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# Probiotic S Dispelling some myths

Parts I, II & III





## Not intended as Medical Advice

- This lecture is informational only and not intended to diagnose or suggest treatments to any individual listening to this lecture.
- We advise you to seek medical direction with your licensed primary care provider.



## Learning Objectives:

- What are probiotics
  - Pre- and Post-biotics for that matter
- How to use them properly
- How GI-Mapping can direct your use
- What can happen when not used properly
- How to heal the gut

## **Define Probiotics**

 Denoting a substance which stimulates the growth of microorganisms, especially those with beneficial properties (such as those of the intestinal flora).

 Microbes in the Human gut that are associated with good health and wellness. "GOOD BACTERIA, VIRUSES and FUNGI"

 Found in health human subjects and a class that is considered good microbes associated with a health microbiome in the gut. Define Prebiotics (not to be confused with Probiotics)

A nondigestible food ingredient that promotes the growth of beneficial microorganisms in the intestines.

Examples: Onions, Jerusalem artichoke, Leeks, Asparagus, Apple, Oats, Bananas, Chicory, Wheat bran, Inulin, Cabbage

## What are probiotics?

## Some of the good guys:

• Lactobacillus: This is a common probiotic found in fermented foods, such as yogurt and other dairy products.

• Bifidobacterium: This probiotic is found in some dairy products and helps with the symptoms of irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).

• Saccharomyces boulardii: This is a type of yeast found in many probiotics. You can find these probiotics and more in supplements and select foods. Keeps Candida at bay.

## Some of the good guys:

- Akkermansia
- There are many others

- There is much confusion and controversy about probiotics. Some can get you rather sick by selecting the wrong ones.
- Spores: There have been 5-strains of research-backed (at this point 7-published studies) that are "spore-based" native to human gut not soil-based. The end result is DNA tested 100% survivable broad-spectrum probiotic clinically shown to help heal the gut and increase barrier function. They survive the gauntlet of the "stomach acid" better than most live microbes.

Foods that can help increase probiotics and postbiotics:

Yogurt, Sauerkraut, Miso soup, soft Cheeses, Kefir, Sourdough breads, Buttermilk, Pickles, Tempeh, Kimchi and Olives (many fermented foods)



## Some of the not-so-good guys:

- List some bad ones here
- Candida
- Parasites of all kinds
- Yersinia, found in pork
- Staphylococcus, found in dairy products, meat, and eggs
- Shigella, found in water and often swimming pools
- Salmonella, found in meat, dairy products, and eggs
- Campylobacter, found in meat and poultry
- E. coli, found in ground beef and salads (not all E.coli is bad; bad is: E. coli 0157:H7)
- Clostridium difficile (C. diff)
- Clostridium perfringens



Infection

BMJ Open Gastroenterology

#### Lost microbes of COVID-19: Bifidobacterium, Faecalibacterium depletion and decreased microbiome diversity associated with SARS-CoV-2 infection severity

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Article

## Ongoing Treatment with a Spore-Based Probiotic Containing Five Strains of *Bacillus* Improves Outcomes of Mild COVID-19

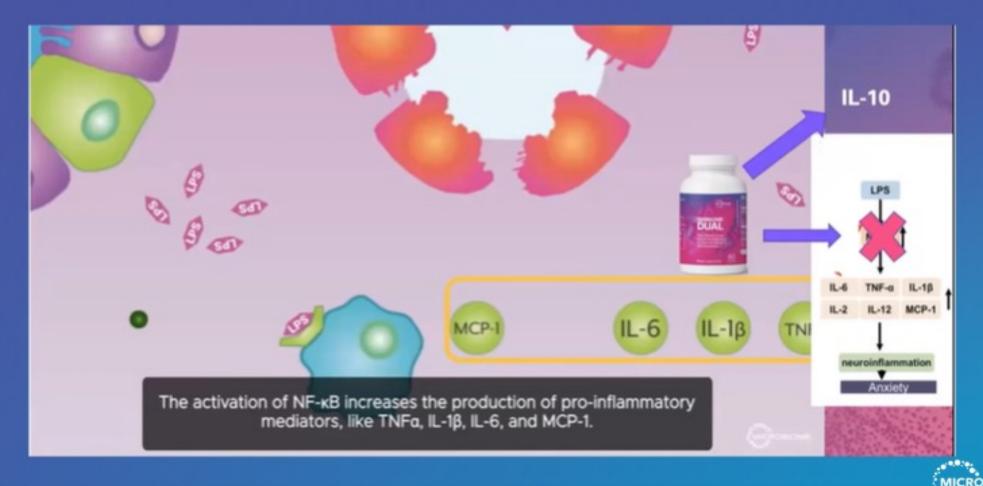
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## **Gut Brain Connection**

