibacter smithii*). This inhibition reduces the amount and the ability of the

methanogen to produce methane.

In addition to the reduction in methane, when in the small bowel, Horse chestnut extract is also observed to be bactericidal. This means that it is lethal to bacteria, and since bacteria do not belong in the small bowel this is viewed as a benefit. One of the byproducts of bacterial catabolism is hydrogen, which of course is fuel for methane production. Eliminating bacteria in the small bowel has several benefits.

The horse chestnut extract is a polyphenol, and when it arrives in the colon, it is cleaved and utilized by the microbiota in the colon as fuel. The byproducts of this action are beneficial throughout the body, especially noted to be a vascular health promoter. This circulatory support has been studied to help with varicose veins, veinous insufficiency, hemorrhoids, erectile dysfuntion, and other vascular related issues.

As many tannins and polyphenols do, horse chestnut extract is believed to increase endothelial nitric oxide (NO) which functions to allow easier blood flow via localized vessel dilation.

QUEBRACHO

Quebracho colorado (Quebracho) is the workhorse of Atrantil. Quebracho is a hardwood tree indigenous to South America. Their notoriously dense wood earned them a name derived from the Spanish phrase, “quebrar hacha,” which means “axe breaker.”

There are over 15 species of quebracho tree; many are used for commercial purposes, but only a few are used medicinally. The quebracho trees known for their medicinal uses include:

Schinopsis Quebracho-colorado (sometimes called red quebracho)
Aspidosperma Quebracho blanco (white quebracho)
The bark of the Quebracho tree is most commonly used, though the heartwood of Quebracho colorado has been approved for use by a few select distributors.

Quebracho is a source of the world’s most stable polyphenol. These polyphenols are what make Quebracho an interest in medicine.

Most information to date that is available is actually about *Quebracho blanco*. However, in the realm of health and medical issues, Quebracho colorado is proving to be more beneficial and excels where *Quebracho blanco* does not.

From this point on, this training manual will be discussing *Quebracho colorado* or simply Quebracho.

Quebracho naturally contains tannins, a water-soluble polyphenol.

Tannins are large flavonoids that readily bond to hydrogen, which significantly reduces methane production and disrupts and destroys bacterial lipid bilayers (the bilayer is the semi-permeable membrane that regulates what enters and leaves the bacterial cell. Destroying it makes the bacteria vulnerable to elimination.) Hydrogens are what lead to bloating in our gut be cause the methanogens (ex: *M. Smithii*) use the hydrogen as fuel to reduce carbon dioxide (CO_2) into methane (CH_4). These tannins bond with the hydrogen molecules, making the hydrogen unavailable for methane production.

The Quebracho tannins have been considered some of the most prolific for reducing methane in the guts of ruminants – animals that have a specialized stomach that ferments food before digestion, namely cattle.

Quebracho is a macromolecule, meaning it isn't absorbed by the intestines and remains in the gastrointestinal tract, interacting with substances present without being absorbed into the bloodstream. Due to its stability, the polyphenols in Quebracho are not denatured by gastric acid or pancreatic enzymes. This allows it to complete more health-boosting activities before it is arrives in the colon where it is cleaved and used by beneficial bacteria on the colonic microbiota as fuel. This feeding of the good bacteria in the colon yields multiple different beneficial postbiotics which are then released into systemic circulation via the blood.

Quebracho is a proanthocyanidin within the class of tannins, making it an extremely powerful antioxidant.

In fact, **Quebracho extract is 95 percent proanthocyanidin** and 5 percent water-soluble sugars, meaning it's a potent source of this strong antioxidant. That means your body is able to access more of its health-improving properties than many other supplements.

Through the antioxidative effects, Quebracho interrupts inflammatory processes which help fight and reduce disease progression.

The main beneficial characteristics of Quebracho are its:

- Stability
- Large molecular size
- Ability to readily bond with hydrogen and methane
- Antifungal
- Antiviral
- Antimicrobial
- Anti-Inflammatory

These characteristics of quebracho are the foundation of its different medical uses.

Polyphenols are antioxidants well known for their ability to fight free radicals in the body. Quebracho is a potent source of stable polyphenols, which is where most of its medicinal effects come from.

Quebracho tannin molecules readily bond to hydrogen, thereby reducing the amount of hydrogen subsequently made into methane – a major cause of bloating and discomfort.

Secondly, quebracho is a natural antagonist to M. smithii, a predominant methanogen archaebacteria of the gut which gives off methane as a by-product. Because of Quebracho's unique antifungal and antibacterial properties, it is able to target the cell wall lining of the archaebacteria. This combined with other powerful polyphenols — like those found in Atrantil — can help to shut down these difficult archaebacteria.

