



**Targeting the Gut–Brain Axis:**

# **A Novel, Clinically Validated Approach to Supporting Psychological Well-Being**

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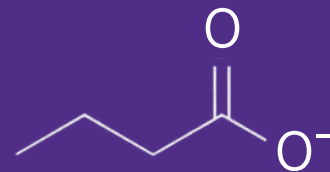
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# Butyrate

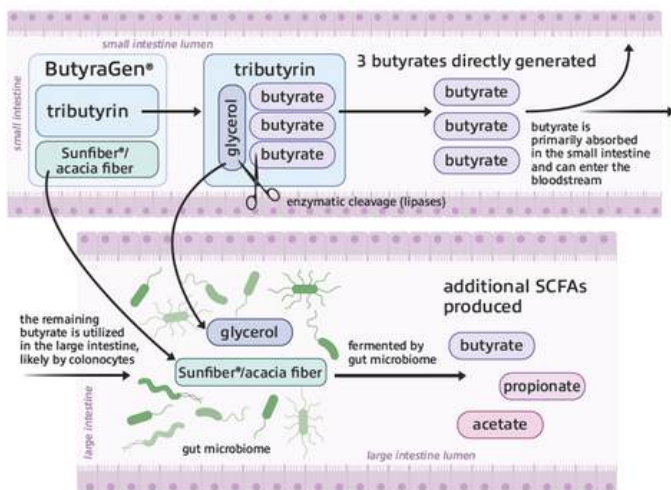
## A Small Molecule with A Big Impact

Butyrate is a naturally occurring short-chain fatty acid (SCFA) essential for gut health and systemic balance. Butyrate plays a critical role in the body supporting intestinal barrier function, immune signaling, and cellular energy production. Butyrate has been shown to influence the gut-brain axis by supporting signaling pathways that communicate with the brain, highlighting the gut as an active regulator of brain health, not just a digestive organ.



## ButyraGen<sup>®</sup> Mechanism of Action

ButyraGen<sup>®</sup> is a novel patent-pending complex that generates butyrate directly in the small intestine, independent of the state of the microbiome.



- Regulates gene expression by inhibiting enzymes and regulating acetylation rates
- Serves as an energy source for colonocytes after being metabolized by the mitochondria
- Promotes anti-inflammatory effects by activating butyrate receptor on colon cells, releasing IL-18, a key player in cell-mediated immunity
- Supports cardiovascular function by activating free fatty acid receptors, regulating metabolic health and influencing immune response

## ButyraGen<sup>®</sup> for Gut Health

A previously published randomized, double-blind, placebo-controlled study demonstrated that ButyraGen<sup>®</sup> delivers fast, clinically significant relief from belly pain and gas/bloating, with improvements in quality of life for people suffering from reflux and constipation in as little as 1 week.<sup>1</sup>

Unlike conventional butyrate sources, ButyraGen<sup>®</sup> delivers a practical, well-tolerated, low-dose solution without the sensory drawbacks of other butyrate options.

# The Gut-Brain Axis

Recent literature has shown short-chain fatty acids may influence systemic processes through the gut-brain axis, a bidirectional communication network linking digestive and neurological function.<sup>2</sup>

The gut-brain axis operates through neural, hormonal, and biochemical signals, including microbial metabolites like SCFAs. Butyrate acts as a histone deacetylase (HDAC) inhibitor, modulating gene expression and improving oxidative stress response.<sup>3</sup> Emerging evidence suggests that butyrate supports neuroprotection, enhances neuroplasticity, and may influence mood regulation, making it a promising candidate for cognitive and emotional health.

## Study Summary

In a 6-week randomized, double-blind, placebo-controlled trial (N=596), participants taking 200 mg/day of ButyraGen® reported **meaningful improvements in psychological well-being**. Outcomes were assessed using validated questionnaires for anxiety, depression, and digestive quality of life (DQLQ).<sup>4</sup>

### Key Findings

Daily supplementation with ButyraGen® led to meaningful improvements in psychological well-being. This includes reductions in feelings of fear and unease, improved focus, and better functional measures such as reduced distraction and greater social engagement, with clinical effects emerging as early as week two. Male participants had an even more pronounced improvement; they were twice as likely to achieve reductions in anxiety compared to the placebo group ( $p = 0.007$ ). Significance appearing in week 2 and continuing through the 6 week study highlights both the fast acting and durable benefits.

### Implications

These findings suggest that ButyraGen® may influence the gut-brain axis both directly and indirectly, through improvement of physiological gut symptoms, but also psychological well-being. These results correlated with digestive quality of life (DQLQ) results, suggesting functional outcomes including being less distracted and more social, underscoring real-world benefits.



# Clinical Evidence

## Depression

Participants with a healthy GI system showed a statistically significant, 2-fold greater likelihood of improvement compared to the placebo ( $p=0.011$ ). Similarly, younger adults (<40 years) exhibited significant improvements in feelings of hopelessness, helplessness, and depression ( $p=0.031$ ,  $0.022$ ,  $0.040$ ). These subgroups experienced the greatest benefits, with a notable, non-significant, trend in score improvement for the overall population (1.29-fold greater likelihood of improvement).