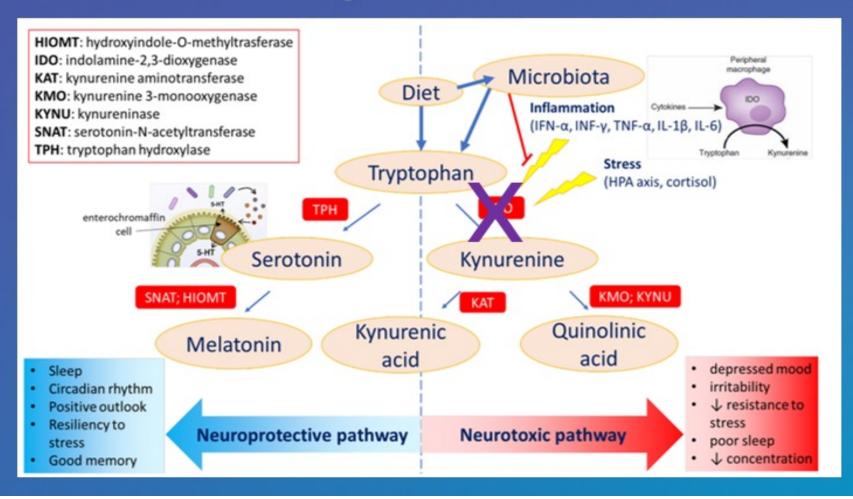
Next two slides illustrate the gut microbiome brain/mood/connection

## Zenbiome Dual blocks NF-kB activation





## Zenbiome Dual blocks tryptophan from breaking down to quinolinic acid, pushing it to serotonin and melatonin.







## Why a GI-map may be helpful

### A typical GI-MAP



Bacterial Pathogens	Result	Range	Units
Campylobacter.	<dl< td=""><td>&lt; 1.0</td><td>x10/3 CFU/9</td></dl<>	< 1.0	x10/3 CFU/9
C. difficile, Toxin A	<dl< td=""><td>&lt; 1.0</td><td>x10*3 CFU/g</td></dl<>	< 1.0	x10*3 CFU/g
C. difficile, Toxin B	<dl< td=""><td>&lt; 1.0</td><td>x10^3 CFU/g</td></dl<>	< 1.0	x10^3 CFU/g
Enterohemorrhagic E. coli	<dl< td=""><td>&lt; 1.0</td><td>x10<sup>4</sup>3 CFU/g</td></dl<>	< 1.0	x10 <sup>4</sup> 3 CFU/g
E. coli O157	<dl< td=""><td>&lt; 1.0</td><td>x10<sup>2</sup> CFU/g</td></dl<>	< 1.0	x10 <sup>2</sup> CFU/g
Enteroinvasive E. coll/Shigella	<dl< td=""><td>&lt; 1.0</td><td>x10^3 CFU/g</td></dl<>	< 1.0	x10^3 CFU/g
Enterotoxigenic E. coli LT/ST	<dl< td=""><td>&lt; 1.0</td><td>x10<sup>4</sup>3 CFU/g</td></dl<>	< 1.0	x10 <sup>4</sup> 3 CFU/g
Shiga-like Toxin E. coli stx1	<dl< td=""><td>&lt; 1.0</td><td>x10<sup>4</sup>3 CFU/g</td></dl<>	< 1.0	x10 <sup>4</sup> 3 CFU/g
Shiga-like Toxin E. coli stx2	<dl< td=""><td>&lt; 1.0</td><td>x10^3 CFU/g</td></dl<>	< 1.0	x10^3 CFU/g
Salmonella.	<dl< td=""><td>&lt; 1.0</td><td>x10<sup>4</sup> CFUig</td></dl<>	< 1.0	x10 <sup>4</sup> CFUig
Vibrio cholerae	<dl< td=""><td>&lt; 1.0</td><td>x10^5 CFU/g</td></dl<>	< 1.0	x10^5 CFU/g
Yersinia enterocolitica.	<dl< td=""><td>&lt; 1.0</td><td>x10^5 CFU/g</td></dl<>	< 1.0	x10^5 CFU/g
Helicobacter pylori	50.0 °H	< 1.0	x10*3 CFU/g