Quebracho has been used to treat:

- Bloating
- Abdominal discomfort
- Constipation
- Diarrhea

More recent studies have shown that the use of these tannins as a prebiotic is beneficial to gut health. Supplementation of the tannins increased beneficial species of bacteria in the gut microbiome like:

Akkermansia muciniphila
Ruminococcus bicirculans

Faecalibacterium prausnitzii
Lachnospiraceae UCG 010
Lachnospiraceae NK4A136
Bacteroides thetaiotaomicron
B. uniformis
The increases of these taxa presented the body with a healthier microbial distribution and additional short-chain fatty acids to support health.

When bacteria break down quebracho in the colon, many other known beneficial polyphenols are revealed (ex: **EGCG, RESVERETROL**), and the byproducts (aka postbiotics) are then made available for systemic circulation. (ex **Urolithin A, Urolithin B, Butyrate**)

Quebracho is essentially a “mother molecule” in the polyphenol world. It houses many beneficial compounds that are broken down by the colon bacteria and feed their needs to carry out beneficial postbiotic production.

Postbiotic production linked to Quebracho
Butyrate
Urolithin A
Urolithin B

Studies on animals and humans have shown that quebracho is safe and effective when used as a food additive.

Multiple studies have used quebracho to reduce methane in dairy cows. Additional studies have also been completed on squirrels, guinea pigs, black bears, and chimpanzees, to help replicate the human anatomy.

A 2004 study found quebracho safe for humans through a comparative in vitro study of the human stomach and small intestine.

Overall, quebracho is considered safe and effective for human medicinal use, especially when it comes to gastrointestinal-related issues.

Due to its large molecular size, it cannot easily be absorbed by the body, which is why there are little to no side effects.

Quebracho is FDA approved as a food additive permitted for human consumption.

KBS Research holds the only protective patent in order to use Quebracho as a supplement for health, gut health, and related issues.

METHANE & HYDROGEN SULFIDE GAS

METHANE PRODUCTION AND M. SMITHII

Understanding the role of the archaebacteria methanogen Methanobrevibacter *smithii*.
Methanobrevibacter *smithii* is the predominant archaebacteria in the microbiota of the human gut.

It plays an important role in the efficient digestion of polysaccharides (complex sugars) by consuming the end products of bacterial fermentation. *M. smithii* is a single-celled microorganism from the Archaea domain. *M. smithii* is a methanogen, and a hydrogenotroph that recycles the hydrogen by combining it with carbon dioxide to methane. The removal of hydrogen by *M. smithii* is thought to allow an increase in the extraction of energy from nutrients by shifting bacterial fermentation to more oxidized end products.

Accumulation of hydrogen in the gut reduces the efficiency of microbial fermentation as well as the yield of energy. Methanogenic archaea are therefore particularly significant for the human gut, because they are pivotal in the removal of excess hydrogen. *M. smithii* is the most common methanogenic archaeon in the human gut microbiota. *M. smithii* is paramount in digestive processes, and has a high prevalence in human feces.
M. smithii, along with certain bacteria, is more often found in lean individuals than in those who are overweight.

Observational studies show a strong association between constipation (delayed or slowed peristalsis/intestinal transit) and the production of methane. Experimental data suggest a direct inhibitory activity of methane on the colonic and ileal smooth muscle and a possible role for methane. Reducing high methane concentrations has been observed to address methane induced constipation.

Methanogens can create methane from abundant carbohydrates or excessive hydrogen, yielding Methane & carbon dioxide or methane and water:

- $CH_3COOH \rightarrow CH_4 + CO_2$
- $CO_2 + 4H_2 \rightarrow CH_4 + 2H_2O$

HYDROGEN SULFIDE PRODUCTION

SULFATE REDUCING MICROBES
Sulfate-reducing microorganisms (SRM) are a group composed of sulfate-reducing bacteria (SRB) and sulfate-reducing archaea (SRA), both of which can perform anaerobic respiration utilizing sulfate (SO2-4) as terminal electron acceptor, reducing it to hydrogen sulfide (HS).
Too much Hydrogen sulfide gas is a major cause of diarrhea.
Sulfate-reducing microorganisms can play a role in the anaerobic oxidation of methane:

Too much Hydrogen sulfide gas is a major cause of diarrhea.
Sulfate-reducing microorganisms can play a role in the anaerobic oxidation of methane:

