

Key Features:

- Specialty enzyme formula for **indigestion of absorbable carbohydrates** and **intolerance of unabsorbable ones**.
- Easier-to-Comply Alternative** to Elemental Diets for SIBO and IBS
- Helps to **reach therapeutic goals of low FODMAP diet** for SIBO/IBS patients.
- Enzyme potencies based on estimated dietary intakes of common FODMAPs – covering 70-100% of average intakes**
- Contain **Butyrate (SCFA)** to **Support Colonocytes & Lining Integrity** during long-term Low FODMAP Diet

Indications:

- Small intestine bacterial overgrowth (SIBO)
- Irritable Bowel Syndrome (IBS)
- Food intolerances, eg. lactose, FODMAP
- Malabsorption & underweight patients

Description:

Low FODMAP ((fermentable oligo-, di-, mono-saccharides, and polyols) diet is a commonly used therapeutic diet to treat symptoms of IBS and SIBO.

However, **low compliance** is the common theme in FODMAP-restricting diets, especially when patients are required to stay on it beyond 3 months. Additionally, there is often a lot of anxiety and stress associated with the regime, which can potentially negate all the beneficial effects from the diet because **stress and anxiety negatively impact our digestion and may exacerbate IBS symptoms.** [3]

Intolerase™ is an ultra-potent, broad-spectrum carbohydrase formula designed to help with intolerances caused by the indigestible and the undigested carbohydrates. By using the right types and doses of carbohydrases, Intolerase™ is able to **help**

Intolerance vs. Hypersensitivity

The key difference between food intolerance and hypersensitivity is body's response.

Food intolerance mainly implies body's inability to process or digest certain food resulting in discomforts (eg. excessive amount of fermentation and gas formation by bacteria). **Food intolerance typically involves carbohydrates and does not trigger an immune response.**

On the other hand, food hypersensitivity usually involves immune responses to certain peptide/protein antigens in foods to cause inflammatory reactions.

Quantity: 84 Vegetarian Capsules

Ingredients (per capsule):

| | |
|---------------------------------------------------------------|------------------------------------------------------|
| Alpha-Galactosidase (from <i>Aspergillus niger</i>)..... | 925 GalU |
| Lactase (from <i>Aspergillus oryzae</i>)..... | 3,000 ALU |
| Amylase (from <i>Aspergillus oryzae</i>)..... | 8,109 DU (contains 7,709 bacterial amylase units) |
| Glucoamylase (from <i>Aspergillus niger</i>)..... | 150 AGU |
| Pectinase (from <i>Aspergillus niger</i>)..... | 90 endo-P |
| Beta-Glucanase (from <i>Trichoderma longibrachiatum</i>).... | 105 BGU |
| Hemicellulase (from <i>Aspergillus niger</i>)..... | 20,000 HCU |
| Invertase (from <i>Aspergillus niger</i>)..... | 2,100 Sumner |
| Xylanase (from <i>Trichoderma longibrachiatum</i>)..... | 1,650 XU |
| Maltase (from <i>Hordeum vulgare</i> seed)..... | 300 DP |
| Protease (from <i>Aspergillus oryzae</i>)..... | 15,000 HUT |
| Acid Protease (from <i>Aspergillus oryzae</i>)..... | 15 SAPU |

Non-medicinal Ingredients: Calcium butyrate (250 mg), microcrystalline cellulose, silicon dioxide, L-leucine, pullulan/hypromellose (capsule).

Suggested Use: Adults - Take 1 capsule with carbohydrate-rich meal, twice a day, or as directed by your health care practitioner. For prolonged use, consult a healthcare practitioner.

reduce the availability of FODMAP to SIBO and take away the tension between patients and their foods.

It can be combined with less strict FODMAP diet - either occasionally or on a regular basis - for patients with SIBO/IBS. Instead of strict restriction, patients can consume fermentable fibers in moderation and enjoy their foods more with the help of Intolerase™ - easing the challenge with compliance, stress and anxiety, and improving patients' quality of life.

Targeting Daily Intakes of FODMAP

Intolerase™ is formulated to reach the target of covering 70-100% of estimated dietary intakes of common FODMAPs. For instance, the average dietary intake of hemicellulose (soluble fibers present in plant cell wall) is about 8 g. Intolerase supplies 20,000 HCU per capsule that can digest 100 g of hemicellulose in 15 minutes.

α -galactosidase, another example, is a non-mammalian enzyme that helps break down galactose-containing oligosaccharides with α -glycosidic linkages, such as raffinose. 925 GalU in each capsule of Intolerase is able to completely digest daily intake of



raffinose (~ 7.5 g) in 15 minutes.

