



Menopause, Microbiome Shifts and Clinical Implications

Samantha Ford, MS
Business Director

The Estrobolome

The Relationship Between Gut Bacteria and Estrogen Metabolism

THE ESTROBOLOME

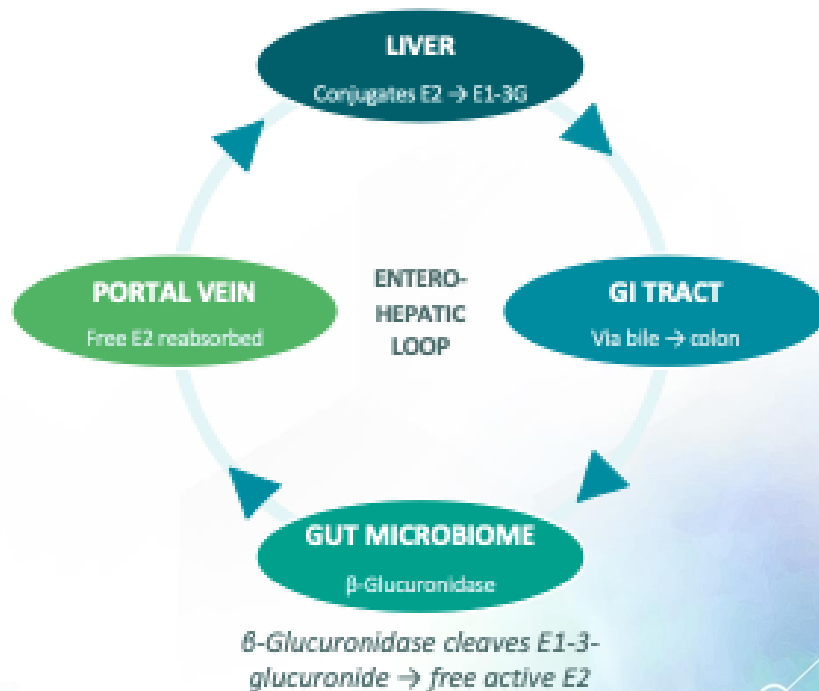
The estrobolome is the aggregate of gut microbiome genes capable of metabolizing estrogens.

KEY ENZYME

β -Glucuronidase (B-glu) deconjugates estrogens in the colon, releasing free E2 for reabsorption into portal circulation.

DYSBIOSIS & DISRUPTION

Altered β -glucuronidase activity disrupts the loop — driving excess estrogen recirculation or estrogen deficit.



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The Ideal Environment

Characteristics of an optimal gut environment for a healthy estrobolome

1

Diverse Ecosystem

Range of B-glu Producers

Examples: *Ruminococcus*, *Clostridium*, *Faecalibacterium prausnitzii* (balance is important vs dominance)

Adequate *Akkermansia*

Critical for maintaining mucus layer and reinforcing the gut lining, preventing endotoxemia and leaky gut.

2

Protective Environment

Ample Butyrate Production

Central to body's immune and anti-inflammatory mechanisms, reduce gut permeability and protect against systemic inflammation.

- Pathogens/Inflammation

Pathogens are opportunistic, can overproduce B-glu enzyme and create conditions of estrogen dominance.

3

Parallel Support

Neurochemical Function

Nervous system regulation, sleep, vasomotor symptoms (all have mechanisms in the gut).

Early signals



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The Window of Vulnerability

Gut-driven inflammation begins years before menopause — a critical opportunity for early intervention