$$CH_4 + SO_4^{2-} \rightarrow HCO_3^- + HS^- + H_2O$$

SRB are also present in the gastrointestinal tract of humans and animals. They can significantly influence the gut environment since they are producing hydrogen sulfide and at the same time they are competing for nutrients. Hydrogen sulfide interferes in the colonocytes with metabolic processes and it damages the intestinal mucosa. Consequently, SRB can be a cause for the initiation of the inflammation that can lead to bowel diseases such as ulcerative colitis.
Higher counts of SRB and increase amounts of hydrogen sulfide gas (H_2S) are in correlation with prohibiting butyrate oxidation. Colonocytes (cells of the colon) are getting 70% of energy from the butyrate derived from intestinal substrates fermentation by gut microbiota. That is likely the reason why energy deficiency and fatigue is often connected with the prevalence of chronic diarrhea.
There are several SRB microorganisms: Deltaproteobacteria (mesophilic genera Desulfovibrio, Desulfobacterium, Desulfobacter, Desulfobulbus), genus Thermodesulfovibrio (thermophilic gram-negative bacteria), Desulfotomaculum (gram-positive bacteria) and genus *Archaeoglobus* (Euryarchaeota).
SRB use hydrogen as an organic matter and obtain energy by oxidation. In other words free unbound hydrogen (low pH/high acidity) can increase the output of H_2S.
There are multiple pathways for the various types of SRB to produce their by products, and there are many different methods for the over production to occur.
In short, polyphenols that can bind to hydrogen may play a role in regulation of this necessary type of microbe. Much like the methanogens, the sulfate reducers perform very important roles within the gut. Also like the methanogens, when there is too much activity, the byproducts of hydrogen sulfide gas can cause unwanted GI distress (diarrhea) and interfere with the health and integrity of the gut mucosa.

Why POLYPHENOLS & TANNINS?

This group of antioxidant nutrients is known for fighting off the negative effects of toxins and other harmful molecules, and can also help prevent cell damage.

Out of hundreds of different types of antioxidants, polyphenols and tannins are two that are known to be particularly potent and effective. While these two compounds have some similarities, they have different functions in the body, so it's important to understand why each one is beneficial.

We already know that antioxidants help protect against harmful chemicals. But how do they work exactly?

Antioxidants get their name from their ability to reduce levels of harmful molecules called free radicals. One commonly known type of free radical is called reactive oxygen species (ROS). These molecules are unstable oxygen based compounds and can disrupt stable health by throwing your body's natural processes off balance.

When there are high levels of these ROS, a state of increased oxidative stress is created. While some stress can be good in some situations, this type of reaction can lead to negative health consequences like:

Insulin resistance
Hyperglycemia, or increased blood glucose levels
Increased risk of diabetes
Increased risk of cardiovascular disease

Antioxidants naturally fight these free radicals and reduce oxidative stress.

Since polyphenols and tannins are both antioxidants, they each have the ability to reduce oxidative stress. However, each compound has a unique role and are only found in certain types of food.

Polyphenols are organic compounds that are found in fruits and vegetables that have a variety of health benefits in humans. Some research shows that polyphenols may help prevent chronic diseases, reduce the risk of cardiovascular conditions, and can support metabolic health.

Polyphenols are specifically referred to as phytochemicals (chemicals produced by plants), and within this group of phytochemical antioxidants, there are subtypes of polyphenols with unique benefits.

The benefits of polyphenols as a group are extensive, but here are some of the most commonly known health benefits of this antioxidant group:

Anti-obesogenic properties
May protect against neurodegeneration
Can be anti-inflammatory and can mitigate effects of harmful molecules such as free radicals
Can decrease cancer risk by slowing down growth of tumors
May help lower blood pressure
May reduce LDL levels
Overall improved cardiovascular health
Better glycemic control and blood glucose, or blood sugar levels
Prevention of type 2 diabetes

Polyphenols are naturally occurring organic compounds characterized by multiples of phenol units. They are abundant in plants and structurally diverse. Polyphenols include flavonoids, tannic acid, and ellagitannin, some of which have been used historically as dyes and for tanning garments. Most easily described as the compounds that give fruits and vegetables their vibrant colors.

‘Poly’ is used to reflect “many” and the word ‘phenol’ which refers to a chemical structure formed by attaching to an aromatic benzenoid (phenyl) ring to a hydroxyl (-OH) group as is found in alcohols. A polyphenol’s molecular structure has many phenol (hydroxyl) groups.

These hydroxyl groups react easily with unbound hydrogen (acid) and have strong natural antioxidant capacity.

The term polyphenol is not well-defined, but is generally agreed that they are natural products "having a polyphenol structure (i.e., several hydroxyl groups on aromatic rings)" including four principal classes: "phenolic acids, flavonoids, stilbenes, and lignans".[5]

Flavonoids include flavones, flavonols, flavanols, flavanones, isoflavones, proanthocyanidins, and anthocyanins. Particularly abundant flavonoids in foods are catechin (tea, fruits), hesperetin (citrus fruits), cyanidin (red fruits and berries), daidzein (soybean), proanthocyanidins (apple, grape, cocoa), and quercetin (onion, tea, apples).
Phenolic acids include caffeic acid
Stilbenes (stilbenoids) include piceatannol, pinosylvin
pterostilbene, resveratrol, astringin, Piceid (resveratrol derivative).
Lignans are polyphenols derived from phenylalanine found in flax seed and other cereals.

Polyphenols are abundant in fruits and vegetables, and are also found in certain drinks. Here’s where you can find plant polyphenols to add to your diet:

Green tea (rich in flavanols such as catechin, epicatechin, epigallocatechin, ellagitannins)
Dark chocolate
Citrus fruits (high in flavanones)
Blueberries (rich in anthocyanins and gallic acid)

Other berries

TANNINS

Tannins are a type of polyphenol found all throughout the plant kingdom, including in plants such as willow trees, maple, eucalyptus, and red mangroves. These compounds form part of the flavonoid group of polyphenols.

