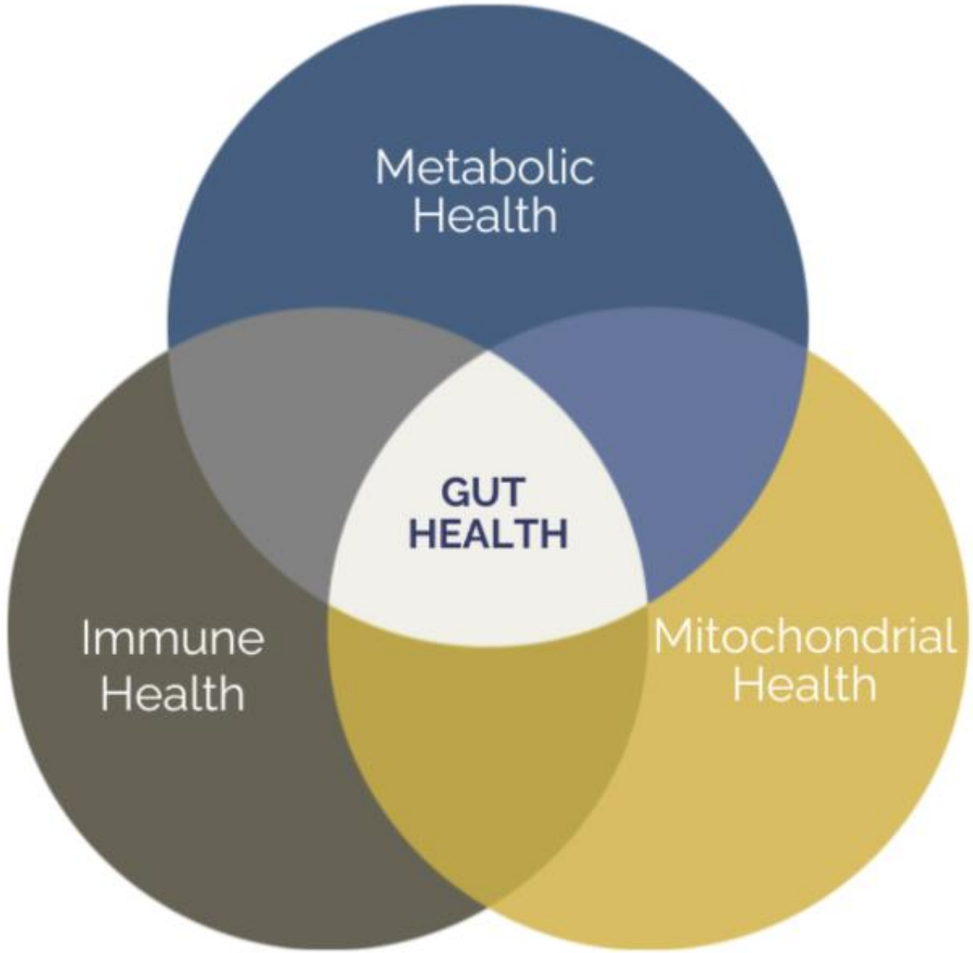
# **Gut Resilience, Redefined**: A Triple-Action Solution for Your Patients

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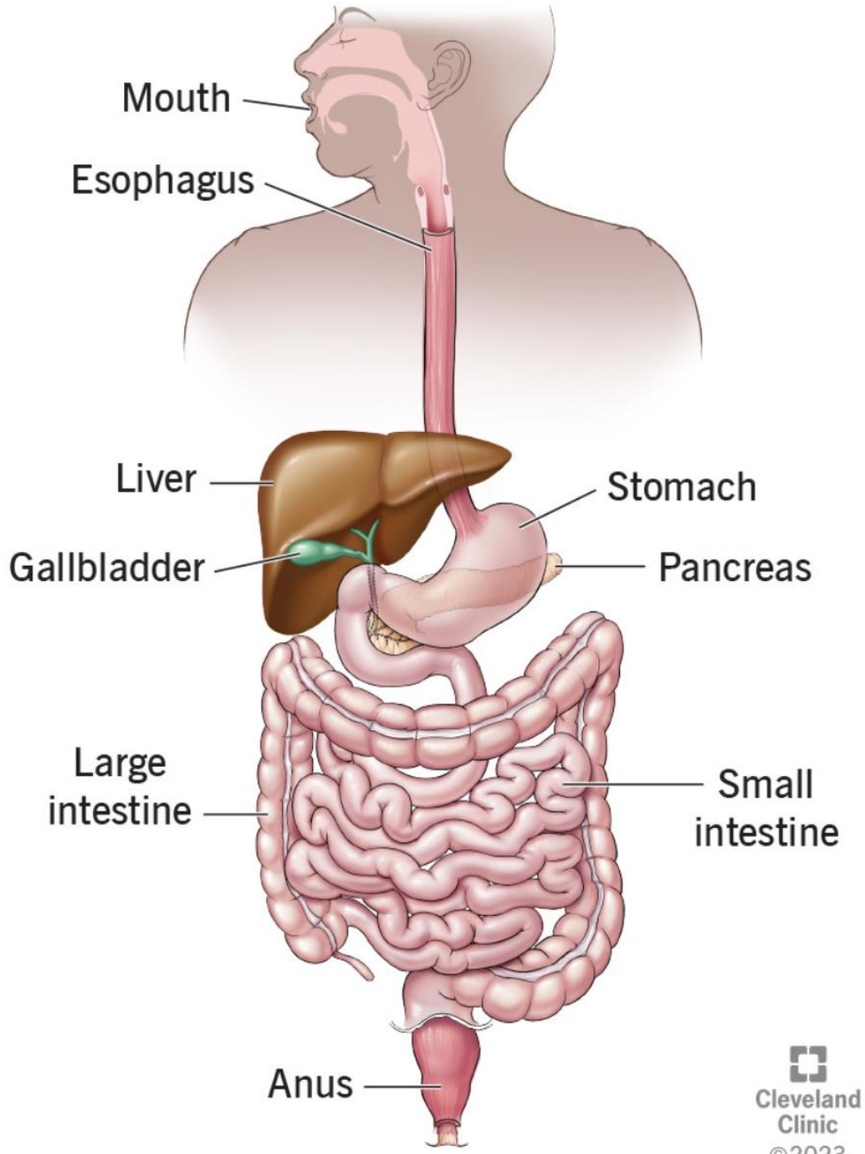
Researched Nutritionals®
solutions for life

# Agenda

- Review of GI anatomy & function
- What constitutes a resilient gut?
- Supportive ingredients: A research deep dive
- A 3-in-1 targeted solution
- Q&A

# Gastrointestinal Tract Anatomy & Function

- ✓ **Regulation:** Nerves, hormones, and gut bacteria
- ✓ **Mouth:** Mechanical digestion & salivary enzymes initiate breakdown
- ✓ **Esophagus:** Peristalsis moves food to the stomach
- ✓ **Stomach:** Churning, hydrochloric acid (HCl), and enzymes continue digestion
- ✓ **Small Intestine:** Enzymes, digestive juices, and gut bacteria break down food; nutrients are absorbed
- ✓ **Pancreas, Liver & Gallbladder:** Release enzymes and bile to aid digestion
- ✓ **Colon:** Houses gut bacteria, absorbs water, and forms waste