ESTROGEN FLUCTUATION

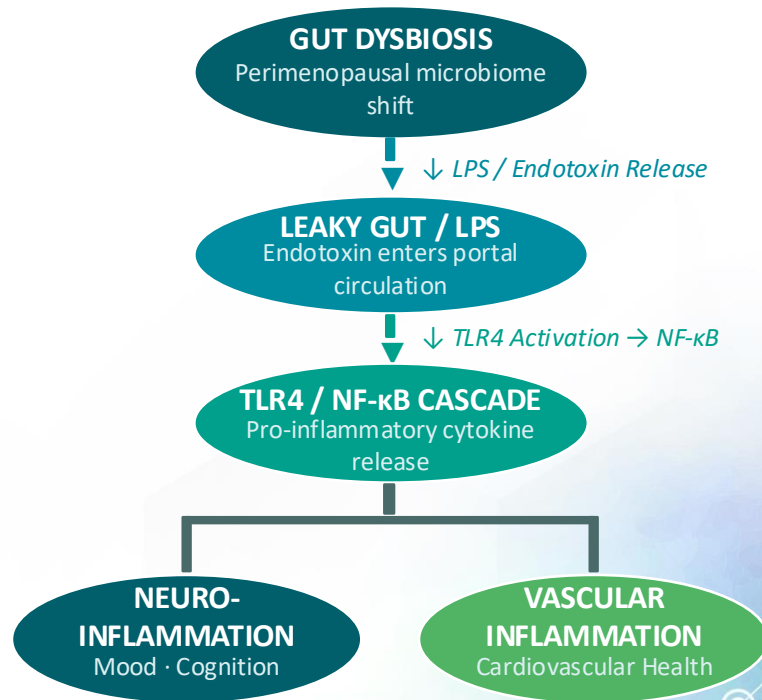
Estrogen levels fluctuate erratically, leading to disrupted gut environment (↓ Lactobacillus, ↓ Bifidobacterium, ↑ Enterobacter).

IMPAIRED GUT BARRIER

The gut mucosal barrier becomes compromised, increasing circulating endotoxins (LPS) and triggering inflammatory response.

SYSTEMIC INFLAMMATION

Stress, brain fog, mood alterations are linked to neuroinflammation and decrease in GABA/serotonin-producing taxa. Vascular inflammation and changes in lipid profile strongly correlated with gut microbial signatures in perimenopause.



Gut microbiome as an upstream therapeutic target — acting before menopause onset

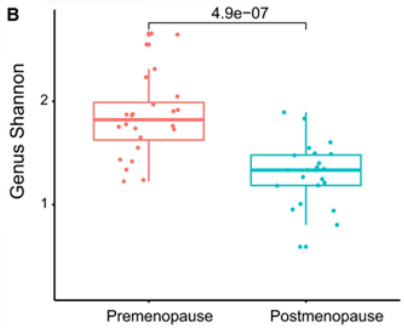
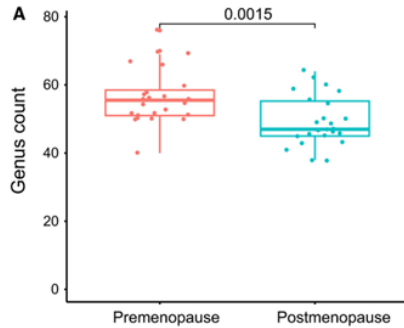


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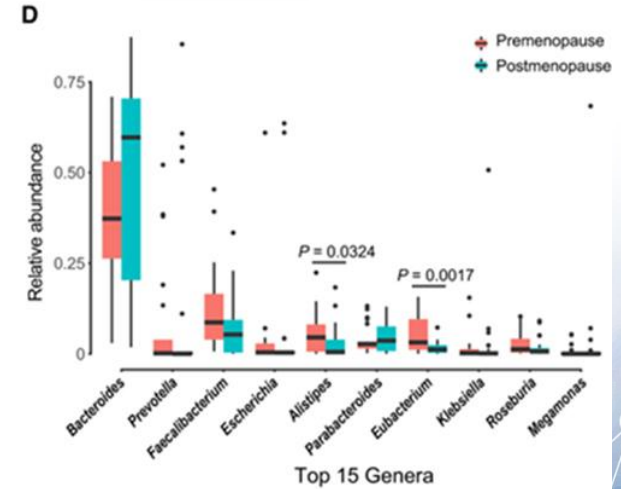
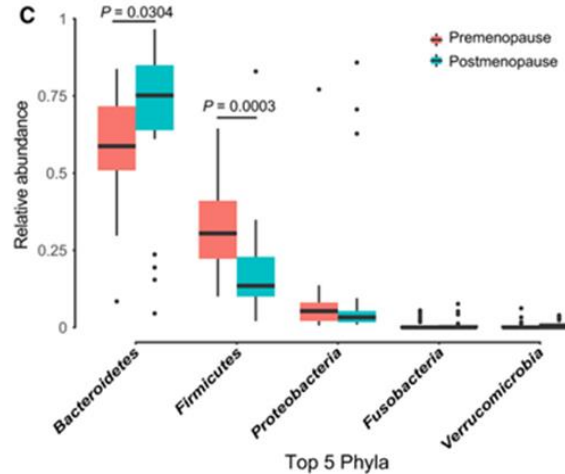