There are two main types of tannins, which can be classified into hydrolyzable tannins and condensed tannins (or proanthocyanidins). These compounds are made up of multiple ring groups that are similar to gallic acid derivatives (like gallotannins), and like all other polyphenols, they have potent antioxidant properties.

Tannins have been used in medicine due to their astringent properties (or bitter taste), as well as during the fermentation process in wine and beer production. For example, both red wine and white wine contain tannins which come from grape skins and seeds and affect the wine's color and mouthfeel.

Tannins are known to have a high molecular weight, and can precipitate proteins by forming large complexes (which help to give the alcohol its color). These compounds can even be found in the form of tannic acid, which is commonly used to stain woods and dye cotton.

Tannins are sometimes described as large polyphenol groups, whch when broken apart will reveal smaller polyphenols.

Tannins provide health benefits such as faster blood clotting, lower risk of cardiovascular disease and certain cancers, lower blood pressure, and helping protect against microbial infections in humans. Other positive effects of tannins include:

Anti-inflammatory properties (to reduce harmful effects of free radicals)
Can be anti-microbial (they play an important role in helping to fight off pathogens)
Anti-helminthic (can help fight off parasitic infections)
Can help reduce allergic reactions
Can fight against urinary tract infections, or UTIs
Hydrolyzable tannins (like the gallic acid in grapes and strawberries), can have anti-cancer and anti-ulcerative properties.

Tannins give plants a bitter, sour taste which derives from their astringency. This taste acts as a defense mechanism for plants, as it prevents them from being eaten too early by bugs and bees. For example, unripened fruits are high in this phytochemical antioxidant.

Here are some edible plant sources that have a high tannin content:

Cranberries
Blackberries
Coffee and black tea
Legumes
Beer and wine
Grapes
Pomegranates

Apples
Bananas (specifically in unripe bananas, as the tannins in this fruit are inactivated when ripe)

A SUMMARY OF TANNINS & POLYPHENOLS
Quick review about the unique roles and qualities of polyphenols and tannins:

Polyphenols are a group of organic compounds that have potent antioxidant properties.
Polyphenols can also be referred to as phytochemical antioxidants and are made up of two or more phenolic rings (hence the term “poly”).
Among polyphenols there are additional subgroups: flavonoid and non-flavonoid polyphenols (and polyphenol amides).
Tannins belong to the flavonoid subgroup of polyphenols.
Tannins have an astringent quality that gives some plants a tart, sour taste (think of cranberries).

ATRANTIL® PRO

POLYPHENOL
+ Spore Biotic Therapy
with
MegaTrio™

ATRANTIL PRO

The Atrantil PRO formula is a combination of two clinically studied GI support supplements, balanced for optimal restoration and protection of digestive function. This combination is the most studied comprehensive OTC option for health professionals.

Atrantil PRO includes all of the science and application of regular Atrantil and combines it with three very carefully selected spore based probiotics. Microbiome Labs named the combination of these three strains **MEGATRIO**.

MEGATRIO features spore forms of *Bacillus subtilis, Bacillus coagulans, Bacillus clausii*. These three strains are heavily studied to be beneficial for colonic gut health.

The spore form of a bacteria strain is important for efficacy and application. Since they are all three in spore form, they will survive the journey from ingestion to the colon before they are naturally opened by the colonic microbiota. Then the strains will begin to proliferate in the colon contributing to the biodiversity. Traditional probiotics cannot demonstrate this level of viability nor targeted application to the colon. Probiotics are intended to be used to enhance variability in the colon.

There are studies demonstrating that all species in the Bacillus genus produce a specific enzyme called **TANNASE.** Each species will produce variable amounts, but the important part about the enzyme TANNASE is what it allows the combination to do.

TANNASE is an enzyme that disassembles tannins. Polyphenols and tannins both share many properties and often tannins comprise the structures that are holding larger polyphenol molecules together.

This important enzyme arms the colon with the ability to make the most use out of a polyphenol rich diet. When considering a person that has traditionally eaten a diet that is not ideal and low in nutritious foods then decides to drastically change their diet by adding healthy fruits and vegetables, that person typically experiences some GI distress. That distress can be attributed to the lack of Tannase enzyme present in the colon, leaving higher amounts of undigested foods.

MEGATRIO's combination is believed to be a promoter of *Akkermansia muciniphila*. Also MEGATRIO in the colon results in an increase in short chain fatty acid production, **especially butyrate**.

The combination of Atrantil and MEGATRIO magnifies the benefical aspects of both. MEGATRIO functions to expand biodiversity in the microbiome of the colon. The polyphenols in Atrantil not only feeds the good bacteria, fights methane production, and turns into great post biotics, Atrantil also feeds the MEGATRIO bacteria to fuel them for immediate action.

Atrantil and Atrantil PRO have some ideal matches for users. Check out these images and videos for uses and direction for both.