#### Comment: Helico Pylori virulence factors will be listed below if detected POSITIVE

H.pylori Virulence Factor, babA	Not Detected
H.pylori Virulence Factor, cagA	Not Detected
H.pylori Virulence Factor, dupA	Not Detected
H.pylori Virulence Factor, iceA	POSITIVE
H.pylori Virulence Factor, olpA	POSITIVE
H.pylori Virulence Factor, vacA	Not Detected
H.pylori Virulence Factor, virB	Not Detected
H.pylori Virulence Factor, virD	Not Detected

iral Pathogens	Result	Range	Units
Adenovirus 40/41	<dl< td=""><td>&lt; 1.0</td><td>x10^10 CFU/g</td></dl<>	< 1.0	x10^10 CFU/g
Norovirus GI/II	<dl< td=""><td>&lt; 1.0</td><td>x10^7 CFU/g</td></dl<>	< 1.0	x10^7 CFU/g

formal Bacterial GUT Flora	Result	Range	Units	
Bacteroides fragilis	7.5	1.6 - 250.0	x10^9 CFU/g	•
Bifidobacterium species	280.0	> 6.7	x10^7 CFU/g	
Enterococcus species	0.5 °L	1.9 - 2000.0	x10^5 CFU/g	•
Escherichia species	8.1	3.7 - 38000	x10^6 CFU/g	
Lactobacillus species	3.6 °L	8.6 - 6200.0	x10^5 CFU/g	•
Clostridium species	331.0	1.2 - 1000.0	x10^3 CFU/g	
Enterobacter species	0.7 °L	1.0 - 50.0	x10^6 CFU/g	•

## Selecting the proper Probiotics

Part II

#### Which Probiotics Strains are Best?

• When it comes to probiotic strains, not all are created equal. And while there are as many as 500 different strains, only a handful have substantial research supporting health benefits.<sup>23</sup> Below are the ones we feel can give you real results.

#### 1. Lactobacillus Gasseri

- Healthy Weight Support: A review of over a dozen human randomized controlled trials concluded that L. gasseri supports healthy weight management. Other studies have shown this strain to support the reduction of fatty tissue and improve metabolism.<sup>24-27</sup>
- Bone Density: Shown to have anti-menopausal effects by increasing bone mineral density and lowering pain sensitivity.<sup>28</sup>

#### • <u>2. Lactobacillus Rhamnosus</u>

- Diarrhea: Helps protect against various causes of diarrhea, including acute watery, antibiotic-related, and trapler-diarrhea. 29-32
- Vaginal Yeast Infections: Reduces the risk of yeast infections by helping inhibit the overgrowth of the harmful bacteria Candida albicans, the most common cause of genital yeast infections.<sup>33-36</sup>
- Mood & Anxiety: Lowers anxiety, reduces stress and boosts mood by changing the expression of the chemical messenger, GABA, which communicates with the brain and produces a calming effect.<sup>37,38</sup>

#### 3. Lactobacillus Reuteri

- Leaky Gut: Helps to strengthen and repair the intestinal barrier, which, when damaged, can allow harmful bacteria to enter the body and cause bloating, gas, cramps, and food sensitivities.<sup>39</sup>
- Urinary Tract Infections: Provides female support to combating and easing the effects of Urinary Tract Infections (UTI's).<sup>40</sup>
- Dental Health: As one of the few probiotics found in the mouth, studies have shown it helps deter the growth of Streptococcus mutans, the bacteria which causes tooth decay. 41
- H. Pylori Defense: May help reduce the presence of Helicobacter pylori (H. pylori), a harmful bacteria which researchers have linked to peptic ulcers and other digestive diseases.<sup>42</sup>