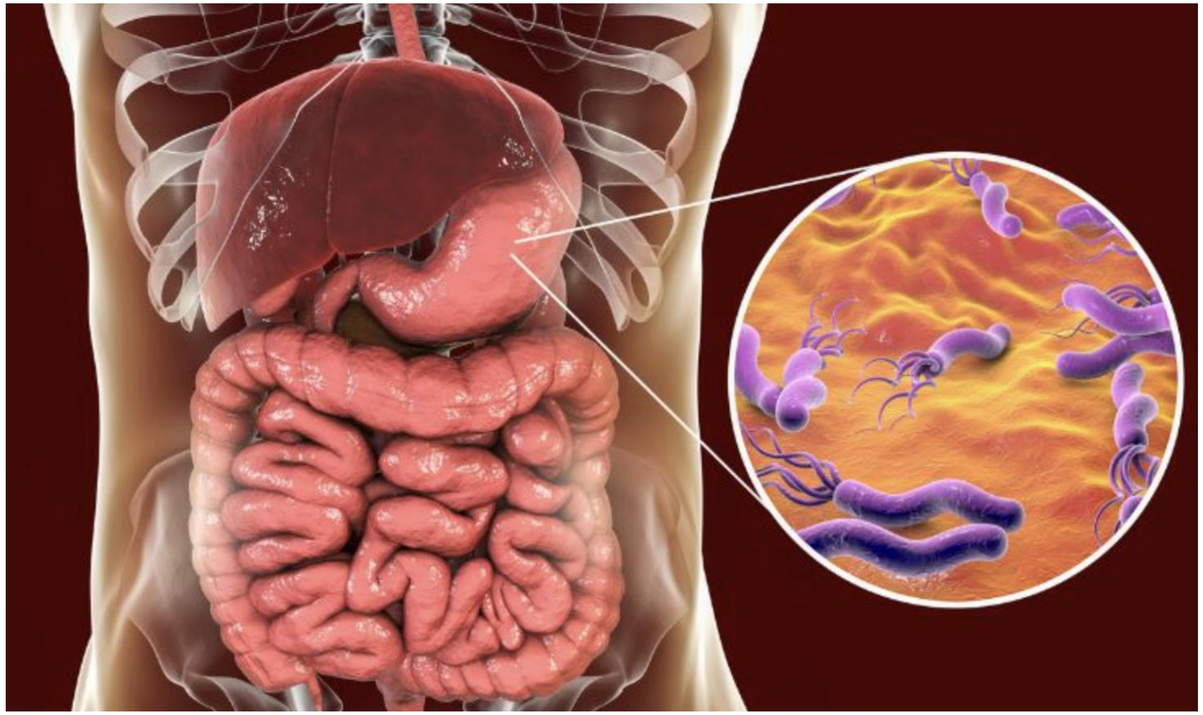



References:[1,2]

# "The Gut"

- ✓ Stomach
- ✓ Small intestine
- ✓ Large intestine

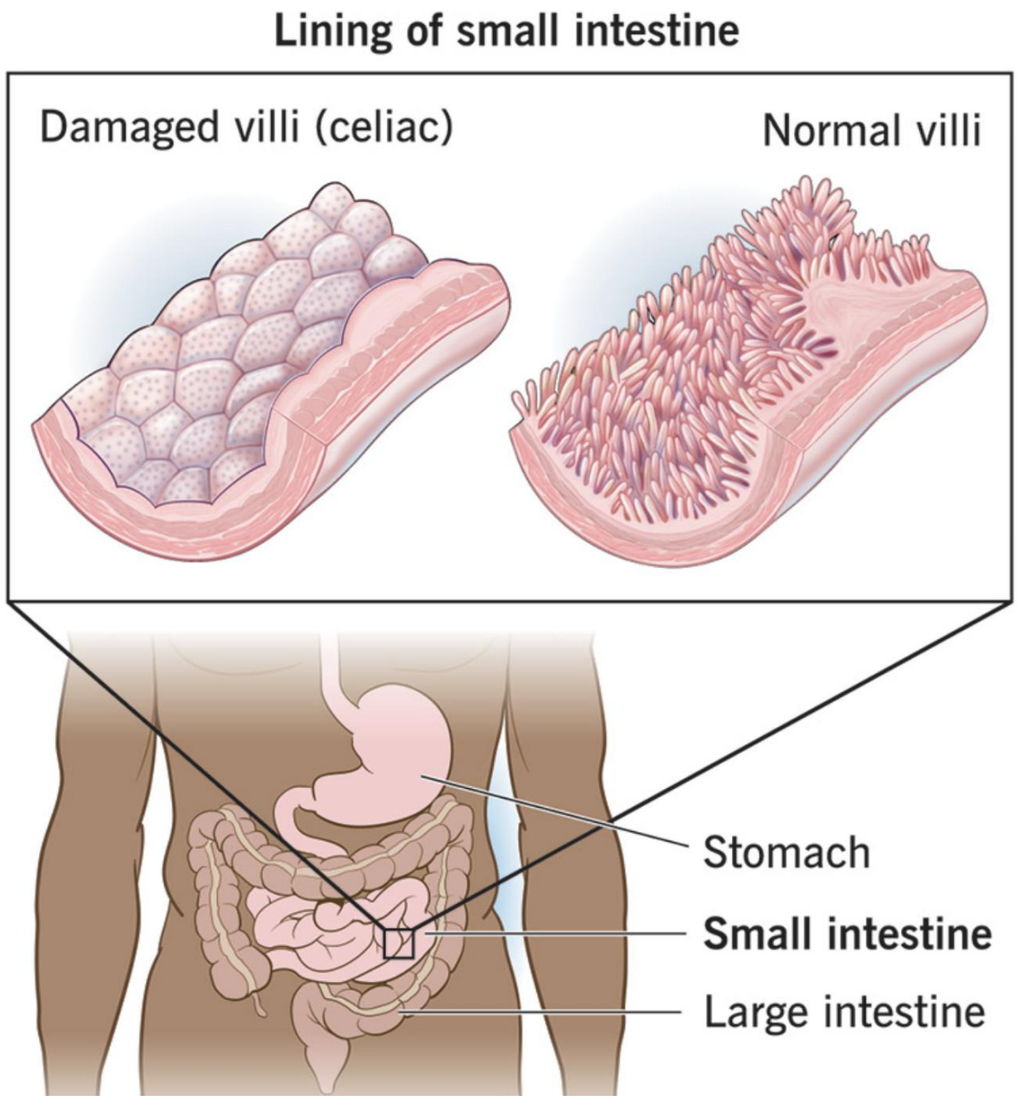
# The Stomach



- ✓ Acidic environment
- ✓ Pathologies:
  - Peptic ulcer disease (*H. pylori*, NSAIDs, stress)
  - Gastritis (*H. pylori*, NSAIDs, alcohol, autoimmune)
  - Crohn's disease (rarely)
- ✓ *Helicobacter pylori* prevalence ~40-50% globally
  - Not all who have it will develop symptoms or complications

References:[3-5]