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Changes in the Gut Microbiome



Metagenome-wide association study with shotgun sequencing, comparing gut microbiota premenopausal vs postmenopausal women (n=48, matched for age and BMI)

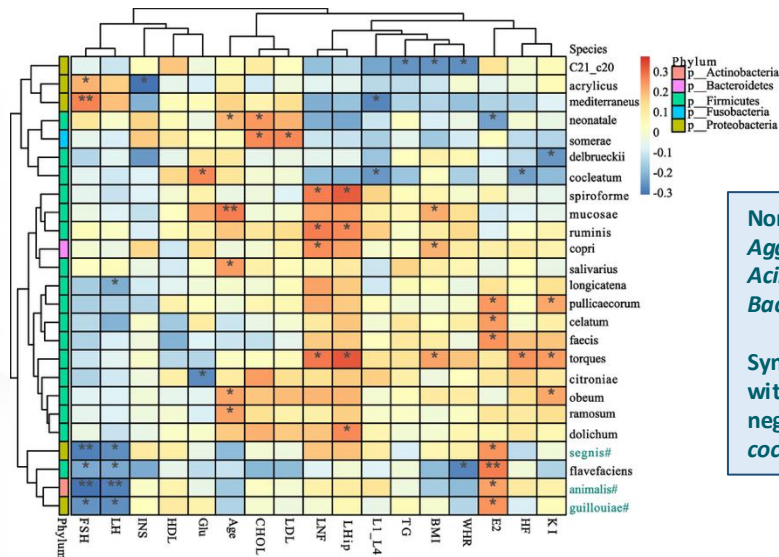


Significant reductions in *Faecalibacterium* and other anaerobic butyrate producers (*Roseburia*)

Significantly lower gut microbial diversity

Menopausal Syndrome

The relationship between menopausal syndrome (MPS) and gut microbes

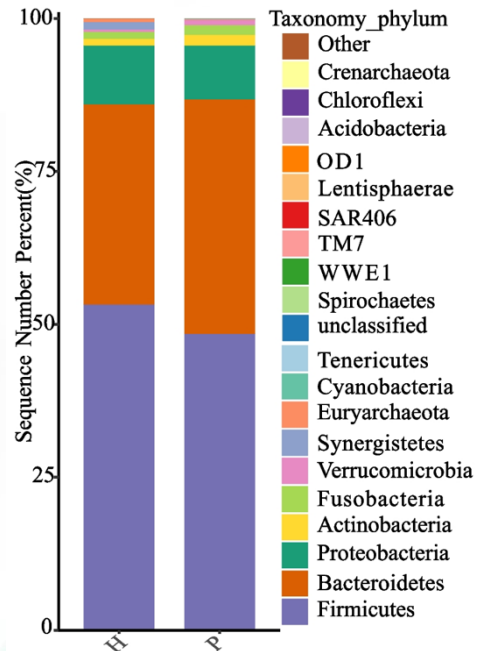


Yellow/red: positive correlation. Blue: negative correlation. *
0.01 ≤ p < 0.05, ** 0.001 ≤ p < 0.01.

Non-MPS had significantly higher:
Aggregatibacter segnis (Proteobacteria),
Acinetobacter guillouiae (Proteobacteria),
Bacteroides animalis (Bacteroides).