#### 4. Lactobacillus Acidophilus

- Dairy Defense: Produces lactase, the enzyme needed to break down the sugar in milk called lactose, helping alleviate diarrhea. 43
- Mineral Absorption: Helps to increase the absorption of minerals such as iron, calcium, and magnesium. 45,45
- Vaginal Health: Produces high lactic acid levels, promoting an acidic environment in the vagina necessary to keep proper bacterial balance and helping to avoid the harmful condition known as Bacterial Vaginosis (BV).<sup>46</sup>

#### • 5. Bifidobacterium Bifidum

- Constipation: Fights chronic constipation by increasing production of mucus in the colon supporting smoother bowel movements.<sup>47</sup>
- Allergy Relief: Reduces allergy symptoms by discouraging histamine production, the chemical that triggers an allergic reaction.<sup>48</sup>
- \*\*\*Stack Tip: Look for a formula that pairs L. Acidophilus with B. Bifidum, as they have been shown to work well together to fight off the harmful effects of antibiotics.

#### 6. Bifidobacterium Longum

- Gluten Defense: Shown to help reduce gastrointestinal symptoms in those with Celiac disease (CD) by reducing intestinal inflammation.
- Liver Health: Human clinical studies show that B. longum paired with the prebiotic FOS plays a beneficial role in combating fatty liver. 52,53
- Immune Support: Helps to strengthen the body's natural defenses against harmful pathogens and improve resistance to respiratory tract infections. 54,55



## **Probiotics, Prebiotics and Post-biotics**



- The term postbiotic appropriately refers to substances derived after the microorganisms are no longer alive.
- A postbiotic bacterial component called muramyl dipeptide, has been shown to relieve glucose intolerance by increasing insulin sensitivity.
- Some may have beneficial properties such as supporting probiotics, controlling inflammation in the gut and diarrhea. Some have antibiotic properties and support the immune system



## Systems to help heal the gut



• Traditionally: Products that contain L-Glutamine, aloe vera, DGL (licorice root extract that is deglycerized) and other herbals are used to "heal" the gut.

 Most of the gut rebuilders on the market have I-glutamine (which may be neuro-toxic for some people making Glutamate), licorice (not good for those with hypertension & can cause electrolyte imbalance if not used properly), and various combinations of herbs some with ASEs.



#### PATIENT EDUCATION



### **Total Gut Restoration**

RECONDITION | REINFORCE | REBUILD

#### **LEAKY GUT**

Leaky gut occurs when cracks or holes develop in the lining of the intestinal tract. These holes allow toxins and unwanted particles to enter into your blood stream and weaken your immune system. If you have leaky gut, it is important to follow an approach that addresses the key layers of a healthy gut. The Total Gut Restoration system can help fix your gut in 3 simple steps.



#### **STEP ONE: RECONDITION**

Reconditioning the gut changes the environment so that it favors your beneficial gut bacteria. MegaSporeBiotic<sup>TM</sup> can change this environment by changing the acidity in the intestines, limiting the presence of harmful bacteria, and producing metabolites that feed beneficial bacteria.



#### **STEP TWO: REINFORCE**

The gut microbiome is a very dynamic environment so it's important to reinforce the beneficial changes from MegaSporeBiotic™ by feeding friendly keystone bacteria. MegaPre™ contains short-chain carbohydrates, known as oligosaccharides, that have been shown to selectively feed beneficial bacteria and enhance gut restoration.



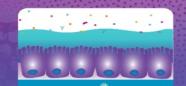
#### **STEP THREE: REBUILD**

In a leaky gut, the protective mucosal layer breaks down and allows toxins to tear through the intestinal lining and into the blood stream. MegaMucosa<sup>TM</sup> contains key amino acids to help your body naturally rebuild your protective mucus layer and immune cells to help fend off any unwanted toxins during the rebuilding process.



#### **TOTAL GUT RESTORATION**

A healthy gut microbiome is multi-faceted and relies heavily upon 3 fundamental aspects of gut health including the microbial population, physical structures, and immune function. For this reason, therapies that only address one layer are often ineffective. This system was uniquely designed to target all three of these areas to help you achieve Total Gut Restoration.