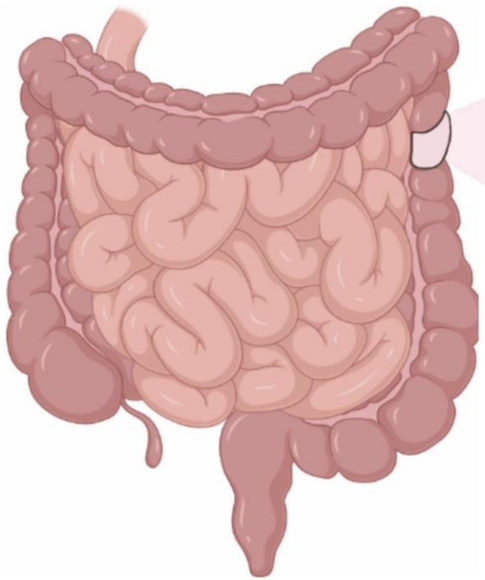
# The Small Intestine

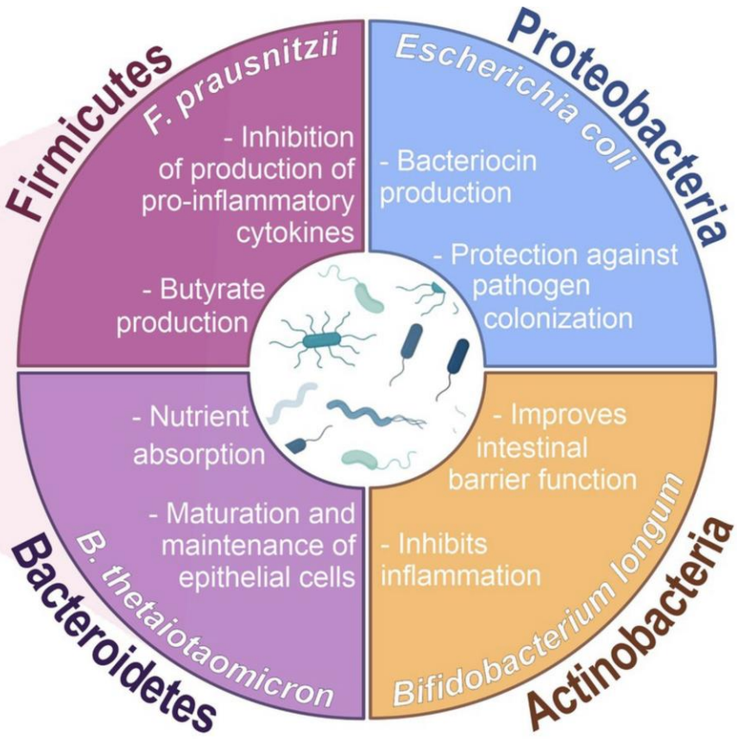



- ✓ Villi AKA "brush border"
  - Enhance surface area for optimal absorption
- ✓ Causes of villous atrophy (damage)
  - Celiac disease
  - Crohn's disease
  - Infections (enteritis)
  - Medication-induced enteropathy
    - e.g., methotrexate, NSAIDs
- ✓ Result: Malabsorption

References:[6,7]

# The Large Intestine (Colon)

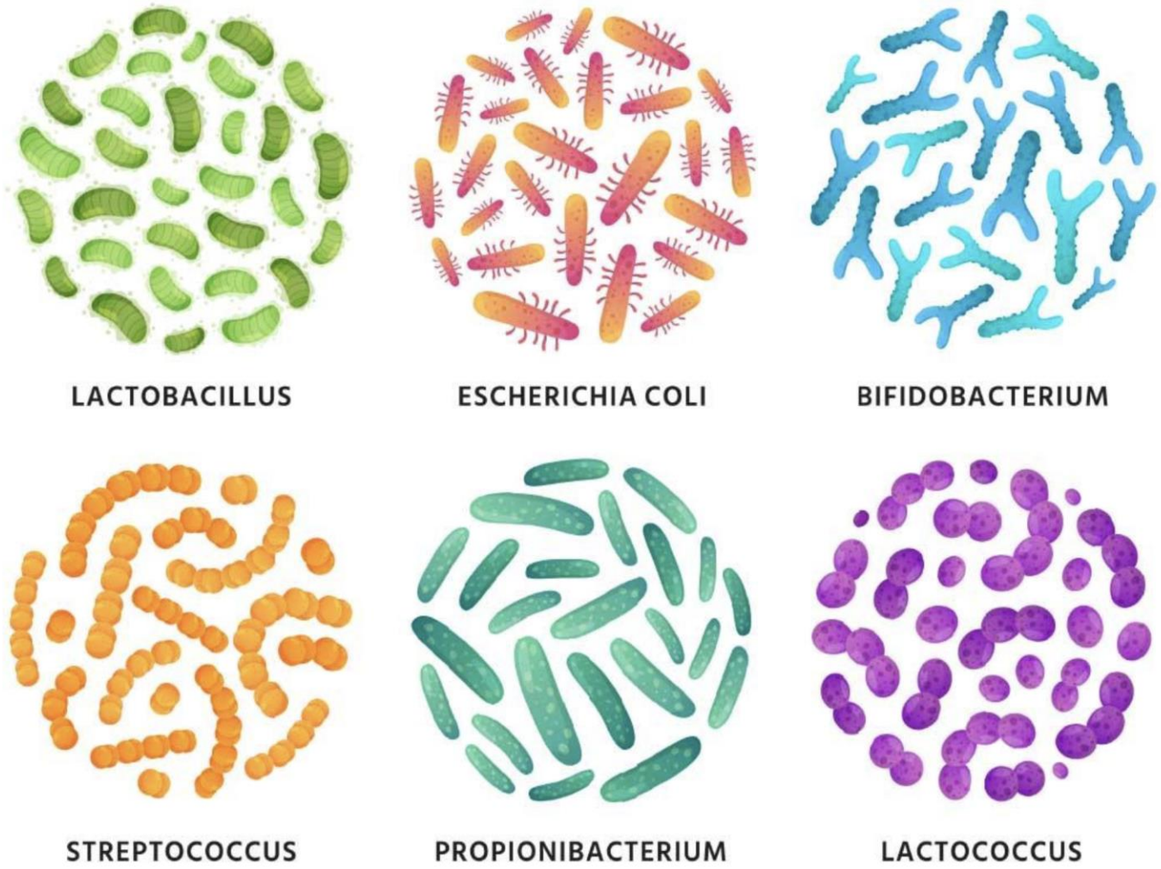





- ✓ Main functions
  - Absorb water & electrolytes
  - Houses the microbiome
  - Form and eliminate feces
- ✓ Pathologies
  - IBS
  - IBD (Crohn's, UC)
  - Diverticulosis & diverticulitis
  - Infectious colitis (*E. coli, Campylobacter, Shighella, Salmonella, C. diff*)

References:[8,9]