Symptom severity positively correlated
with *Ruminococcus torques* (Firmicutes)
negatively correlated with *Clostridium
cocleatum* (Firmicutes).

Average relative abundance of microbiota at the phylum level in healthy (H) vs menopausal syndrome (P)



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Gut Microbiome Modulation as a Mechanistic Target for Early Intervention

01 BOOST MICROBIAL DIVERSITY

PRECISION PREBIOTICS

Actazin®

Green kiwifruit powder supports improved microbiome diversity and a healthy gut ecosystem by stimulating mucin production (important for *Akkermansia* to thrive)

PreticX® XOS

Xylooligosaccharides selectively feed *Bifidobacterium* and support gut barrier function.

Restores microbial diversity → supports
estrobolome balance and gut barrier integrity

02 PROTECT AGAINST INFLAMMATION

PROTECTIVE FLAVONOIDS AND POLYPHENOLS

GutGard®

Flavonoid-rich glycyrrhiza glabra (≥3.5% glabridin)
COX-2 / NF-κB inhibition, tight junction support
Reduces LPS-driven intestinal permeability

Livaux®

Gold kiwi polyphenols increase relative abundance of SCFA-producing microbes and support anti-inflammatory gut mechanisms

Breaks the LPS → TLR4 → NF-κB cascade —
the perimenopausal inflammatory driver

03 SUPPORT THE GUT-BRAIN AXIS

GABA-PRODUCING PROBIOTICS

L. plantarum LMG S-33253

Carries GAD gene system
Glutamate → GABA conversion

L. brevis LMG S-33254

Confirmed GAD gene — dual GABA-producing strain
combination for neurochemical support via the gut-brain axis

Produces GABA in situ → supports mood, stress
resilience, and sleep via vagal signaling

Formulate for the full pathway: gut ecology → inflammation control → neurochemical support



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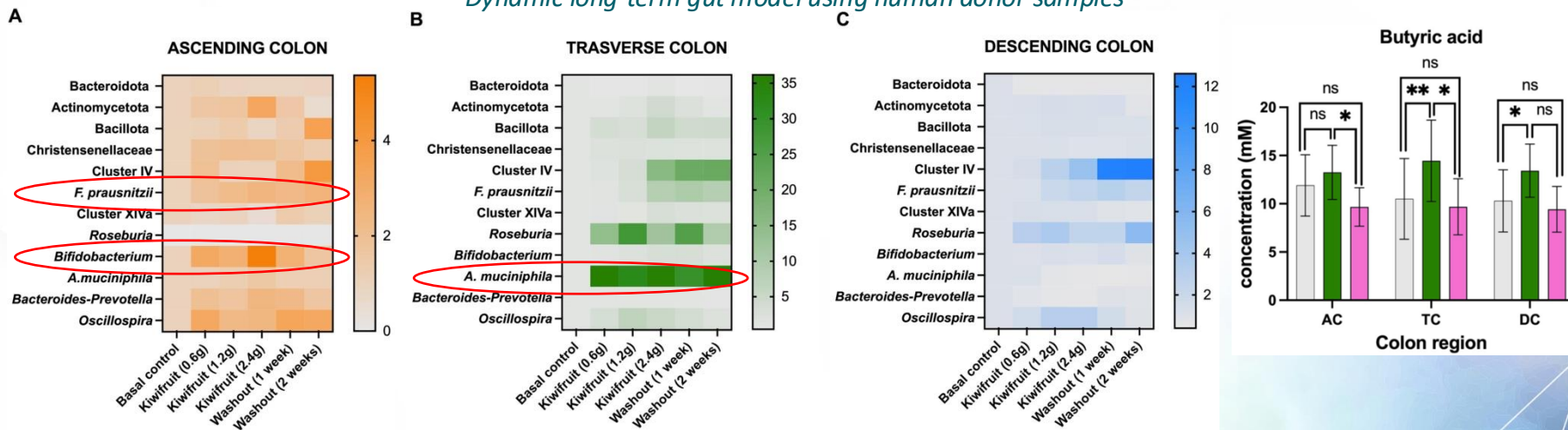
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Actazin® promotes the growth of Akkermansia, Bifidobacteria, and Faecalibacterium and increases butyrate