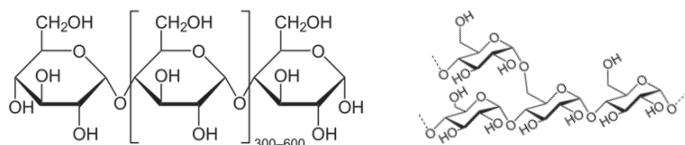
Other specific FODMAP-digesting enzymes include: Pectinase, Beta-Glucanase, Xylanase, Lactase, Maltase, and Invertase.

Timely & Complete Digestion of Starch - Crucial in IBS & SIBO

Other than dealing with FODMAP, efficient digestion of starch is also very important in IBS/SIBO patients because having **slow, partial digestion of starch** can **feed the overgrowth present in the duodenum and proximal part of the jejunum in those patients.**

There are two major types of starch in our foods: **single-chain (amylose)** and **branched-chain (amylopectin)**. Both are comprised of glucose subunits linked by 1,4-glycosidic bonds; amylopectin utilizes the additional **1,6-glycosidic bonds** (~1/3 of all linkages) to yield branched-chain configuration (Figure 1).

Figure 1. Structures of amylose [left] and amylopectin [right].



Amylose and amylopectin can be digested by 3 types of amylases - alpha-, beta-, and gamma-amylases, as well as maltase. (Table 1)

Alpha-amylase is the main carbohydrase produced by our pancreas; however, its efficiency to completely break down starch to glucose or maltose is not great because of its randomly selective nature (ie. large presence of oligosaccharides); and it leaves branched-chain 1,6-linkages untouched. This is probably why amylopectin-rich vegetables such as taro, yam and sweet potato often cause gas and bloating.

Gamma-amylase - also known as glycoamylase - is the enzyme of choice to help digest amylopectin-rich foods via its actions on 1,6-bonds, as well as 1,4-linkages.

Beta-amylase selectively breaks 1,4-glycosidic bonds at non-reducing ends, one maltose at a time.

By utilizing **beta-, gamma-amylases, and maltase, starch digestion is much more efficient and thorough.**

Table 1. Digestive Activities of Different Amylases & Maltase

| Enzymes | Produced by | Actions | End-Products |
|---------------------------------------------|-------------------------------------------------|--------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| Alpha-amylase (dextrinizing units; DU) | Salivary glands and pancreas | Randomly breaks 1,4-glycosidic bonds | Saccharides in various lengths: mono-, di-, and oligo-saccharides; 1,6-linked disaccharides |
| Beta-amylase (bacterial amylase units; BAU) | Bacteria, eg. <i>Bacillus amyloliquifaciens</i> | Selectively breaks 1,4-glycosidic bonds at non-reducing ends | Maltose |
| Gamma-amylase (amyloglucosidase unit; AGU) | Fungi eg. <i>Aspergillus niger</i> | Randomly breaks both 1,4- and 1,6-glycosidic bonds | Saccharides in various lengths: mono-, di-, and oligo-saccharides; |
| Maltase | Barley | Breaks maltose into glucose | Glucose |

Why Need Butyrate?

One nutrient largely overshadowed by Low FODMAP Diets is short-chain fatty acids (SCFAs) such as butyrate. They are produced by beneficial bacteria, mostly in our large intestine, **via fermentation of the FODMAP. SCFAs are an important food source for colonocytes and colonic lining integrity.**

Restricting FOMDAP in our diets significantly limit our dietary intake of soluble fibers, **and can potentially compromise the regeneration of colonocytes and the microbiota balance in our lower bowel.** In fact, safety of long-term low FODMAP diet has not been investigated and should, therefore, not be taken lightly.

Caution:

Consult a health care practitioner prior to use if you are pregnant or breastfeeding; if you have a GI lesion/ulcer; if you are taking an anticoagulant/blood thinner or an anti-inflammatory; if you are having surgery; or if you have diabetes. Hypersensitivity/allergy has been known to occur; in which case, discontinue use.

Reference:

1. Lauritano EC, Gabrielli M, Scarpellini E, Lupascu A, Novi M, Sottili S, Vitale G, Cesario V, Serricchio M, Cammarota G, Gasbarrini G, Gasbarrini A. Small intestinal bacterial overgrowth recurrence after antibiotic therapy. *Am J Gastroenterol.* (2008). 103(8): 2031-5.
2. Fialho A, Fialho A, Thota P, McCullough AJ, Shen B. Small intestinal bacterial overgrowth is associated with non-alcoholic fatty liver disease. *J Gastrointest Liver Dis.* (2016). 25(2): 159-65.
3. Wang JB, Lu SH, Zhao SJ. Post-infectious and non post-infectious irritable bowel syndrome: a comparative study. *Pak J Med Sci.* (2016). 32(1): 116-119.
4. Deng YY, Misselwitz B, Dai N, Fox M. Lactose intolerance in adults: biological mechanism and dietary management. *Nutrients* (2015). 7(9): 8020-35.

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