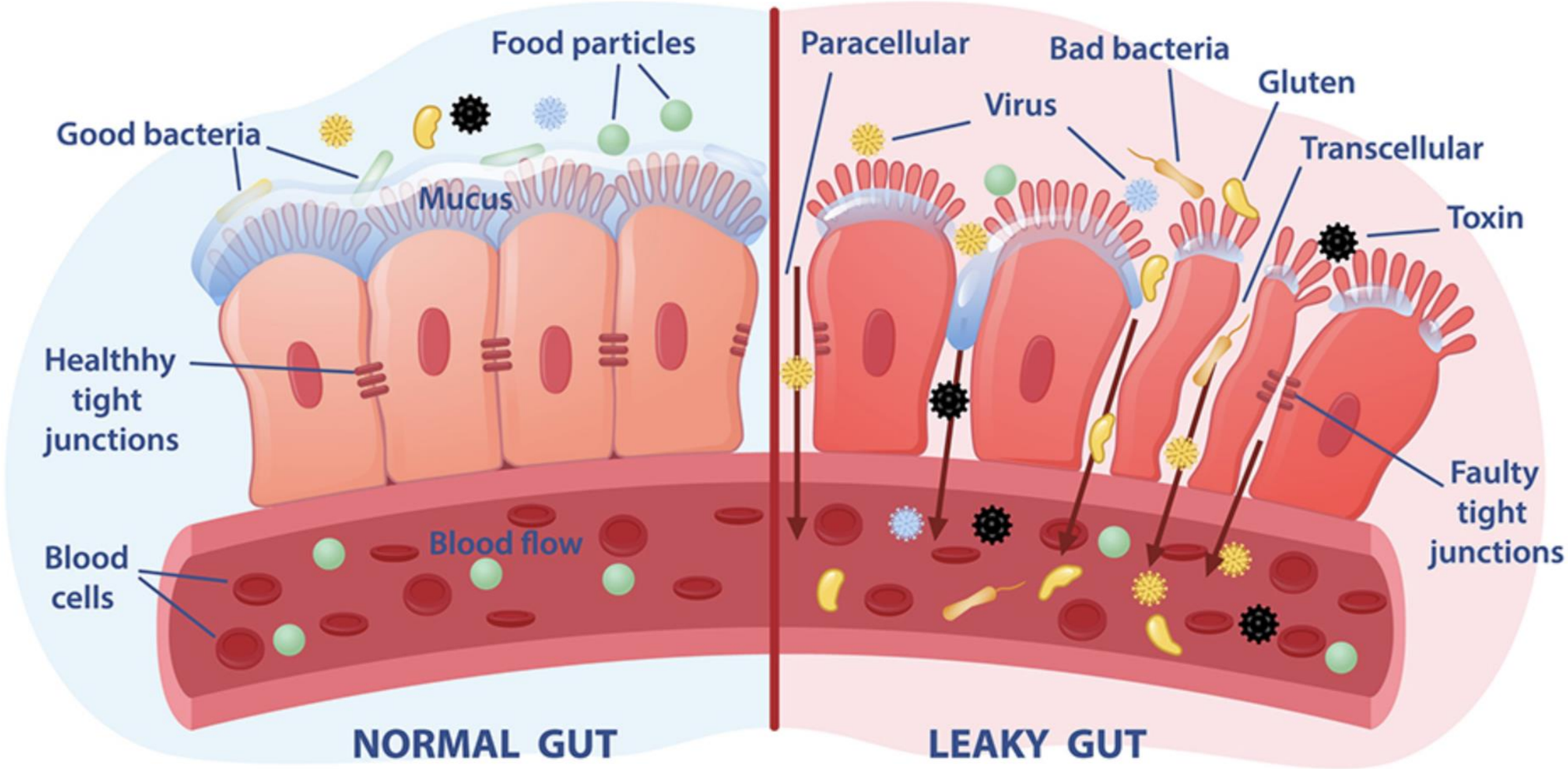
# The Microbiome




- ✓ **Many functions**
- ✓ Maintains the gut barrier
- ✓ Protects against pathogens
- ✓ Fermentation of dietary fibers to produce short-chain fatty acids (SCFAs)
  - Enhance tight junction integrity
  - Feed colonocytes
  - Control inflammation
- ✓ Immune modulation
- ✓ Release enzymes to produce vitamins (Vitamin K, B vitamins)

References:[10-12]

# "Leaky Gut"




References:[13,14]

# Leaky Gut Causes

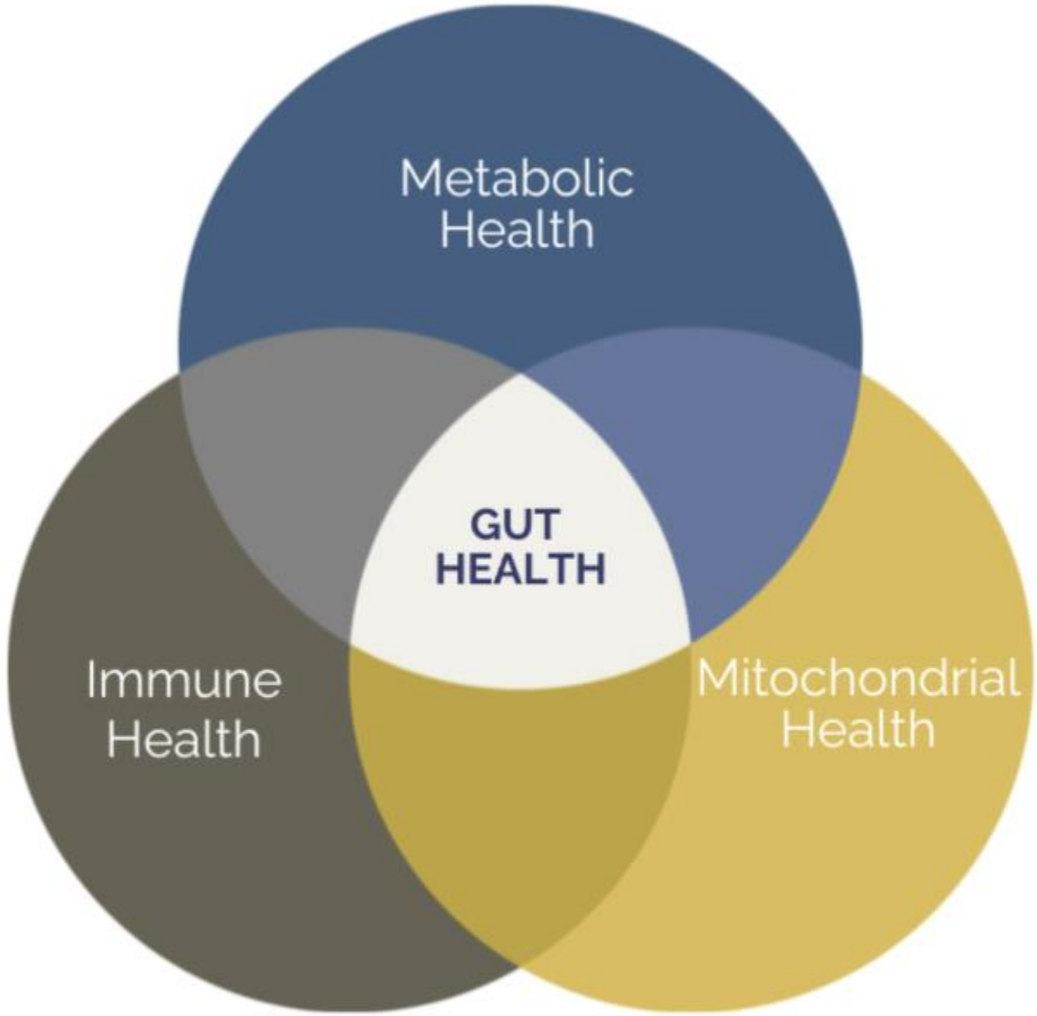
- Chronic inflammation (IBD, celiac)
- Stress
- Food particles/eating your sensitivities
- Infections
- Medications (chronic NSAID use)
- Toxins (alcohol, chemo/radiation)
- The list goes on...

# Leaky Gut Symptoms

- Fatigue
- Gut issues (gas, bloating, diarrhea, IBS)
- Allergies & food sensitivities
- Brain fog
- Headaches
- Mood dysregulation
- Sleep issues
- Hormone imbalances
- Associated with autoimmunity
- The list goes on...

References:[15,16]

# **Gut Health**: A Key Regulator of Systemic Function




References:[17-22]

# **The Microbiome**: Systemic Influences

- ✓ **Mitochondrial Health**:
  - A healthy microbiome ferments dietary fiber into short-chain fatty acids (SCFAs) such as butyrate, important regulators of mitochondrial health
  - Butyrate has been shown to promote mitochondrial biogenesis and oxidative phosphorylation, supporting cellular energy metabolism
  - Disruptions in these pathways have been associated with changes in immune signaling

- ✓ **Immune Health**:
  - Gut microbiome imbalances can compromise gut barrier function, activating immune cells, driving the production of pro-inflammatory cytokines, and contributing to metabolic imbalances

- ✓ **Metabolic Health**:
  - Changes in gut microbiota composition has been linked to changes in insulin sensitivity and glucose metabolism
  - SCFAs like butyrate may help support glucose regulation by modulating gut hormone secretion, including GLP-1, and balancing inflammatory pathways

References:[17-22]

# **Building a Resilient Gut**:
## Essential Targets for a Comprehensive Formula

- ✓ **Structural integrity**
  - Intact tight junctions & strong epithelial barrier
  - Healthy, protective mucus layer
- ✓ **Microbiome health**
  - Diverse, resilient microbial ecosystem
  - Optimal fermentation & short-chain fatty acid (SCFA) production
- ✓ **Gastrointestinal comfort**
  - Soothed, nourished tissues
  - Healthy histamine metabolism
- ✓ **Immune & inflammatory balance**
  - Healthy cytokine signaling
  - Regulated immune responses
- ✓ **Metabolic wellness**
  - Gut-mediated metabolic signaling
  - Healthy glucose metabolism

References:[10,11]