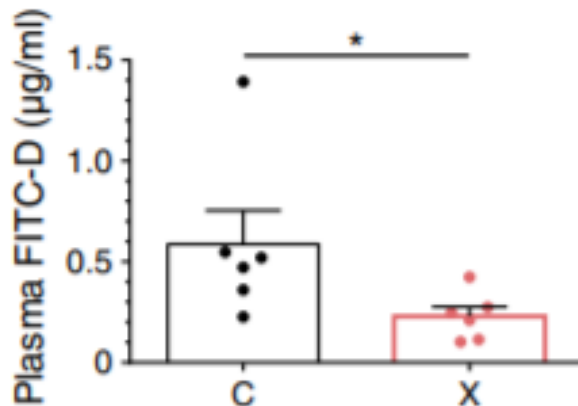
Simulator of the Human Intestinal Microbial Ecosystem (SHIME®)

Dynamic long-term gut model using human donor samples

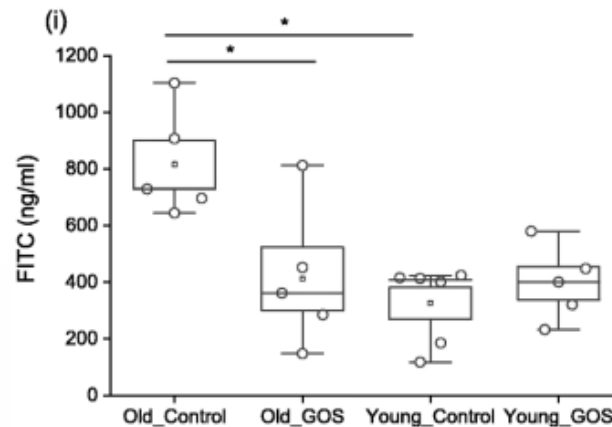


Prebiotic Xylooligosaccharides and Galactooligosaccharides improve gut barrier function and reduce intestinal permeability in animal models

Prebiotic structure is important. Precision prebiotics like XOS have a higher specificity when feeding gut bacteria, leading to more meaningful alterations in the microbial ecosystem.



Spectrophotometric analysis of plasma FITC-dextran (FITCD) level 2 h post oral gavage at 7 weeks of age in non-obese diabetic mouse model supplemented with XOS (X) vs control (C)



FITC-dextran assessment of gut barrier function old (n=24) and young (n=24) mice showed significantly increased intestinal permeability in old vs young mice, with decreased values in old animals fed GOS

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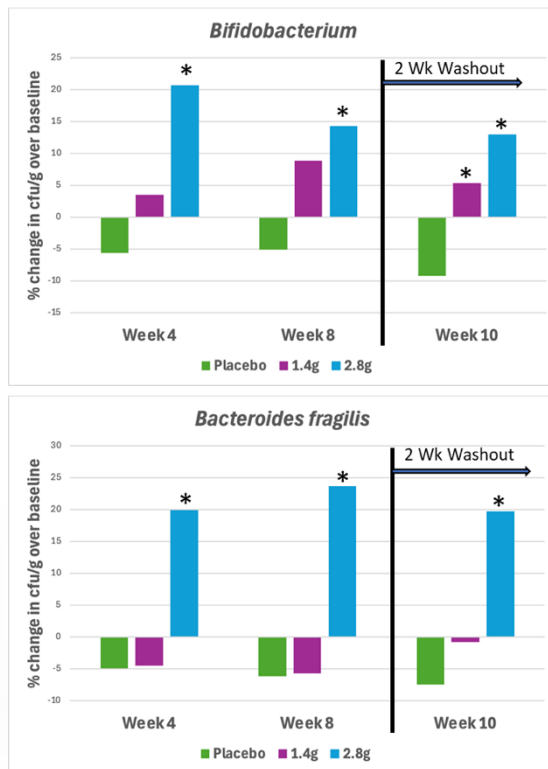
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Design