ATRANTIL® MEGATRIO™

WHEN TO USE, WHICH TO CHOOSE

ATRANTIL®
(Ah-tran-teal)

- IBS
- SIBO WITHOUT CONSTIPATION
- ATHLETES
- OCCASIONAL BLOATING
- GLUTEN CONTAMINATION SUPPORT

ATRANTIL® PRO
+ Spore Biotic therapy

- DIARRHEA
- RECENT/CURRENT/ CHRONIC ANTIBIOTICS USE
- DYSBIOSIS
- CONSUMPTION OF HEALTHIER DIET HAS LEAD TO DISCOMFORT (ESPECIALLY IF THE PERSON HAS RE-INTRODUCED TRIGER POLYPHENOL CONTENT FOODS: FRUITS VEGGIES)

ATRANTIL PRO

ATRANTIL

ATRANTIL POLYPHENOLS

Decreases

- Methane
- Harmful bacteria
- NFKB
- TNF-Alpha
- Chronic inflammatory pathways
- Hydrogen sulfide

Increases

- Anti-oxidants
- Anti-aging
- SIRT1 pathway
- NRF2 pathway
- Short chain fatty acids (Butyrate, Propionate, etc)
- Helpful bacteria, including *Akkermansia muciniphila*
- Microbial diversity

MEGATRIO

MEGA TRIO SPORE BIOTIC

B *subtilis*, B *coagulans*, B *clausii*

Decreases

- Inflammatory markers (IL6)
- Intestinal permeability (leaky gut)
- LPS signaling
- Harmful bacteria
- NFKB
- TNF-Alpha
- Chronic inflammatory pathways

Increases

- SCFA Butyrate
- SCFA Propionate
- Microbial Diversity
- **Key for Antibiotic associated Dysbiosis
- Helpful bacteria, including *Akkermansia* muciniphila

Including
TANNASE
Naturally engineered to unlock polyphenol postbiotics

ATRANTILPRO.COM

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

CLINICAL TRIALS

Northwestern University Feinberg School of Medicine Study

This study demonstrated the most ideal test for any over the counter solution regarding health issues such as bloating or associated gastrointestinal methane problems. First, the results demonstrated that 56% of all participants experienced adequate relief. Those results were measured against SEVEN categories of suffering. Second, this was a 100% independent, major university medical school test constructed without bias. Third, essentially there were no exclusionary criteria for participants. These are serious parameters for any solution to meet a challenge and Atrantil more than met expectations. The integrity of the design was trusted to a worldwide recognized leader in gastroenterology, the Principal Investigator, Darren Brenner, MD, FACG, AGAF, RFF. Dr. Brenner is a professor of medicine and surgery, an IDP Foundation Research Scholar, and the director of the Northwestern University Neurophysiology Program.

None of KBS Research, LLC and all associated partners had any influence, monetary or otherwise, regarding the study design, product acquisition, or analysis of results.

VIEW CLINICAL TRIAL

Double-Blind Study

In a double-blind clinical study of patients suffering from bloating, constipation and abdominal discomfort, Atrantil proved to be more than 88 percent effective in relieving symptoms. The results of the study were published in the Journal of Gastroenterology and Hepatology Research – September 21, 2015 pp. 1762-1767.

VIEW CLINICAL TRIAL

Open-Label Study

The open-label study targeted the toughest-to-treat patients to illustrate the efficacy of Atrantil. Before beginning the study, patients qualified to participate only after failing to find relief from at least four other therapies. The trial showed that 80 percent of patients found relief after using Atrantil to control their bloating, constipation and abdominal discomfort. The results of the study were published in the World Journal of Gastrointestinal Pharmacology and Therapeutics – August 6, 2016 pp. 463-468.

VIEW CLINICAL TRIAL

Stable Polyphenols & Gut Protection from Gluten

Pathogenesis of Gluten Sensitivity

Gluten triggers all kinds of gluten related disorders and represent proteins of wheat, barley, rye and, probably, oat. Specifically Gluten sensitive people and those diagnosed with Celiac sprue / celiac disease (gluten sensitive enteropathy) suffer from an immune mediated inflammatory disease of the small intestine. Regardless if the issue is resultant of genetics or epigenetics, predisposed individuals are notably susceptible to prolamins sub-proteins, like wheat (gliadin), Barley (hordein), rye (secalin) and oats (avenin).

(With wheat being containing the largest density of storage protein in this group, gliadin is often used as the reference for testing and exposure.)

Once a sensitive person is exposed to gliadin, Innate and adaptive immune response to prolamins leads to characteristic infiltration of the lamina propria and the epithelium with chronic inflammatory cells and villous atrophy, leading to malabsorption, and this is followed by compromised nutrition.