# Supportive Ingredients

## Barrier Integrity, The Microbiome, and Beyond

- ✓ **Collagen peptides**
  - Enhances tight junction protein expression & gut barrier function*
  - Supports healthy bacterial colonization & SCFA levels via prebiotic activity*

- ✓ **N-acetyl D-glucosamine (NAG)**
  - Enhances tight junction protein expression & gut barrier integrity*
  - Promotes healthy inflammatory responses*
  - Mucin layer support*

- ✓ **DGL (deglycyrrhizinated licorice)**
  - Removal of glycyrrhizin associated with fewer potential side effects
  - Promotes healthy inflammatory responses*
  - Mucin layer support*
  - Soothes the GI tract & promotes comfort*
  - Promotes microbial balance*

- ✓ **Zinc carnosine**
  - Supports tight junctions & stimulates gut repair processes*

References:[23-33]

# Supportive Ingredients

## Fostering Healthy Gut Histamine Responses

- ✓ **Black cumin seed** (*Nigella sativa*)
  - Targets histamine within the GI tract*
  - Promotes healthy inflammatory responses*

- ✓ **Luteolin**
  - Promotes mast cell stability*
  - Promotes healthy inflammatory responses*
  - Soothes the GI tract*

References:[34-36]

# Supportive Ingredients

## Gut-Driven Immune & Metabolic Resilience

### ✓ Tributyrin

- A triglyceride form of butyrate designed for targeted delivery to the colon where it's needed most (unlike pure butyrate)
- Supports gut barrier function*
- Promotes microbial balance*
- Supports bowel regularity*
- Helps maintain immune balance, healthy inflammatory responses, and metabolic wellness*

### ✓ Pasteurized *Akkermansia muciniphila*

- A stable, bioavailable postbiotic form of this beneficial microbe, suitable even when the gut mucus layer is compromised*
- Supports gut barrier integrity*
- Promotes microbial balance and mucin layer health*
- Helps maintain immune balance, healthy inflammatory responses, and metabolic wellness*

References:[37-48]

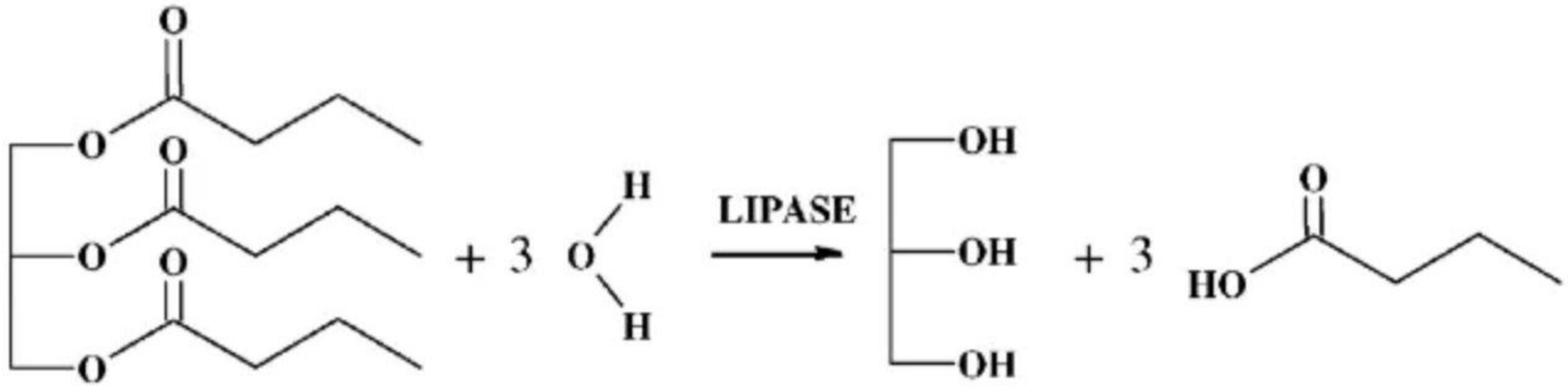
# More on Tributyrin

- ✓ Metabolized in the body to release butyrate
  - Butyrate = A short-chain fatty acid (SCFA)
    - Formed by bacterial fermentation of fiber
    - Provides a direct energy source for colonocytes
    - Supports gut barrier, immune modulation, healthy cytokine activity
    - Insufficient fiber intake → poor SCFA production (prevalent issue)

- ✓ A triglyceride form of butyrate (3 butyrate molecules attached to a glycerol backbone)
  - Unique structure enables it to **reach the colon where it is needed most**
    - ***Standard butyrate supplements are rapidly absorbed in the small intestine, limiting their availability in the colon***

References:[37]

# Tributyrin Metabolism




**Tributyrin** **Glycerol** **Butyric Acid**

A triglyceride composed of 3 butyrate molecules esterified to a glycerol backbone

Hydrolyzed by pancreatic lipases in the small intestine, releasing glycerol and free butyrate, where it is then absorbed in the large intestine (colon)

References:[37]

# **Tributyrin:** Mechanisms of Action

- ✓ **Supports gut barrier function***
  - Upregulates tight junction proteins
  - Downregulates serum zonulin & lipopolysaccharide (LPS)
- ✓ **Helps maintain immune balance & a healthy inflammatory response***
  - Studies suggest it positively impacts TNF-α, IL-6, IL-1β & the NLRP3 inflammasome
- ✓ **Provides support for beneficial gut bacteria, including butyrate producers, to promote a balanced microbiome, SCFA production, and bowel regularity***
- ✓ **Supports intestinal health and microcirculation (to the villi)***
  - Protects the endothelium, promotes healthy levels of oxidative stress, and promotes vasodilation
- ✓ **Promotes gut-brain communication, skin health, and metabolic wellness***

References:[37-40]

# More on Butyrate…

- ✓ **Histone deacetylase inhibitor (HDACi)**
  - Shown to influence gene expression and protein function → Supports **healthy cytokine signaling** and a balanced immune response
  - Helps maintain **pancreatic β-cell health**
    - Supports **healthy glucose metabolism** by influencing expression of glucose-6-phosphate and subsequent gluconeogenesis
  - Supports the body's natural mechanisms for removing **damaged or aged cells**
- ✓ Stimulates release of **GLP-1** from intestinal L-cells
  - Involved in glucose and appetite regulation
- ✓ Supports **mitochondrial function** & metabolic efficiency by influencing key pathways involved in energy production and fat metabolism (e.g., AMPK & PGC-1α)

References:[49-51]

# *Akkermansia muciniphila*

- ✓ Commensal bacterium: Comprises 1-4% of the microbiome (in healthy individuals)
- ✓ Abundant in infants & declines with age
- ✓ Higher levels seen in centenarians (100+)
  - Longevity, lower inflammation, healthy aging?
- ✓ Lower levels observed in:
  - IBD
  - Obesity & Type 2 diabetes
  - Autism
- ✓ Resides in the mucus layer
  - Degrades mucins, thereby stimulating its production by host tissues
  - Supplementing as a probiotic:
    - Can be detrimental to an already-damaged gut barrier due to mucin-degrading activity
    - Colonization & survival is uncertain
- ✓ Supports gut barrier integrity (once reconditioned)
- ✓ Reduces pathogen abundance

References:[52-54]

# Pasteurized *Akkermansia muciniphila*

- ✓ **Heat-killed strain (postbiotic)**
  - Pasteurization inactivates the bacteria's metabolic activity while preserving its structural integrity and bioactive components
  - ***Maximizes the overall physiological benefits for the patient according to a body of research***
    - Metabolic effects
    - Gut barrier integrity
    - Immune modulation

- ✓ **Benefits of pasteurization**:
  - Stability (stomach acid, temperature, shelf-life)
  - Consistent dosage
  - Bioavailability
  - Safety profile
    - Suitable for immunocompromised individuals
    - ***May be used even when the gut tissues are not intact***
      - Mucin-degrading activity of live forms can worsen epithelial damage in such patients