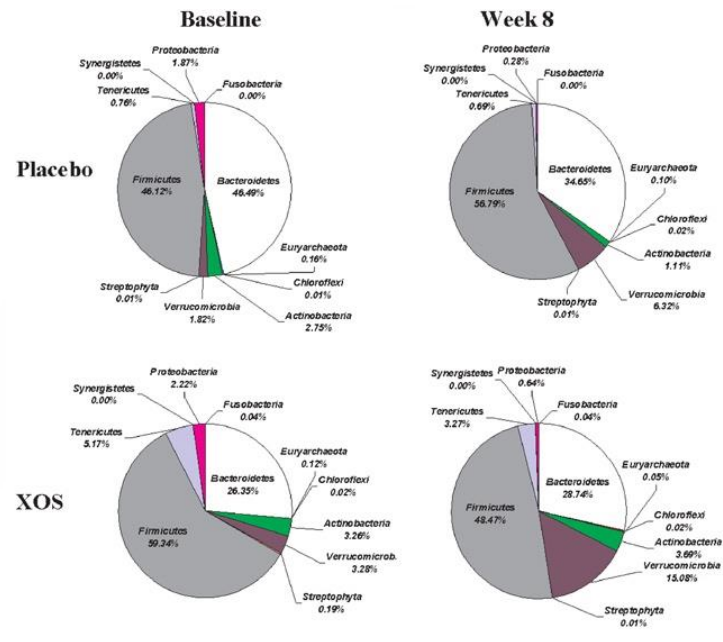
- Double-blind, randomized, placebo-controlled
- 32 healthy adult participants
- 1.4g or 2.8g of PreticX® per day, or placebo
- 8-week supplementation with 2-week washout

Results

- Increase in absolute *Bifidobacterium* from baseline significantly greater
- Increase in absolute *Bacteroides fragilis* from baseline significantly greater (2.8g) at all time points
- Significant increase in relative *Akkermansia* (2.8g) vs placebo ($p=0.041$)



Effects of XOS supplementation on gut microbiota in healthy participants



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Flavonoid Rich Licorice Extract



Flavonoids are prebiotic and support digestive health

Flavonoids are a class of polyphenolic secondary metabolites found in plants widely researched to benefit digestive health



01

Flavonoids and flavonoid metabolites can **shape gut microbiota** by **inhibiting** the **growth of** various **pathogens** and **increasing beneficial genera**