## MUCIN BUILDING BLOCKS



### Specific Amino Acids Increase Mucin Synthesis and Microbiota in Dextran Sulfate Sodium-Treated Rats

Magali Faure,\*1 Christine Mettraux,\* Denis Moennoz,\* Jean-Philippe Godin,\* Jacques Vuichoud,\* Florence Rochat,\* Denis Breuillé,\* Christiane Obled,† and Irène Corthésy-Theulaz\*

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ABSTRACT During the anabolic response associated with inflammation, mucin synthesis and colonic protection may be compromised by the limited availability of specific amino acids. We therefore determined the effect of dietary amino acid supplementation on the microbiota, mucin status, and mucosal damage in dextran sulfate sodium (DSS)-treated rats. From 8 d before to 28 d after colitis induction, male Sprague-Dawley rats (10 mo old, n = 8/group) were fed a control diet supplemented or not with 2 different doses of an amino acid cocktail containing t-threonine, t-serine, t-proline, and t-cysteine. All diets were isonitrogenous (adjusted with t-alanine). The higher dose of amino acids increased the number of Muc2-containing goblet cells in the surface epithelium of the ulcerated area, stimulated mucin production in the colon, and restored the mucin amino acid composition and mucosal content to healthy, control values. The colonic mucin synthesis rate was specifically stimulated by 95%, whereas the protein tumover was unchanged. All bacterial populations, markedly altered by the DSS treatment, were promoted. In conclusion, in inflammatory situations, an increase in threonine, serine, proline, and cysteine dietary supply can promote mucin synthesis, reequilibrate the gut microbiota, and thus favor colonic protection and mucosal healing. J. Nutr. 136: 1558–1564, 2006.

KEY WORDS: • mucin • amino acids • protein synthesis • intestine • rats

L-threonine,
L-serine,
L-proline &
L-cysteine
increased
colonic
mucin
synthesis
by 95%



## TOTAL GUT RESTORATION RECONDITION - REINFORCE - REBUILD













#### **Immunoglobulins**

Bind and neutralize toxins

#### Amino acids

- Increase mucin2 production
- Rebuild mucosal barrier

#### Citrus polyphenols

- Antioxidant properties
- Increase short-chain fatty acid production
  - Reduce inflammation
  - Increase microbial diversity





Article

## Probiotic Bacillus Spores Together with Amino Acids and Immunoglobulins Exert Protective Effects on a Rat Model of Ulcerative Colitis

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## **Supplement Facts**

Serving size: 1 capsule

Servings per container: 30

Amount per capsul	e	% DV
Akkermansia	100 million AFU	†
(Akkermansia mucin	iphila WB-STR-0001)	
Chicory Inulin	276ma	+

+ Daily Value (DV) not established.

#### Other ingredients:

microcrystalline cellulose, hypromellose (vegetarian capsule), L-leucine, silica

Adults take 1 capsule daily with food.

Refrigerate for optimal quality.

## **UltraFl** ra





## **More Alternatives and add ons:**





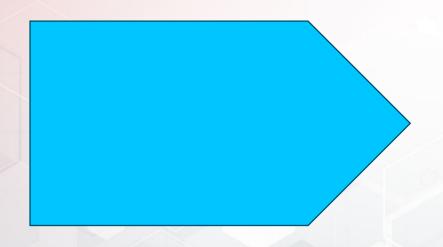


## Seed's DS-01<sub>TM</sub> vs. OTC Probiotics

FEATURES	<b>DS-01</b> тм	OTC PROBIOTICS
Proprietary ViaCap Delivery Technology	•	0
Broad Spectrum formulation with multiple strains from within species (24 strains)	•	Rare
Research-derived potencies (53.6B AFU)	•	Rare
Systemic benefits beyond the gut	•	Rare
Produces specific beneficial SCFA (short-chain fatty acids)	•	Unknown
100% survival through simulated digestions* (stomach acid, bile salts, and digestive enzymes	•	0
Non-fermenting prebiotics compatible with FODMAPS diet	•	Unknown
No skip-lot testing for over 400 allergens and pesticide residues at 3rd party accredited laboratories	•	Unknown
Active Fluorescent Units (AFU) testing via flow cytometry for precise enumeration of viable cells in multi-strain formula	•	Unknown
Precision release at top of gastrointestinal tract	•	Unknown
Whole-genome testing via shotgun sequencing of microbial DNA	•	Unknown
Oxford nanopore fully assembled closed genome sequencing for strain characterization	•	0
Heat, moisture, and light protected no refrigeration required	•	Rare
Heat testing to ensure viability through shipping conditions	•	Rare