References:[54,55]

# Pasteurized *Akkermansia*: Multiple Mechanisms of Action

| Target | Mechanisms Supported by Research* |
|---|---|
| **Metabolic** | • Influences GLP-1 release via **P5** protein and FFAR2 (GPCR) activation [42]<br>• Via **Amuc_1100** protein & TLR2 activation:<br>▪ Helps maintain healthy glucose metabolism and insulin function [43, 55, 56]<br>▪ Supports healthy lipid metabolism and body composition [43, 44, 56]<br>▪ Promotes metabolic homeostasis [43, 56, 58] |
| **Gut Barrier** | • Via Amuc_1100 protein & TLR2 activation:<br>▪ Supports intestinal barrier integrity/tight junctions [43, 44, 46, 48]<br>▪ Encourages SCFA production and microbial balance [44, 45]<br>▪ Supports mucin production [48]<br>• Supports gut-brain communication and gut sensory function [46] |
| **Immune** | • Helps maintain mucosal immune function via CD8+ T cells and balanced cytokine signaling (↓TNF-α, ↓IL-6, ↑IL-10) [44, 57]<br>• Supports healthy inflammatory pathways (↓TLR4, ↑TLR2) [43, 44, 48]<br>• Promotes immune homeostasis via Amuc_1100 [43, 44, 57, 58] |

| Target | Pasteurized AKK | Live AKK |
|---|---|---|
| **Mucin Production** [48, 52] | Amuc_1100:<br>• Stimulates mucin production (TLR2 activation on goblet cells)<br>• Promotes healthy gut & SCFA generation (activate goblet cell activity) | • Degrades mucins, thereby stimulating host mucin production<br>• Promotes SCFA generation, activating goblet cell activity |
| **Microbiome Composition** [45, 48, 52] | • Improves overall microbial balance<br>• May increase *Akkermansia* abundance | • Colonizes mucus layer (survival through GI tract uncertain) |
| **Metabolic Support** [43, 47, 55, 58] | More pronounced improvements in:<br>• Lipid metabolism, glucose homeostasis, and body composition | Some benefit, less pronounced |
| **Gut Barrier Integrity** [44, 48, 55, 59] | Amuc_1100:<br>• Stronger upregulation of tight junction proteins<br>• Stimulates mucin and promotes SCFA production | • Upregulation of tight junction proteins<br>• Stimulates mucin and promotes SCFA production |

| Target | Pasteurized AKK | Live AKK |
| --- | --- | --- |
| **Pathogen Defense Support**<br><br>[48, 60] | Enhances macrophage antimicrobial activity via ↑:<br>• NLRP3 (selective activation)<br>• Reactive oxygen species (ROS)<br>• Nitric oxide (NO)<br>• Inflammatory cytokines (ALL critical for pathogen clearance) | • Antimicrobial peptide secretion<br>• Competes with pathogenic mucin-degraders |
| **Immune Modulation**<br><br>[44, 57, 59, 60, 61] | • Promotes healthy cytokine & immune responses | • Benefits observed, but less potent |
| **Safety, Stability & Bioavailability**<br><br>[43, 44, 48, 61, 62, 63] | • More stable & bioavailable (resistant to environmental conditions)<br>• Negligible risk of toxicity/adverse reactions | • Less stable & bioavailable (sensitive to oxygen, stomach acid, temperature)<br>• Higher risk of adverse reactions<br>• Higher levels observed in Parkinson's & MS |

# Researched Nutritionals®

## RenewGut *Thrive*™

GI Optimizer &
3-in-1 Wellness Solution

# RenewGut Thrive™

***Suggested Use**:* As a dietary supplement, take **5 capsules first thing in the morning with food** or as directed by your healthcare professional.

- Optimizes absorption
- Promoting comfort
- Tributyrin (pancreatic lipases activated with meals)
- Most metabolically active during the day
- May be taken without food if necessary (not ideal)

## Supplement Facts

**Serving Size: 5 Capsules | Servings Per Container: 30**

| Amount Per Serving | | %Daily Value** |
|---|---|---|
| **Zinc** (from Tight Junction Enhancer) | 15 mg | 136% |
| **Tight Junction Enhancer**<br>Hydrolyzed collagen peptides (type I & III), N-Acetyl D-glucosamine, GutGard® deglycyrrhized licorice, Zinc Carnosine | 1725 mg | † |
| **Mast Cell Manager**<br>Black Cumin (*Nigella sativa*) (seed), Luteolin | 175 mg | † |
| **ImmunoMetabolic Booster**<br>Tributyrin (as CoreBiome®), *Akkermansia* (as pasteurized *Akkermansia muciniphila*) | 350 mg | † |

** Percent Daily Values are based on a 2,000 calorie diet.

† Daily Value not established.

**Other Ingredients:** Gelatin (capsule).

Manufactured without milk, eggs, fish, tree nuts, peanuts, shellfish, sesame, wheat, soy and gluten. Produced in a facility that may process other ingredients containing these allergens.

# RenewGut Thrive™

## Ingredients & Benefits

| Each Capsule Includes: | | |
|---|---|---|
| **Features** | **Constituents/Actions** | **Benefits*** |
| **Tight Junction Enhancer** | Hydrolyzed collagen peptides (type I & III), N-Acetyl D-glucosamine, GutGard® deglycyrrhized licorice, Zinc Carnosine | • Supports gut lining integrity, including tight junctions and mucin layer health<br>• Supports beneficial probiotic bacteria for a resilient microbiome<br>• Helps maintain GI comfort<br>• Promotes healthy cytokine activity<br>• GutGard® is a patented DGL extract with high flavonoid content, requiring a smaller effective dose<br>• GutGard® has lower levels of glycyrrhizin to minimize potential side effects |
| **Mast Cell Manager** | Black Cumin (*Nigella sativa*) (seed), Luteolin | • Supports histamine balance within the digestive tract<br>• Helps maintain GI comfort<br>• Promotes healthy cytokine activity |
| **ImmunoMetabolic Booster** | Tributyrin (as CoreBiome®), *Akkermansia* (as pasteurized *Akkermansia muciniphila*) | • Promotes a healthy immune response<br>• Supports metabolic health<br>• Fuels colon cells with short-chain fatty acids (SCFAs)<br>• Supports gut barrier function and microbial diversity |

# **CoreBiome® Tributyrin**: Research Highlights

## ***In vitro*** **study:**

**Objective:** Researchers examined separate and combined effects of: Probiotics (*Lactobacillus rhamnosus* GG & *Bifidobacterium animalis* BB-12), a prebiotic (bacteriophage blend), and a postbiotic (tributyrin) on intestinal permeability using an *in vitro* gut barrier model.

**Methods:** Used a lab model to simulate a weakened barrier (mimicking leaky gut). Intestinal permeability was measured with transepithelial electrical resistance (TEER).

**Results:**

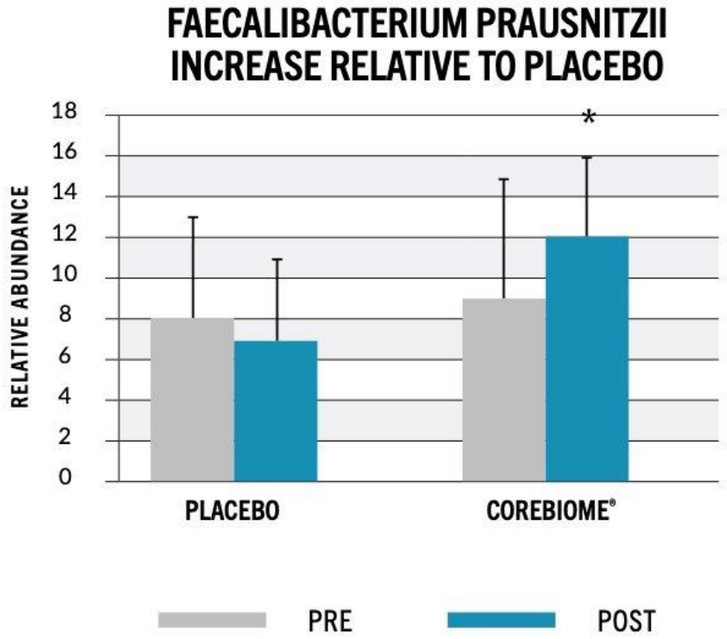
- The full combination of ingredients **significantly improved gut barrier strength**. The **postbiotic (tributyrin) was also effective alone** ($p < 0.05$).
    - Also reported reduced gut inflammatory markers **IL-6 & TNF-α**.