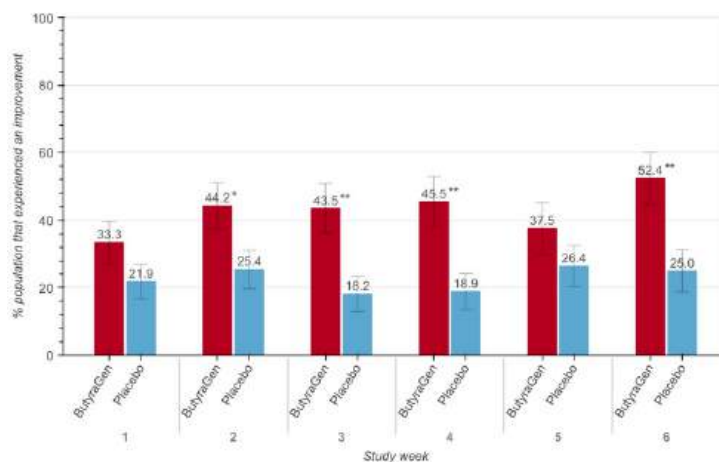
## Anxiety

Men were over twice as likely to achieve clinically meaningful improvement ( $p=0.007$ ).

Improvements appeared rapidly in 2 weeks and persisted through week 6. Significant reductions in feelings of fear and unease across all participants was observed, with enhanced feelings of focus among men (Fig. 1). Additionally, a non-significant, but meaningful trend in anxiety scores was observed in the general population. A 9.29% higher rate of clinically meaningful improvement versus placebo was observed in the general population ( $p=0.140$ ).

## DQLO

Active group participants reported reduced distraction (17.15% lower rate) and greater willingness to engage in social activities (12.16% higher rate), indicating relatable improvements in daily functioning, suggesting a potential modulation to the gut-brain axis through physiological improvements in gut health.



**Figure 1:** Temporal (week-to-week) changes in Anxiety 4A % male participant improvement over the course of the 6-week study.

# Multiple Mechanisms

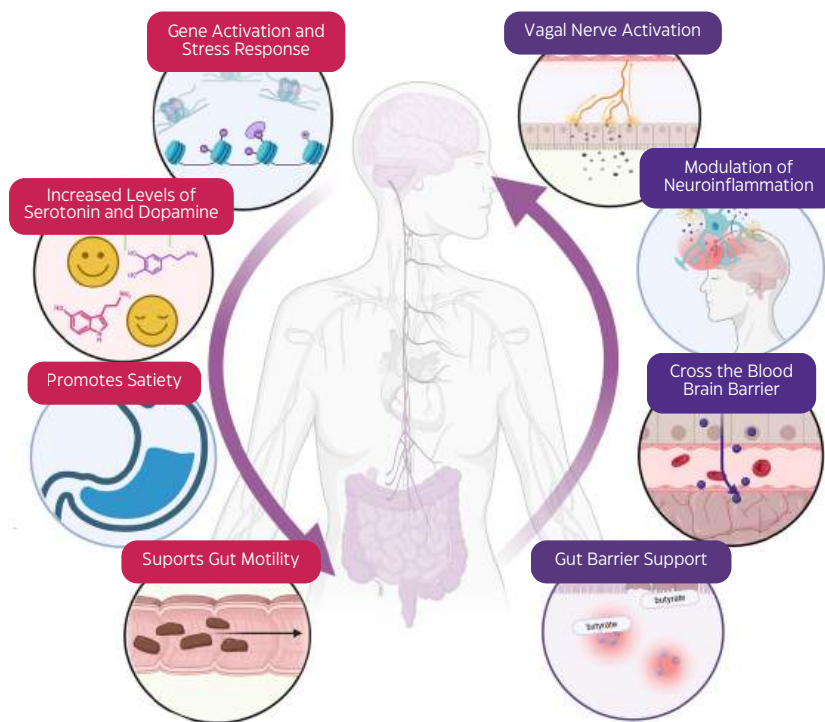
ButyraGen® may support the gut-brain axis through two complementary pathways:

## Indirect:

Direct butyrate generation can improve gut physiology—enhancing barrier integrity and reducing inflammation, which supports psychological well-being via vagal, immune, and hormonal signaling.<sup>2</sup>

## Direct:

Butyrate can cross the blood-brain barrier, influencing neurotransmitter synthesis and gene expression, contributing to mood regulation and cognitive resilience.<sup>5</sup>



## Conclusion

ButyraGen® offers a science-backed approach to supporting both gut and brain health. By generating butyrate in the small intestine, it delivers fast-acting, clinically meaningful benefits for anxiety, mood, and functional well-being, particularly in men, younger adults, and those with healthy GI functions. For brands seeking innovative solutions at the intersection of digestive and cognitive health, ButyraGen® provides a low-dose, well-tolerated ingredient with broad potential for enhancing quality of life.

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5. De Sousa RAL, Cassilhas RC. Microglia role as the regulator of cognitive function. *Rev Assoc Med Bras*. 2023;69(7). doi:10.1590/1806-9282.20230412

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