\*To evaluate the survival of Seed's DS-01 probiotic, they use a Simulator of the Human Intestinal Microbial Ecosystem -- the closest system developed to model digestion and the gut.

## Study:







Submit a Manuscript: http://www.f6publishing.com

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ISSN 2150-5330 (online)

ORIGINAL ARTICLE

#### **Prospective Study**

#### Oral spore-based probiotic supplementation was associated with reduced incidence of post-prandial dietary endotoxin, triglycerides, and disease risk biomarkers

Brian K McFarlin, Andrea L Henning, Erin M Bowman, Melody A Gary, Kimberly M Carbajal

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Brian K McFarlin, Andrea L Henning, Kimberly M Carbajal, Department of Biological Sciences, University of North Texas, Denton, TX 76203, United States

Author contributions: McFarlin BK designed the study, collected data, interrupted findings, and prepared manuscript; Henning AL, Bowman EM, Gary MA and Carbajal KM collected data, interrupted findings, and prepared manuscript.

Institutional review board statement: The study was reviewed and approved by the UNT Institutional Review Board for Human Subjects Research.

Informed consent statement: Subjects provided written and oral consent to participate using an IRB-approved informed consent form specific to the study in question.

Conflict-of-interest statement: The present study was funded in part by a competitive research grant from Microbiome Labs, LLC (Glenview, IL) to the University of North Texas. The UNT team did not receive direct funding associated with the completion of the present study. The funding agency was not involved in the data collection, analysis, interpretation, and manuscript preparation. Double blind procedures and confidentially were used to conduct the present study in a sound and unbiased manner. As such, the authors report no conflict of interest associated with completing the present study.

#### Data sharing statement: None.

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#### Abstract

#### AIM

To determine if 30-d of oral spore-based probiotic supplementation could reduce dietary endotoxemia.

#### METHOD!

Apparently healthy men and women (n=75) were screened for post-prandial dietary endotoxemia. Subjects whose serum endotoxin concentration increased by at least 5-fold from pre-meal levels at 5-h post-prandial were considered "responders" and were randomized to receive either placebo (rice flour) or a commercial spore-based probiotic supplement [Bacillus indicus (Hu36), Bacillus subtilis (HU58), Bacillus coagulans, and Bacillus licheniformis, and Bacillus clausii] for 30-d. The dietary endotoxemia test was repeated at the conclusion of the supplementation period. Dietary endotoxin (LAL) and triglycerides (enzymatic) were measured using



## One spore option

One study showed a 42% improvement in leaky gut after taking 2 MegaSporeBiotic every day for 30 days.





MegaSporeBiotic™ is one of the most recognized names in the probiotic industry. It is Microbiome Labs' flagship probiotic product—a pioneering and trend-setting all-spore formula designed to support gut microbiome reconditioning.

MegaSporeBiotic™ is a 100% spore-based, broad-spectrum probiotic clinically tested to support and maintain gut microbial diversity, healthy levels of commensal gut bacterial species, and intestinal barrier function. This unique blend of spore-based probiotic species is designed to maintain survivability, efficacy, and potency throughout the digestive process. Boasting a 3-year shelf-life, MegaSporeBiotic™ doesn't require refrigeration or a high colony-forming unit (CFU) count to be effective—unlike non-spore-forming strains (*Bifidobacterium* or *Lactobacillus spp.*), which are typically vulnerable to destruction at room temperature and in the digestive tract.\*\*