- Gliadin is recognized by the CXCR3 receptor on intestinal epithelial cells
- The CXCR3 receptor stimulates the production of Zonulin
- Zonulin triggers pericellular leakage
- Gliadin passes through the laminar propria creating a release of Interleukin (IL-15)
- IL-15 recruits intraepithelial lymphocytes (IEL)
- IEL infiltration of the intestinal barrier
- Normal performance of T-cell lymphocytes are impaired and are ineffectively expressed
- For severe Celiac sufferers, this is a risky catalyst potential for lymphoma

Symptoms of gluten exposure

Celiac disease has been diagnosed in just over 1% of those that consume a western modern diet with a presence of processed food. That's over 3 million in the US alone. (It is estimated that there are roughly an additional 11-12 million celiac sufferers that are undiagnosed.)

In addition there are roughly 15-18 million in the US that have gluten sensitivity.

Although celiac patients are differentiated from those that are gluten sensitive by a detectable autoimmune issue, the symptoms and early signs are often very similar as are the causes.
People may experience the following symptoms for several hours or
days after they consume glute

- Abdominal Pain
- Anemia
- Anxiety
- Bloating
- Brain fog, or trouble concentrating.
- Depression
- Diarrhea or constipation
- Fatigue
- Joint Pain
- Skin rash
- Irritable Bowel Syndrome (IBS)

Accidental Gluten Exposure

Given that gluten sensitive and celiac sufferers usually work to avoid the obvious foods that make them ill, many sources of the pathogenic protein still sneak into their diets unintentionally. It can happen at restaurants, family gatherings, dinner with friends, or just not clearly defined on a package of food. Sharing of utensils or even the cooking surface can transmit the protein to foods that usually are not thought to contain gluten. Many times well intentioned gluten avoidance is breached when gluten is in a filler that is not clearly declared by the manufacturer.
The following foods are often the biggest culprits:

- Cereals, breads, or other grain products that include wheat, rye, barley, or oats. This includes white or whole-wheat flour (including cookies, crackers, cakes, and most other baked goods), semo lina, couscous, bread crumbs, most pastas, and malt.
- Processed cheese, cheese mixes, low-fat or fat-free cottage cheese, or sour cream.
- Dairy products such as yogurt or ice cream that contain fillers or additives.
- Canned soups or soup mixes.
- Creamed vegetables.
- Products that contain modified food starch, food starch, hydrolyzed vegetable protein, stabilizers, or fat replacers or substitutes. (Examples of fat replacers include cellulose, gelatin, dextrins, gums, modified dietary fibers, whey protein, microparticulated egg white, and milk protein.) Check the label for these ingredients.
- Prepared or processed meats.
- Beer, gin, and whiskey.
- Flavored coffee, malted milk, or herbal tea with malted barley.

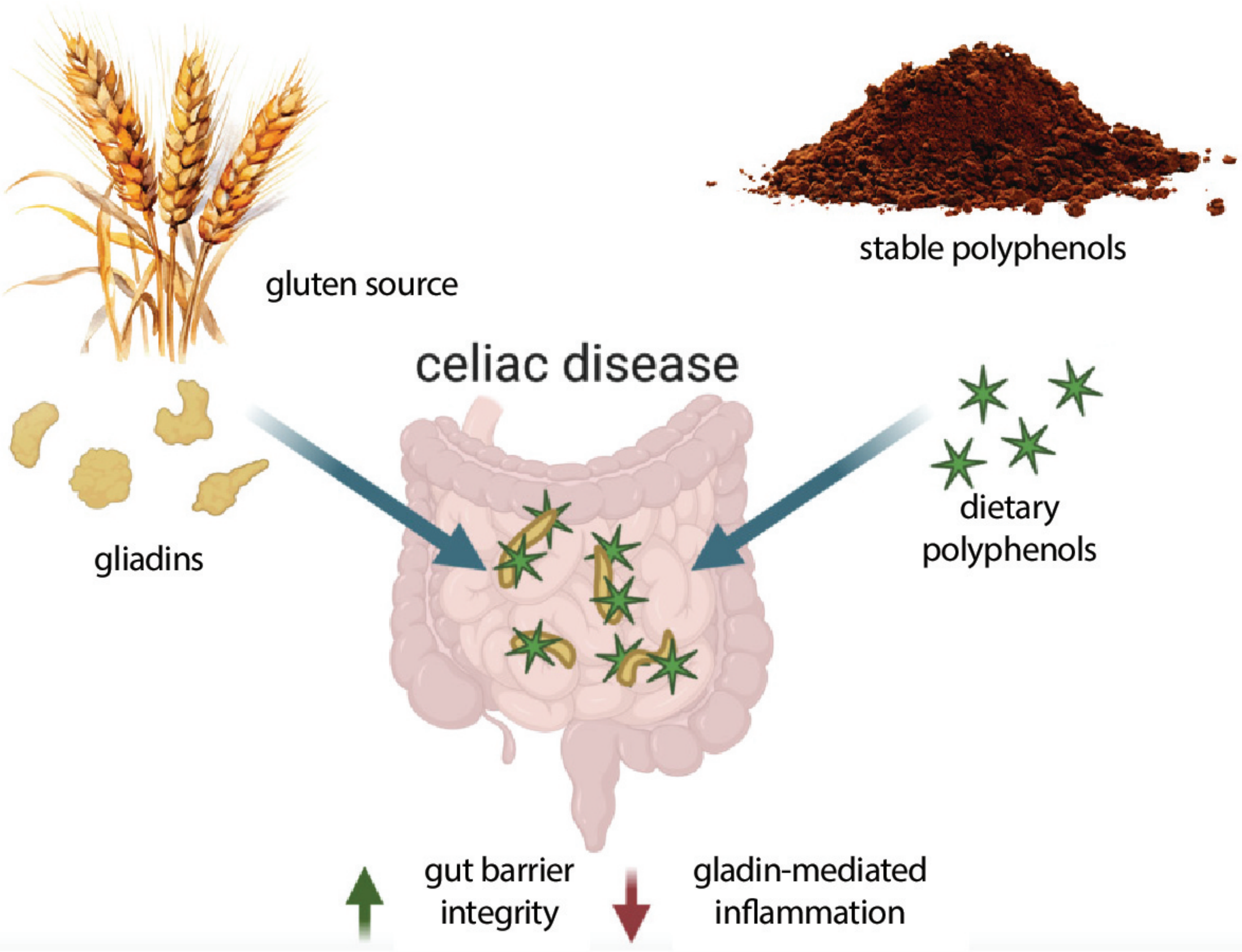
POLYPHENOLS – Protection Against Gluten Exposure