02

Flavonoids **inhibit gut inflammation**

03

Flavonoids are studied to **improve gut immunity**



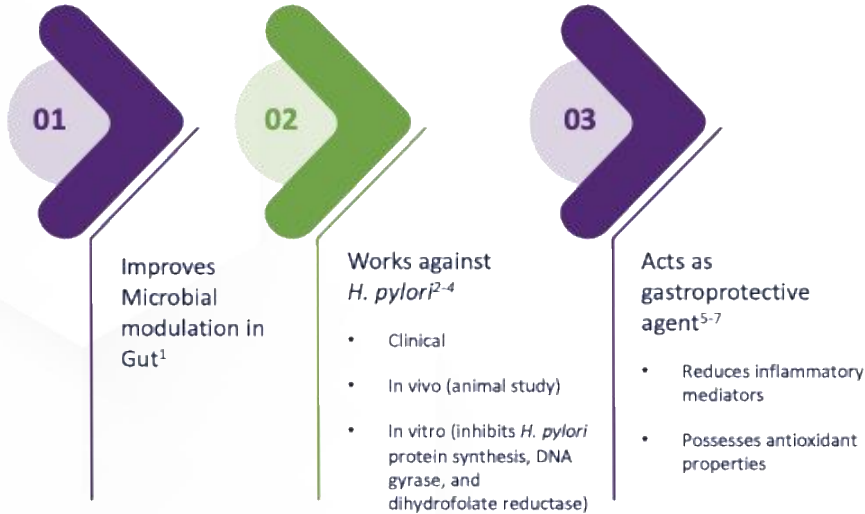
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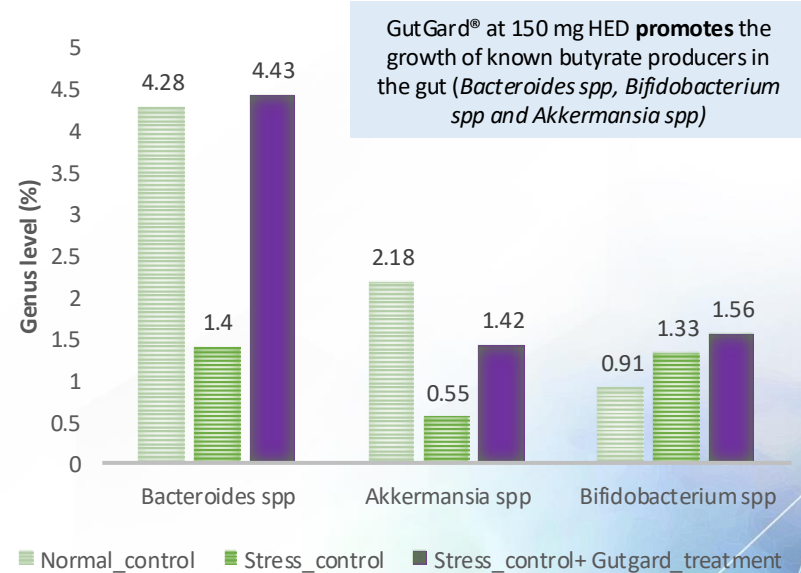
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Flavonoid Rich Licorice Extract

Gastroprotective and supports pathogen inhibition



GutGard® significantly improves stress-induced gut dysbiosis





Livaux®

Gold Kiwi Polyphenols Significantly increase *Faecalibacterium prausnitzii*

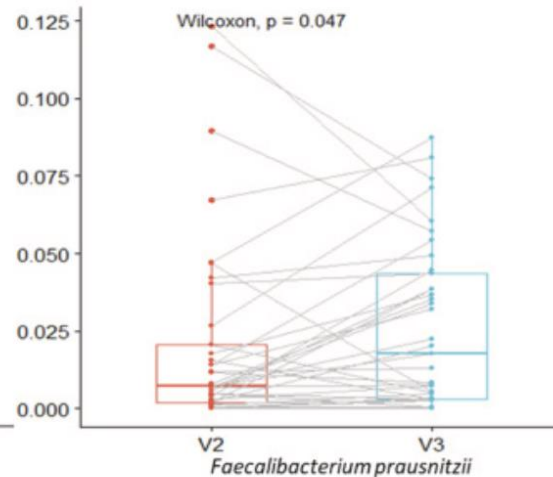
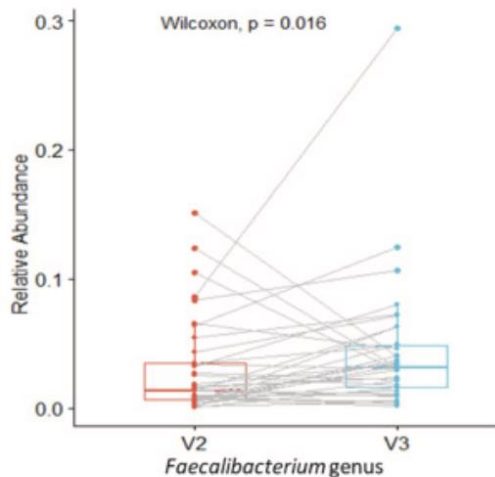
A major SCFA producer in the gut, energy source for colon cells and supports anti-inflammatory mechanisms

Design:

- Double-blind, randomized, placebo-controlled, parallel-arm trial
- 85 healthy adults (ages 18–60)
- 600 mg Livaux/day or placebo
- 28 days

Outcomes:

- Significant increase in *Faecalibacterium prausnitzii* ($p = 0.047$)
- Decrease in hydrogenotrophic *Blautia* spp.
- Decrease in bloating



Maintaining or increasing *F. prau* with dried gold (Gold3) kiwifruit

Increasing fatty acid levels and *F. prau* with dried gold (Gold3) kiwifruit

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The GABA Probiotic Pair

Proprietary Strains *L. plantarum* LMG S-33253 + *L. brevis* LMG S-33254 — supporting the gut-brain loop at the GAD gene level

WHY GABA?