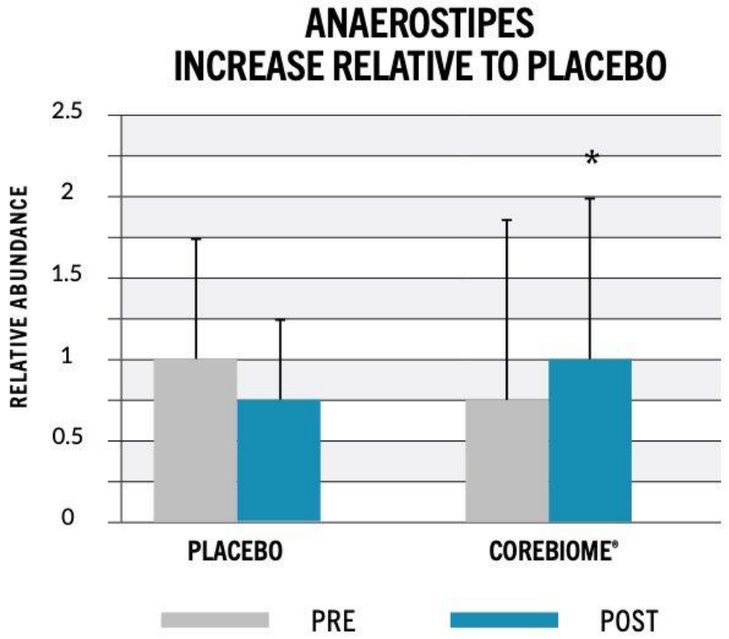
References:[64]

# CoreBiome® Tributyrin: Research Highlights

**3-week human pilot study (randomized controlled trial):**

- ✓ 300 mg CoreBiome® vs. Placebo
- ✓ Significantly **increased abundance** of *Faecalibacterium prausnitzii* and *Anaerostipes* after 3 weeks



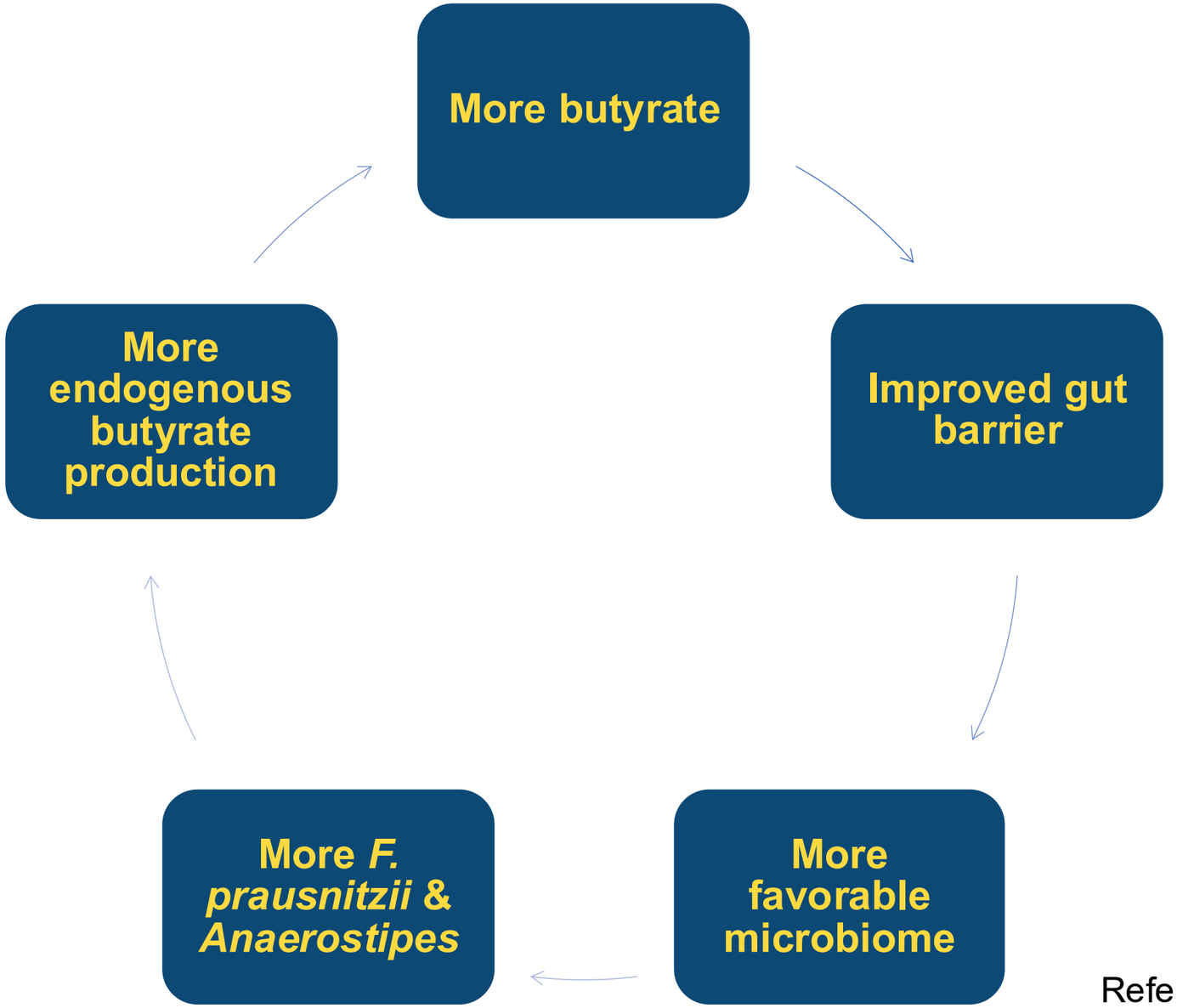




- Butyrate-producing beneficial bacteria involved in:
  - A healthy microbiome
  - Immune modulation
  - Healthy inflammatory responses
- Low levels seen in IBD, colorectal cancer, and obesity

References:[23]

# CoreBiome®: Positive Feedback Loop

**Boosts butyrate-producing bacteria in a *positive feedback loop**




References:[37,65]

| Feature | CoreBiome® Tributyrin | Butyrate (e.g., sodium butyrate, calcium butyrate) |
|---|---|---|
| **Absorption** | Hydrolyzed by pancreatic lipases in the small intestine, releasing glycerol and free butyrate, which is then absorbed in the large intestine (where it is needed most) | Rapidly absorbed in the small intestine, limiting delivery to the colon |
| **Stability & Bioavailability** | More stable/bioavailable; More controlled/gradual delivery of butyrate (reported to be 2.5 to 4x more potent) | Less stable/bioavailable; May degrade before reaching target areas |
| **Tolerability** | Generally more tolerable; Low FODMAP certified; Less intense odor | Can be harsh on the GI tract; Strong, unpleasant odor |
| **Dosing** | 300 mg – lower dose due to high bioavailability | Higher dosing (often gram-level) |

References:[38,41,65]