- Supports gut microbial diversity\*\*
- Supports healthy gut barrier and immune function\*\*
- Maintains levels of key, health-supportive, commensal gut bacteria\*\*
- Maintains healthy gut microbiome function\*\*
- Unique spore-based Bacillus probiotic blend supports gut reconditioning\*\*
- Designed to maintain efficacy, potency, and 99.99% survivability throughout the digestive process\*\*
- Supports keystone bacterial species that produce valuable short-chain fatty acid (SCFAs) metabolites, including butyrate\*\*
- Backed by multiple research studies and extensive clinical validation\*\*
- 3-year shelf life\*\*
- Stable at room temperature\*\*



## Three things to avoid:



#### 3 Things To **AVOID**

When Buying A Probiotic Supplement

#### 1. LACK OF STRAIN DIVERSITY

Clinical studies have shown that specific probiotic strains can help with particular health concerns. While the human gut contains thousands of different bacterial strains, most probiotics only include a few generic Lactobacillus or Bifidobacterium strains. Look for a probiotic that has at least 14 unique strains to support proper microbiome balance.

#### 2. CHEAP GENERIC STRAINS (Most OTCs)

Store shelves are filled with brands selling probiotics, listing cheap generic forms of popular strains on their labels. A 2018 study showed that **not all probiotic strains produce the same results**, even if they have the same name.<sup>21</sup> Like most things in life, it all comes down to the details.

A high-quality brand will list the strain and a combination of letters and numbers, such as **L. acidophilus La-14<sup>™</sup>**, known as a **substrain.** This unique identifier tells you that one or more **clinical studies back the strain** being used. **Avoid probiotics that don't list substrains**, as that could be a warning sign that low-quality, generic, and possibly ineffective strains are used in the formula.

#### 3. PLASTIC BOTTLES

Moisture vapor transmission rate (MVTR) studies on probiotics packaged in **plastic bottles** have shown that they **can allow too much moisture to enter**, causing **lower strain survival rates** and a **shorter shelf life** overall.<sup>22</sup>
Don't throw away your hard-earned money on probiotics in cheap plastics bottles that can allow harmful elements to enter during storage and shipping, risking your probiotics arriving dead at your doorstep.



## **Four Criteria for Quality Probiotics**



#### **Top 4 Essential Criteria For A Quality Probiotic Supplement**

Below are the 4 most essential criteria to consider when deciding on which probiotic brand is best for your needs.

#### \_#1 High CFU Counts

•You can have the highest quality strains, but if you don't have them in a potent enough dose, they will not be very effective amongst the trillions of other bacteria in the gut. The quantity aspect of a probiotic is measured in Colony Forming Units (CFUs). Look for a formula that contains a minimum of 45 Billion CFUs per dose.

#### **#2 Clinically Studied Strains**

- •Supply chain issues and inflationary pricing has driven many manufacturers to pursue more readily available cheap generic strains that have not been proven effective in clinical testing.
- •Check the supplement facts section of a probiotic label to see if it has the trademark ™ or registered symbol ® next to each strain's substrain. This symbol is your indication that the strain has undergone clinical testing. Remember, not all strains perform the same, even if they have the same general name.

#### **#3 Prebiotics**

•Once probiotics make their way to your gut, they begin to feed off prebiotics, a fiber-based form of food needed to help them survive, grow and populate. We suggest looking for a formula that explicitly includes the prebiotic **NutraFlora®** that has twenty years of research and **over 200 studies** proving it helps **stimulate the growth of probiotics**. Don't just take a brand's word that they include a prebiotic. Check the back of their label to make sure NutraFlora® and not some generic form is on their list of ingredients.

#### **#4 Glass Bottle**

•Moisture is the number one element that can destroy the stability of probiotics, even if freeze-dried.<sup>57</sup> Studies have shown that glass bottles are the best packaging for probiotics as they allow for nearly zero moisture to enter.<sup>58</sup> For **maximum shelf life and effectiveness**, look for a probiotic that comes in a **dark amber glass bottle**, as only glass can **keep out harmful moisture and light**.



### **More Alternatives and add ons:**



LDN how this can heal the gut, IBS and IBD

Low Dose Naltrexone has been shown to have a bi-directional helpful/healing property with the gut

>helps heal gut and benefits by better bioavailability (absorption)

#### References:

www.ldnresearchtrust.org





#### References

- Throughout this presentation on slides additional here:
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