Declining estrogen reduces GABA-A receptor sensitivity → GABAergic deficit → hot flashes, anxiety, disrupted sleep, and mood dysregulation.¹

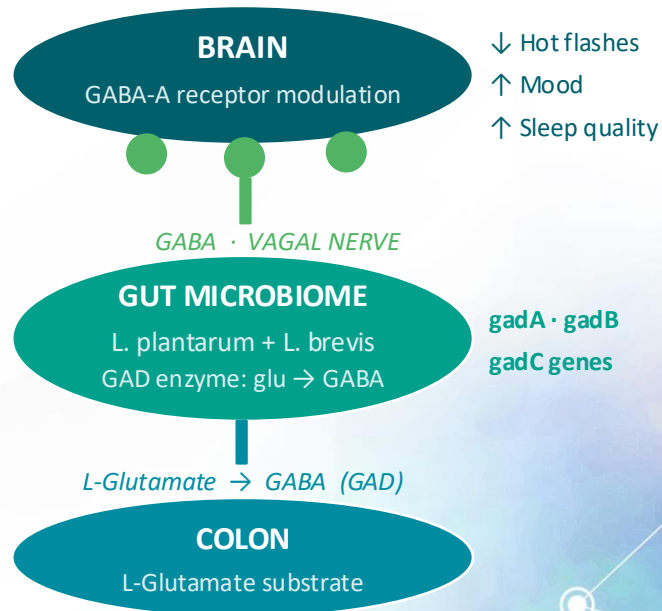
L. plantarum LMG S-33253

- GAD gene system confirmed: *gadA* · *gadB* · *gadC* (glutamate decarboxylase)
- Converts L-glutamate → GABA in situ within the colon
- Human clinical data: ↑ GABA/glutamate ratio; ↑ mood scores; ↑ sleep quality

L. brevis LMG S-33254

- GAD gene confirmed (*gadB*) — one of highest GABA-yield species in literature
- Dual-strain combination = enhanced output
- Supports vagal nerve GABA signaling → systemic neurochemical effects

THE GUT-BRAIN GABA PATHWAY



SUMMARY

The Gut Influences Menopause by Modulating Estrogen Metabolism

Huge opportunity exists to develop targeted solutions for hormone regulation via the gut-axis

01 GUT ECOLOGY

BALANCE THE ESTROBOLOME

Targeted Prebiotics

- Bifidobacterium abundance ↑
- Microbial diversity ↑
- β-Glucuronidase modulation
- Gut transit time ↓

SYNERGY:

Estrobolome restoration:
better E2 recirculation balance

Gut microbiome support

Digestive wellness

Hormone balance
support

02 INFLAMMATION

CLOSE THE LOOP

Flavonoids and Polyphenols

- LPS endotoxin load ↓
- NF-κB signaling ↓
- Tight junction integrity ↑
- Systemic inflammation ↓

SYNERGY:

Amplifies prebiotic effect:
barrier healing enables colonization

Anti-inflammatory
support

Gut lining health

Immune balance

03 NEUROCHEMICAL SUPPORT

SUPPORT THE BRAIN AXIS

Gene-Encoding Probiotics

- GABA production ↑ (GAD gene)
- Vagal nerve signaling
- Mood + stress resilience ↑
- Sleep quality ↑

SYNERGY:

Completes the gut-brain loop:
targeted neurochemical output

Mood + stress support

Sleep support

Cognitive wellness



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