# **GutGard® DGL**: Unique Attributes & Research Highlight

- ✓ High levels of active flavonoids allows for a lower effective dose* (vs. other forms of DGL)
- ✓ Lower levels of glycyrrhizin vs. standard licorice
  - May reduce the risk of electrolyte imbalances and blood pressure-related effects
- ✓ **2013 published research** findings:
  - 150 mg GutGard® for 2 months
  - Associated with a statistically significant reduction in ***H. pylori*** presence vs. placebo, measured by:
    - Stool antigen test
    - Urea breath test

References:[66]

# **GutGard® DGL:** Emerging Evidence

- ✓ Promotes the growth of beneficial bacteria (*Bacteroides spp.*, *Bifidobacterium spp,*, and ***Akkermansia*** *spp.*) associated with enhanced **butyrate** production*
- ✓ Supports appetite control*
- ✓ May support GLP-1 activity through microbiome modulation via enhanced **butyrate** production*

**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.*

# RenewGut Thrive™: Suggested Use

- ✓ As a dietary supplement, take **5 capsules once daily first thing in the morning with food** or as directed by your health care professional.
  - Optimizes absorption when taken with a meal
  - Promotes GI comfort
  - Tributyrin is hydrolyzed by pancreatic lipases (activated in response to meals)
  - Body is most metabolically active during the day
  - May be taken without food if necessary (not ideal)
- ✓ **Caution:** Not for use by women who are pregnant or may become pregnant.
- ✓ **Allergen info:** Shellfish-free; Contains corn

# RenewGut Thrive™

## Multiple Mechanisms of Action

- **Fortifies gut lining & tight junctions to promote healthy intestinal mucosal barrier***
- **Promotes healthy cytokine activity***
- **Provides healthy histamine support in the gut (both histamine absorption & degranulation)***
- **Improves microbiome balance in the digestive tract***
- **Supports short-chain fatty acid (SCFA) levels (the primary energy source for colon cells), promoting microbial diversity and immune health***
- **Supports metabolic health, including insulin function & lipid metabolism***

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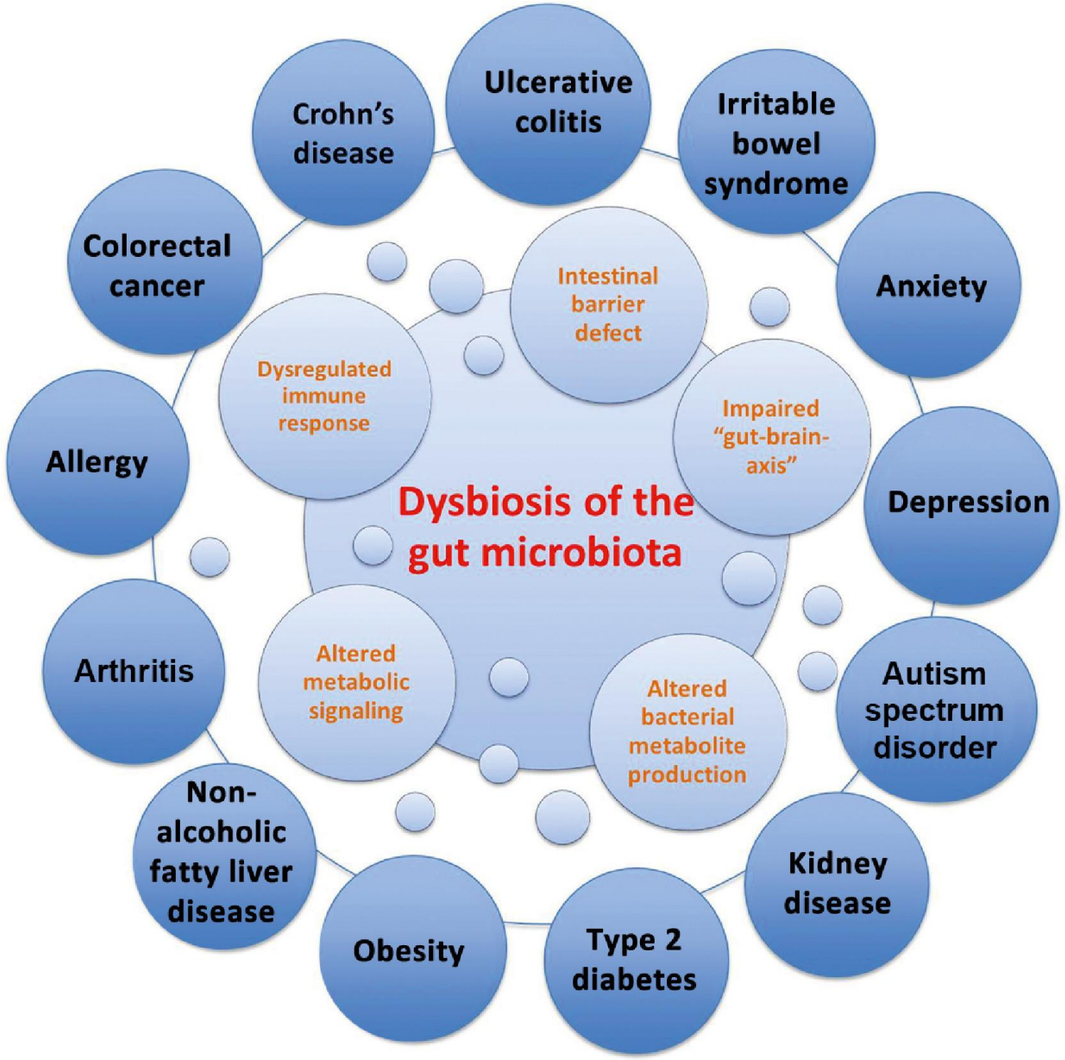
# RenewGut Thrive™

## Indications/Patient Profile

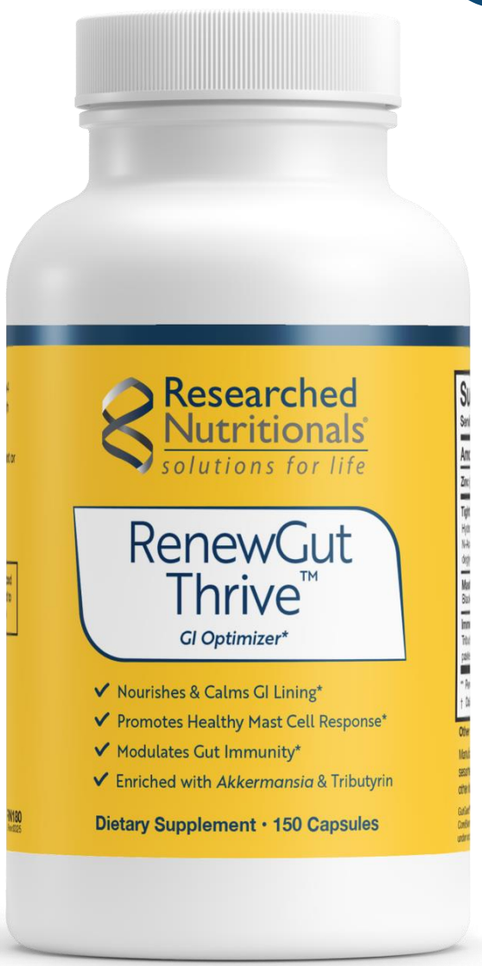



**Promotes healthy**:

- ✓ Intestinal barrier integrity
- ✓ SCFA levels, especially in those with low-fiber diets or low fiber tolerance
- ✓ Bowel irregularity/fast stool transit
- ✓ Colon and digestive comfort
- ✓ Balance of gut flora
- ✓ Balanced immune responses
- ✓ Metabolic wellness
- ✓ Glucose metabolism

References:[37,67-70]

# Q&A

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**Suggested Use**: As a dietary supplement, take **5 capsules first thing in the morning with food** or as directed by your healthcare professional.

# Disclaimer

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*All content is based on currently available scientific research and is intended for use by healthcare professionals. References are provided to support the mechanisms and functions discussed and do not constitute medical claims.*

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