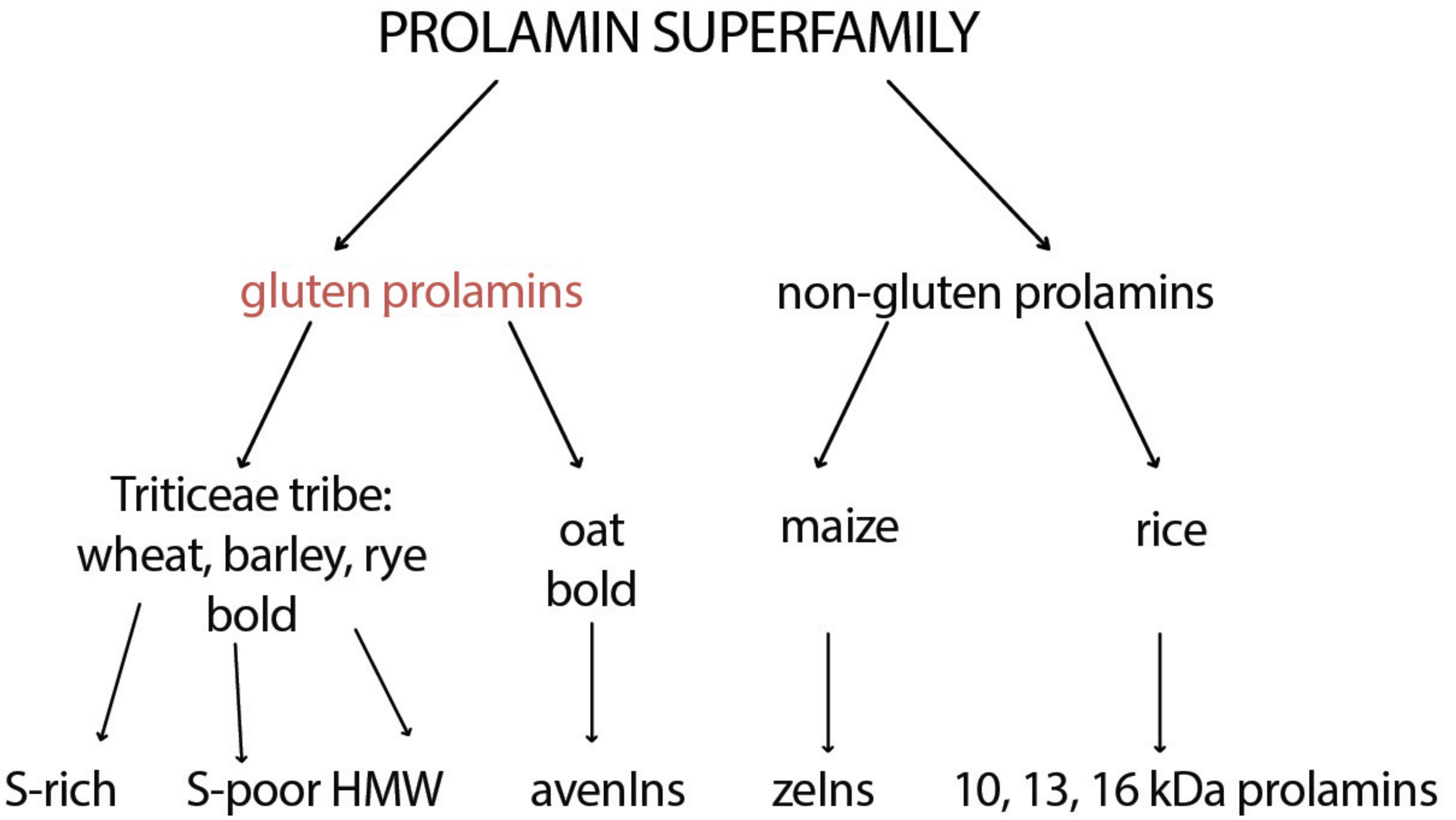
It is never recommended for a gluten sensitive or celiac sufferer to willingly ingest gluten regularly. However, even with the most diligent gluten avoidance routines, there is always a risk of accidental exposure whenever all aspects of food preparation cannot be controlled.

So how can polyphenols work to protect the gut from the gluten threat?

Simply put, the sub protein particle of gluten, gliadin, is the inflammatory trigger. Large stable polyphenols (Quebracho) can bind to the gliadin before the gliadin can bind with the dendrites of the enteric nervous

system. The occupation of that binging site on the gliadin naturally protects by preventing the cascade of inflammation. The polyphenol bound gliadin is then essentially undigested as it passed through the GI tract.




PROLAMIN SUPERFAMILY
gluten prolamins
non-gluten prolamins
Triticeae tribe:
wheat, barley, rye
bold
oat
bold
maize
rice
S-rich
S-poor
HMW
avenIns
zeIns
10, 13, 16 kDa prolamins

COMMON COMPETITORS

IBGard

- MOA- being constituted of only one active ingredient (peppermint oil), the benefits of IBGard are limited to the results of slowing duodenal spasm.
- IBGard markets “SST” site specific technology. This is a synthetic covering around the peppermint oil, which is intended to not expose the lower esophagus or upper gastric area to the peppermint in order to reduce the occurrence of reflux.
- IBGard does not address methane nor any other causes of unwanted gas production.
- Relatively safe, no adverse events
- Efficacy IBGard was 66% successful in reducing abdominal discomfort compared to 42% placebo arm (24%)
- Nestle

Probiotics (non-spore based)

- MOA unproven recolonization, premise is 100% hypothetical based upon in vitro studies.
- Low to moderate Cost, Almost always OTC
- Ubiquitous Placement, several notable brands
- No Clinical trials with proven efficacy (over 3600 studies featuring non-spore probiotics, results are almost uniformly “inconclusive” when evaluated against improvement of disease or symptom)
- No proven effect regarding SIBO/IBS
- Incongruent storage for some brands- refrigerated strains are subject to immediate denature upon ingestion, body temperature is well over 96F.
- Non-spore probiotics are not naturally engineered to survive either gastric acid or pancreatic enzymes.
- If the strains have residual survival, they risk contributing to the free hydrogen issue in the small bowel.

Amitiza (Lubiprostone)

- MOA By increasing intestinal fluid secretion, increases motility in the intestine, thereby facilitating the passage of stool and alleviating symptoms associated with chronic idiopathic constipation.
- Indication IBS-C/OIC Opioid Induced Constipation/CIC Chronic idiopathic constipation/
  Hemorrhoids
- Dose 24mcg twice daily
- Efficacy 8.2% improvement over placebo
- Side Effects diarrhea, constipation, abdominal swelling
- Metabolized mostly occurs in stomach and jejunum, excreted Renal (60%) Fecal (30%)
- Cost Over $300/month (cash)
- Financial power, Takeda

Xifxan (Rifaximin)

- Possible Need for adjunctive therapy Neomycin/Flagyl (Metronidazole)
- Indications Traveler's Diarrhea, Hepatic encephalopathy
- MOA-Binds to Beta subunit of Bacterial RNA polymerase, halting tran scription of bacteria (Note-Xifaxan is structural analog of Rifampin)
- Efficacy 11% better vs placebo for IBS SANS constipation
- Dose 1100mg up to 1600mg/day (caps in 200mg or 550mg)
- Cost of Therapy Over $400 (cash pay) Roughly $23-24 per 550mg cap
- Side effects N-V, bloating, gas pain, urgent bowel, fatigue, headache, taste loss, dysentery /Contraindications allergy to Rifampin
- Metabolism is Hepatic, Excreted Fecal (97%)
- Antibiotic, systemic, multiple use = decreasing efficacy
- Well known, good financial power, Valeant-Salix

Linzess (Linaclotide) {Constella is another trade name}

- MOA- Peptide agonist of Guanylate Cyclase 2C thereby reducing pain sensation and activating colonic motor neurons promoting bowel movement. Increase in cGMP = Excretion of Cl- and HCO3 (Bicarbonate)
- Indication IBS-C/CIC
- Efficacy Beat placebo by 13% in PIII trial
- Side effects Diarrhea (may require re-hydration measures), abdominal pain, distension, viral gastroenteritis, sinusitis, /Contraindications
- Dose IBS-C 290mcg/day—CIC 145mcg/day (each is 30min before meal)
- Cost $280/month for 30 caps regardless of 290 or 145mcg caps
- MFG-Marketing Forest Laboratories in US, Almirall in Europe, Astellas Pharma in Asia